Novel approaches to evaluate the impact of the SAFE strategy on trachoma and other neglected tropical diseases in Amhara National Regional State, Ethiopia

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Summary

***Background*:** Trachoma, a blinding bacterial disease of the ocular surface, is the leading cause of infectious blindness, responsible for the visual impairment of 2.2 million people worldwide and an estimated economic loss of US$ 5.3 billion annually. Blinding trachoma, considered a neglected tropical disease, is targeted for global elimination as a public health problem by the year 2020. To achieve elimination, the World Health Organization (WHO) recommends implementing an integrated intervention package of surgery, antibiotics, facial cleanliness, and environmental improvement, known as the SAFE strategy. Surgery aims to correct trichiasis, the blinding anatomical condition of inward turning lashes touching the eye. Antibiotics are distributed annually to endemic communities to treat relatively asymptomatic ocular *Chlamydia trachomatis* infections to reduce the infectious reservoir. The promotion of facial cleanliness and environmental improvements, use of water and latrines for hygiene and sanitation, both target interrupting transmission of the infection. Of the 325 million persons estimated living in trachoma endemic communities, over 70% reside in sub-Saharan Africa. Within the region, Ethiopia, Nigeria, and South Sudan are estimated to have the highest burden of disease. The SAFE strategy in Ethiopia has been implemented since 2007 targeting all 17 million residents of the Amhara National Regional State.

***Goals and specific objectives*:** The goal of this PhD thesis was to investigate novel approaches of measuring the impact of SAFE interventions on trachoma and other neglected tropical diseases within the context of a national elimination programme as implemented in the Amhara National Regional State of Ethiopia. The specific operational research objectives were to determine whether areas receiving 3-5 years of interventions had achieved elimination by applying new evaluation guidelines; whether new electronic data collection technology could facilitate impact evaluation; whether SAFE interventions had any impact on trachomatous scarring (TS) among children; whether school-based surveys might serve as an alternative method to assess trachoma; and whether SAFE interventions have had any impact on intestinal parasitic infections.

***Methods*:** Data collection for the thesis project occurred in three phases. The first phase involved the implementation of a population-based, cross-sectional study utilising a cluster random sampling design to survey 360 communities in South Wollo zone to estimate prevalence of trachoma after three years of SAFE interventions. Data was collected using standard paper-based questionnaires. The second phase involved the development and field-testing of a new electronic data collection system in a pilot study utilising a mixed, quantitative and qualitative, study design. The last phase involved the implementation of another population-based cross-sectional study in South Gondar zone after receiving five

years of SAFE interventions. The same sampling methodology was used to survey another 360 communities, yet integrating both assessment of trachoma and intestinal parasitic infections. Additionally, data was collected strictly by the newly developed electronic system. Clinical signs of trachoma were individually assessed using the WHO simplified trachoma grading system. Intestinal parasitic infections among children aged 2-15 years were determined by concentrating preserved stool specimens with ether for microscopic examination.

***Results*:** From 714 communities in the two zones, 72,452 persons were examined for trachoma. The prevalence of trachomatous inflammation follicular (TF) among children aged 1-9 years was 26.4% in South Wollo and 25.9% in South Gondar zone. Trachomatous inflammation intense (TI) was less prevalent than TF; 4.3% and 7.0% in South Wollo and South Gondar respectively. TT prevalence in the two zones suggest that over 59,000 persons are estimated to have trichiasis and in need of surgery. In South Gondar the prevalence of TS among children under the age of 11 years has declined from 24.9% in 2000 to 2.2% in 2011. While declines in intense inflammation and scarring were observed among children since intervention, the WHO targets for elimination have not been achieved.

The android-based tablet computer and the standard paper questionnaire were comparable in regards to time required to collect data during the pilot study, proportion of mistakes made while recording data and costs when considering data entry of paper questionnaires. Data recorders preferred to collect data electronically even though initially they felt the tablet interrupted their connection with the interview respondents. Electronic data collection resulted in completion of the large-scale surveys from preparation to presentation of results in 35% less time (one month earlier) than the standard paper-based surveys.

An analysis of 75,864 children examined in community-based surveys in Ethiopia (from field work described in this thesis), Mali, Niger, and Nigeria found that differences between children who attend and do not attend school varies across survey settings in regards to age, gender, having a clean face, and participation in antibiotic distribution for trachoma control. Meta-analysis of the data found that TF was less likely (odds ratio=0.71) among school-attendees than non-attendees when controlling for age, sex, and clustering at the household and community levels. Children attending school did not represent the target age group recommended for assessment of trachoma prevalence.

Stool specimens from 2,338 children aged 2-15 years from 99 communities in South Gondar were assessed for intestinal parasites. The prevalence of any helminth infection was 24.2%, which represented a 50% reduction from a previously published study prior to the SAFE interventions. Over 70% of children had at least one type of intestinal protozoan

infection. Significant increases were observed in household latrine ownership, access to water, use of an improved water source for drinking, and face washing behaviour since the start of the interventions.

***Conclusions*:** Trachoma remains a public health problem in South Wollo and South Gondar zones of the Amhara National Regional State of Ethiopia and ongoing interventions are warranted to control transmission to prevent incident blinding disease and provide surgery for prevalent and incident cases of trichiasis. The application of new WHO guidelines to evaluate trachoma at the sub-district level was feasible, but required significant resources. Electronic data capture facilitates the implementation of such large-scale impact evaluation surveys for neglected tropical diseases allowing the results to be generated immediately with as few mistakes as were made with paper-based data collection. Measuring prevalence of TS among children over time offers an additional way to monitor impact of the SAFE strategy. Children under the age of 11 years have substantially benefited from having lived in an environment where the SAFE strategy has been implemented for five years. The use of school-based sampling approaches for assessing trachoma prevalence risks underestimating true prevalence in the community. The prevalence of intestinal helminths among school-aged children has declined alongside significant increases in household-level indicators of water, sanitation, and hygiene since the implementation of the SAFE strategy in South Gondar. Yet, there is ongoing transmission of intestinal parasitic infections warranting improved control interventions. Integrating both the assessment of trachoma and intestinal parasitic infections in community-based surveys was a feasible approach to evaluate a broader impact of the SAFE strategy in a programmatic setting. Overall, the operational research presented in this thesis successfully generated evidence for health system decisions, contributed new information to the respective scientific fields, and identified areas warranting additional research.

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List of abbreviations

CI	Confidence interval
CLTS	Community led total sanitation
CO	Corneal opacity
Ct	*Chlamydia trachomatis*
DALY	Disability-adjusted life year
DT	Development team
Eb	Elementary bodies
EOS	Enhanced outreach service
EU	Evaluation unit (sub-district)
HEW	Health extension worker
IECW	Integrated eye care workers
MDA	Mass drug administration
MDG	Millennium Development Goal
NA	Not applicable (or not available)
NTD	Neglected tropical disease
OR	Odds ratio
PCT	Preventive chemotherapy (for helminth infections)
PSU	Primary sampling unit
Rb	Reticulate bodies
SAFE	Surgery, antibiotics, facial cleanliness, environmental improvement strategy for trachoma control
STH	Soil-transmitted helminth
TF	Trachomatous inflammation follicular
TI	Trachomatous inflammation intense
TS	Trachomatous scarring
TT	Trachomatous trichiasis
UNICEF	United Nations Children's Fund (formally United Nations International Children's Emergency Fund)
WASH	Water, sanitation, and hygiene
WHO	World Health Organization

Figure 1.1. An Ethiopian woman with trichiasis waiting for surgery (courtesy of The Carter Center)

"I feel as if someone's pricking my eyes with a thorn." - Woman with trichiasis;
quote courtesy of The Carter Center, Stephanie Palmer

1. Introduction

1.1. Blinding trachoma – global public health problem

In some of the world's poorest communities, what starts as uncomfortable, but mostly asymptomatic childhood eye infections, may over time lead to a painful, disabling disease resulting in blindness. Trachoma, the world's leading cause of avoidable, infectious blindness is responsible for 3% of global blindness and in 2012 an estimated 334,000 disability-adjusted life years (DALYs) (WHO (2012a; Murray et al., 2013)). An estimated 325 million people are living in areas where trachoma is suspected but the true extent of the disease is unknown because trachoma has not been assessed in all countries or within all regions of known endemic countries (WHO, 2012b). An estimated 1.2 million persons are irreversibly blind from trachoma and an additional one million are visually impaired by the disease (Pascolini and Mariotti, 2012). An estimated 7.3 million persons have trichiasis, the disabling stage of disease leading to blindness, and who could benefit from surgery (WHO, 2012b). The economic loss due to trachoma impaired vision and blindness is estimated to be US$ 5.3 billion annually, of which 10% is due to the requirement of a sighted household resident to care for the person with trachoma, clearly demonstrating that trachoma not only impacts the potential economic productivity of the individual, but of the entire family unit (Frick et al., 2003). If potential productivity losses were to include persons with trichiasis, the economic loss could be as high as US$ 8 billion (Burton and Mabey, 2009).

Figure 1.2 displays the global distribution of trachoma with 53 countries considered trachoma endemic, of which 29 (55%) are located in the Africa region where >70% of the total endemic population reside (WHO, 2012b). Within the Africa region, Ethiopia, Nigeria, and South Sudan have the highest burden of infection (ITFDE, 2011). Yet, adequate data remain unavailable for Nigeria in addition to India and China, which together could greatly influence the global estimates of trachoma. Efforts are currently underway to assess suspected areas to complete the map.

1.2. Aetiology

Blinding trachoma begins by ocular infection with *Chlamydia trachomatis* (*Ct*) serovars A, B, Ba and C. These gram-negative bacteria typically remain localised to epithelial surfaces of the conjunctiva and mucous membranes of the genital tract (genital serovars D-K) (Mabey et al., 2003). The development cycle of *Ct* involves two stages (Figure 1.3), the infectious elementary bodies and the metabolically active reticulate bodies. Elementary bodies are transmitted when carried from an infected eye to uninfected susceptible host, become metabolically active and initiate a new infection.

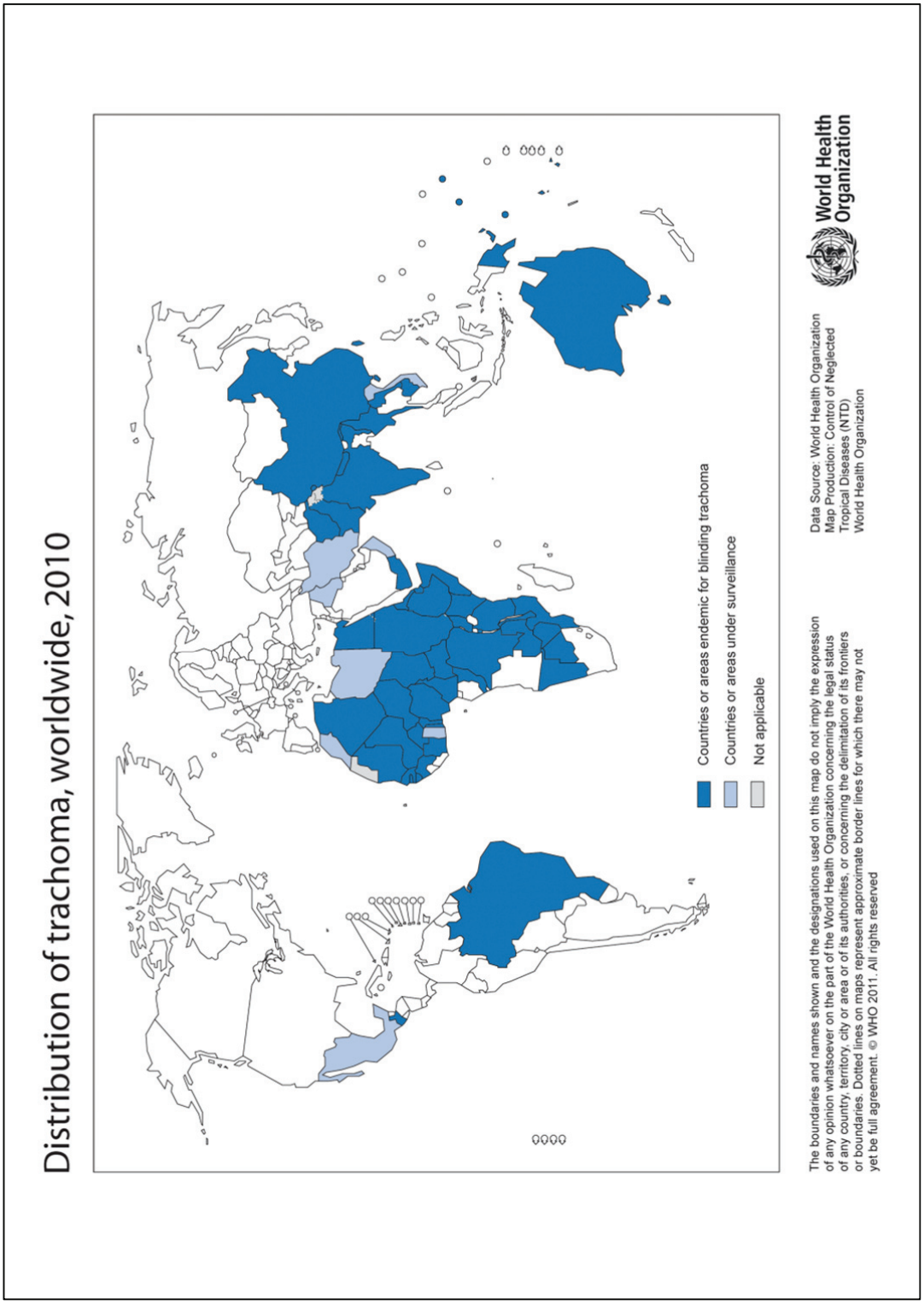

Figure 1.2. Global distribution of trachoma in 2010 (source: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_trachoma_2010.png)

*Chlamydia*e are obligate intracellular pathogens which, upon elementary body inclusion of host epithelial cells in the conjunctiva, transform to reticulate bodies for replication through binary fission. New reticulate bodies transform back to elementary bodies, which are expelled upon lysis of the host cell. Released *Ct* elementary bodies make their way into the environment mainly through ocular discharge. This development process of internalisation, replication and release takes about two to three days (Barron, 1988).

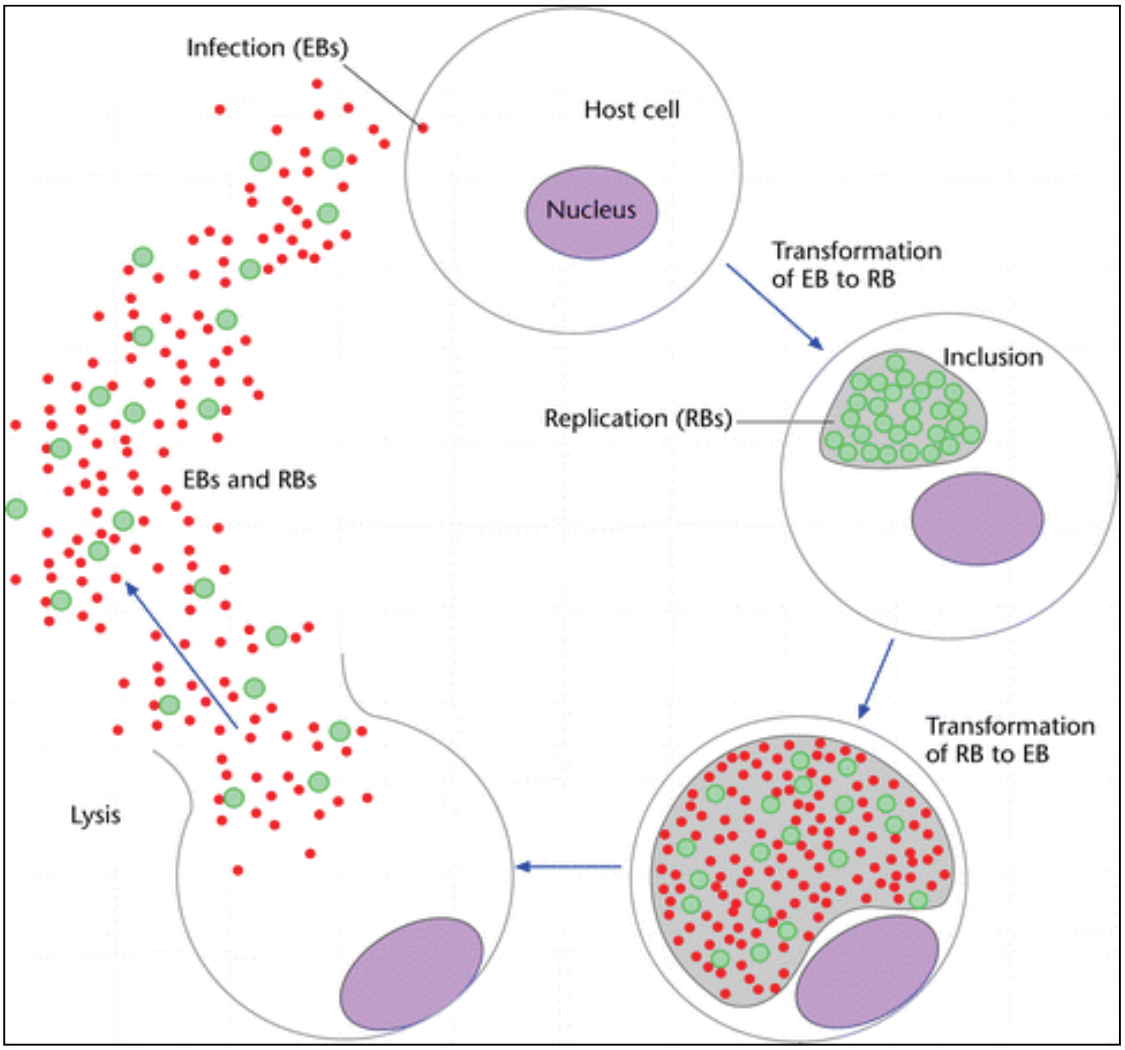

Figure 1.3. Developmental cycle of *Chlamydia trachomatis*. EB, elementary body (red dots); RB, reticulate body (green dots) (source: http://chlamydiae.com/twiki/bin/view/Cell_Biology/GrowthCycle diagram by Dr. Karin D. Everett)

1.3. Pathology

Trachoma is an immunopathogenic disease with severity and progression being driven by multiple bouts of infection, reinfection, and inflammation due to the host immune response (Grayston et al., 1985). With the first infection, trachoma manifests as a self-limiting conjunctivitis that takes several months to resolve. Subsequent infections trigger an immunopathogenic response resulting in chronic inflammation characterised by lymphoid follicles (Figure 1.4.B.) and papillary hypertrophy (Figure 1.4.C.) seen in the tarsal conjunctiva, follicles along the limbus and possible vascularisation of the cornea (Mabey et al., 2003). Inactive reticulate bodies may persist and continue to present antigen, but whether these antigens continue to provoke chronic inflammation, is not clearly understood (Taylor, 2008). As the inflammatory response resolves, emerging scar tissue distorts the anatomy of the eyelid. It is the development and progression of scarring (Figure 1.4.D.) that leads to trichiasis and then corneal damage and blindness.

After repeat exposure and infection with *Ct* there is an acquired immunity which shortens the time required for clearance of the infection but does not protect from reinfection (Bailey et al., 1999; Grassly et al., 2008). *Chlamydial* antigens have been targeted for vaccine development, but so far none have shown promise. Given the immunopathology, the concern is that the antigens targeted in the vaccine must not promote the deleterious immune response.

Cellular mediated and innate immune responses are likely involved in both protective and pathogenic effects. T-helper lymphocytes and natural killer cells produce IFNγ which is thought to be involved in clearing *Ct* infection. The T-cell responses, while helpful in clearing *Ct* infection, may also lead to tissue damage and stimulate fibrosis within the conjunctiva, but the evidence is inconclusive (Abu el-Asrar et al., 1998; Hu et al., 2013). An alternate explanation of trachoma pathology suggests that the pro-inflammatory cytokines of the infected epithelial cells that recruit a cellular infiltrate of macrophages, neutrophils and natural killer cells to aid in clearing infection, bring about prolonged inflammation and potential scarring development (Stephens, 2003). Thus, scar tissue formation in the conjunctivae is brought about by tissue damage and stimulation of fibroblasts during the immune response to infection.

Progressive scarring of the subtarsal conjunctiva deforms the lid margin causing the eyelid to fold inwards directing lashes towards and touching the eye, a condition known as trichiasis (Figure 1.4.E.). In addition, the protective tear film is disrupted as goblet cells and meibomian glands are damaged as well as the lacrimal glands, leading to “dry eye” (Tabbara and Bobb, 1980; Blodi et al., 1988; al-Rajhi et al., 1993).

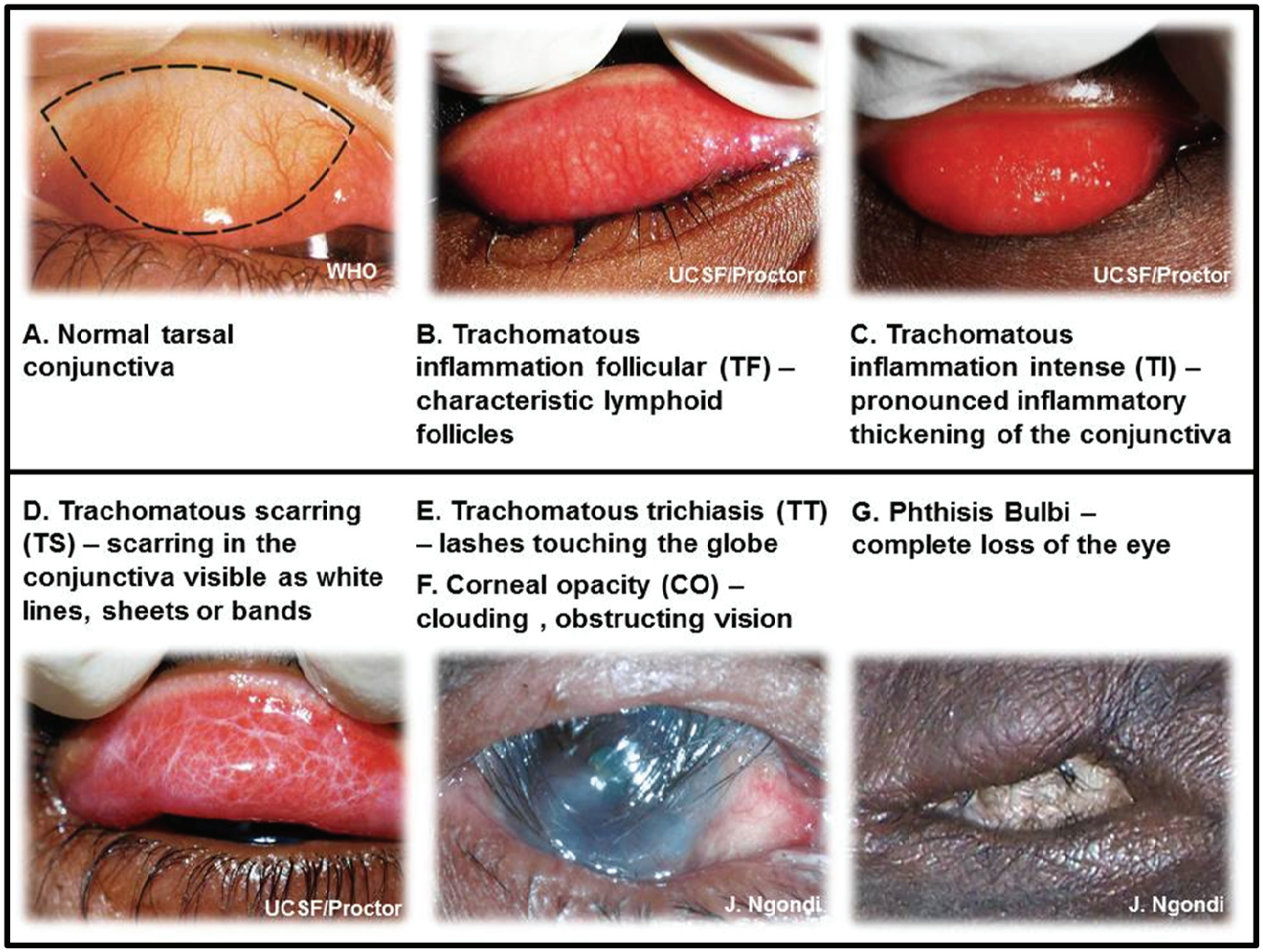

Figure 1.4. Clinical presentation of blinding trachoma. The signs of the WHO Simplified Trachoma Grading System TF, TI, TS, TT and CO are indicated (Thylefors et al., 1987)

The absence of the tear film alone leaves the cornea susceptible to infection, but in trichiasis, lashes abrade the cornea with each blink or movement of the eye. This chronic scratching makes the cornea susceptible to bacterial, viral and fungal infections, which result in corneal ulcers (Bowman et al., 2001, 2002; Rajak et al., 2010, 2012b). The resolution of these ulcers causes scarring directly within the cornea which is observed as clouds or opacities (Figure 1.4.F.). Opacities in the cornea covering the pupil margin cause severe visual impairment and blindness. If nothing is done for the patient, severe trichiasis can end with Phthisis Bulbi (Figure 1.4.G.), the complete loss of the eye.

1.4. Diagnosis of trachoma in public health programmes

1.4.1. Natural history of infection and disease

When discussing diagnosis of trachoma, it is important to note the natural history of *Ct* infection. The relationship of infection and disease has been modeled using prospective data from The Gambia (Grassly et al., 2008). Figure 1.5 describes the natural history of duration of infection with *Ct,* and subsequent disease presentation. Clinical presentation of active disease (follicular and intense inflammatory response, Figures 1.4 B and C) occurs approximately 2-3 weeks after infection and persists several weeks after infection has cleared. Infection is present before development of clinical signs in a short latent phase, infection and signs seen together in a patent phase and finally in the recovery phase, infection has resolved, but clinical signs persist. Therefore, it is not surprising that studies have often found a lack of good correlation between clinical signs of trachoma and evidence of infection (Miller et al., 2004b; Wright and Taylor, 2005; See et al., 2011). The persistence of clinical signs might also suggest that *Ct* may not be the only pathogen to elicit such inflammatory response (Burton et al., 2011a).

1.4.2. Current laboratory diagnostic methods

Highly sensitive and specific laboratory diagnostic methods are available to detect *C. trachomatis* (Bailey et al., 1994; Mabey and Solomon, 2003). The current methods most frequently used by trachoma researchers are nucleic acid amplification techniques for ribosomal RNA and DNA from the common cryptic plasmid (Yang et al., 2009). Recent field research in Ethiopia suggests that RNA assays are more sensitive than, and as specific as, the DNA tests (Keenan et al., 2012b). Typically, these assays are performed on ocular swabs taken in the field under non-sterile conditions. There is no single standardised protocol for collection of ocular swabs, transport of specimens to equipped laboratories or procedures. These techniques are used in the context of research, are cost-prohibitive on a large scale, and currently are not recommended by the World Health Organization (WHO)

for use in national trachoma programmes (Solomon et al., 2004b). However, detecting little or no infection in areas that have had mass drug administration (MDA) of antibiotics would indicate impact of successful interventions. Additionally, in some settings, the cost of employing these tests to evaluate prevalence of infection is hypothesised to save resources in the long run by avoiding additional, unnecessary rounds of MDA where *Ct* infection cannot be detected (Yohannan et al., 2013). A point-of-care test to detect *Ct* antigen has been developed but the current formulation did not perform well under field environmental conditions (Michel et al., 2006; Harding-Esch et al., 2011). Currently, antibody-based tests are under investigation that can be integrated with other disease assessments and might prove to be valuable for trachoma surveillance once interventions have stopped (Goodhew et al., 2012). A rapid, field diagnostic assay to detect *Ct* infection would be invaluable in supporting decisions concerning MDA.

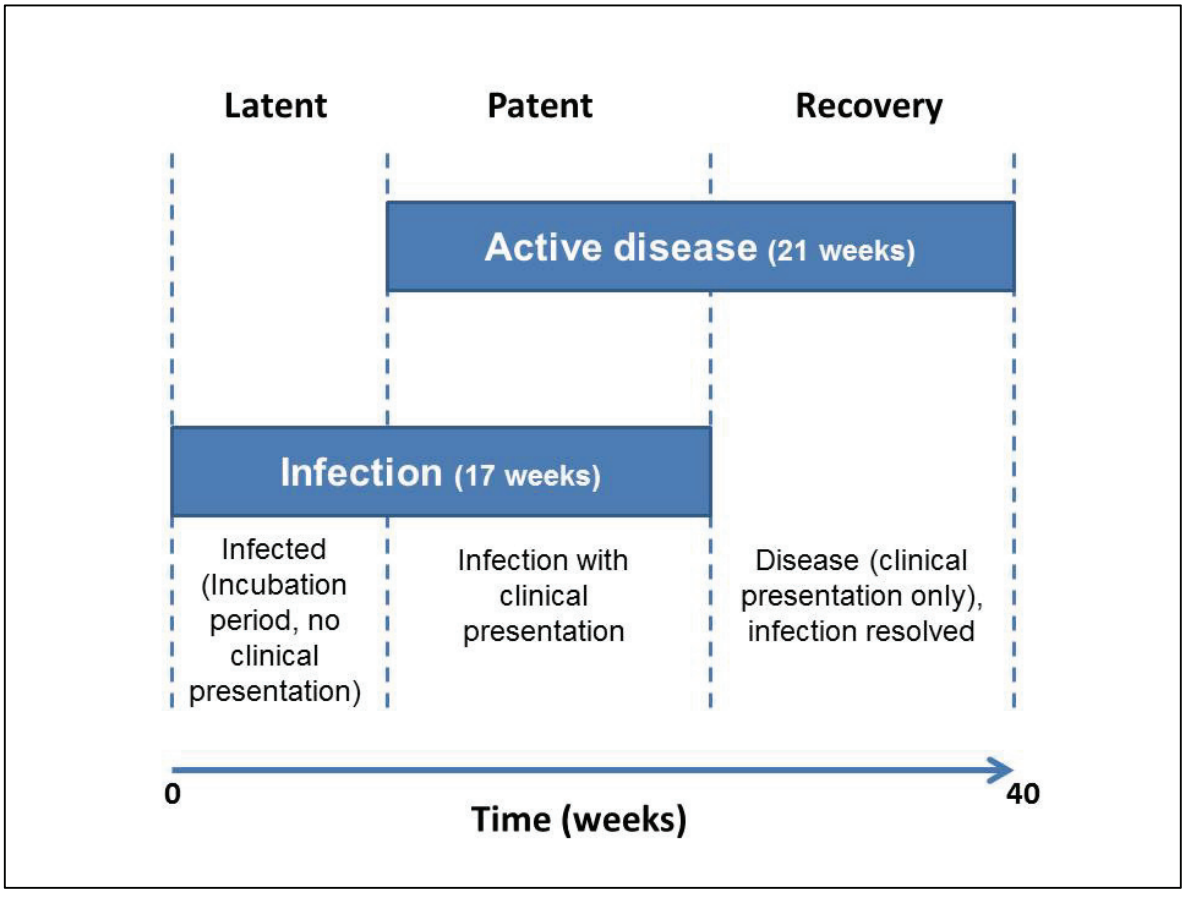

Figure 1.5. Natural history of *Chlamydia trachomatis* infection and clinical response (modified from Grassly et al., 2008)

1.4.3. Clinical diagnosis

The classification systems to diagnose the clinical manifestations of trachoma have been reviewed in detail (Solomon et al., 2004b). The required clinical skills of an ophthalmologist and, in some instances, the use of a slit lamp are among the limitations of the earlier trachoma grading systems particularly prohibitive to large-scale programmatic utilisation. In 1987, the detailed classification of trachoma clinical signs was simplified into a standardised classification of five, differentiated clinical signs of trachoma. This became known as the WHO Simplified Trachoma Grading System, which remains the recommended tool for national trachoma elimination programs because of feasibility and comparability across programs (Thylefors et al., 1987).

Grading signs of trachoma using this WHO recommended diagnostic system limits signs visible within the central area of the tarsal conjunctiva where clinical signs of inflammation due to trachoma are most evident (Figure 1.4.A.). As mentioned in the previous section, lymphoid follicles are characteristic of inflammation due to *Ct* infection. They are elevated collections of lymphoid cells that range in size from 0.2 to 2 mm in diameter. While just a few follicles may be indicative of trachoma, the simplified grading system limits the definition of trachomatous inflammation follicular (grade “TF”, Figure 1.4.B.) to five or more follicles each greater than 0.5 mm in diameter. Intense inflammation is marked by pronounced vascular engorgement where the conjunctiva is bound to the tarsal plate. The combination of vascularisation and thickening of the conjunctiva obscures the large underlying blood vessels. Trachomatous inflammation intense (grade “TI”, Figure 1.4.C.) in the simplified grading system is defined as such vascularisation and thickening that obscures more than half of the underlying vessels. Trachomatous scarring (grade “TS”, Figure 1.4.D.), can be seen as white lines, bands or sheets and may obscure underlying blood vessels. At least one eyelash touching the globe or evidence of removal of inturned lashes is defined as trachomatous trichiasis (grade “TT”, Figure 1.4.E.). Corneal opacity (grade “CO”, Figure 1.4.F.) is defined as visible opacities in the cornea that cover all or part of the pupil.

The system is easy to learn and it is relatively simple to assess the capacity of newly trained examiners to apply the system. At the systems inception, inter-observer reliability was measured and very good agreement among multiple examiners was documented for TF (kappa=0.70, range 0.66-0.74), TS (kappa=0.75, range 0.67-0.79) and TT (kappa=0.76, range 0.68-0.81). Agreement on TI among multiple observers in the first studies was not as good (kappa=0.45, range 0.38-0.49) (Thylefors et al., 1987). A validation study thereafter in Tanzania reported substantial agreement among examiners on TF (kappa=0.79), TI (kappa=0.95), and TS (kappa=0.87) after extensive training (Taylor et al., 1987). However, clinical grading will always be limited by the fact that the grade is subjective to the

determination of the examiner. While the system is capable of identifying areas with endemic trachoma warranting interventions, further research is needed to determine the ability of the system to detect rare disease, on which decisions to withdraw interventions will be made.

1.4.4. Interpretation of the WHO Simplified Trachoma Grading System

It is the simplicity, repeatability and transferability of the simplified system that makes it currently, the best clinical diagnostic system for large-scale public health programmes. Additionally, each grade is differentiated from the other and can be interpreted to provide informative information about trachoma in the community. The presence of active trachoma (TF and/or TI) serves as a proxy for recent or current infection in a patient and a community indicating transmission of *Ct* and a need for control interventions. As patients, they should be treated with antibiotics. Separately, TI is more severe than TF, given that it is seen with severe inflammatory response and persons with persistent TI in longitudinal studies are more likely to progress to scarring than those with TF (MacCAllan, 1931; West et al., 2001a). Detecting the presence and a greater quantifiable load of *Ct* is more common from ocular swabs of patients with TI than from patients with TF alone (Burton et al., 2003; Solomon et al., 2003, 2004b).

The observed decline of TF prevalence after control interventions has been variable and seems to be related to the level of TF at baseline (WHO, 2010). Recent prospective studies measuring impact of mass drug administration (MDA) of antibiotics on trachoma in hyper-endemic areas of Ethiopia have observed a slower decline in TF than in *Ct* infection (Gebre et al., 2012). Additionally, observed declines in TI have been greater than declines in TF in South Sudan and Ethiopia following control interventions (Ngondi et al., 2006b, 2009a). There is new evidence that TF is associated with non-*Ct* bacterial infections and the impact this might have on TF prevalence in control programmes should be investigated (Burton et al., 2011a).

TS in a trachoma endemic area demonstrates that the patient has or has had repeated inflammation due to *Ct* infection and infers risk of progression to TT. The presence of TT identifies persons who are disabled and will develop corneal opacity and visual loss. TT indicates a need for corrective surgical intervention.

1.5. Epidemiology of trachoma

1.5.1. Age and gender-specific patterns

Clinical signs of trachoma are associated with age and gender. For example, TF and TI are most prevalent in children aged 1-9 years (Dawson et al., 1976; West et al., 1991). Figure 1.6 demonstrates the typical relationship observed between trachoma and age. Infection tends to follow the pattern of active trachoma, is most prevalent among those under five

years of age, but is not uncommon in adults (Bailey et al., 1999; West et al., 2005; Grassly et al., 2008; House et al., 2009). TS, TT, and CO appear to be irreversible and accumulate with age. Not all persons with scarring will progress to TT and CO (Burton et al., 2006; Ngondi et al., 2009c). Typically, the higher endemicity of TF and TI among children relates to a greater burden of blinding trachoma in adults. Also, where trachoma is hyper-endemic and transmission abounds, younger age groups have likely experienced more repeated infections and present with blinding trachoma at an earlier age than persons living in a low-endemic setting (Ngondi et al., 2006a; King et al., 2008). With gender, a recent meta-analysis of 25 cross-sectional studies found that women are nearly two times more likely than men to have trichiasis (Cromwell et al., 2009a). This gender disparity has almost always been reported in any trachoma assessment and is possibly due to increased exposure and reinfection experienced during childcare. Disparities in active disease between girls and boys have been inconsistent, but *Ct* infection may be more common in girls than boys (Courtright and West, 2004).

1.5.2. Transmission

Ct is transmitted by fingers, fomites, and flies. Infectious *Ct* elementary bodies are shed in ocular discharge and nasal discharge which can be wiped directly from one child to the next by dirty hands or indirectly by shared towels and also by eye-seeking flies. *Musca sorbens* are vectors of trachoma and are prevalent nearly worldwide, thriving in areas without basic sanitation (Emerson et al., 2000a). *Ct* has been isolated by polymerase chain reaction (PCR) from flies captured on the faces of children (Miller et al., 2004a; Lee et al., 2007). Reductions in the density of the *M. sorbens* population have been associated with decreased trachoma prevalence (Emerson et al., 1999, 2004).

1.5.3. Risk factors

The association of clinical signs of trachoma with various other individual and household factors has been assessed in multiple studies and reviewed (Emerson et al., 2000b; Taylor, 2008). Most of the analyses are limited to cross-sectional data and thus temporality and measures of risk are difficult to determine. The statistical significance of associations is not always consistent between studies.

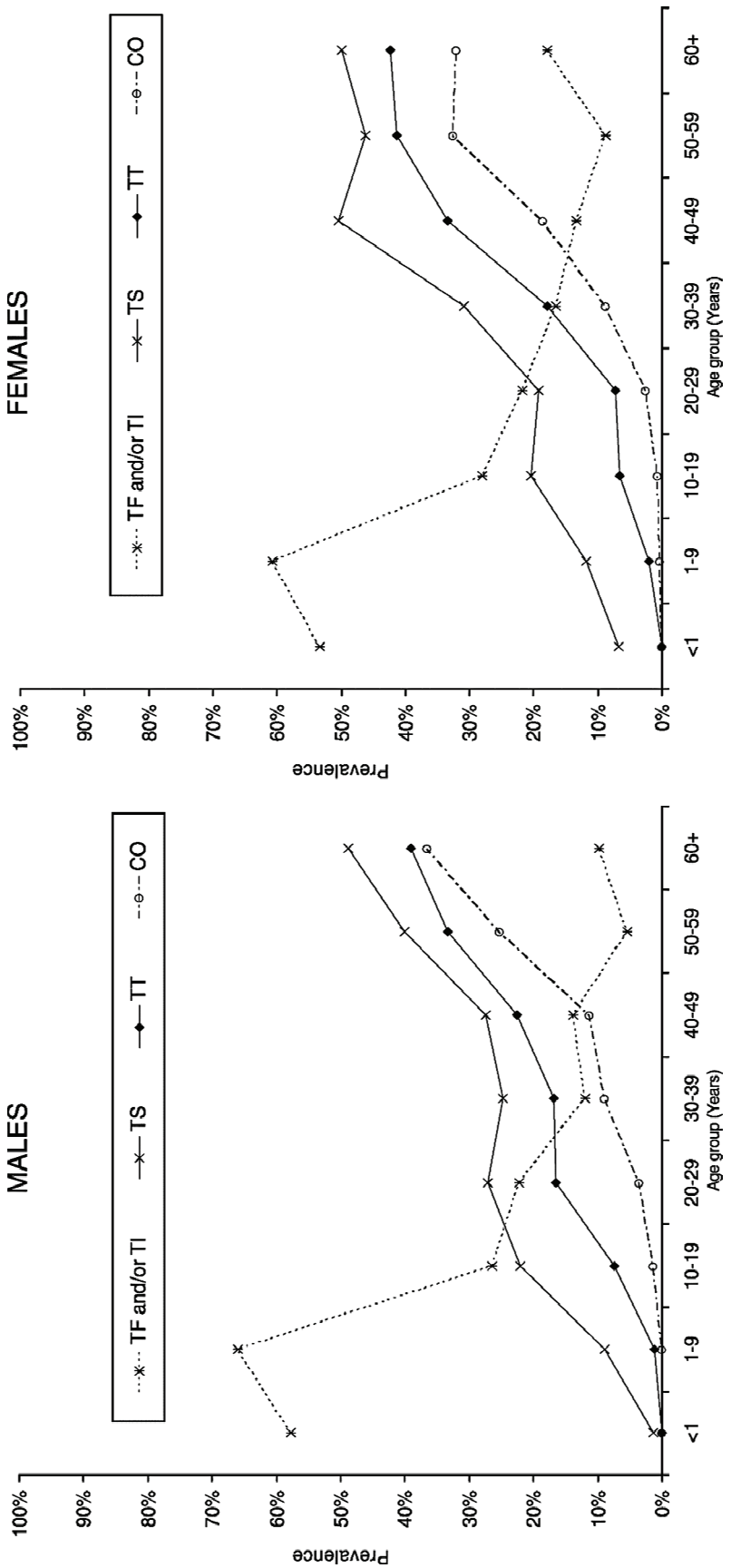

Figure 1.6. Age-specific prevalence of trachoma clinical signs by sex in South Sudan (Ngondi et al., 2006a)

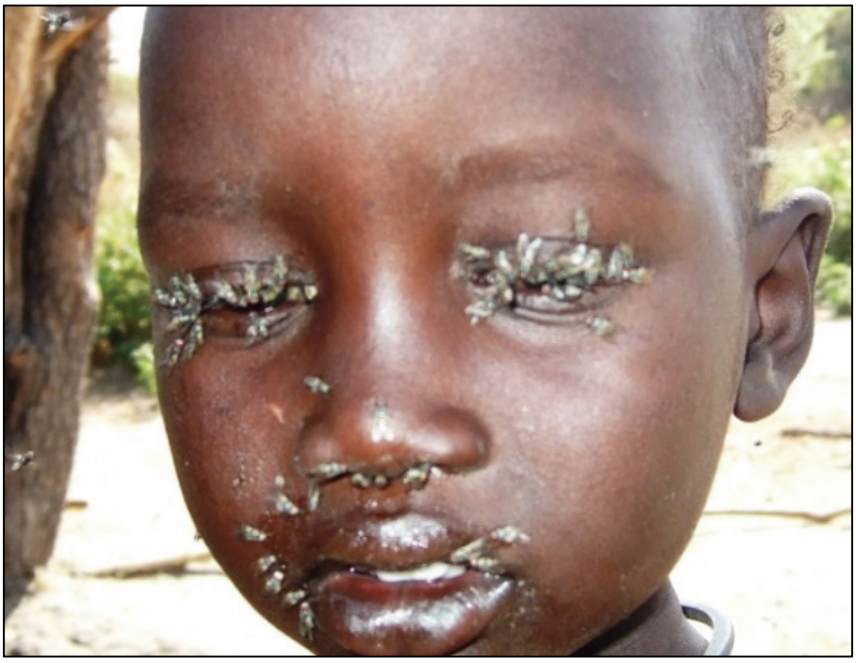

Figure 1.7. Child in South Sudan with active trachoma and *M. sorbens* feeding on ocular and nasal discharge (courtesy of The Carter Center South Sudan)

Table 1.1 lists some of the risk factors assessed and the consistency of their reported relationship with TF. Various indicators of low socio-economic status, lack of parental education, household size, and crowding are usually associated with increased odds of trachoma in children but not always statistically significant. We know that trachoma transmission clusters within a household and having a sibling with TF is always associated with increased odds of having TF (Barenfanger, 1975; Burton et al., 2003; Polack et al., 2005). Owning animals, keeping farm animals close to the living quarters, presence of flies, absence of a household latrine, distance to a water source, and the time to collect water have in some studies been shown to be associated with increased odds of trachoma in children. Ocular discharge has consistently been shown to be associated with trachoma in children likely because it is a direct result of the inflammatory response; not that it is a risk factor; although ocular discharge not related to trachoma may attract eye-seeking flies (Abdou et al., 2007). Studies have shown a reduced odds of trachoma in children with a sustained clean face and increased observed or reported frequency of face washing or bathing (West et al., 1996; Schemann et al., 2002, 2003). While typically trachoma is found endemic in hot, dry undeveloped areas, it was not always the case as at the turn of the 19th century, trachoma caused blindness in the slums of London, Dublin and Paris (Taylor, 2008). Few studies have assessed indicators of climate and geography with trachoma and the relationships have not been well established.

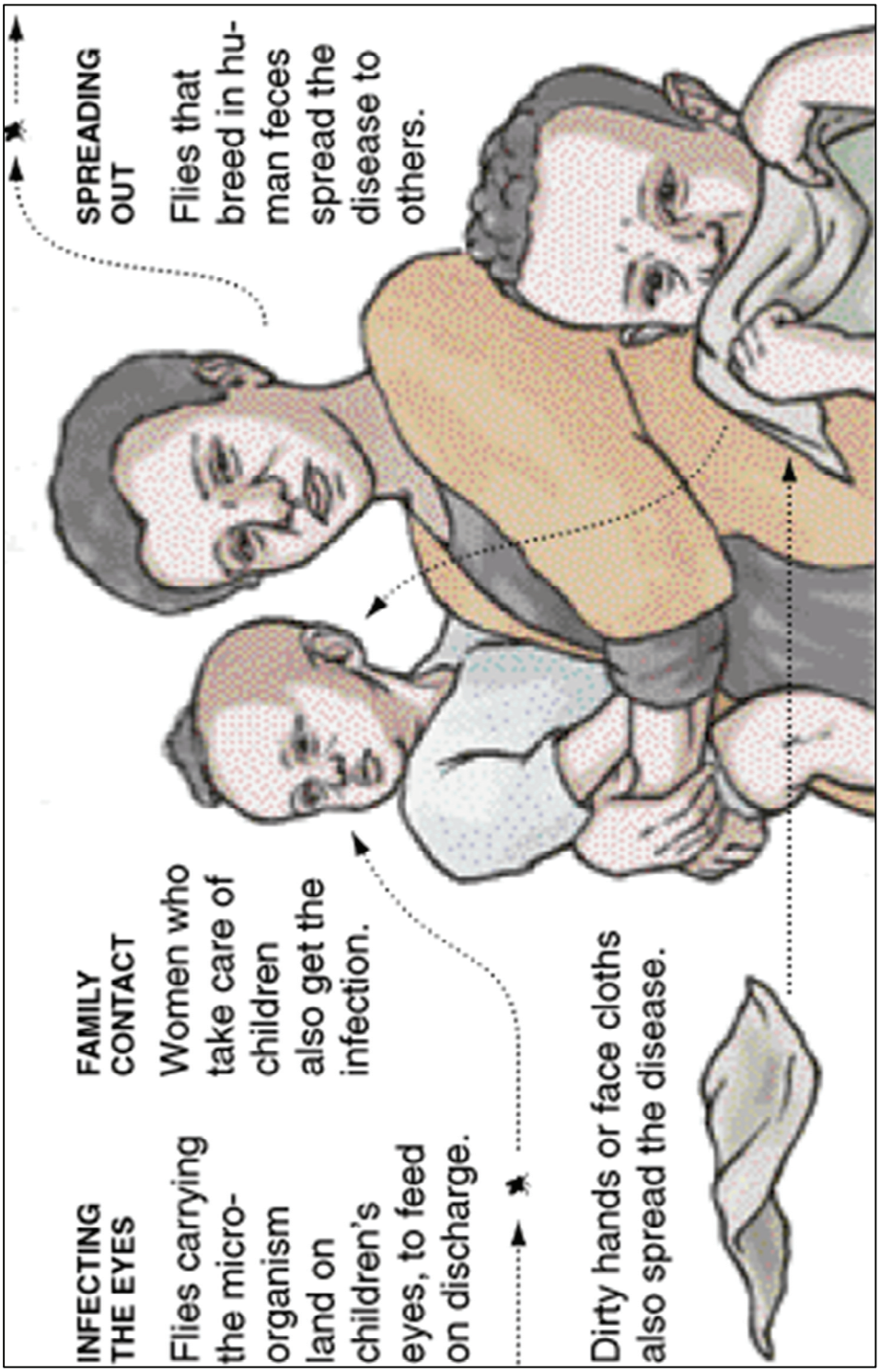

Figure 1.8. Transmission cycle of *Chlamydia trachomatis*. (Modified from sketch by artist Al Granberg The New York Times courtesy of The Carter Center)

Table 1.1. Relationship of individual and household factors with TF.

Factor	Relationship with TF	Consistency
Poverty (various SES indicators)	Increased odds	Usually
Lack of paternal education	Increased odds	Usually
Household size	Increased odds	Usually
Crowding	Increased odds	Usually
Sibling with trachoma	Increased odds	Always
Animal ownership	Increased odds	Sometimes
Animals in compound	Increased odds	Sometimes
Absence of household latrine	Increased odds	Sometimes
Presence of flies	Increased odds	Sometimes
Time to collect water	Increased odds	Sometimes
Ocular discharge on face	Increased odds	Always
Nasal discharge on face	Increased odds	Usually
Frequency of face washing	Decreased odds	Usually
Frequency of bathing	Decreased odds	Usually
Water use for washing	Decreased odds	Usually
Climate (various indicators)	Not established	-

1.6. The SAFE strategy

SAFE is an acronym for the integrated package of measures to treat, control and ultimately prevent any new blinding case of trachoma, namely through **S**urgery, **A**ntibiotic distribution, **F**acial cleanliness, and **E**nvironmental improvement (Francis and Turner, 1993). The SAFE strategy was adopted by WHO in 1996 as a result of recent developments in trachoma control, specifically: a standardised surgical procedure for trichiasis, development of strategies of community-based control activities, new information on risk factors of trachoma, and research showing effective treatment of active trachoma with azithromycin (WHO, 1997a).

1.6.1. Surgery

The aim of the surgery component (S) is to reverse the pathological anatomical condition, correcting the eyelid to keep the lashes from touching the eye. In major trichiasis cases, corrective surgery has been shown to improve comfort and visual acuity in patients (Reacher

et al., 1992; Burton et al., 2005a). There are multiple procedures, some of which do not require a surgical theatre and can be conducted in the field. The procedures can be taught to and effectively performed by nurses or integrated eye care workers (Alemayehu et al., 2004). National programmes often implement the surgery component of SAFE through community outreach campaigns in addition to providing surgery in tertiary hospitals or specialty eye care clinics (Rajak et al., 2012a). Regardless of the location of surgery or technique, in the best outcomes, approximately 10% of patients will have recurrence of trichiasis after surgery, but a range from 7% to 62% of operated trichiasis cases have been reported to have at least one recurrent lash after three years of follow-up (Rajak et al., 2012a). Despite variable recurrence rates, surgery improves visual outcomes and reduces pain and photophobia among trichiasis patients (Woreta et al., 2009). Recent qualitative research in Niger suggests that operated patients have a high level of tolerance, regardless of recurrence (Palmer, 2013). The factors related to recurrence are not fully understood and are currently being investigated.

1.6.2. Antibiotics

Antibiotic therapy (A) resolves *Ct* infection in the individual patient in >90% of cases. The aim of MDA with antibiotic in trachoma control is to treat all persons in a defined geographical area where signs of disease exceed a predetermined threshold. MDA is conducted without knowledge of and regard to whether persons are actually infected or not, in the anticipation that infected persons serving as the reservoirs of *Chlamydia* in the community will receive treatment. This was determined to be more effective at preventing reinfection than individual treatment (Schachter et al., 1999). A recent review found antibiotics to reduce both the risk and prevalence of infection and clinically active trachoma according to currently recommended regimens (Evans and Solomon, 2011). The current regimens recommended by WHO are: 1% tetracycline eye ointment applied twice per day for six weeks or a single, oral dose of azithromycin 20 mg/kg up to 1 g given annually for at least 3-5 years through MDA depending on prevalence of TF among children aged 1-9 years (WHO, 2006b, 2010). Recent research on the optimal frequency of MDA found no added benefit of biannual treatment over the current annual MDA recommendation (Gebre et al., 2012). Pfizer Inc. donates azithromycin (Zithromax®) to national programmes for the elimination of blinding trachoma (Mecaskey et al., 2003). Investigation of the use of topical azithromycin 1.5% ophthalmic solution for trachoma control is ongoing, but the multi-dose regimen (one drop twice a day for three days) may be challenging to implement on a programmatic scale (Amza et al., 2010; Huguet et al., 2010).

1.6.3. Facial cleanliness

The aim of the “F” component is to reduce contamination by keeping faces, and thus, hands and household items such as towels and washcloths free of infectious discharge. This strategy involves promoting behaviour change. There is some evidence that the promotion of face washing relates to changed behavior and decrease in prevalence of severe inflammatory trachoma compared to villages where face washing was not promoted (Lynch et al., 1994; West et al., 1995). But, as mentioned before, it has been difficult to establish a causal relationship as inflammation due to *Ct* infection produces ocular discharge. This inherent relationship also makes it difficult to monitor uptake of the promoted behaviour. In an earlier study not included in this thesis, we attempted to develop a standardised, repeatable definition of a clean face that programmes could employ to measure face washing behaviour. Unfortunately, ocular and dry nasal discharge were the only signs assessed that had some correlation with the face being washed and only moderate inter-observer agreement (King et al., 2011a). Thus, the monitoring of facial cleanliness has been limited to keeping record of the number of communities in which active promotion of face washing is occurring.

1.6.4. Environmental improvement

The “E” component aims to improve sanitation and hygiene in communities to reduce transmission of trachoma and prevent reinfection. Trachoma elimination from North America and Europe was not due to intervention with mass distribution of antibiotics, rather improvements in development (Taylor, 2008). *M. sorbens* preferentially oviposit in human faeces on the soil surface and do not oviposit in faeces within pit latrines (Emerson et al., 2001). Fly control with insecticide has been demonstrated to reduce trachoma and diarrhea in the Gambia (Emerson et al., 1999). Latrine construction and use are promoted due to evidence that populations of *M. sorbens* may be reduced, reducing fly-to-eye contacts and the transmission of trachoma (Emerson et al., 2004). It is unclear what additional effects latrines may have on controlling trachoma in areas receiving MDA or after MDA has been ceased (Stoller et al., 2011), but it is plausible that increasing use of latrines will help sustain reduction of transmission where antibiotics have reduced *Ct* infection in the community.

While accessibility of water is important, whether or not the water is used for hygiene seems to be most important in trachoma prevention. Where water is not accessible, household use of a limited supply of water may not be prioritised for bathing (West et al., 1989; Bailey et al., 1991; Polack et al., 2006). Where water is available, it must be used for hygiene to reduce transmission of trachoma. The low allocation of scarce potable water for hygiene purposes might explain the identification of trachoma in the Pacific Islands (Dethlefs, 1982; Mathew et al., 2009; Kline et al., 2013).

1.6.5. Potential ancillary benefits

The SAFE strategy is an integrated control strategy that likely has impact beyond control of blinding trachoma. Surprisingly, research to document these collateral impacts, until recently, has been scarce and most of the potential benefits discussed here are hypothesised. Benefits from the SAFE strategy are thought to include improvements in household economy, education, and both physical and mental health. Improvement in physical function has been documented among patients receiving surgery to correct trichiasis (Wolle et al., 2011). The reduction in disability probably decreases the risk of injury or perhaps mortality and might allow the patients and their caretakers to resume work contributing to the household income and shrinking the economic losses estimated in section 1.1. A successfully operated patient is likely to experience reduced stigma and improved self-perception as a contributor to the economic well-being of the household. These potential social impacts deserve documentation through qualitative research to define the extent of the benefits experienced by the patients and their families.

Mass distribution of azithromycin to children and adults is effective against trachoma, but also may reduce morbidity and mortality from other infections such as pneumonia, *Haemophilus influenzae*, bacterial dermatitis, and sexually transmitted infections (STIs). One study in Ethiopia found a 50% (95% confidence limit was 10-70%) lower rate of mortality among children less than five years of age who took azithromycin compared to children who did not receive azithromycin (Porco et al., 2009). Currently, a trial designed to reproduce this finding and specifically identify which factors of mortality are impacted is in preparation. Any reduced morbidity among treated children may lessen the number of school days missed improving learning. There has been some evidence that children receiving azithromycin in MDA have lower rates of diarrhea than children not receiving MDA for up to three months after the distribution (Coles et al., 2011). Therefore, it is not unreasonable to postulate that persons with resolved infections may have lower healthcare expenditures and experience feelings of increased vigor, which may explain anecdotal field reports of demand for continued antibiotic distribution.

The promotion of facial hygiene involves washing the face to prevent transmission of *Ct*, and perhaps as a result, reduce infectious ocular and nasal discharge of other ocular and respiratory infections. If in the process of face washing, the hands are also washed, transmission of other infections spread by contact with infectious material would be prevented, particularly respiratory and faecal-oral transmitted infections. Pneumonia and diarrhea are the leading causes of mortality among children aged 1-5 years and nearly half of the deaths due to these diseases occur in Sub-Saharan Africa where trachoma is highly endemic (Liu et al., 2012). Hand washing can reduce diarrheal illness by 47% and thus avert a significant burden of mortality due to diarrhea (Curtis and Cairncross, 2003). One could

assess whether households in trachoma endemic areas that prioritise water for face washing are more likely to prioritise water use for overall hygiene including hand washing.

The Millennium Development Goal 7c, to reduce by half the proportion of households that lack basic sanitation, is directly addressed through the E component in trachoma endemic areas where SAFE is being implemented (Emerson et al., 2012). Globally in rural areas, it is estimated that nearly one billion people practice open defecation and 1.8 billion lack access to an improved sanitation facility (UNICEF, 2012). This lack of sanitation is a major contributing factor to child mortality due to diarrheal disease. Managing human waste through household latrine use reduces contamination of the environment and reduces transmission and new infections of faecal-oral diseases (Mara et al., 2010). Recent meta-analysis found significant protective effect of household sanitation on soil-transmitted helminths (Ziegelbauer et al., 2012). The availability of water improves the chances of water use for bathing as mentioned in 1.6.4. Availability of potable water when used for drinking reduces risk of infection from water-borne diseases (Prüss-Üstün et al., 2008). Together, these environmental improvements in water and sanitation should impact transmission of guinea worm, diarrheal diseases, respiratory tract infections and intestinal parasites (helminths and pathogenic intestinal protozoa) (Esrey et al., 1991). While these collateral benefits are hypothesised, little research has been conducted to document such benefits as an effect of the SAFE strategy.

1.7. Global elimination of blinding trachoma

In 1997 The Global Alliance for the Elimination of Blinding Trachoma (GET 2020), a collaborative force of donors, international NGOs, academic institutions, corporate sponsors, and national governments, met to bring about the realisation of global trachoma elimination. Shortly after their first meeting, recognising the severe health burden due to trachoma and that the disease is preventable through simple and available strategies, the World Health Assembly (WHA) called for the global elimination of blinding trachoma as a public health problem by the year 2020 in WHA resolution 51.11 adopted in May 1998 (WHO, 1998). Specifically, the resolution called on member states to map blinding trachoma in the remaining endemic areas and where needed, implement the SAFE strategy to achieve elimination. A recent review of trachoma elimination by the International Task Force for Disease Eradication highlighted that trachoma elimination, as defined, was achievable (ITFDE, 2011).

1.7.1. Elimination defined

The aim of the global programme is interpreted as the ‘elimination of blinding trachoma as a public health problem’ and targets neither ocular *Ct* nor the disease for elimination. Low

levels of active trachoma (TF and/or TI) felt to no longer contribute to chronic reinfection and inflammation leading to the deleterious anatomical condition and few incident cases of TT will be acceptable. Therefore, the term 'elimination' in this thesis will be used to align with WHO terminology, but essentially this is a global control programme. The proxy targets assumed to meet this aim are together: the existence of less than one case of TT per 1,000 population and <5% prevalence of TF among children aged 1-9 years (Resnikoff et al., 2007; WHO, 2010). Currently, there are no recommended measures of elimination for infection with *Ct* or for any other clinical signs of the simplified trachoma grading system such as TI and TS.

1.7.2. Programme strategy as recommended by WHO

A surgical backlog is calculated to be the total number of persons with TT based on the most recent prevalence estimates. Where the prevalence of TT is >1% among adults, surgical interventions should be prioritised including outreach campaigns in combination with the existing eye care services. According to WHO guidelines, areas with ≥10% TF among children 1-9 years of age (TF_{1-9}) warrant behaviour change communication to promote the F and E components and at least three rounds of annual MDA with azithromycin (WHO, 2006b). Where district-level prevalence of TF_{1-9} is <10%, prevalence at the sub-district level should be assessed (WHO, 2010). Sub-districts having ≥10% TF_{1-9} warrant MDA for at least three years. F and E interventions, at minimum, and targeted MDA are recommended for sub-districts having 5-9% TF_{1-9} (WHO, 2010). Where TF_{1-9} is <5% no MDA is needed, but efforts should be made to ensure that F and E are being implemented (WHO, 2006b).

Trachoma elimination programmes should aim to achieve 100% coverage of the total population targeted with the SAFE interventions (WHO, 2010). Specifically the targets are as follows: 100% of TT cases (total estimated backlog) registered and offered surgery; 100% of persons taking antibiotics during MDA; 100% of communities receiving behaviour change communication on facial cleanliness and environmental improvements; 100% of households with basic sanitation (latrine); 100% of households with access to water within 30 minutes round-trip collection. These targets are referred to as the ultimate intervention goals (UIG).

Evaluation of disease outcomes is not necessary before three years of intervention with SAFE in areas with a baseline prevalence of TF_{1-9} between 10-30%, whilst evaluation is not necessary before five years in areas with a baseline prevalence of TF_{1-9} >30%. Modeling of the natural history of trachoma in The Gambia and recent analysis of data from Ethiopia suggest the timing of the outcome evaluation should be no earlier than six months since the last round of MDA (Grassly et al., 2008; Ngondi et al., 2010). In areas (districts) that have been receiving mass antibiotic distribution, if the evaluation survey finds that TF_{1-9} is >10%, then A, F, and E interventions should continue for an additional three years.

Previous guidelines (WHO, 2006b) had indicated decisions to stop MDA be made at the community level, implying that each community need be assessed. Realising the logistical challenges this would present programmes, a consensus was reached that the sub-district level is the unit on which stopping interventions be made (WHO, 2010). In sub-districts where TF_{1-9} is between 5-9%, targeted MDA in combination with F and E should continue for an additional three years. Where TF_{1-9} is <5% at the sub-district, MDA is no longer warranted, but F and E interventions should continue whilst post-endemic surveillance activities are put in place.

1.7.3. Recommended "post-endemic" surveillance

As countries implementing SAFE start to see levels of blinding trachoma decline, national programmes must plan activities to ensure the achievements are sustained. The objective of trachoma surveillance is to monitor the presence of active disease and TT incidence to detect and respond to potential resurgence. Additionally, eye care services must continue to identify and operate new and recurrent TT cases. Surveillance activities should be planned and tested in some of the first "post-endemic" areas that achieve <5% TF_{1-9} and subsequently implement the activities as other districts become post-endemic. At minimum, WHO recommends selecting two communities per district per year biased to the least developed and suspected most endemic. In these communities, all school entrance-aged children (5-6 years) in school are to be examined for TF where attendance is >90% and there is no gender bias (WHO, 2008). In areas with lower attendance, at least 50 children aged 5-6 years in the community may be examined. Where TF among the sample of children is >5%, a series of further investigations and response with A, F, and E activities is suggested cascading from community level back to the district if necessary (WHO, 2008). To monitor incidence of TT, national programmes are recommended to continue collection and analysis of TT surgical output data and to incorporate TT into existing national health information systems. TT cases identified and reported through the health systems should be classified as recurrent, prevalent (already offered surgery), or incident (not yet offered surgery). This health system surveillance for trachoma should be maintained for at least 10 years (WHO, 2008). Additionally, in each community assessed for TF, TT should also be assessed in adults and any cases should be classified and offered surgery. Active surveillance for TF can be stopped if after three years an additional prevalence survey were to find TF_{1-9} to remain <5% (WHO, 2008, 2010).

1.7.4. Progress towards elimination

Currently, of the 53 trachoma endemic countries, 36 are implementing the SAFE strategy (WHO, 2012b). Nine countries (Algeria, Ghana, Iran, Libya, Mexico, Morocco, Oman, The

Gambia, and Vietnam) have reached their elimination targets and are in the post-endemic surveillance phase (WHO, 2012b). Of these nine, Ghana and The Gambia give great hope that elimination of trachoma in Sub-Saharan Africa is feasible through concerted efforts to implement the SAFE strategy.

A third of the estimated 325 million persons at risk for trachoma are living in districts where trachoma has been mapped and confirmed endemic. For the remaining two-thirds, the estimates will be made clearer as a current grant from the UK government is supporting mapping surveys in the remaining 1,293 districts to be completed by 2015. In all suspected endemic areas, 80% of the populations at risk live in 14 countries and with the exception of Pakistan, all are located in Sub-Saharan Africa (ICTC, 2011). Ethiopia alone accounts for 22% of the global population at risk. Since the inception of GET 2020 until 2010, approximately 900,000 persons have received surgery for trichiasis and 250 million antibiotic treatments have been distributed (WHO, 2012b). To meet the 2020 goal, an estimated 500,000 persons with TT need be operated per year to clear the estimated backlog of 4.6 million persons with TT and up to 380 million doses of antibiotic would be warranted for distribution in the confirmed endemic areas (ICTC, 2011). Clearly, there is much work to be done and continued collaborative efforts are needed as well as financial resources to achieve elimination. An important first step is to confirm all suspected areas and establish the true targets on which to measure progress.

1.8. Methods for mapping trachoma and evaluating impact of the SAFE strategy

1.8.1. Objectives of the trachoma assessment

"The epidemiology of the disease is such that only population-based assessments are relevant" (WHO, 1997a). This quote from the first global scientific meeting on trachoma clearly indicates the type of data needed for trachoma control programmes. The goal of the trachoma assessment is to identify endemic areas warranting interventions. The specific aims are to:

1. Determine prevalence of TF_{1-9} on which to plan interventions and use as a baseline on which to measure programme success
2. Determine prevalence of TT in the population on which to estimate the total backlog of cases to be operated and to prioritise areas for surgical outreach
3. Measure the facial cleanliness of $children_{1-9}$ and the reported frequency of face washing
4. Measure the existing household sanitation coverage (proportion of households with at minimum, a household latrine)
5. Measure household access to water (proportion of households within 30 minutes round-trip collection to water source)

Regardless of whether the assessment is for initiating a programme (mapping), monitoring the progress or evaluating the impact after interventions have been implemented, the above objectives remain consistent. After MDA, surveys may include measurement of reported antibiotic coverage, defined as the proportion of the total surveyed population that reported taking antibiotics when distributed during the campaign (WHO, 2006b). Estimating prevalence in each time point allows the same repeated measures to be compared over time to interpret success of the interventions.

1.8.2. WHO recommendations

Currently, WHO recommends national programmes conduct baseline prevalence surveys to identify endemic areas. There are three WHO manuals providing guidelines for assessing trachoma in the community. The first from 1993, *Trachoma Epidemiological Survey Protocol*, recommends population-based, cluster surveys be conducted (WHO, 1993b). The method adheres to the principles of random probability sampling where 20 clusters are selected with probability proportionate to population size (PPS) and households are selected through random systematic sampling. It suggests all residents of selected households be examined for all clinical signs of the simplified trachoma grading system. Finally, it calls for the estimation of prevalence of active trachoma (TF and/or TI and TI alone) among children aged ≤10 years and TT among women at the district level.

The second manual, *Guidelines for the Rapid Assessment for Blinding Trachoma*, came in response to the perception that population-based cluster surveys were difficult to conduct in resource-poor settings. The idea behind the trachoma rapid assessment (TRA) was to prioritise trachoma endemic areas for intervention as quickly as possible without having to conduct prevalence surveys in all areas (Negrel AD, 2001). Instead of district-level surveys, TRA involves two phases, desk-top review of any existing data including key informant interviews to categorise areas, and then field assessments to confirm reports. The TRA assumes that reports including trachoma data are available and that people interviewed will be knowledgeable about trachoma in the community. The field assessments are biased to the suspected most endemic sites or least developed areas in order to confirm endemicity. Once areas of trachoma have been identified, there is additional need to determine the level of facial cleanliness and coverage of water and sanitation. The assumed advantages are that large areas can be classified and prioritised for intervention rapidly. The disadvantages are that active and blinding trachoma prevalence in a district cannot be estimated upon which to make intervention decisions or measure progress according to WHO recommendations.

Trachoma Control: a guide for programme managers contains the most recent guidelines for conducting trachoma assessments (WHO, 2006b). Similarly to the 1993

protocol, population-based prevalence estimates of active and blinding trachoma are generated at the district level from cluster random sampling (CRS). Communities are also similarly selected via PPS, but suggested household selection is performed via spinning a bottle and surveying households in the direction of the bottle top until the desired sample size of children is met. Different from the original protocol, only children under 10 years of age and adults 15 years of age and older are suggested for examination. The limitations of this current approach is that using the bottle spin approach with a rule for stopping once the sample size is achieved, violates the principles of probability sampling. The probability that a person is examined cannot be calculated and is different from cluster to cluster. Additionally, limiting the examination to only adults prevents the direct estimation of the prevalence of TT in the total population on which the elimination target is defined.

1.8.3. Alternative and integrated methods applied

Population-based prevalence surveys are considered the gold standard and, for the most part, are currently being applied in the field (Wright et al., 2005; Ngondi et al., 2009b). However, there have been methods, influenced by quality assurance strategies in the manufacturing industry, applied in trachoma mapping surveys that determine whether an unacceptable threshold of trachoma in the community has been exceeded (Myatt et al., 2003, 2005). These lot quality assurance sampling (LQAS) designs are able to determine the need for trachoma interventions and may require smaller sample sizes, but require strict adherence to simple random sampling from complete population census data. Additionally, these methods are unable to provide population-based prevalence estimates on which programmes monitor success (Ngondi et al., 2009b). A modification of the LQAS method was applied in Senegal which allowed an estimation of community-level prevalence by examining all targeted children without stopping at a given threshold of positives (Faye et al., 2006). The modified method was quite similar to CRS, yet the number of clusters sampled was more than what would have been in a recommended cluster survey. Additionally, a limited age range was randomly sampled and the method did not generate TT prevalence through random sampling of the population.

The recent global push for an integrated approach to NTD control programmes prompted discussion of integrated methods for mapping, monitoring, and evaluation (Baker et al., 2010). The strengths of integrated disease assessment are that efforts can be harmonised into one field activity to conserve limited resources. The challenges to integration are that the recommended methodologies of each programme have different target populations and different venues of sample selection. For instance, the schistosomiasis and soil-transmitted helminthiasis control programmes assess disease burden in school-aged children through a random sample of 50 children in schools (WHO,

2002a). As mentioned previously, the recommended age group for assessing trachoma prevalence and basing intervention decisions is children aged 1-9 years and blinding disease in adults.

Despite these differences, efforts have been made to align surveys of multiple NTDs. Children in all government primary schools in eight districts of central Nigeria were randomly selected for either urine analysis for schistosomiasis or active trachoma depending on their ages (King et al., 2009). In that specific setting, integrating trachoma examinations in schools was useful in identifying endemic communities that were not identified through the recommended population-based cluster survey, yet no estimates of trichiasis were possible through the approach. Also, the method employed allowed district-level estimates of TF prevalence to be generated that were not different than estimates generated by the recommended methodology assessing all children in the community. In the same study, efforts to assess urinary schistosomiasis through community-based CRS method of the trachoma programme were not as successful given the focal nature of schistosomiasis and the fact that the school-aged children in this area were in school when survey teams were in the community and thus very small sample sizes were achieved. School-based integrated NTD assessments have also been conducted in Burkina Faso to serve as baseline data for programme decisions and to serve as sentinel sites on which to monitor schistosomiasis and trachoma control programmes (Koukounari et al., 2011).

Schools have also served as the sampling venue of another integrated disease survey approach, Integrated Threshold Mapping, whereby trachoma, soil-transmitted helminths, schistosomiasis and lymphatic filariasis are assessed (Pelletreau et al., 2011; Dorkenoo et al., 2012). Intervention decisions are made based on whether the proportion of positive children examined for each disease in four communities (two purposefully selected for schistosomiasis and two randomly selected) per sub-district exceeds the prevalence thresholds recommended in WHO guidelines for identifying areas warranting interventions. However, this method employs neither LQAS, random or population-based sampling strategies and is unable to generate estimates of prevalence of any of the diseases.

The key to integrated disease assessment is to align methods where it makes sense and coordinate where there is no compromise. However, further research is warranted to identify the right compromise of existing programme standards, but yet maintain the principles of random sampling and provision of prevalence estimates which can be consistently measured over time to determine programme success.

2. Goal

The investigations included in this thesis are aimed to address relevant programmatic issues, solutions to which would improve the ability of national trachoma elimination programmes to measure success of interventions. The overarching goal of this PhD project was to investigate novel approaches for evaluating the impact of the SAFE strategy, primarily on trachoma, but also other neglected tropical diseases (NTDs), namely intestinal helminth infections. This operational research was designed and carried out in the context of a national trachoma elimination programme.

2.1. Specific objectives and research needs addressed

Objective 1. Determine whether implementation of the SAFE strategy in South Wollo and South Gondar has reduced the prevalence of TF_{1-9} below 5% at the sub-district level and MDA can be stopped.

National programmes implementing the SAFE strategy to eliminate blinding trachoma need guidance in determining when mass distribution of antibiotics can be stopped. When starting MDA is based upon prevalence estimates at the district level (population 100,000-250,000), new guidelines from the WHO state that MDA can stop if the programme demonstrates that TF_{1-9} has fallen below 5% (defined as 4±2%) at the sub-district level (population ~50,000) (WHO, 2010). The feasibility of conducting such sub-district level surveys in large population areas has not been established and there is no standard methodology (i.e. parameters recommended most recently have yet to be applied in programmatic settings). Additionally, a reduction in TF_{1-9} to below 5% has yet to be observed in such hyper-endemic areas as the Amhara region of Ethiopia.

Null hypothesis: There is no difference between prevalence of TF_{1-9} prior to and post intervention with the SAFE strategy.

Alternate hypothesis: The prevalence of TF_{1-9} at the sub-district level is less than 5% in South Wollo and South Gondar after the implementation of the SAFE strategy.

Objective 2. Determine whether a novel electronic data management and collection tool can facilitate the completion of surveys to evaluate the impact of the SAFE strategy.

The requirement of greater precision (i.e. from district-level to sub-district-level prevalence estimates) upon evaluating impact of interventions inevitably will require more data to be collected and substantial resources required for data management. The application of new technology for the electronic collection of trachoma survey data might be feasible to reduce time and costs in managing such large data collection activities.

Null hypothesis: There is no difference in cost, time to survey completion, data entry errors, or respondent participation rates between a novel electronic data collection system and standard paper-based surveys.

Objective 3. Determine whether children exposed to SAFE interventions are less likely to present with trachomatous scarring (TS) than children having never been exposed.

Currently WHO recommends assessing TF as an outcome measure to evaluate impact of the SAFE strategy. As mentioned before, the clinical sign of TF serves as a proxy for infection and indicator of transmission. However, research in high trachoma prevalence areas has shown that TF prevalence may not decline after several rounds of MDA with antibiotics even when *Ct* infection in the community is low to nearly undetectable. This generates great concerns that even after concerted efforts have been put forth to implement the SAFE strategy, national programmes may not meet their elimination targets and MDA will continue after ocular *Ct* has been eliminated. The impact of SAFE interventions on other clinical signs, particularly scarring among children, would suggest that the interventions are having immediate and long-term effects on averting blindness, but this has not been investigated.

Null hypothesis: There is no difference in the risk of presenting TS between children exposed and not exposed to the SAFE strategy.

Objective 4. Determine whether school-based surveys might serve as a valid, alternative approach to assess the impact of the SAFE strategy on trachoma.

Realising the substantial resources likely to be required for generating prevalence estimates at the sub-district level to evaluate the SAFE interventions on a programmatic scale, ways to simplify sampling methods should be explored. Schools have been used as primary sampling units on which to estimate community prevalence of schistosomiasis and soil-transmitted helminthiasis. Currently, schools are being used to assess and monitor integrated NTD programmes. Yet, it has not been clearly determined whether children who attend school are representative of children in the community and whether their disease prevalence is similar to children who do not attend school. Any differences between these groups might affect the validity of disease prevalence estimates derived from school-based survey methods.

Null hypothesis: There is no difference in active trachoma between children who attend and do not attend school.

Objective 5. Determine whether the prevalence of intestinal helminths among children has declined in an area where the SAFE strategy has been implemented.

Theoretically, trachoma disappeared from industrialised nations due to improvements in hygiene and sanitation, yet the evidence of the impact of improved sanitation on trachoma has been demonstrated only in few studies. Unfortunately, current programmes pertaining to NTDs primarily focus on preventive chemotherapy dependent on pharmaceutical donations rather than efforts to improve sanitation. While hygiene behaviour and latrine construction are being promoted through the SAFE strategy, national programmes could strengthen advocacy efforts by documenting potential collateral benefits of household latrine use such as reduced prevalence of soil-transmitted helminth infections. Combining the assessment of intestinal parasites with trachoma impact evaluations also establishes the proof of concept that integration of NTD assessments is feasible in community-based surveys.

Null hypothesis: There is no difference between the prevalence of intestinal helminthiasis among school-aged children prior to and post implementation of the SAFE strategy

3. Study site

The study site of this project is the Amhara National Regional State of Ethiopia. The state has a total population of 17,232,709 persons living in 3,468 *kebeles* (clusters of villages) in 151 *woredas* (administrative districts) from 10 zones (Ethiopia, 2007). People from the ethnic group *Amhara* make up the majority of residents and *Amharic* is the official language. Additionally, English is taught within the education system. Persons living in the regional capital, Bahir Dar, and other large zonal towns are considered to be at little or no risk of trachoma, but this has not been well established. An estimated 16,591,836 persons within the region are living in known trachoma endemic areas. The specific locations of data collection were all *woredas* (equivalent to a district) of South Gondar and 13 *woredas* from South Wollo zones of the Amhara National Regional State (Figure 3.1.). The estimated total population living in South Gondar zone in 2007 was about 2 million and 2.5 million total population live in South Wollo (Ethiopia Central Statistical Agency).

A country-wide blindness and low vision survey conducted in 2006 found trachoma, both TT among adults (5.2%) and TF (39.1%) or TF/TI (62.6%) among children, to be highest in Amhara compared to the other regional states (Berhane et al., 2006). Shortly after the survey, The Federal Ministry of Health with Regional State Health Bureaus developed a strategic plan outlying full implementation of the SAFE strategy to eliminate blinding trachoma by 2015. Although pilot trachoma interventions were initiated within four *woredas* of Amhara in 2001, it was not until a recent collaboration in 2006 between The Carter Center, Lions Clubs International Foundation and the Amhara National Regional State Health Bureau that has allowed the widespread implementation of the full SAFE strategy to all endemic areas in Amhara. Surgery for trichiasis is conducted at static health facilities and during mobile outreach campaigns. Mass antibiotic distribution is carried out solely through integrated mass campaigns called MalTra weeks. MalTra weeks involve short, intense periods of community mobilisation and mass antibiotic distribution as well as fever screening febrile patients, testing, and treatment for malaria at central distribution sites. The extensive network of Health Extension Workers (HEWs) and health volunteers provide the human resources to reach millions of residents within two weeks. HEWs are year-round health education and service providers of the health system, who also promote the F and E components of the SAFE strategy. Facial cleanliness and hygiene are part of a trachoma specific primary school health curriculum. Additionally, HEWs demonstrate construction and promote use of household latrines using local materials.

The implementation of SAFE interventions in Amhara represents a model effort for the global trachoma elimination programme given the high endemicity of disease, investment of resources, partnerships, political commitment, and magnitude of output. The total

cumulative output of SAFE activities through December 2010 (the date prior to initiating field work for the thesis project) in Amhara as reported by the Health Bureau include:

- 220,333 persons operated to correct trichiasis
- 59,227,132 doses of antibiotic distributed
- 3,468 *kebeles* with ongoing trachoma specific health education
- 2,021,382 household latrines constructed

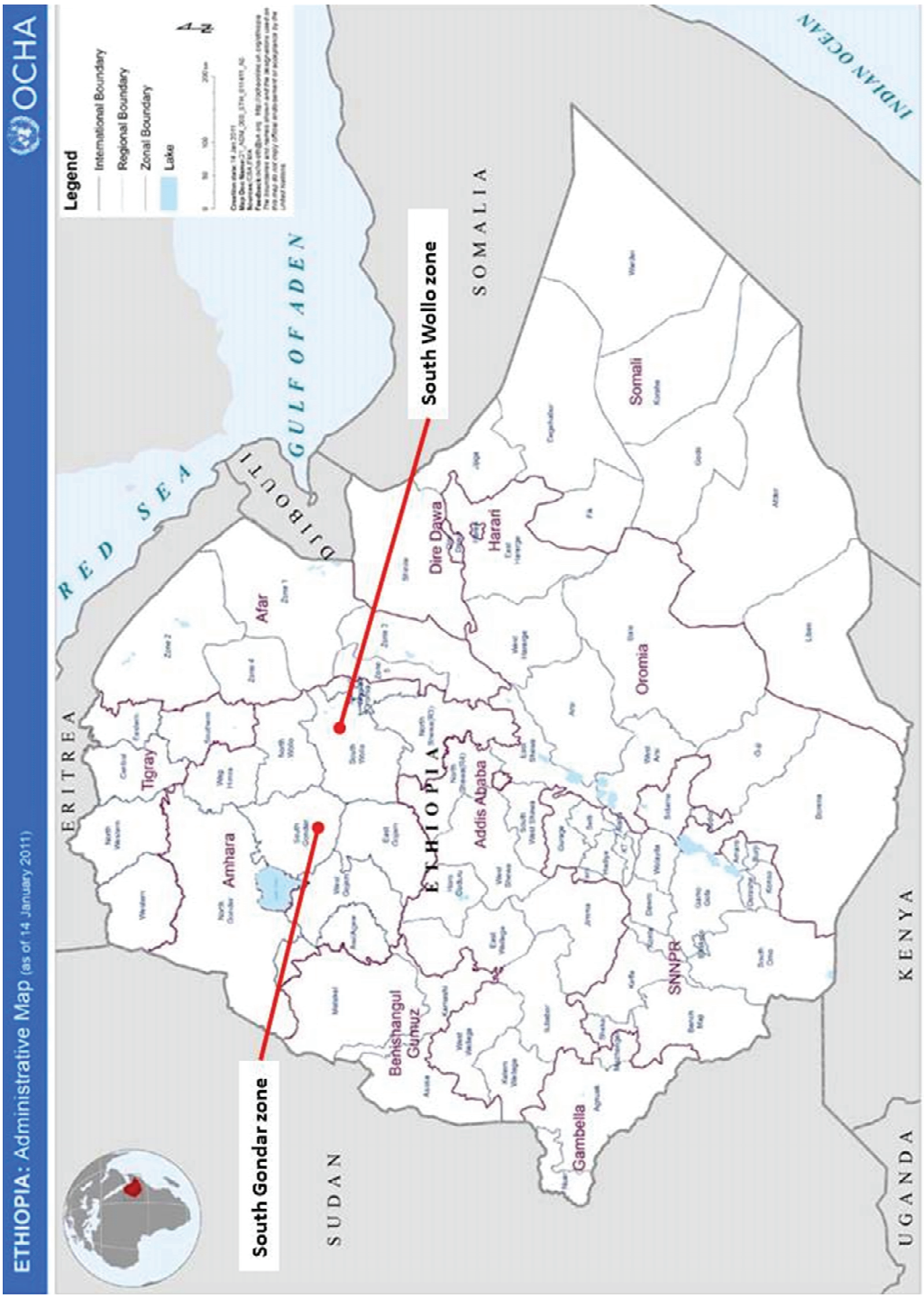

Figure 3.1. Location of study sites: South Gondar and South Wollo zones of the Amhara National Regional State, Ethiopia (modified from http://www.usaid.gov/news-information/frontlines/child-survival-ethiopia-edition/ethiopia-land-contrasts-nation)

Figure 4.1. The author demonstrates how to hold small children for trachoma examinations during the survey training in South Wollo Zone, Ethiopia (courtesy of Mary Rose King)

4. Prevalence of trachoma at sub-district level in Ethiopia: determining when to stop mass azithromycin distribution

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4.1. Abstract

Background: To eliminate blinding trachoma, the World Health Organization recommends implementing the SAFE strategy which includes annual mass drug administration (MDA) with azithromycin to the whole population of endemic districts. Proposed impact assessment guidelines suggest stopping MDA when the prevalence of trachomatous inflammation follicular (TF) among children aged 1-9 years is below 5% at the sub-implementation unit (sub-district). We conducted surveys powered to estimate prevalence simultaneously at the sub-district and district in two zones of Amhara, Ethiopia to determine whether MDA could be stopped.

Methodology**:** Seventy-two separate sub-district surveys were conducted in 25 districts. In each survey all residents from 10 randomly selected clusters were screened for clinical signs of trachoma. Data were weighted according to selection probabilities and adjusted for correlation due to clustering.

Principal Findings: Overall, 89,735 residents were registered from 21,327 households of whom 72,452 (80.7%) were examined. District-level prevalence of TF in children aged 1-9 years ranged from 0.9% to 67.0% and 0.9-76.9% at the sub-district level. Six sub-districts and two districts were below the stopping threshold of 5% TF in children aged 1-9 years. TF in none of the districts receiving at least five rounds of MDA was reduced below 5% among children. In only one district was the prevalence of trichiasis below 0.1%.

Conclusions/Significance: The experience from these zones in Ethiopia demonstrates that impact evaluation designed to give a prevalence estimate of TF at sub-district level are possible, although the scale of the work was challenging. Interpretation was not as simple as stopping MDA in sub-districts below 5% given programmatic challenges of exempting sub-districts from a highly-regarded programme and the proximity of hyper-endemic sub-districts. Analysis of the spatial distribution of trachoma between sub-districts and prevalence of *Chlamydia trachomatis* infection may be useful additional evidence for MDA-stopping decisions.

4.2. Author Summary

Trachoma, the leading cause of preventable blindness, is targeted for elimination by the year 2020. National programmes are implementing the recommended strategy of surgery, antibiotics, facial cleanliness, and environmental improvement (SAFE) to meet the target. Many programmes are currently facing the decision of when to scale down interventions, particularly mass drug administration (MDA) of azithromycin. We implemented large population-based surveys in two different zones of the Amhara National Regional State of Ethiopia following a novel approach to measure the prevalence of trachoma at sub-district level and to determine whether to stop MDA according to World Health Organization guidelines. We compared the current disease situation with that of the trachoma situation before the full implementation of the SAFE strategy. Over 72,000 people in 714 communities in 72 sub-districts were examined for clinical signs of trachoma. The clinical data suggest some decline in trachoma within these areas since the SAFE strategy was implemented. However, we identified only six sub-districts that met criteria for being able to stop MDA. The study demonstrates that determining the prevalence of trachoma at sub-district level is feasible but requires significant resources.

4.3. Introduction

Trachoma accounts for 3% of global blindness and is targeted for elimination as a public health problem by the year 2020 (WHO,1998, 2012a). Trachoma is estimated to be endemic in 53 countries of which 35 have begun scaling-up or have fully implemented the recommended SAFE strategy for reaching the elimination targets (WHO, 2012b). SAFE is the acronym for an integrated package of interventions to treat, control and ultimately prevent new cases of blinding trachoma through surgery (S), antibiotic distribution (A), facial cleanliness (F), and environmental improvements (E) (Francis and Turner, 1993). Elimination as a public health problem, the ultimate intervention goal (UIG), is defined as achieving a transmission target: trachomatous inflammation follicular (TF), in children aged 1-9 years to less than 5%, and a morbidity target: less than 1 case of trachomatous trichiasis (TT) per 1,000 population (Resnikoff et al., 2007).

The World Health Organization (WHO) recommends annual mass drug administration (MDA) with azithromycin or tetracycline ophthalmic ointment in areas where the district-level prevalence of TF among children aged 1-9 years is greater than 10% (WHO, 2006b). A major challenge faced by national programmes currently implementing SAFE is determining when to stop MDA. According to guidelines issued after the 2nd global scientific meeting (GSM) on trachoma in 2003, the impact of SAFE on the prevalence of trachoma should be assessed after at least three years of implementation and MDA stopped where the prevalence of TF in children aged 1-9 years is determined to be less than 5% in any community (WHO, 2004, 2006b).

Realising that estimating trachoma prevalence in every community in sub-Saharan Africa places a heavy burden on resource-limited programmes, the 3rd GSM on trachoma was convened by WHO in July 2010 with the purpose of reviewing and clarifying guidelines for the implementation of impact assessment surveys, including the administrative level at which impact must be measured to stop MDA. These new guidelines state that a district is the largest unit on which to estimate trachoma prevalence for outcome surveys and specifically that “outcome surveys can be used to pronounce achievement of UIG for TF, if the sample size is powered to calculate estimates at the sub-district level” (WHO, 2010). The purpose of this study was to apply this recommendation from the 3rd GSM in two different programmatic settings in the Amhara region of Ethiopia by conducting trachoma outcome surveys at the sub-district level to determine where MDA might be stopped. Secondary aims of the study were to compare current estimates to baseline prevalence and to estimate blinding trachoma, defined as TT in the total population to calculate the remaining backlog of TT patients requiring surgery to guide future provision of surgical services.

The new guidelines suggest conducting outcome surveys at the district level first, interpreting the results and then conducting additional surveys at the sub-district-level where

district-level estimates of TF are below 10% (WHO, 2010). In each zone, we chose to implement surveys in a single exercise to estimate the prevalence of TF among children aged 1-9 years at the sub-district level in all districts eligible for outcome surveys. Using aggregate data from sub-districts allowed us to generate trachoma prevalence estimates at the district level simultaneously. We chose this strategy for one main reason: to obtain a definite answer for all areas in the two zones within a timeframe feasible for mobilising and implementing an annual MDA.

4.4. Methods

4.4.1. Ethics Statement

The study protocols for surveys in both South Wollo and South Gondar were reviewed and approved by the ethical review committee of the Amhara Regional State Health Bureau. Additionally, the study activities were approved by Emory University Internal Review Board under protocol 079-2006. Due to the high rate of illiteracy, verbal informed consent was obtained and recorded prior to data collection rather than written information and a signed statement. Consent for trachoma examination and household interview was obtained from heads of households, individuals, and parents of minors according to the principles of the declaration of Helsinki.

4.4.2. Study Site and Time Frame

Widespread implementation of the full SAFE strategy to all endemic areas in Amhara was initiated in 2007, which included outreach camps to provide surgery in addition to the existing static service; annual MDA with antibiotics; promotion of facial cleanliness and hygiene in schools and communities by health extension workers; community-level promotion of latrine construction and use through the health extension workers and environmental health officers. Provision of improved water sources was simultaneously supported by the development sector.

Previous data indicate that 6-12 months since the last round of MDA is the ideal time to conduct impact surveys to assess trachoma (Ngondi et al., 2010). The outcome survey in South Wollo was conducted in December 2010 in 13 *woredas* (districts) which had received a third consecutive round of MDA in April of 2010. The remaining eight *woredas* in South Wollo had not yet received three rounds. In South Gondar, training and field collection activities were conducted in the rainy season from late June to early August 2011 covering all 12 *woredas* in the zone. All *woredas* in South Gondar had received at least five rounds of MDA, the last round of which took place in November 2010.

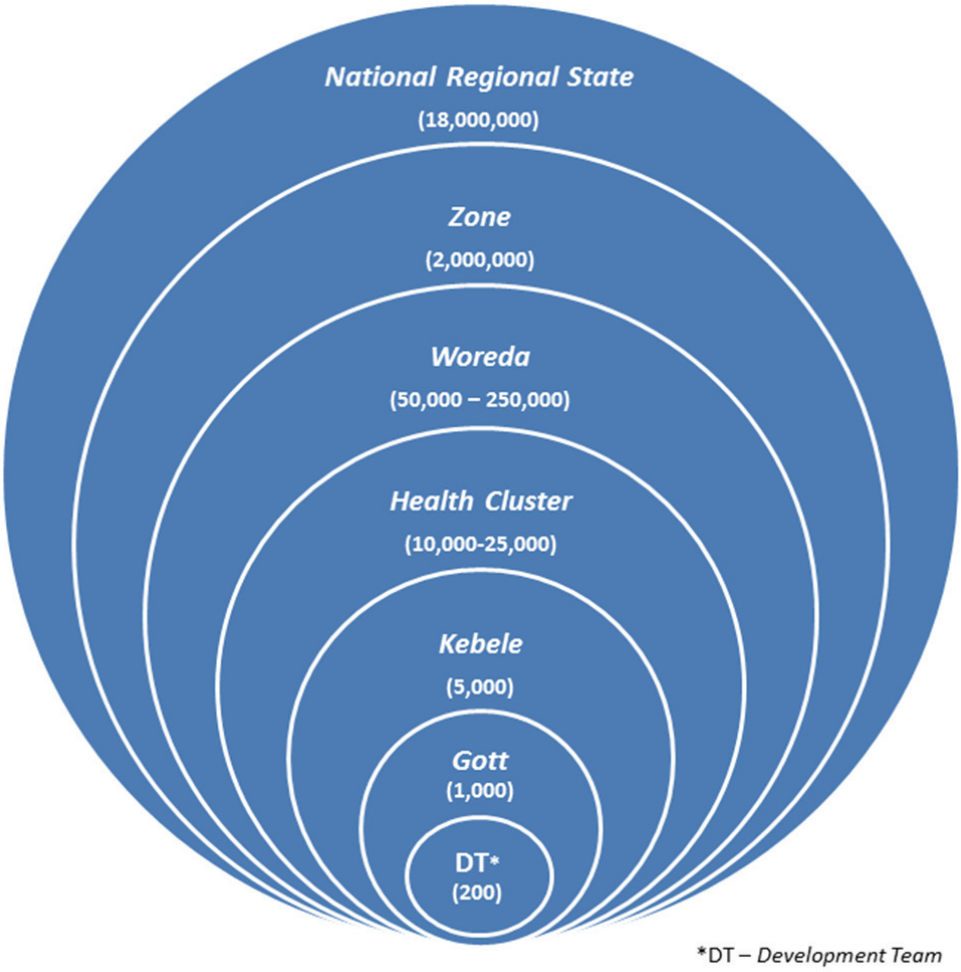

Figure 4.2. Administrative levels and respective population structure of Amhara National Regional State, Ethiopia

4.4.3. Sampling Methodology and Sample Size

The administrative levels of this area of Ethiopia and the respective population at each tier are presented in Figure 4.2 with the *woreda* being the district-level equivalent. From the 3rd GSM report, a sub-district is defined as three or more villages with combined total population of at least 30,000 persons (WHO, 2010). Since no existing administrative level matched this description exactly, we joined geographically adjacent *health clusters* in groups to create a sub-district evaluation unit of approximately 50,000 cumulative population. *Gotts* are the smallest administrative unit for which there is population data available, which we used as our primary sampling unit or cluster. For each evaluation unit surveyed, *gotts* were selected from a line list arranged according to geographical distribution using a standard methodology (UNICEF, 2006a). *Gotts* are broken down into smaller administrative units called *development teams* (DT), which made ideal segments on which to base a modified

segmentation design for equal probability sampling (UNICEF, 2006a). One DT was randomly selected in each *gott* and all persons present or absent residing in all households within the selected DT were registered and those present examined. Absent households were registered as non-consenting and were not replaced. Heads of household (or their adult representative) were interviewed in consenting households. Physical characteristics were recorded from direct observation.

To detect whether the prevalence of TF was 3% with 2% precision, we calculated a sample size of 558 children aged 1-9 years per sub-district. This was based on a 5% level of significance, design effect of 2, five persons per household with children aged 1-9 years composing 30% of the total population. To obtain the target sample size, population-based, cluster random sampling was utilised for both surveys. We surveyed 10 clusters per sub-district, including 40 households per cluster, which, based on our assumptions, would allow for an 8% non-response rate in children.

4.4.4. Training and Quality Control

Prior to the survey data collection, teams participated in a 7-day, applied training and skills examination. Trachoma graders were responsible for diagnosing the clinical signs of trachoma using the simplified trachoma grading system (Thylefors et al., 1987). Potential graders were trained to classify signs of trachoma using digital photographs, followed by examination with a standardised set of photographs where agreement was calculated for all signs. Poor performing participants were given additional instruction or assigned other duties. Remaining participants practiced examination and diagnosis of trachoma for at least two days in volunteer subjects of all ages resident in communities not selected for the survey. Finally, the participants took a reliability exam to measure their agreement with the "gold standard" grading of volunteer subjects. The "gold standard" was the consensus grade of the course trainers (ophthalmologist, trachoma programme director, and trachoma survey consultant) experienced with the simplified trachoma grading system. Additionally, in South Wollo, digital photos were taken of each eye included in the inter-observer exam and reviewed to obtain consensus when trainers' grades were discordant. The agreement for all signs was generated, but selected graders were those achieving greater than 84% agreement and a Kappa ≥0.7 on grade TF. Training for data recorders consisted of classroom instruction and field practice, which included testing and refining the data collection tools, applying the sampling strategy in the field, and taking geographical coordinates of survey households. Persons trained to serve as data recorders were also evaluated to assess their ability to follow protocol, perform the interview, and record responses correctly. The top performers were selected to work with selected graders to form

the final survey teams. A total of 21 teams were deployed in South Wollo and 13 teams deployed in South Gondar.

4.4.5. Data Collection, Management, and Analysis

Each head of household was interviewed to assess demographics of the households and uptake of the SAFE strategy. All household residents were examined for the presence or absence of all five clinical signs of the simplified trachoma grading system in both eyes using a 2.5x binocular loupe and adequate light (Thylefors et al., 1987). Additionally in 99 *gotts* of South Gondar, DNA specimens of the tarsal conjunctivae of one randomly selected child aged 1-5 years per household were collected using ocular swabs for detection of infection with *Chlamydia trachomatis* by polymerase chain reaction (PCR) (results not yet available).The surveys also included non-trachoma indicators to measure outcomes of integrated programme interventions for malaria in South Wollo and intestinal parasites in South Gondar. These data will be presented elsewhere.

Data were collected by recorders on paper survey forms in South Wollo zone. Forms were reviewed for completion by a team leader prior to leaving the *gott*. Data in South Gondar were collected electronically using tablet computers operating on the Android platform (Google Inc.). In South Gondar, data recorders reviewed survey data after completing each household prior to initiating the next house. In both zones, supervisors met with each team at least once per two clusters surveyed to provide needed materials and collect completed forms. Data collected electronically were copied to an external micro SD card and downloaded every 2-3 days by the team's supervisor.

Paper-based survey data were double-entered in Microsoft Access by separate entry clerks, compared for discordance, and corrected with the original hard-copy. Electronic data was downloaded at the end of the survey separately for each team and converted from html to csv format. Data were analysed using SAS version 9.3 (SAS Institute Inc., Cary, United States of America). The inverse of the selection probabilities was calculated and used to weight the data in the analysis. Additionally, the data were adjusted for correlation within the data due to clustering by using a robust method to estimate the standard error and inflate confidence limits. Current prevalence estimates were compared with a regional baseline survey that provided zonal level trachoma prevalence in 2006 (Emerson et al., 2008) and in South Gondar, from cross-sectional trachoma surveys prior to pilot interventions. The statistical significance of differences were assessed with a chi-square (X^2) statistic accounting for the survey designs.

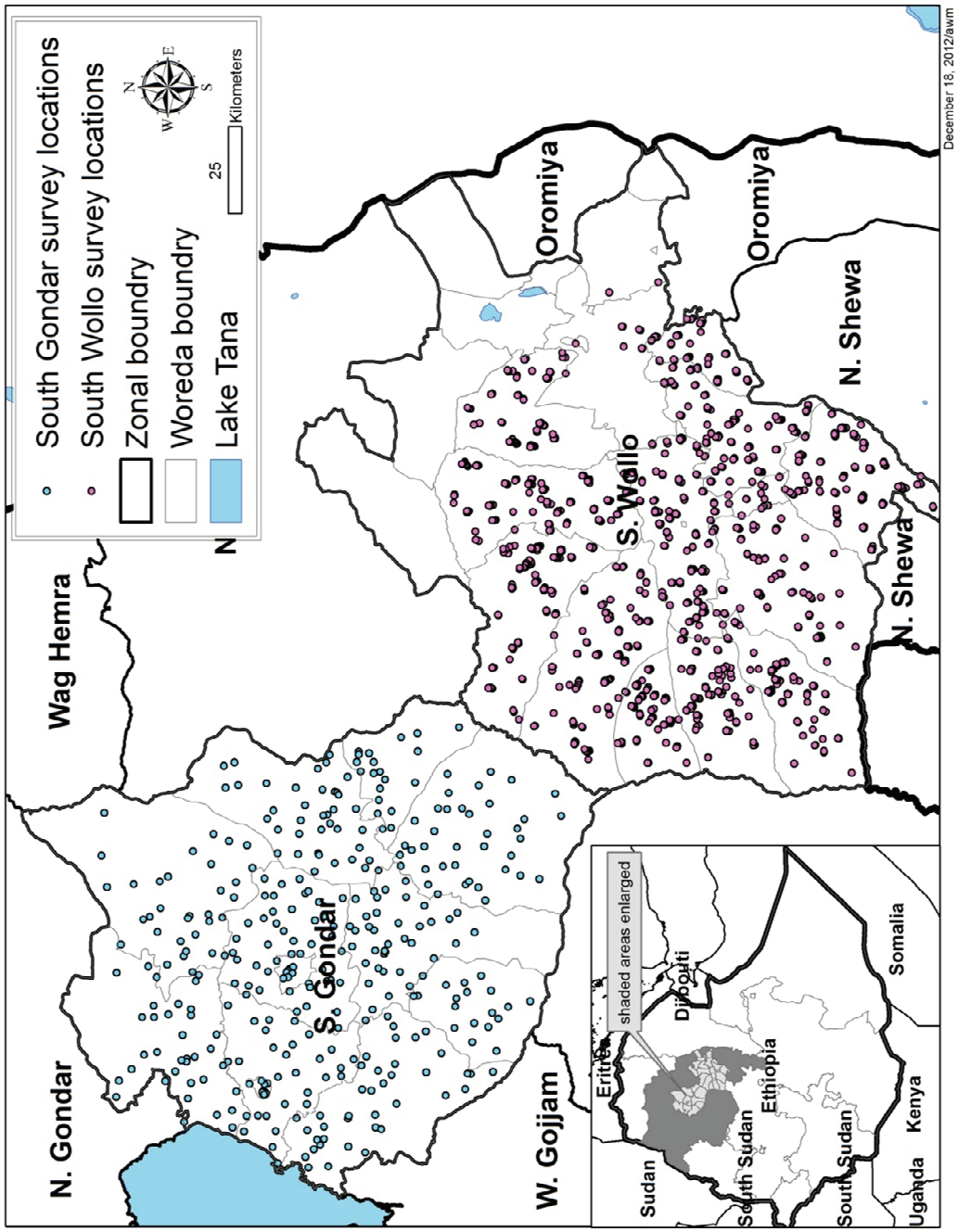

Figure 4.3. Surveyed communities in South Gondar and South Wollo zones of Amhara National Regional State, Ethiopia

4.5. Results

Teams successfully surveyed 714 of 720 communities from 72 evaluation units across the 25 *woreda*s in the two zones. The six *gotts* not surveyed were all in South Gondar and inaccessible during the rainy season. Figure 4.3 shows the geographical distribution of the 714 communities in the two zones of Amhara National Regional State, Ethiopia. A total of 89,735 residents were registered from 21,327 households of whom 72,452 (80.7%) were examined for clinical signs of trachoma. A summary description of the sample stratified by zone is shown in Table 4.1. Less than 2% of households encountered in selected *gotts* refused to participate in the survey. A higher proportion of residents were not available for examination (absent from the house) in South Gondar than in South Wollo (X^2=1,725, p <0.001). The proportion of enumerated residents examined was lowest among the adult male population (data not shown). Among the target population, children aged 1-9 years, 95.8% and 94.9% of the enumerated children in South Wollo and South Gondar were examined respectively.

The prevalence of TF in the target age group for the combined area in South Wollo zone was 26.4% (95% confidence interval (CI) 23.7-29.1%; range by *woreda* 0.9-67.0%; range by evaluation unit 0.9-76.9%) [Table 4.2]. Prevalence of trachomatous inflammation intense (TI) was 4.3% (95% CI 3.2-5.4%; range by *woreda* 0.7-22.0%; range by evaluation unit nil-28.6%). The mean number of children in the 1-9 year age group sampled in each evaluation unit was 269.7 (standard deviation (SD) 50.6). The mean number of persons examined of all ages in each evaluation unit in South Wollo was 938.9 (SD 192.0). Among all residents, the prevalence of TT was 1.3% (95% CI 1.1-1.5%; range by *woreda* 0.0-3.1%; range by evaluation unit nil-4.3%).

In South Gondar [Table 4.3], TF prevalence among children was 25.9% (95% CI 23.8-27.9%; range by *woreda* 8.6-44.9%; range by evaluation unit 8.6-55.7%). Prevalence of TI was 7.0% (95% CI 6.2-7.8; range by *woreda* 4.3-10.7%; range by evaluation unit 1.4-13.4%). The prevalence estimates at the evaluation unit were based on a mean sample size of 487.0 (SD 45.8) children 1-9 years of age and 1073.7 (SD 106.8) total persons examined per evaluation unit. The prevalence of TT was 1.8% (95%CI 1.6-2.0%; range by *woreda* 1.0-3.5%; range by evaluation unit 0.6-4.2%) among the total examined population.

In South Wollo, the prevalence of TF among children aged 1-9 years for the combined 13 *woredas* was higher than the baseline zonal-estimate in 2006 (p=0.013, Figure 4.4). The prevalence of TI in the current survey was lower than the 10.6% estimate in 2006 (p=0.053). Compared to estimates from two previous, cross-sectional, cluster random surveys in South Gondar, the prevalence of TF among children decreased from 2003 (p <0.001) but did not change significantly from the estimate in 2006 (p=0.509). The current TI

prevalence among children in South Gondar was lower than previous estimates, 35.8% in 2003 ($p<0.001$) and 23.3% in 2006 ($p<0.001$).

The *woreda*-level and evaluation unit prevalence of TF, classified as <5%, 5-9%, and ≥10% is shown for both zones in Figure 4.5. Overall, the prevalence of TF among children aged 1-9 years was below 5% in six evaluation units and between 5-9% in an additional three evaluation units in South Wollo (Table 4.4.). According to the proposed WHO guidelines, where the *woreda*-level TF prevalence is <10%, MDA with azithromycin may be stopped in evaluation units where TF prevalence is less than 5%. In two *woredas* (Albuko and Mehal Saiynt), at both the evaluation unit and *woreda* levels, the prevalence of TF was below the 5% threshold and warranted stopping MDA in the entire *woreda.* One additional evaluation unit in Tenta *woreda* also warranted stopping MDA under the guidelines. The additional evaluation unit with TF prevalence below 5% in Legambo, while not identified in the suggested way of district then sub-district surveys, meets the UIG criteria, but would not have been found if assessment was conducted first at the district and subsequently at the sub-district level. Neither at the *woreda*-level nor in any single evaluation unit was the prevalence of TF below 5% among children in South Gondar. Targeted MDA at the sub-district level is recommended in three *woredas* (Tenta and Mekidela in South Wollo, Debre Tabor in South Gondar) where TF prevalence was between 5% and 9%. For all 20 other *woredas* across the two zones, guidelines suggest continued MDA with azithromycin.

In only one *woreda* (Albuko), were no cases of TT identified and thus the point estimate for the prevalence of TT is assumed to be below the elimination threshold of less than 0.1% among the total population. In all other *woredas* the prevalence of TT is greater than 0.1% and programmes to provide surgery to correct TT should continue. An estimated total of 21,376 (95% CI 11,499-31,356) TT patients in the 13-*woreda* area of South Wollo and 37,784 (95% CI 23,060-52,710) TT patients in South Gondar zone need to be operated on to meet the elimination threshold for TT prevalence of less than 1 per 1,000 total population.

Table 4.1. Sample description in South Wollo and South Gondar by *woreda* (district) and sub-district evaluation unit (EU)

Woreda	Total EU*	Total *gotts*	Houses		Individuals		Proportion male		Adults 15+		Children 1-9 yr	
			surveyed	%**	examined	%**	examined	enumerated	examined	%**	examined	%**
Adjibar Saiynt	3	30	793	100	1,113	98.7	40.4	44.9	1,375	79.8	747	97.8
Albuko	2	20	440	89.2	1,504	69.7	46.6	51.9	894	69.2	429	79.7
Borena	3	30	895	98.7	3,360	90.6	46.3	48.6	1,829	94.7	971	99.7
Jamma	3	30	893	99.2	3,622	95.7	48.5	49.3	2,152	95.2	965	98.1
Kelala	3	30	719	92.7	2,415	77.8	44.4	48.8	1,342	75.9	711	88.0
Kutaber	2	20	477	96.4	1,798	87.6	46.8	49.7	1,036	85.0	451	94.6
Legambo	4	40	859	99.0	3,279	86.4	46.8	50.2	1,832	82.2	952	97.3
Legahida	2	20	421	100	1,725	96.6	49.3	50.3	962	95.3	493	98.4
Mehal Saiynt	2	20	506	100	1,942	87.4	45.6	48.7	1,021	82.6	622	98.1
Mekidela	3	30	991	99.8	3,819	98.6	47.4	47.4	2,285	99.1	1056	99.3
Tenta	3	30	751	99.7	2,349	74.0	43.1	49.9	1,368	69.7	657	92.9
Wogedi	3	30	792	99.9	2,714	86.5	43.3	46.5	1,472	83.0	841	96.3
Woreillu	3	30	726	99.3	2,903	89.7	45.3	48.0	1,640	86.3	813	98.2
South Wollo	36	360	9,263	98.2	33,800	87.0	45.8	48.6	19,208	84.9	9,708	95.8
Debre Tabor	1	10	368	100	1,109	69.7	36.7	44.4	515	55.8	519	96.1
Dera	4	39	1,325	99.9	4,350	78.0	41.6	48.2	1,903	65.8	2,128	96.4
East Estie	4	35	1,186	99.7	3,861	74.1	41.6	48.3	1,776	62.3	1,828	96.5
Ebinat	4	40	1,309	100	4,256	79.1	41.3	47.8	1,915	67.1	2,036	97.5
Farta	4	40	1,269	100	4,248	75.5	43.3	49.3	1,984	64.9	1,907	96.2
Fogera	3	30	985	98.6	3,415	77.2	43.3	49.1	1,607	69.4	1,399	92.9
Lay gayint	4	40	1,457	99.3	4,497	75.1	39.5	46.4	2,193	66.1	1,971	94.0
Libokem	3	30	1,020	99.3	3,289	74.3	41.0	48.3	1,529	65.8	1,482	92.9
Simada	4	40	1,407	99.5	4,135	73.7	38.8	46.1	2,011	65.5	1,800	91.0
Tach gayint	2	20	690	99.9	2,185	79.4	39.3	46.3	1,092	71.7	937	93.8
West Estie	2	20	689	100	2,180	77.6	42.4	47.7	1,033	67.6	1,011	96.0
Woreta town	1	10	359	100	1,127	75.5	39.3	46.7	509	62.5	543	96.8
South Gondar	36	354	12,064	99.6	38,652	76.0	41.0	47.6	18,067	65.8	17,561	94.9

*Sub-district evaluation unit (EU) ; ** percent of enumerated does not include 1.8% and 0.4% of total households in South Wollo and South Gondar for which consent could not be obtained

Table 4.2. Prevalence* of trachoma clinical signs by sub-district evaluation unit (EU) and *woreda* in South Wollo 2010

South Wollo *woredas*	EU	Children 1-9 years	TF		TI		All ages	TT	
			%	95% CI	%	95% CI		%	95% CI
Adjibar Saiynt	1	284	27.2	6.1-48.2	2.2	0.0-4.6	1011	1.5	0.6-2.4
	2	206	15.2	2.3-28.1	4.8	0.0-10.4	638	1.4	0.1-2.8
	3	257	56.9	49.5-64.4	9.2	6.3-12.1	721	4.3	2.6-5.9
woreda-level		747	30.7	18.9-42.5	4.6	2.4-6.9	2370	2.1	1.3-2.9
Albuko	1	203	1.0	0.0-2.6	4.8	0.3-9.3	769	.	.
	2	226	0.9	0.0-2.0	3.6	0.4-6.7	735	.	.
woreda-level		429	0.9	0.0-1.9	4.2	1.4-7.1	1504	.	.
Borena	1	284	15.7	10.7-20.8	2.3	0.0-5.5	1066	1.7	0.7-2.6
	2	352	16.2	12.2-20.2	2.1	0.8-3.4	1191	1.2	0.6-1.9
	3	335	12.8	5.5-20.1	0.5	0.0-1.4	1103	0.7	0.0-1.3
woreda-level		971	15.1	12.0-18.2	1.7	0.6-2.8	3360	1.2	0.7-1.7
Jamma	1	303	18.5	0.3-36.7	3.8	0.0-8.0	1095	3.5	1.6-5.5
	2	368	25.0	7.8-42.2	6.6	3.8-9.4	1388	0.3	0.0-0.7
	3	294	23.3	16.9-29.7	6.1	3.8-8.4	1139	0.6	0.2-1.0
woreda-level		965	21.8	11.5-32.2	5.3	2.8-7.7	3622	1.7	0.8-2.6
Kelala	1	214	19.6	13.3-25.9	1.8	0.0-3.9	778	2.8	2.2-3.4
	2	260	26.4	13.8-39.1	3.8	0.2-7.4	876	1.5	0.8-3.3
	3	237	36.7	25.7-47.8	2.4	0.0-5.6	761	2.3	1.3-3.2
woreda-level		711	28.9	21.4-36.4	2.6	0.7-4.4	2415	2.3	1.7-2.8
Kutaber	1	190	20.8	10.2-31.3	7.7	0.0-16.5	821	1.7	0.0-3.7
	2	261	22.4	12.7-32.1	0.7	0.0-1.7	977	0.5	0.2-0.8
woreda-level		451	21.7	14.6-26.7	3.8	0.0-8.2	1798	1.1	0.1-2.1
Legahida	1	281	76.9	66.0-87.8	28.6	13.5-43.7	917	2.0	0.8-3.3
	2	212	55.7	39.7-71.6	7.1	2.3-11.9	808	0.6	0.1-1.1
woreda-level		493	67.0	55.0-78.9	22.0	10.5-33.6	1725	1.6	0.7-2.5
Legambo	1	243	4.2	0.7-7.6	0.0	.	889	.	.
	2	217	7.5	3.9-11.0	0.0	.	723	.	.
	3	259	38.4	28.8-48.0	2.6	1.2-4.0	887	0.7	0.0-1.3
	4	233	24.4	19.5-29.2	1.8	0.0-3.9	780	0.5	0.1-0.9
woreda-level		952	20.7	14.6-26.7	1.3	0.5-2.1	3279	0.3	0.1-0.6
Mehal Saiynt	1	313	1.1	0.0-2.7	2.4	0.1-4.7	1005	1.0	0.3-1.7
	2	309	3.5	1.1-5.8	2.5	0.4-4.5	937	1.2	0.0-2.7
woreda-level		622	2.2	0.5-3.8	2.4	0.8-4.0	1942	1.1	0.4-1.9
Mekidela	1	384	10.4	1.5-19.2	0.4	0.0-1.0	1429	0.2	0.0-0.4
	2	319	6.9	2.5-11.3	1.2	0.1-2.3	1070	0.8	0.1-4.2
	3	353	13.7	0.5-26.9	2.1	0.1-4.1	1320	0.1	0.0-0.2
woreda-level		1056	9.5	4.7-14.2	1.2	0.5-2.0	3819	0.5	0.1-0.9
Tenta	1	219	15.1	8.3-22.0	0.4	0.0-1.0	776	2.5	0.7-4.2
	2	222	3.6	1.0-6.3	1.2	0.1-2.3	833	0.7	0.0-1.3
	3	216	7.8	2.5-13.1	2.1	0.1-4.1	740	0.3	0.0-0.8
woreda-level		657	8.5	4.9-12.1	0.7	0.0-1.5	2349	1.1	0.4-1.7
Wogedi	1	313	30.8	18.7-42.9	7.2	0.0-14.6	1048	3.0	2.0-4.1
	2	273	23.0	9.6-36.4	5.4	1.8-9.0	858	2.7	1.6-3.9
	3	255	40.8	32.9-48.6	11.7	4.1-19.3	808	3.7	2.6-4.9
woreda-level		841	30.9	23.2-38.6	8.0	4.2-11.7	2714	3.1	2.4-3.8
Woreillu	1	241	48.3	38.3-58.4	3.7	0.9-6.4	903	1.3	0.6-2.0
	2	280	61.8	54.2-69.5	3.7	0.7-6.6	961	1.4	0.1-2.7
	3	292	38.0	29.2-46.9	1.1	0.1-2.1	1039	0.6	0.1-1.1
woreda-level		813	46.5	40.0-53.0	2.3	1.1-3.5	2903	0.9	0.5-1.4

*estimates weighted according to selection probabilities adjusted for correlation in the data due to clustering; CI, confidence interval

Table 4.3. Prevalence* of trachoma clinical signs by sub-district evaluation unit (EU) and *woreda* in South Gondar 2011

South Gondar *woredas*	EU	Children 1-9 yr	TF		TI		all ages	TT	
			%	95% CI	%	95% CI		%	95% CI
Debre Tabor	1	519	8.6	2.1-15.1	3.9	0.5-7.3	1109	1.0	0.0-2.2
Dera	1	606	31.0	15.6-46.4	6.9	4.4-9.3	1188	1.3	0.6-2.0
	2	447	30.1	17.7-42.5	2.7	1.3-4.1	954	2.4	1.3-3.6
	3	550	23.0	14.3-31.6	2.5	0.3-4.7	1133	1.0	0.2-1.8
	4	524	26.1	13.4-38.8	5.5	1.8-9.2	1075	0.8	0.0-1.7
woreda-level		2128	27.3	20.7-33.8	4.5	2.9-6.2	4350	1.3	0.8-1.8
East Estie	1	353	18.3	11.4-25.3	3.9	3.1-4.6	705	2.7	1.3-4.0
	2	474	24.5	19.3-29.6	9.2	3.0-15.4	1008	1.7	0.5-2.9
	3	486	14.5	9.5-19.5	5.6	3.1-8.2	1004	0.6	0.0-1.2
	4	514	16.7	9.1-24.3	3.9	0.4-7.3	1144	1.1	0.7-1.4
woreda-level		1828	18.9	15.7-22.2	6.1	3.7-8.5	3861	1.4	0.8-2.0
Ebinat	1	538	31.7	19.1-44.2	7.9	4.8-11.0	1173	1.9	0.9-2.8
	2	446	44.8	35.0-54.7	12.7	8.8-16.7	991	3.4	1.5-5.3
	3	506	55.7	48.0-63.4	13.4	5.5-21.3	971	1.9	0.5-3.3
	4	537	43.4	35.2-51.5	8.4	0.6-16.2	1121	1.1	0.4-1.8
woreda-level		2036	44.9	38.7-51.1	10.7	7.1-14.3	4256	2.0	1.3-2.6
Farta	1	458	22.3	16.2-28.4	6.0	2.5-9.4	962	2.0	0.6-3.3
	2	516	10.6	7.2-13.9	1.4	0.7-2.2	1206	1.2	0.6-1.7
	3	487	21.5	13.0-30.1	4.9	2.2-7.7	1159	2.4	1.4-3.4
	4	446	22.2	17.8-26.6	7.1	3.8-10.3	921	2.1	0.8-3.4
woreda-level		1907	17.8	14.2-21.4	4.3	2.8-5.8	4248	1.8	1.3-2.4
Fogera	1	437	28.9	23.1-34.7	6.0	3.8-8.2	1108	1.2	0.0-2.3
	2	518	39.1	22.6-55.6	9.8	5.4-14.1	1227	2.2	1.1-3.2
	3	444	28.7	22.4-35.1	8.1	2.7-13.5	1080	1.5	0.5-2.5
woreda-level		1399	33.3	25.2-41.3	8.1	5.6-10.6	3415	1.7	0.9-2.4
Lay gayint	1	487	14.3	4.9-23.7	4.6	0.1-9.0	1142	1.1	0.4-1.8
	2	512	15.3	10.9-19.8	7.8	5.3-10.3	1077	2.4	0.5-4.3
	3	489	16.8	5.6-27.9	4.4	1.8-7.0	1246	1.6	0.7-2.5
	4	481	30.0	15.9-44.0	8.4	4.2-12.7	1032	1.7	1.1-2.2
woreda-level		1971	18.8	12.8-24.8	6.2	4.3-8.2	4497	1.6	1.1-2.2
Libokem	1	474	20.2	10.3-30.0	7.3	3.6-11.1	1048	1.2	0.3-2.1
	2	496	19.1	12.2-25.9	6.0	2.3-9.8	1087	1.8	1.2-2.3
	3	512	32.3	20.1-44.6	6.5	3.5-9.4	1154	1.3	0.6-1.9
woreda-level		1482	24.3	17.3-31.4	6.5	4.4-8.5	3289	1.5	1.1-1.9
Simada	1	430	24.5	16.2-32.9	8.1	4.5-11.7	1043	4.2	2.3-6.0
	2	503	25.0	19.4-30.5	10.3	5.9-14.8	1100	4.0	1.8-6.2
	3	447	24.5	15.5-33.5	13.0	8.9-17.1	1115	2.2	0.6-3.8
	4	416	21.3	11.3-31.3	2.7	1.0-4.4	877	4.5	2.9-6.0
woreda-level		1800	23.9	19.7-28.1	8.8	6.4-11.2	4135	3.5	2.5-4.6
Tach gayint	1	455	36.5	23.4-49.6	10.5	5.5-15.5	1091	1.4	0.7-2.1
	2	482	31.1	12.6-49.5	9.0	1.5-16.5	1094	2.7	1.1-4.3
woreda-level		937	33.8	22.1-45.5	9.7	5.1-14.4	2185	2.0	1.1-3.0
West Estie	1	508	31.5	23.3-39.6	7.0	3.1-10.9	1169	1.1	0.6-1.5
	2	501	29.1	17.1-41.1	11.8	5.7-18.0	1011	3.0	1.8-4.1
woreda-level		1009	30.6	23.3-37.9	9.5	5.7-13.2	2180	2.0	1.3-2.7
Woreta town	1	543	17.2	9.1-25.4	6.7	3.1-10.2	1127	1.0	0.0-2.1

*estimates weighted according to selection probabilities adjusted for correlation in the data due to clustering; CI, confidence interval

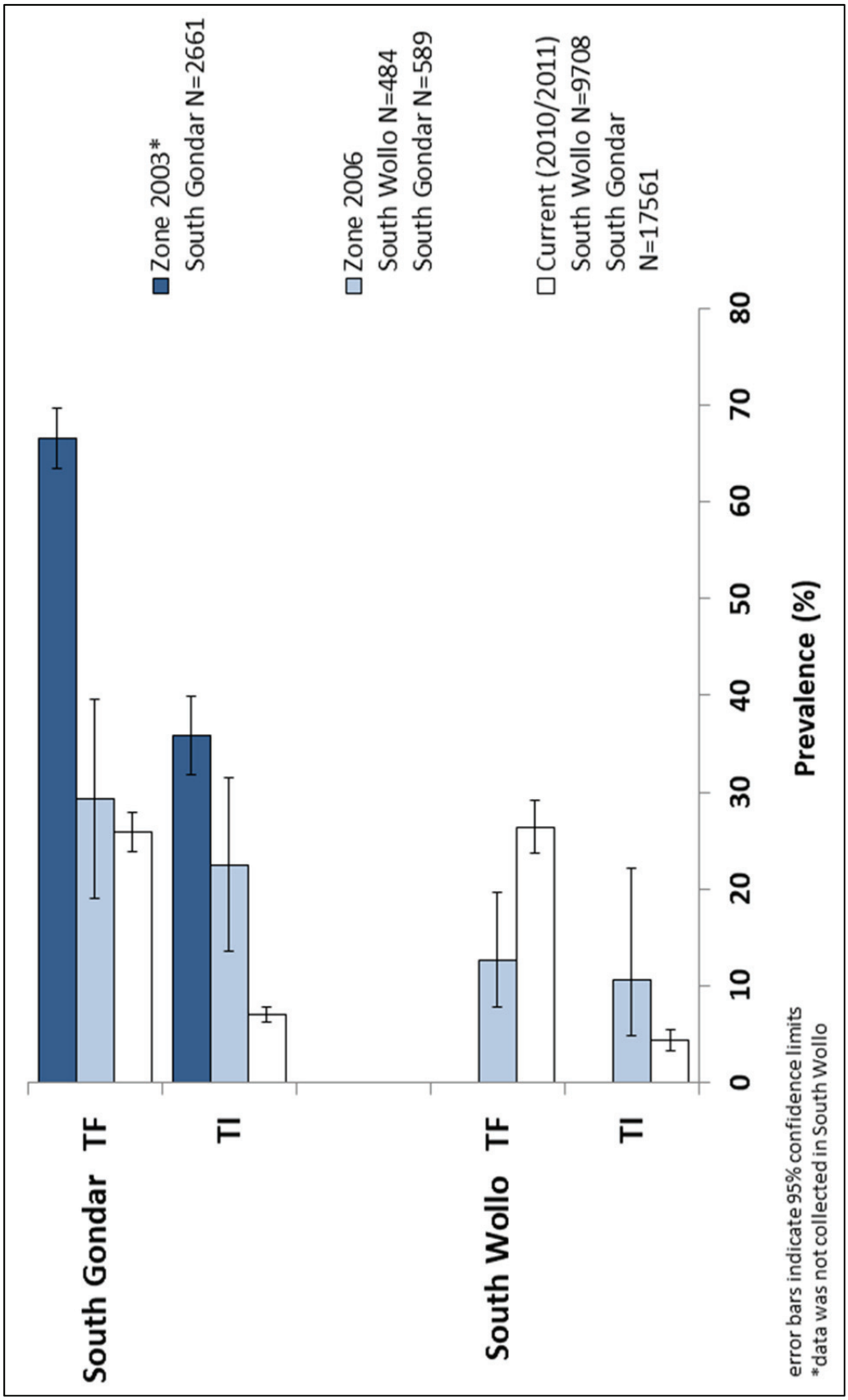

Figure 4.4. Prevalence of active trachoma, clinical signs among children aged 1-9 years, 2003, 2006 and 2010-2011

Table 4.4. Summary of survey findings and recommended programmatic strategy for trachoma elimination in South Wollo and South Gondar Zone

	South Wollo	South Gondar
EU* with TF <5%	6 / 36	0 / 36
EU* with 5% < TF < 10%	3 / 36	1 / 36
***woreda* TF <5%**	2 / 13	0 / 12
***woreda* 5% < TF < 10%**	2 / 13	1 / 12
***woreda* TT<0.1%**	1 / 13	0 / 12
TT case backlog**	21,376 (11,499-31,356)	37,784 (23,060-52,710)
Recommended Programme Strategy‡	Stop MDA in 2 / 13 *woredas* and 2 additional EU with TF <5%. Conduct targeted MDA in 2 other *woredas* TF 5-9%. Continue district-wide MDA in 9 *woredas* for 3 more years. Provide surgery to 21,376 estimated TT cases.	Conduct targeted MDA in 1 *woreda* with TF 5-9%. Continue district-wide MDA in 11 *woredas* for 3 more years. Provide surgery to 37,784 estimated TT cases.

*sub-district evaluation unit (EU)
**total number of TT patients targeted for provision of corrective surgery in order to achieve less than 1 per 1000 population (95% confidence interval)
‡ interpretation of WHO guidelines

4.6. Discussion

Implementation of the full SAFE strategy, including five consecutive, annual mass azithromycin distribution campaigns did not result in a reduction of TF prevalence below the elimination target in any sub-district within the trachoma hyper-endemic setting of South Gondar in Ethiopia. The impact on TF after three consecutive years of SAFE implementation was not as clear in South Wollo, where the overall prevalence of TF was higher than the zonal-level prevalence estimated prior to SAFE interventions. Yet, TF prevalence in a fraction of the sub-districts assessed and two of 13 districts were below the 5% threshold. According to WHO guidelines these areas are eligible to stop MDA for trachoma. Our sample of 9,708 children aged 1-9 years across 360 communities in South Wollo provided much more accurate and precise estimates than at baseline surveys. Indeed, the baseline prevalence estimates for the entire zone of South Wollo were derived from 484 children across 16 communities (Emerson et al., 2008). The 12.6% estimate for South Wollo in 2006 was the lowest for all 10 zones in the region and the only zone estimated below 20% TF prevalence. In South Wollo, the observed difference in TF prevalence compared to the baseline survey was likely the results of an underestimate of the true TF prevalence at baseline due to chance. Four of the randomly selected communities in 2006 were

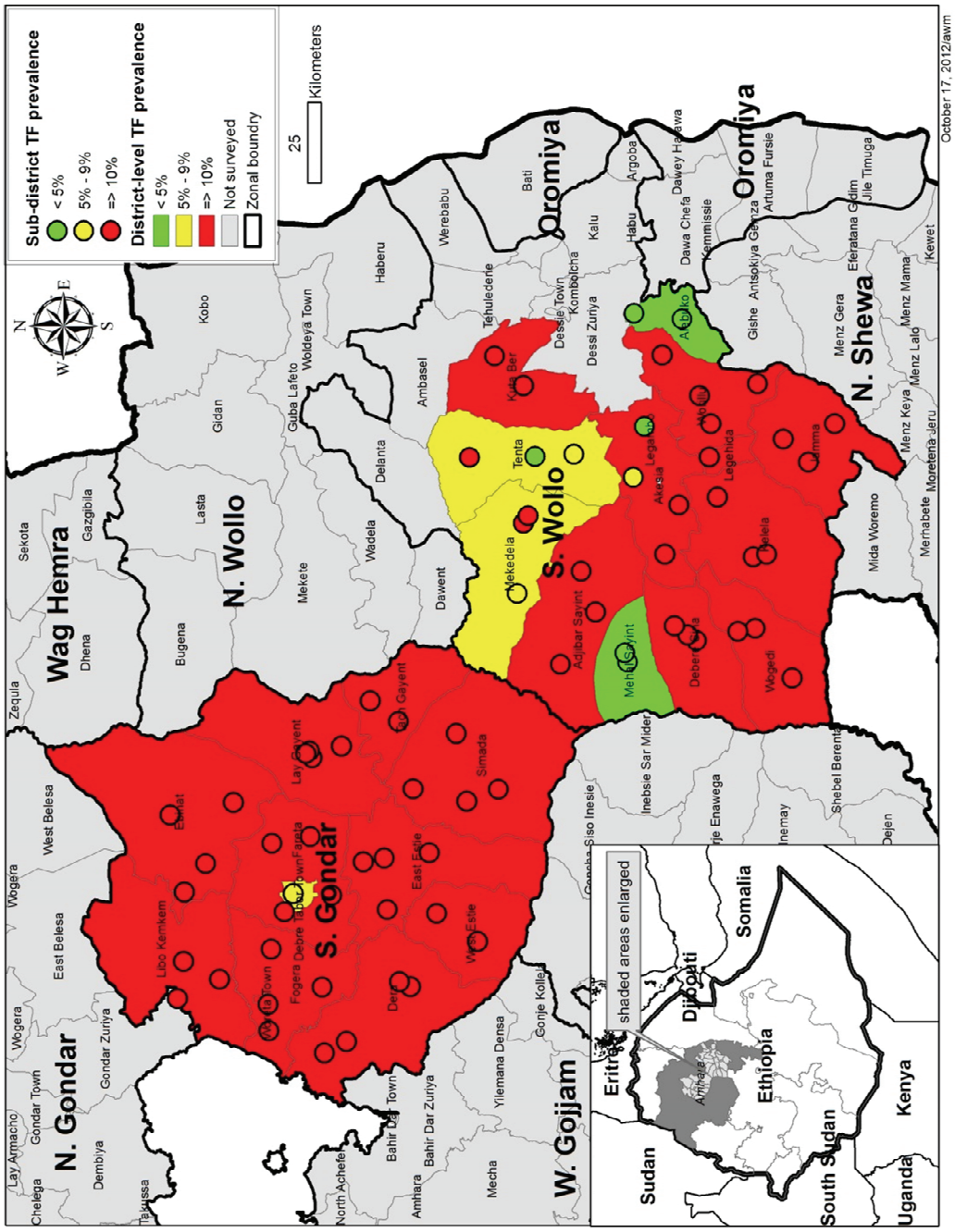

Figure 4.5. Distribution of trachomatous inflammation follicular (TF) among children aged 1-9 years by woreda and evaluation unit

from *woredas* where the current prevalence was lowest which might have contributed to a lower prevalence estimate if TF prevalence was also less common at baseline in these areas.

Additional prevalence data from South Gondar prior to 2006 suggest a decline of TF prevalence since the initiation of the programme (Figure 4.4), but a reduction in TF from 2006 to 2011 was not observed in the recent survey. Reduction in TF below 5% among children aged 1-9 years has been documented in other programmes after SAFE implementation, but in those settings the prevalence of TF at baseline was lower than in Amhara (Solomon et al., 2008; Yayemain et al., 2009). TF prevalence in South Sudan (also hyper-endemic for trachoma) was reduced to below 5% after high community uptake of SAFE interventions but this was observed only in one of four intervention sites (Ngondi et al., 2006b).

One conclusion that could be made from the results is that a lack of reduction in TF indicates that trachoma has not been controlled and continued MDA is needed. Alternatively, trachoma research studies from another region of Ethiopia have documented a delay in the resolution of clinical signs after MDA has successfully reduced infection (Keenan et al., 2011). In one study, although a mean prevalence of 43.5% TF was measured among children post 3 years of azithromycin MDA, in a third of the participating communities there was no evidence of *C. trachomatis* infection (Keenan et al., 2012a). A separate study from the same area found infection prevalence of 2-3% in the context of 35% TF and/or TI prevalence after three years of either annual or biannual MDA of azithromycin (Gebre et al., 2012). These studies suggest TF alone may not be a suitable marker for impact after multiple rounds of MDA on which to determine stopping antibiotic distribution. A reduction in the more severe active trachoma grade, TI, was observed in our surveys compared to baseline in both zones. A reduction in TI was also documented in the first impact assessment conducted in five *woredas* after 3 years of SAFE implementation in Amhara (Ngondi et al., 2009a). An ordinal analysis of that data suggested a combination of TF and TI might serve as a better impact indicator than TF alone, which is also supported from a recent study in Tanzania (Ngondi et al., 2007; Muñoz et al., 2011). A recent latent class analysis concerning trachoma diagnosis concluded that TF was sensitive but not specific whereas TI lacked sensitivity but had high specificity indicating usefulness of both signs(See et al., 2011).

According to current WHO guidelines, all *woredas* of South Gondar warrant ongoing MDA with antibiotics (WHO, 2006b). After having received five rounds of MDA, the prevalence of *C. trachomatis* infection is uncertain, but data from other studies in the Amhara region raise the question of whether additional rounds will provide further specific trachoma-related benefits (Ngondi et al., 2009a; Gebre et al., 2012; Keenan et al., 2012a). In

hyper-endemic communities from a different region where region-wide trachoma control interventions are not yet underway, a rebound of *C. trachomatis* infection was observed 6-24 months after no evidence of infection could be determined post azithromycin distribution (Lakew et al., 2009). In the Amhara setting where there is region-wide intervention and fewer opportunities for exposure to reinfection, infection data will provide crucial, additional evidence for MDA decisions even though relative stopping thresholds based on infection have only been suggested from mathematical models (Ray et al., 2009). We have not had the ability to process the collected conjunctival DNA swabs to date due to constraints in the local availability of reagents and national policies regarding exporting clinical specimens; reasons which might suggest why assessing infection has not been included in WHO guidelines.

Recommendations of the 3rd GSM report suggested that after *woreda*-level surveys indicated a prevalence of TF below 10% among children aged 1-9 years, sub-district-level estimates indicating the same were then required before making a decision to stop MDA (WHO, 2010). Planning and implementing impact surveys are vital but compete for time and resources against the ongoing implementation of programme interventions which require decisions for planning well ahead of scheduled activities. For instance, submission of the application for donated azithromycin and planning of its distribution occurs 8-20 months in advance of the intended distribution. Instead of having a scenario where two surveys need to be completed prior to the forecasting of drug needs, we felt a single survey, powered to estimate the prevalence of both the sub-district and the district was preferred. The experience from implementing these large-scale surveys in both zones, demonstrates that such surveys designed to simultaneously measure disease prevalence at the sub-district and district levels to evaluate impact of an elimination programme are indeed feasible. However, the process was neither without challenge nor the outcome without limitations. Over 50 people were required to implement each survey, including data recorders, clinical examiners, drivers, supervisors, logisticians, and a coordinator. During the training in both zones, only about half of the clinical examiners met our pre-set criteria to participate in the study even after several days of applied training. The final number of survey teams is dependent on the number of examiners who can accurately apply the trachoma grading system. If fewer examiners meet the criteria, fewer teams can be deployed, which increases the number of clusters each team must cover and the total number of days in the field. In Amhara, the majority of *gotts* are accessible only on foot or horseback. Once in the community, teams walked long distances between houses within a selected development team to survey each household and often slept overnight in the community to repeat the process the next day. Accessibility in the field is further constrained when surveys are conducted in the rainy season; however, due to MDA forecasting needs and programme

implementation schedule, carrying out the survey in the rainy season was unavoidable in South Gondar. In South Wollo, around 12,000 paper-based surveys were distributed to survey teams for data collection. The printing, sorting, labeling, and distributing of these forms took 18 person-days. Double data entry, comparison and correction took over 200 person-days and seven rental laptop computers. Electronic data collection in South Gondar streamlined data management and saved substantial time and resources, as has been documented in other programmes (Yu et al., 2009; Rajput et al., 2012; Wilcox et al., 2012). Overall, from planning to data analysis, each of these surveys took approximately three months to complete, including 30 days of field work. Our survey cost estimates are incomplete until the ocular swab specimens are processed, but a generalisable median cost per cluster of US $ 311 for conducting population-based prevalence surveys of trachoma clinical signs was estimated previously (Chen et al., 2011).

Although these surveys are a landmark for trachoma control, our results should be interpreted in the context of the following limitations. The actual sample size achieved at the sub-district level was lower than the estimated sample size desired. We assumed a household size of five persons based on prior experience, when in fact the mean household size was smaller, (four). The number of households in a development team was not 50 households as projected, but varied greatly within a district. In South Wollo, we found the development teams to be much smaller than anticipated. To correct for this observation in South Gondar, multiple development teams were randomly selected in each cluster. Yet, even in South Gondar the actual sample size did not meet expectations. Selecting different numbers of segments per cluster results in unequal probability sampling which had to be adjusted for by weighting the analysis according to the selection probabilities and doing so decreases the precision of the estimates. If the actual point prevalence findings for TF at the sub-district level had been near the stopping threshold, then this may have been a reason for concern; however, most of the sub-districts were well above 5% so this should not bias decisions regarding MDA implementation. Another limitation inherent with utilising clinical signs of the simplified trachoma grading system is that diagnosis is subjective and has high variability between examiners of the same patients (Miller et al., 2004b). While we took every means possible to select the most capable, reliable graders, there will always be the chance of systematic misclassification. Taking photographs of the everted lid has been shown to provide an objective measure of findings in some studies, but not in all settings and not at the scale of the current study (West and Taylor, 1990; Solomon et al., 2006; Roper and Taylor, 2009). We used photographs only during the standardisation of the graders but capable cameras were not deployed with any of the 34 survey teams. With the rapid development in technology of devices which are used for electronic data collection, it might

be useful to explore the capability of the device to capture photos of the tarsal conjunctivae (Bhosai et al., 2012).

The decision to stop MDA is not straight forward. Strictly following WHO guidelines, Amhara Regional Health Bureau could stop MDA in six evaluation units in South Wollo. Programmatically, planning and coordination of interventions is done by the district and it is very difficult (politically and logistically) to exempt part of the district while the other part continues to receive a perceived benefit from the intervention. Scientifically, these six evaluation units are within *woredas* geographically surrounded by areas where the prevalence of TF warrants continued MDA (Figure 4.5). The spatial distribution of trachoma and correlation of trachoma between sub-districts may have implications on how stop MDA decisions are made. Additionally, identification of factors at the community and geographical level associated with trachoma might assist in the prediction of the presence or absence of trachoma post-intervention and perhaps help minimise the amount of communities to be surveyed.

The total cumulative output of SAFE activities through December 2010 in Amhara, as reported by the Health Bureau include: 192,922 persons operated to correct trichiasis, 50.9 million doses of azithromycin distributed, 3,428 kebeles with ongoing trachoma-specific health education and over 1.8 million household latrines constructed [unpublished data]. Facial cleanliness was specifically promoted in 1,324 schools but the proportion of children with clean faces is not routinely recorded because a clean face is not a good predictor of a washed face (King et al., 2011a). Field reports of antibiotic coverage ranged from 80-95% in each round, but these administrative reports were not validated (Cromwell et al., 2012). In addition to clinical evaluation criteria on which to determine trachoma elimination, the compliance with the SAFE interventions, particularly hygiene and sanitation should be required. Low prevalence of clinical trachoma signs in areas with low compliance of F and E interventions might be interpreted differently than areas where household latrine coverage, water access, and use for face washing is high. Such indicators have been measured in these zones (reported elsewhere) and show increases in household sanitation and water access. Additional investigation is warranted to determine whether high coverage of household-level access to water and sanitation supports sustained reduction of trachoma prevalence after MDA has stopped. Given the current situation, a district-level randomised clinical trial might be possible, to compare both clinical signs and infection between *woredas* stopping and continuing MDA and measured uptake of F and E interventions.

In conclusion, this study demonstrated that our methodology was capable of providing estimates at both the district and sub-district levels in a single survey, although minor adjustments would be needed to consistently meet the required sample size at the sub-district level. Implementing the survey at the sub-district level irrespective of the district-

level TF prevalence might identify sub-districts which have met the elimination threshold for TF when the district level prevalence remains above 10% such as we found in Legambo *woreda* of South Wollo. However, to obtain the sub-district level estimates, 360 communities in a single zone had to be surveyed. While more feasible than surveying every village as suggested by the previous WHO recommendations, this number of clusters surveyed in each zone was greater than that surveyed in some national-level standardised surveys such as the multiple indicator cluster survey and malaria indicator survey. Realising the logistical challenges posed by carrying out sub-district-level surveys and our feeling that TF alone may not be sufficient to confidently make programme decisions, begs the question: is there a more efficient way to determine whether MDA could be stopped?

4.7. Acknowledgements

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Figure 5.1. Data collector conducting a household interview using tablet computer (courtesy of the author)

5. A novel electronic data collection system for large-scale surveys of neglected tropical diseases

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5.1. Abstract

Background: Large cross-sectional household surveys are common for measuring indicators of neglected tropical disease control programmes. As an alternative to standard paper-based data collection, we utilised a novel paperless technology to collect data electronically from over 12,000 households in Ethiopia.

Methodology: We conducted a needs assessment to design an Android-based electronic data collection and management system. We then evaluated the system by reporting results of a pilot trial and from comparisons of two, large-scale surveys conducted seven months apart; one with traditional paper questionnaires and the other with tablet computers, including accuracy, person-time days and costs incurred.

Principle Findings: The electronic data collection system met core functions in household surveys and overcame constraints identified in the needs assessment. Pilot data recorders took 264 (standard deviation (SD) 152 sec) and 260 sec (SD 122 sec) sec per person registered to complete household surveys using paper and tablets, respectively (P=0.77). Data recorders felt a lack of connection with the interviewee during the first days using electronic devices, but preferred to collect data electronically in future surveys. Electronic data collection saved time by giving results immediately, obviating the need for double data entry and cross-correcting. The proportion of identified data entry errors in disease classification did not differ between the two data collection methods. Geographic coordinates collected using the tablets were more accurate than coordinates transcribed on a paper form. Costs of the equipment required for electronic data collection was approximately the same cost incurred for data entry of questionnaires; whereas repeated use of the electronic equipment may increase cost savings.

Conclusions/Significance: Conducting a needs assessment and pilot testing allowed the design to specifically match the functionality required for surveys. Electronic data collection using the Android-based technology was suitable for the large-scale health survey, saved time, provided more accurate geo-coordinates, and was preferred by recorders over standard paper-based questionnaires.

5.2. Introduction

Large-scale national and sub-national surveys are needed to map the distribution of a health condition, establish baseline prevalence and incidence data for planning, and monitoring the impact of neglected tropical disease control interventions (Emerson et al., 2008; Brooker et al., 2009; Baker et al., 2010; Dorkenoo et al., 2012). These surveys often involve collection of a combination of geospatial and disease prevalence data from multiple households within multiple communities across many different regions of a country. Sample sizes vary according to programme-specific methodologies, but typically thousands of individual, household, school, and community records are obtained on paper forms (Sturrock et al., 2009; Bamani et al., 2010b; King et al., 2010; Kabatereine et al., 2011; Forrer et al., 2012; Gosoniu et al., 2012). Paper forms must be printed, transported to the field, distributed, filled in, collected, organised, collated, and kept secure prior to data entry. Once data have been collected, forms must then be entered manually into computer databases. To ensure quality of stored data, the forms should be entered twice by separate data entry clerks and then compared to remedy discordant entries against the original hard copy forms. Finally, in good practice, the paper forms must be stored securely for a minimum time period (no less than 2 or 5 years after publication) according to national and international regulations (WHO, 2002b; IEA, 2007).

As neglected tropical disease control and elimination programmes seek to assess impact of interventions (e.g., elimination), large sample sizes are required to have the power to determine low levels of disease (WHO, 2011). For example, while 10 communities may be acceptable for estimating the need to initiate control interventions to over a million population in a “super district” suspected hyper-endemic for trachoma, 10 or more clusters per 50,000 population in a sub-district are required to document low-level disease before stopping interventions (WHO, 2010). Applying sub-district-level surveys in only two zones (population of 3.8 million) of the Amhara National Regional state in Ethiopia required collecting data from over 21,000 households in 714 communities(King et al., *at review*). A 4-page paper survey tool was employed and administered to each household. Needless to say that paper-based surveys at this magnitude require significant time, financial and human resources, and physical storage space.

Electronic data collection has been proposed as a solution to the challenges posed by paper-based surveys and several advantages have been discussed (Lane et al., 2006). Devices such as mobile phones, using short message service (SMS), have been effectively used to manage drug-stock in rural health facilities, push health communication messages to target populations and for disease surveillance (Barrington et al., 2010; Jian et al., 2012; Deglise et al.,

2012). However, the amount and complexity of the data collected and sent with SMS is limited (Hillebrand, 2010). Personal data assistants (PDAs) allow the capture of more complex data and efficient use of PDAs has been documented in disease surveillance and clinical research, as well as national surveys (Dale and Hagen, 2007, Blaya et al., 2008, Yu et al., 2009, Jima et al., 2010). With the development of the Android (Google Inc.) platform, applications such as Open Data Kit (ODK, www.opendatakit.org) and EpiCollect (www.epicollect.net) have broadened the options in mobile data collection in public health to so-called 'smart' devices (primarily touch-screen mobile devices, such as smart phones and tablet computers) (ODK, Aanensen et al., 2009). Many of these devices offer the additional advantage of having built-in global positioning systems (GPS) to automatically capture geographic coordinates from external GPS devices, as opposed to transcribing coordinates to paper-surveys from external GPS devices, thus minimising transcription errors in the field.

The purpose of this study was to evaluate the use of a novel electronic data collection system for use on tablet computers operating on the Android platform, and to determine whether this system was feasible and as effective as standard paper-based forms in collecting data in large-scale household surveys in a remote area of Ethiopia with poor infrastructure. Additionally, an effort was made to estimate person-time days and cost incurred by the two approaches of data collection.

5.3. Materials and Methods

5.3.1. Ethics Statement

The pilot study reported here was integrated into a training exercise for the trachoma impact assessment surveys approved under Institutional Review Board protocol 079-2006 of Emory University and by the Amhara National Regional Health Bureau ethical review committee. Data obtained from these surveys and used for the current comparison are the property of the Amhara National Regional State Health Bureau and The Federal Ministry of Health of Ethiopia and made accessible to The Carter Center under a memorandum of understanding, but are not publically available. Details of the ethical consideration for these surveys and training have been explained elsewhere (King et al., *at review*). Participants involved in needs assessment discussions were aware of the intent to publish from the outset of the discussion, are authors on the present paper and have consented to the contents of this paper.

Box 5.1. Description of hardware and software utilised for electronic data collection during the study activities

Activity	Hardware	Software
Pilot Study		
Design electronic questionnaire	Desktop / Laptop computer	Build ODK: *browser application* Google Chrome browser
Data collection in field	Wistec A81E 7-in tablet computer Blue-tooth external GPS	Android 2.0 Swift Insights Mobile 1.0 *Android App*
Data download and processing	Laptop computer	*KoBoSync Post Processor : Java application for aggregating data*
Large-scale deployment		
Design electronic questionnaire	Desktop / laptop computer	Swift Insights Desktop: *Java application* Mozilla Firefox browser
Data collection in field	Samsung Galaxy Tab GT-P1010 7-inch tablet computer	Android 2.1 Swift Insights Mobile 1.1 *Android App* Barcode scanner 4.3.1 *Android App* Amharic Android keyboard
Data download and processing	Laptop computer	Swift Insights Desktop: *Java application*

5.3.2. Study Preparation

We consulted freelance volunteers (senior computer science undergraduates) with experience, expertise, and interest in seeking to apply their technical skills in a philanthropic project. In a first step, we conducted a needs assessment prior to proposing an electronic data collection system aimed at improving efficiency in large-scale household surveys. This involved group discussions with the volunteer computer scientists, epidemiologists, and public health programme professionals with extensive experience in cross-sectional household surveys to identify core, functional needs of both hardware and software when implementing a survey and identifying potential constraints of electronic data collection under typical field conditions in resource-constrained settings. Next, we piloted a proposed, novel electronic data collection system in a setting where such a system would be deployed to further refine the design and provide developers first-hand experience of real constraints faced in the field. This pilot involved the following activities: training data recorders experienced in paper-based surveys to use an Android device and electronic questionnaire; recording the time required for data recorders to collect data using the same household questionnaire by either paper and pencil, or electronically on a tablet computer; and finally, documenting the perceptions of the data recorders about using the electronic data collection system. The hardware and software used for electronic data collection in the study activities are described in Box 5.1.

5.3.3. Training and Study Implementation

The pilot survey team consisted of eight members who had previously been deployed in a large-scale trachoma survey in Ethiopia. The same survey tool (paper questionnaire, see Appendix S1) that was used by the teams in the large-scale survey was designed electronically and loaded onto tablet computers.

The data recorders were trained for one day in a classroom on how to operate the tablet computer and collect data using the Android application, including capture of geographic coordinates. This was followed by one day of practice in a nearby community whereby the eight members were split into two teams of four (two data recorders and two trachoma examiners) and followed the exact protocol of previous surveys. At each household, one data recorder administered the questionnaire and collected data using the tablet, while the other recorded data on the paper questionnaire. The recorders took turns using the tablet and alternating lead interview roles at each household for a total of 20 households. The next two days the same process was repeated in two separate communities. Without the data recorders' knowledge, the team supervisors recorded the time required for the data recorder to implement the survey at

each house and whether it was administered by paper or tablet. On each day of applied training, the participants' perceptions on using either paper-questionnaires or electronic questionnaires were documented through focus group discussions (FGDs). Using a grounded theory approach, these discussions were semi-structured around a core set of questions (Appendix S2) and new themes identified in one FGD were explored in subsequent FGDs until saturation of themes was reached (Glaser et al., 1967). Additionally, the participants were given the same questions on individual questionnaires and were asked to share any comments they felt were not adequately discussed or did not want to openly share in the discussion. Two observers entered separately the responses and any additional comments provided by the participants which were compared for consistency. The discussion notes were reviewed by the coauthors and emerging common themes extracted as has been done in other programmes (King et al., 2011b). The findings from the FGDs were used to revise the survey instrument and functionality of the data collection programme, and were re-tested among the study participants.

5.3.4. Data Comparison

The electronic data collection system was further refined and implemented in a large-scale trachoma prevalence survey using the same protocol and questionnaire as implemented seven months prior in a neighboring zone of the same region of Ethiopia. The methods and results of these surveys are described in detail elsewhere (King et al., *at review*). Of note, the cluster size was increased in the survey using electronic data collection by randomly selecting one segment of 40 rather than 30 households as done in the previous survey in order to meet the target sample size for estimating prevalence of trachoma among children aged 1-9 years.

The first survey collected data on standard paper-based questionnaires and the other utilised the modified electronic data collection system both using the survey tool (Appendix S1). The survey tool consisted of one interview per household to obtain household characteristics, head of household demographics, knowledge of trachoma, knowledge of prevention measures, reported behaviour of face washing and household indicators of water, sanitation, and hygiene. Nested within the household interview, data was collected from all individual household residents including demographics, reported school attendance among children and participation in antibiotic mass distribution, and clinical examination for trachoma, hence creating the hierarchical structure of parent (household) to child (individual resident). An additional questionnaire was employed for one randomly selected school-aged child per household by branching to a separate electronic form linked to the parent and child data with a unique

identification number. This additional questionnaire was not used in the survey employing paper questionnaires and thus is not compared in the analysis.

5.3.5. Analysis

We assessed the raw data sets from the two large-scale trachoma impact assessment surveys conducted 7-months apart. We compared the difference in frequencies of survey refusals and identified data entry errors using a X^2 test and t-test corrected for the survey design where appropriate. We focused on data entry errors that could have the most impact on disease prevalence estimates: number of blank fields (i.e., missing data where data should have been recorded according to protocol); age and sex of participants; availability for examination; incorrect unique identifying number; a blank field in the classification of trachoma clinical signs, or an impossible combination of clinical signs (e.g., no signs and clinical signs recorded for the same eye).

Geographic coordinates as recorded by the GPS were collected for every household, in each community cluster, for both surveys. Using the recorded household coordinates, we calculated the median location for each community surveyed to serve as the cluster centroid. We then computed the distance between the coordinates for each household to the cluster centroid, and compared the two surveys with a t-test. The Euclidian distance was calculated using the Haversine formula (Sinnott, 1984), and cross-checked in ArcGIS version10 (Esri; Redlands, CA, United States of America) by re-projecting the latitude and longitude (in decimal degree) into Northing and Eastings (in meters, UTM Zone 37). We also compared the frequency of obvious outlying household coordinates, defined as ≥ 4 km away from the cluster centroid. Finally, we mapped all households linked to their cluster centroid to visually assess the differences in accuracy of each data collection method. Statistical tests were conducted in Stata version 12.0 (Stata Corp.; College Station, TX, United States of America).

To estimate costs associated with paper-based data collection, we used 10.9% of a median cost per cluster of US$ 311 (inter-quartile range [IQR]: US$ 119-393) estimated from a previous study of trachoma prevalence surveys in 165 districts across eight countries (Chen et al., 2011). This was the overall proportion of total costs due to data entry of paper questionnaires. An additional 1.5% of total cluster cost was assumed to cover the cost of the paper and printing for questionnaires. For a conservative estimate of the cost of electronic data collection, we simply took the sum of equipment costs for the tablet computer and accessories, assuming a one-time use.

Table 5.1. Needed functionality of electronic data collection in household surveys and the solutions implemented

	Description of need	Final solutions implemented
Software		
Creation	• Simple design of new surveys • Update of existing surveys • Display multiple languages	• No Internet connection required for design, drag and drop survey builder • Create and save templates for fast production of new surveys • Entry of multiple translations in form builder • Export labels for faster, bulk translation
Collection	• Simple entry of data • Accommodate skip patterns • Generate unique identification numbers for each household and individual • Maintain parent-child relationships of household-level and individual-level data • Generate random samples of entered records • Track external specimens • Minimise errors • Input text in multiple languages	Android application with base functionality of Open Data Kit plus: • Ability to generate relational databases so that data entered once applies to all related records • User defined survey preferences • Generation of unique record identification • Select enumerated residents randomly • Save listing of absent persons for ease of review and completion • Side-by-side view of enumerated residents and repeating data fields (Figure 5.2) • Capture input from internal or external GPS and camera • Language specific keyboards
Management	• Efficient distribution of survey forms • Minimal risk of data loss • Append data from multiple devices • Convert data to a generic file format for broad compatibility • Reduce time to data availability	• Data written to external storage on device • Without Internet or mobile network connection, from a local desktop user-friendly interface: 1. Distribute forms 2. Upload and append collected data 3. Convert data to useable format
Hardware		
Durability	• Withstand heat, cold, moisture, and dust; • Battery life for at least 1 working day • Ease of recharging	• Android tablet computer 7” display • Internal battery minimum capacity 6-8 hr • Protective case • Portable external battery pack • AC and DC to multiple USB plugs for charging
Capability	• Capacitive touch screen • Visible display in bright sunlight • Collection of geographic coordinates • Camera for scanning barcodes • Recoverable data	• Tablet computer with 3.5 mega pixel camera • Auto-brightness display setting • Internal GPS • Removable, external micro SD cards

5.4. Results

5.4.1. Design of Electronic Data Collection System

The summary of the findings of the needs assessment and developed solutions are listed in Table 5.1. In brief, the proposed electronic data collection system incorporated a desktop user-friendly interface, which readily allowed survey planners to design, modify, and update electronic questionnaires, without the need for Internet connection, in an intuitive drag-and-drop form builder. Additionally, the Android application to collect data was able to capture recurring data from individuals within a data record collected from the household. Unique identification numbers were generated based on survey preferences set on the tablet in the home screen of the application and from minimal input of the data recorder. Data fields for each individual enumerated in a household record were arranged alongside the list of enumerated individuals, which allowed flexibility of alternating between individuals as a survey team encountered each one for examination (Figure 5.2). From this same display, the random selection functions were accessible, allowing random selection of an eligible individual enumerated in the household record for additional assessment (e.g., submission of stool sample for the diagnosis of intestinal parasite infection). Eligibility was defined as set by the user in survey preferences accessed from the home screen. To manage the survey, the user interface allowed the distribution of created forms, uploading, and appending collected data through USB connection without Internet connection.

With regards to hardware (Box 5.1), during the pilot testing, we used a tablet computer with a 7-inch resistive touch screen display with exchangeable batteries. The resistive screen was tough, but not sensitive to normal touch and the external batteries proved problematic to exchange on-the-go and keep charged. Hence, for the full deployment, we used a tablet with 7-inch capacitive touch display enabling softer touches to the screen and a more responsive user experience. The deployed tablet had an internal battery providing 6-8 hours of use, which could then be recharged through a USB connection to AC/DC or external battery pack charging units. An internal GPS allowed the direct capture of geographic coordinates. To minimise errors in linking results to household and individual records and maintain privacy of survey volunteers, a camera with autofocus allowed use of an application (Barcode Scanner 4.3.1; see http://code.google.com/p/zxing) to capture of random identification numbers from 0.25”x0.25” QR codes on 1.18”x0.5”labels used to uniquely link external specimens (in this case, stool specimens; see Figure 2). Data were stored on an external micro SD card to reduce risk of data loss.

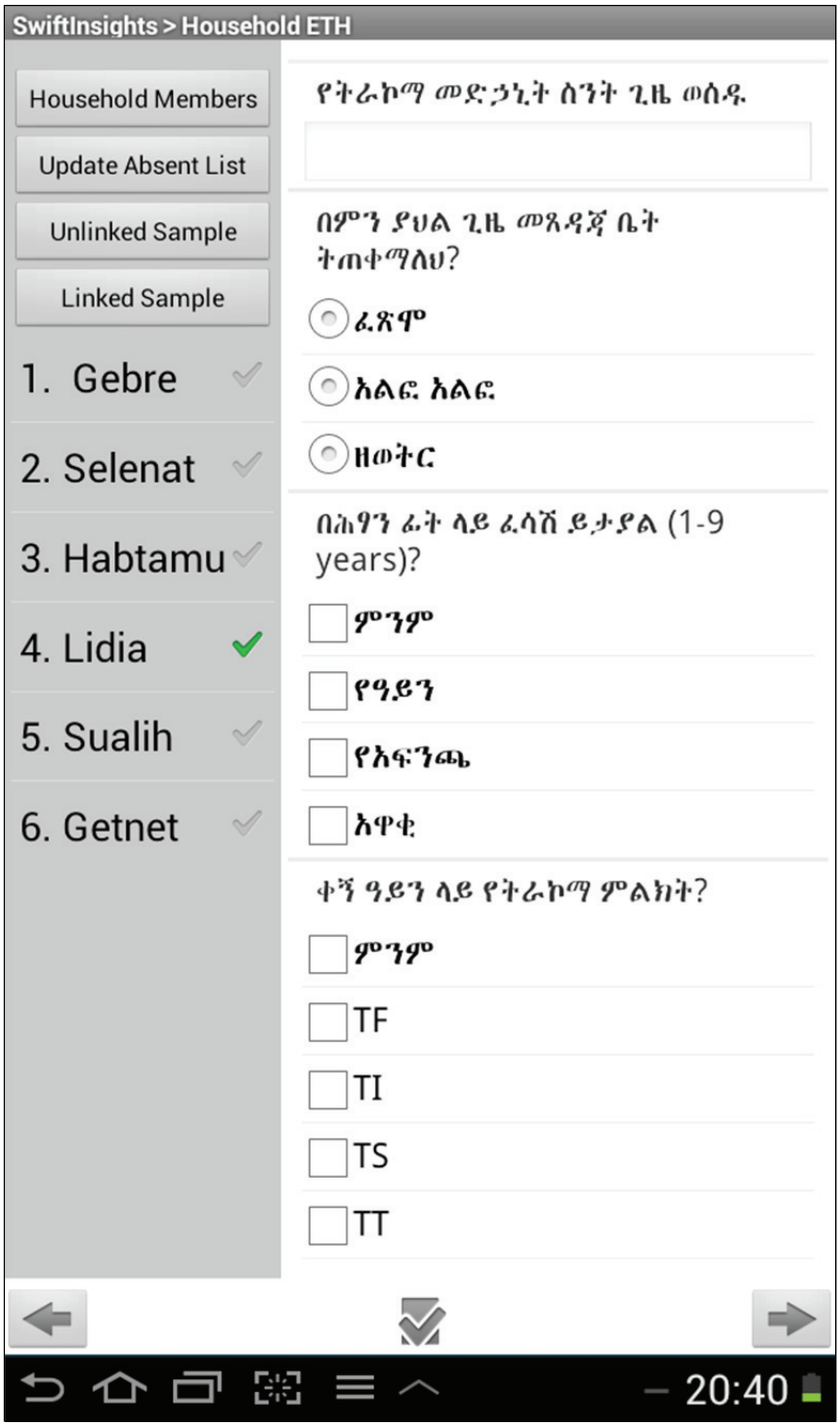


Figure 5.2. Example screen shot: looping fields for members grouped within a household record. As seen in a novel Android application for collecting data in household surveys

Figure 5.3. Collecting the identification number from a barcode-labeled stool specimen. Integrated survey of neglected tropical diseases in Amhara National Regional State, Ethiopia (courtesy Aisha Stewart)

5.4.2. Results from Pilot Investigation

A total of 40 households were surveyed over two days in two separate communities during pilot testing. There was no difference in the time required to collect data between the paper-based and electronic method over the 2-day observation period (Table 5.2). The time taken to enter data when the survey was administered with tablets was 48 sec per person more on the first observed day (day 2) and 54 sec per person less on the second observed day (day 3) compared to paper surveys. These differences, however, were not statistically significant (*P*=0.20 and *P*=0.50, respectively).

Table 5.2. Time to complete paper-based and Android-based electronic questionnaires during a pilot trial in Ethiopia 2011

	Paper*	**Tablet***	H_0: Paper = Tablet**
Day 2			
Total number of households surveyed	10	10	
Mean number of residents per household	4.9 (1.8)	4.5 (2.9)	
Mean time (sec) to enter data per person registered	268 (101)	320 (119)	z=-1.29 *P*=0.20
Day 3			
Total number households surveyed	10	10	
Mean number residents per household	3.8 (1.2)	3.9 (1.2)	
Mean time (sec) to enter data per person registered	260 (197)	201 (97)	z=0.68 *P*=0.50
Combined 2-Day Results			
Mean time (sec) to enter data per person registered	264 (152.4)	260 (122)	z=-0.30 *P*=0.77

* SD- standard deviation

**Wilcoxon rank-sum test

Table 5.3. Data recorders' perceptions of electronic data collection post 3-day pilot trial in Ethiopia

Aspect explored	Summarised perceptions
Time	▪Paper questionnaire took less time to complete than the electronic questionnaire
Preparation	▪No printing, sorting, stapling, and labeling with unique numbers is required with electronic data collection
Transporting	▪Tablet computers were portable, lighter, and less bulky than paper
Communication with respondents	▪Less eye-to-eye contact with respondent, but was less of a problem once familiar with the tablet computer
Recording data	▪Transcribing GPS coordinates onto paper forms was a difficult task and the direct capture of GPS coordinates via the tablet was preferred ▪Writing district, village, and community names on a paper form for every household was tedious ▪No writing necessary for electronic data collection ▪Recorders must be attentive to skip patterns on a paper form, but the skip patterns were automatic on the electronic form ▪Entering text, moving the cursor, and editing text fields were most challenging tasks using the tablet computers ▪Accidental selections on single select (i.e., yes or no) questions when the question did not apply could not be de-selected only switched to either option ▪Mistakes on paper forms can be erased and corrected ▪More difficult to return to a completed electronic form and add information than a paper form (i.e., an absent person presents for examination after the survey team has moved to a new household)
Data management	▪Risk of losing the data was greater for tablets than for paper forms because paper is tangible ▪Paper forms are difficult to keep clean, dry, and in order
Training	▪Ability to use tablets may be enhanced by experience in using computers ▪Data recorders should become familiar with questionnaires first before using tablets ▪Power management must be covered
General concerns	▪Keeping device charged where there is no access to electricity
General preferences	▪Enjoyed learning new technology ▪Questions on the electronic form and entry of data in *Amharic* (native language) are preferred ▪Use electronic data collection rather than paper questionnaires in future trachoma surveys

After the field work, recorders shared their perceptions concerning electronic data collection with key findings summarised in Table 5.3. Recorders felt the paper survey took less time to complete, but they enjoyed learning the new technology and preferred to collect data electronically in future surveys. Recorders expressed a lack of connection to the respondent

when first learning to use the data collection device due to less eye-to-eye contact while administering the questionnaire. The training curriculum was modified to address attentiveness and connection to the respondents in future surveys. The greatest concern about using electronic data collection was the ability to keep the electronic device charged under field conditions. We also included modules in future survey trainings to address power management and common data collection mistakes or difficulties as reported by the pilot data recorders (Table 5.3).

Data loss with paper surveys was perceived less risky than with electronic data collection since the paper questionnaires were tangible, enabling the immediate review, identification and correction of mistakes. Paper surveys were also perceived to be easier to manipulate, to add or change data, including an absent household member who was later encountered by the survey team. To address these concerns the Android application was modified to allow identification of absent persons in a household, and aggregate these people in an absent list that facilitates finding the correct household record and completing the necessary fields of the presenting absent person.

5.4.3. Results from Large-Scale Surveys

Outcomes from the paper-based and electronic data collection in separate, large-scale surveys utilising the same sampling methodology and questionnaire are presented in Table 5.4. The surveys were equivalent in scope and scale. Refusals to participate in the survey were rare, but significantly more common among household residents when using the electronic device (0.8%, 95% confidence interval (CI), 0.7-1.0%) compared to paper-based surveys (0.3%, 95% CI 0.2-0.4%) (P<0.01). The number of empty entries for the fields age, sex, and availability of enumerated household residents was fewer with electronic data collection than paper-based collection by 0.2% (P=0.01). There were fewer errors identified in the unique identifying numbers of each household in the electronically collected data set (1.8%) than the paper-based data set (2.3%, P=0.09). There was no difference in the amount of errors made when recording the trachoma clinical diagnosis between the two data collection approaches (0.2% *vs.* 0.2%, P=0.26).

When comparing the capture of geographic coordinates, 0.5% more empty fields were observed in the data collected with tablets than in the paper-based data (P<0.01). Outliers, defined as household coordinates ≥4 km from the median geographic coordinate in the surveyed cluster or more than 1000 m elevation from median elevation in the cluster, were more common in paper-based collection than electronic collection (1.4% *vs.* 0.6%, P<0.01). The

mean distance from a household in a cluster to the cluster centroid was 400 m greater in the survey where coordinates were transcribed to paper questionnaires compared to electronic survey application ($P<0.01$). Variability of this distance is seen in Figure 3, where each point represents a household and each solid circle represents the cluster centroid. Each household is connected by a line to its cluster centroid circle. The displayed size of the circle is proportional to the maximum distance between a household and the centroid in that cluster.

The total time taken to prepare, implement, and process the data was 511 and 790 person-days for electronic and paper-based data collection, respectively. The proportion of time taken to complete activities involved with data collection is presented in Figure 5.5 for both surveys. The two survey methods required approximately the same amount of time to develop the questionnaire, obtain translations and edit. An additional person day was required to convert the paper-questionnaire to an electronic platform. For either method, the length of training was approximately one full week. The paper-based questionnaires (over 9,000 in total) took 18 person-days of preparation to print, collate, staple, and distribute prior to deploying teams for actual fieldwork. Preparing the electronic survey and loading to 20 electronic collection devices took less than one person-day. Collecting data in the field in South Wollo (paper-based survey) took 21 survey teams 26 days to complete, while in South Gondar (electronic survey) it took13 teams 38 days which was 52 less person-days. Including the time required for survey teams to access the selected clusters, one cluster was completed every one and half days per team in both surveys. Upon completion of field work, data collected electronically was uploaded to the survey coordinator's computer, appended, and converted to a usable data set in less than one day using the desktop interface. Completed paper questionnaires were collected from all teams, transported back to a central office where 14 data entry clerks working 8-10 hours per day for 14 days double-entered the data into separate databases. An additional 5 days was required to compare the duplicate data sets for discordant records, find the respective hard-copy questionnaires, and identify the correct entry before a final data set was available. Together, these data entry and correction activities accounted for 26.6% of the total time spent on the paper-based survey.

Table 5.4. Data comparison of paper-based and electronic data collection from two large-scale, cluster surveys in Ethiopia

Indicator compared	Paper-based data collection	Electronic data collection	X^2 or *t*-test (p-value)
Sample			
Clusters	360	354	NA
Households surveyed	9,263	12,064	NA
Individuals enumerated	38,851	50,858	NA
Individuals examined	33,800	38,652	NA
Refusals			
Individual-level	0.3% (N=38,852)	0.8% (N=50,884)	27.96 (*P* <0.01)
Identified data entry errors			
% Individuals enumerated with at least 1 blank field in census record (age, sex, availability)	1.7% (N=38,851)	1.5% (N=50,858)	6.61 (*P* =0.01)
% households with incorrect unique identifying number	2.3% (N=9,433)	1.8% (N=12,112)	6.83 (*P* =0.01)
Disease classification	0.2% (N=33,800)	0.2% (N=38,652)	1.28 (*P* =0.26)
Geographic coordinates			
Blank entries	0.6%(N=9,263)	1.1% (N=12,064)	12.14 (*P* <0.01)
Outlying entries‡	1.4%	0.6%	38.92 (*P* <0.01)
Mean household distance in meters to cluster centroid (SE)	687 (81)	288 (7)	t=-5.53 (*P* <0.01)

‡Defined as recorded households with coordinates more than 4 km from cluster centroid, or more than 1,000 m elevation from median elevation of the cluster

NA, not applicable

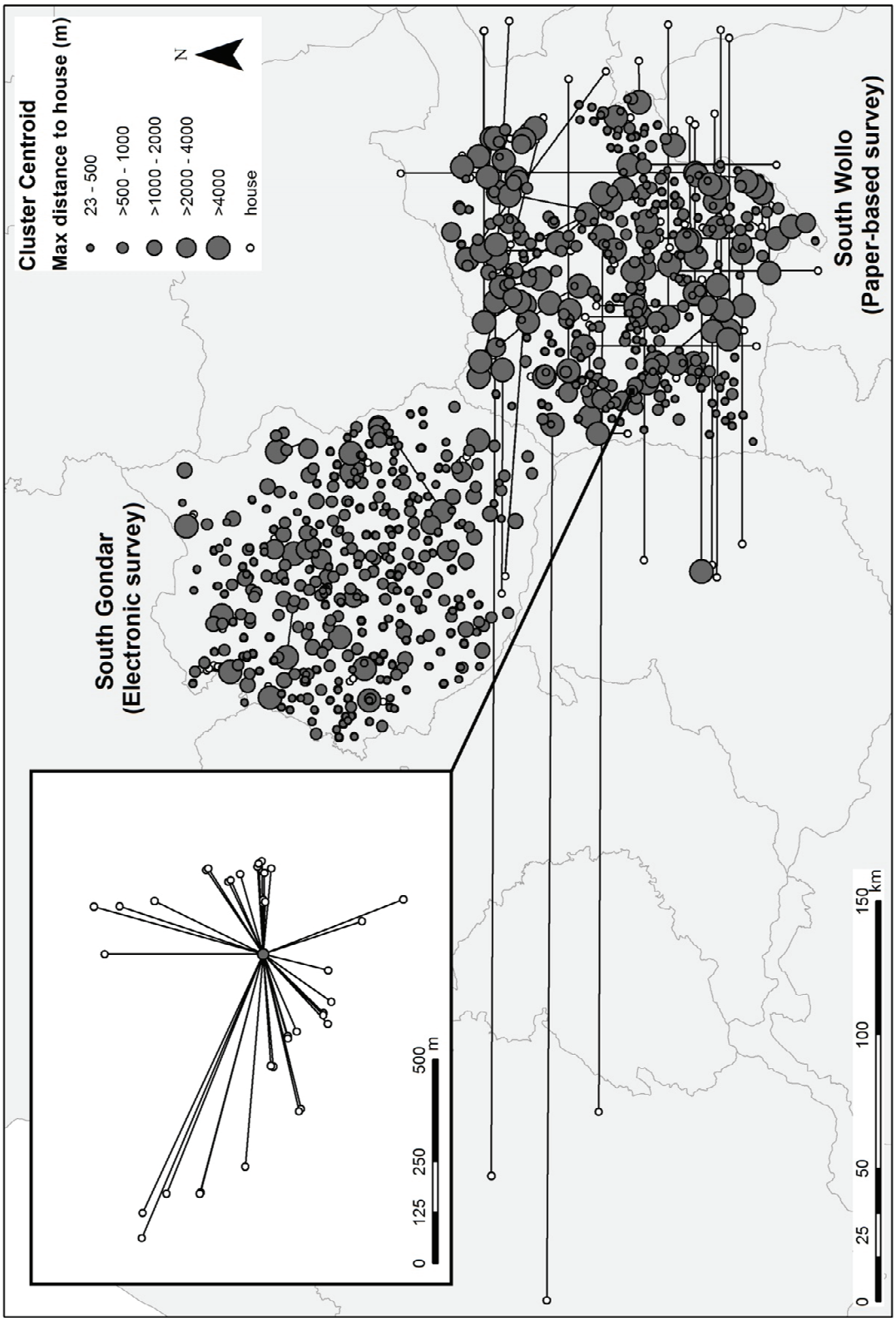
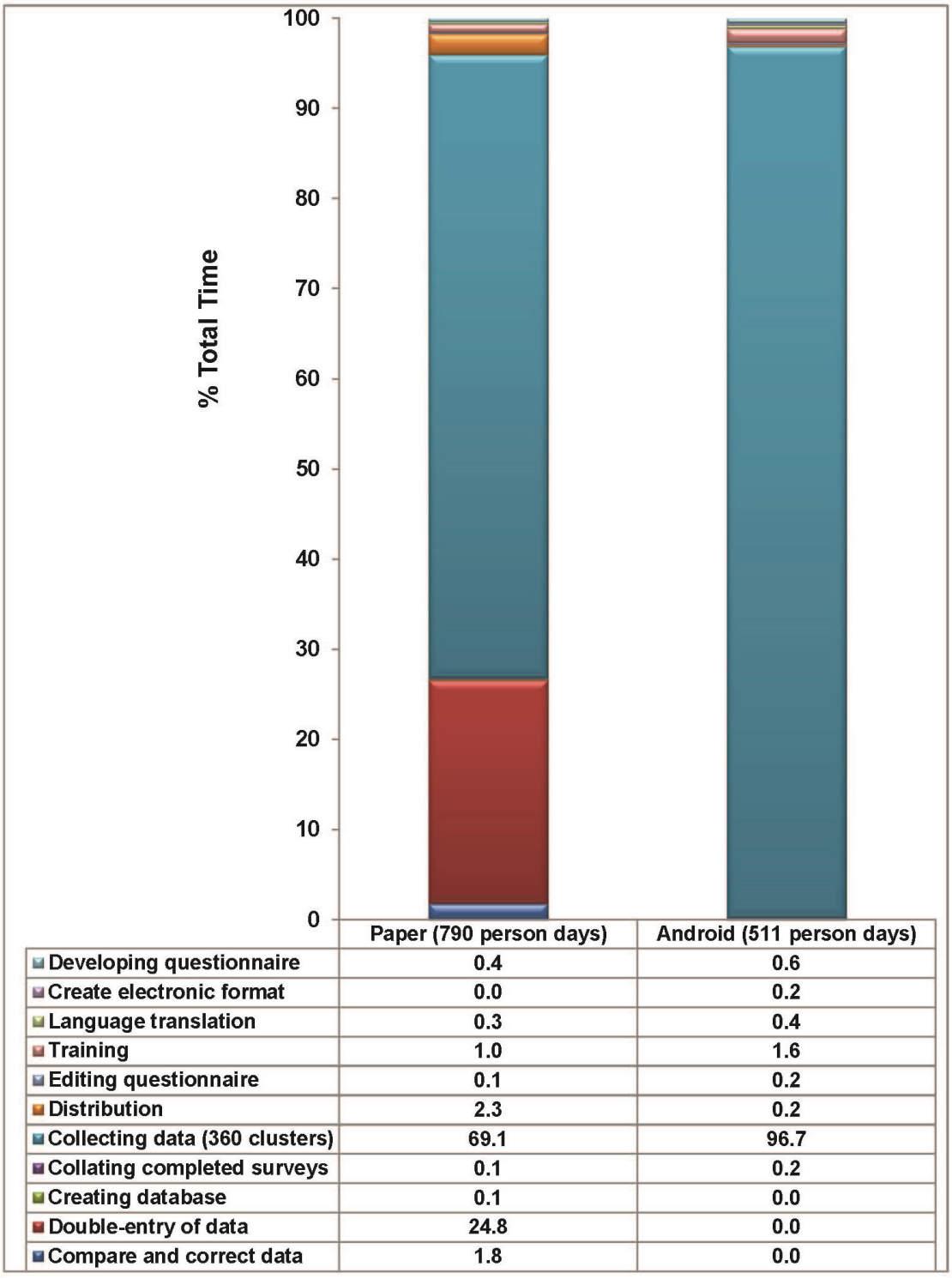


Figure 5.4. Distance between the recorded location of a surveyed household and the cluster centroid. Households surveyed in trachoma impact assessments in South Wollo (paper-based questionnaire 2010) and South Gondar (electronic data collection 2011), Ethiopia



	Paper (790 person days)	Android (511 person days)
Developing questionnaire	0.4	0.6
Create electronic format	0.0	0.2
Language translation	0.3	0.4
Training	1.0	1.6
Editing questionnaire	0.1	0.2
Distribution	2.3	0.2
Collecting data (360 clusters)	69.1	96.7
Collating completed surveys	0.1	0.2
Creating database	0.1	0.0
Double-entry of data	24.8	0.0
Compare and correct data	1.8	0.0

Figure 5.5. Proportion of total time (person days) required to complete survey activities by collection method. Time as implemented using paper-based questionnaire and Android-based electronic form in two large-scale (360 clusters each) trachoma impact assessments in Ethiopia 2010 and 2011.

5.4.4. Cost Estimates

Costs associated with paper-based data collection in the compared survey were US$ 13,883 (IQR US$ 5,312-17,543), which included an estimated cost of US$ 1,679 (IQR, US$ 642-2,122) for paper and printing of questionnaires plus US$ 12,204 (IQR US$ 4,670-15,421) for entering the data from questionnaires twice by separate data entry clerks into a database. The incremental survey costs associated with electronic data collection were US$ 10,320, which included 24 tablet computers (US$ 299 per piece), carry cases (US$ 15), micro SD memory card for external data storage (US$ 12), two external batteries for charging the tablet in absence of electricity (US$ 40 each), AC-USB adapter for charging with electricity (US$ 12), and DC-USB adapter for charging in a vehicle (US$ 12). These equipment costs assume a single use, which, more realistically, may be used for multiple surveys thus lowering incremental costs. Additionally, four of 24 tablet computers were not needed and never deployed during the survey.

5.5. Discussion

In this study, electronic data collection was at least as accurate as data collected using conventional paper-based questionnaires. Importantly, the novel electronic data collection system was less time consuming and our preliminary cost evaluation suggests that it is less costly. There was no evidence of differences in the amount of data entry errors identified by the two data collection methodologies. However, the differences in accuracy and precision observed between the captured geographic locations of surveyed households were significant, which, in turn, could affect subsequent spatially explicit data analysis. The accuracy of data entry using the electronic system could be further enhanced with additional logic statements and by blocking impossible combinations of entered data. The costs of the equipment required for electronic data collection was approximately the same cost required for data entry of paper-based questionnaires in a single survey, which was a conservative estimate. Use of the electronic data collection equipment in additional surveys would further reduce costs.

In the pilot study, there were no differences in time to completion of the household surveys between the methods, which was also reported in a comparison of smartphone administrated interviews among attendees of maternal health clinics in the People's Republic of China (Zhang et al., 2012). In comparing the two large-scale surveys, more households and individuals were examined in the electronic survey because of a modification in protocol to select more households per cluster. Yet, even with the increased work load, teams collected

more data in less time, as expressed in person-days to collect data using electronic capture. A total of 265 person-days were gained when using the electronic data collection system. The majority of time saved came from obviating the need for post-field collection data entry and translated into having the final data set available for analysis nearly one month sooner. Time saved is invaluable in programme settings, as it allows for immediate reporting of results to decision makers within the health system and creates lead time for preparation of needed interventions or importation of commodities such as donated drugs. Because impact surveys where data is collected electronically requires less time than conventional paper-based methods, the flexibility of when the survey is conducted within the programme schedule is increased. This is a critical advantage in neglected tropical disease control programmes due to the tight and often complex calendar of planning annual mass drug administration campaigns and other community-based interventions (Rotondo and Seligson, 2011; WHO, 2012c; Hanson et al., 2012; Knopp et al., 2012).

Pilot testing was crucial and identified additional flexibility needed in the electronic data collection system and further insight into the type of hardware required. It also introduced us to the perspectives of the experienced data recorders from previous paper-based data collection, which raised important issues that were addressed in the final system and provided insight to the training curriculum used in the large-scale deployment. We tailored the selected Android device to fit the needs of the survey and field conditions, which required extended battery life, internal GPS, touch screen, no stylus or external keyboard, and automatic adjustment of display brightness.

We applied a novel electronic data collection system in this study that did not require short-cuts or redesigning the survey forms to absolute minimum requirements due to limited functionality, as observed in use of PDA and SMS-based systems (Carroll et al., 2002; Kuntsche and Robert, 2009). The software was designed to fit the need, rather than the survey designed to fit the capabilities of the electronic system. The Android application for collecting data was designed to mimic the protocol of the survey team and offer sufficient flexibility to match the dynamics of interactions with household residents, which may have been contributing factors to explain why experienced, paper-based data recorders wished to use electronic data collection in the future. For example, household information needed entry only once for each individual in a household. Each household resident could be registered regardless of availability and data collection could occur for each resident in any order simply by selecting the person in the side-by-side view and entering the individual's trachoma signs (or other information). This

system also provides the flexibility to have multiple translations and input data in multiple languages, like Amharic, which was a cited preference of the pilot data collectors.

The desktop user interface allowed a multi-level survey prepared first on paper, to be transferred to an electronic form and applied in an application on any Android device within a day, without requiring mobile phone or Internet connections. Forms can be uploaded to survey devices for deployment in minutes while simultaneously downloading collected data held on the device. Data are protected securely on the device using a log-in code or pattern, stored on an external disc housed within the collection device minimising risk of data loss. We were not able to compare the frequency and type of lost data between the paper-based and electronic-based surveys, and therefore cannot address the perceptions from data recorders of the greater risk of data loss with electronic collection. We had three out of 24 devices temporarily power-off and fail to reboot, though data was recovered by removing and downloading data stored on the external SD card. The devices were set aside, but most importantly, all three rebooted after a 48 hour charge and remained functional even though not needed for the rest of the survey. Data were downloaded to the password-protected laptops of supervisors at least every second day, which further minimised risk of data loss should the device be stolen or lost, or the SD card not be retrievable at the end of the survey. In the future, encrypting the data on the SD card would enhance data security, whereas storing data both on internal and external memory would further minimise risk of data loss. At completion of the survey, records were downloaded to local computers, staying in country without having to be transmitted over mobile phone networks or the Internet to a foreign server, maintaining sovereignty and physical possession of the data set by the host country.

There are alternatives to data storage, such as uploading to a cloud server via telecommunications networks or the Internet, or downloading from an internal disk on the device to a local computer. Each alternative has strengths and limitations. Methods for data collection must be designed to function within the limits of the local infrastructure and adherence to local guidelines on data management and security is mandatory. At the time our survey was conducted, the Internet connectivity infrastructure in Ethiopia has been given a score of 1 (thin) on a scale of 0 (non-existent) to 4 (immense) (ITU, 2002). The software we used had the capability of web-based form design, deployment and data transfer, but our experience with connectivity during the pilot activities motivated us to pursue an off-line solution.

There were limitations in our study and these are offered for discussion. First, the comparisons made between data entry errors identified were from two different surveys implemented in different zones at different times of the year. Second, inherent to electronic data

collection, there is little opportunity to confirm collected data by field teams simply by reviewing the data set as we did to identify errors. Yet, this same limitation applies to paper-based questionnaires; we assume that the recorded data were the actual response. Third, time to administer the survey as recorded in the pilot might be affected by factors other than the recorder's ability to use the data collection tool, i.e., survey is interrupted by a neighbor or the respondent goes out to collect his/her children. We assumed that these external factors were, on average, the same for the two methods during the 2 days of observation, and hence do not affect the overall results. Fourth, the differences in mean distance to the cluster centroid should be interpreted with caution. Either households in South Wollo were simply more dispersed within community settlements than in South Gondar or the household distances from the cluster centroid were inflated due to systematic inaccuracies in transcribing household coordinates to paper in several clusters. The plots on Figure 5.4 and greater proportion of outlying households recorded in South Wollo suggest the latter. Finally, in estimating cost, we did not include the value of the time volunteered by the computer scientists (approximately 4 months of part-time work) to design and refine the system. Our reasoning was that free electronic data collection systems have now become available, although with less specific functionality, but could be deployed for survey use with only the added equipment costs and possibly training of survey coordinators on designing electronic forms and managing collected data. We also did not include the long-term value of the electronic equipment, which has continued to serve four other large-scale surveys in multiple countries at the time this manuscript was prepared for submission. Additional costs not considered were potential import duties levied on data collection devices and accessories as the regulations and amounts are setting specific, but should not be ignored when budgeting.

In summary, use of a novel system for electronic survey design, collection on an Android platform, and local management was feasible in a large-scale trachoma impact assessment survey. Electronic data collection saved time, was less costly, was at least as accurate as standard paper-based questionnaires, and was preferred by experienced paper-based data recorders. These advantages were similar as those advertised in recent applications of Android-based data collection applied to animal health and surveillance of zoonotic diseases (Karimuribo et al., 2012; Madder et al., 2012). Such systems could be readily applied to other large-scale neglected tropical disease control surveys as well as national initiatives, such as the malaria indicator surveys (MIS), the demographic and health surveys (DHS), the UNICEF multiple indicator cluster survey (MICS), or the regular household surveys done by the health

demographic surveillance systems (HDSS) of the INDEPTH net-work (USAID, 2012; UNICEF, 2006a; INDEPTH).

5.6. Acknowledgements

We gratefully acknowledge the residents of selected communities who gave freely of their time to participate in the pilot and actual surveys. We thank the pilot survey team that provided useful feedback for refining the electronic data collection system. We appreciate the time, effort, and attitude of all field teams, supervisors, drivers, trainers, and coordinators of the survey. We appreciate Adam Wolkon from US Centers for Disease Control and Prevention for sharing his experience regarding currently available technology and accessories. We thank Darin Evans, Greg Noland, Lisa Dickman, Aryc Mosher, Amy Patterson and Aisha Stewart from The Carter Center Health Programs for applying the system in other surveys and providing ideas on further development. Finally, we appreciate Georgia Institute of Technology graduate volunteers, Joy Buolamwini, Andrew Panfel, and Jessica Watson who have considerably improved the survey process through their collaboration in designing the electronic data collection and management system, *Swift Insights*.

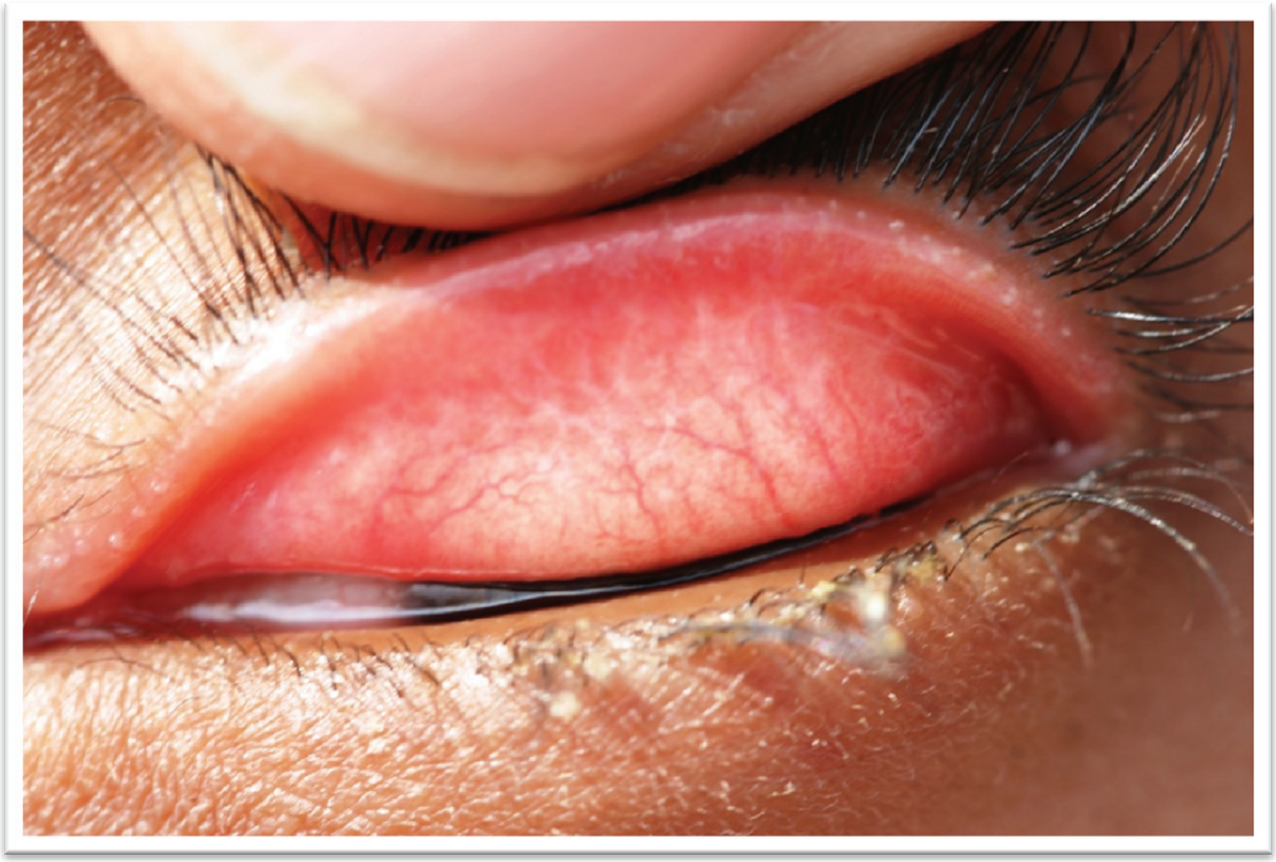


Figure 6.1. Trachomatous scarring (TS) as observed in the tarsal conjunctiva of an Ethiopian girl (courtesy Mary Rose King)

6. Impact of the SAFE strategy on trachomatous scarring among children in Ethiopia: a repeated cluster randomised cross-sectional study

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[this manuscript is currently at review in *Lancet*]

6.1. Abstract

Background: An integrated package of surgery, antibiotics, facial cleanliness, and environmental improvements, known as the SAFE strategy is prescribed for the elimination of blinding trachoma. Previous studies have assessed the impact of the SAFE strategy on trachoma transmission by monitoring infection and trachomatous inflammation among children. We aimed to determine whether any impact on cicatricial trachoma was evident among children living in a hyper-endemic area of Ethiopia since the implementation of SAFE.

Methods: Data from four cross-sectional, cluster randomised surveys conducted between 2000 and 2011 were analysed to determine age-specific patterns of trachomatous scarring (TS) among children aged 1-10 years. Impact was assessed by comparing the odds of TS among children having lived under the SAFE intervention with those assessed in surveys prior to this intervention in a multi-level logistic regression model, controlling for secular variation between survey years, various potential confounder variables, and random effects due to clustering at community and household levels.

Findings: The prevalence of TS has reduced from 24.9% in 2000 to 2.2% in 2011 among children aged 1-10 years. Having lived during SAFE implementation was associated with reduced odds of TS for children aged 1-9 years (range odds ratio=0.27-0.66). Children aged 5 years in 2011 had the lowest odds ratio of TS (odd ratio=0.27, 95% confidence interval (CI) 0.18-0.40) when compared to 5-year-old children before interventions began. Interventions independently associated with reduced odds of TS were living in a household reporting frequent face washing and where round-trip water collection took less than 30 min.

Interpretation: Our results provide optimism that the SAFE strategy is preventing the risk of blinding trachoma by reducing the development of scarring among the most vulnerable age groups.

Funding: The Lions Club International Foundation, The Lions Club Ethiopia and The Carter Center (surveys). Swiss Tropical and Public Health Institute (analysis and interpretation).

6.2. Introduction

Trachoma is the leading infectious cause of blindness responsible for 3% of total blindness worldwide (WHO, 2012a). In 2010, trachoma was responsible for an estimated 334,000 disability-adjusted life years (Murray et al., 2013). The severe, disabling sequelae of trachoma are the end result of an immunopathogenic response prompted by repeat episodes of ocular infection with *Chlamydia trachomatis* inducing severe inflammation (Grayston et al., 1985; West et al., 2001b; Mabey and Fraser-Hurt, 2003). Resolution of inflammation leads to development of fibrosis in the subtarsal epithelium, which can be seen as white lines, bands, or sheets of scarring. Further progression alters the anatomy of the normal lid margin rotating eyelashes inwards until lashes eventually contact the globe and abrade the cornea, a condition called trachomatous trichiasis (TT) (Mabey et al., 1992; Mabey and Fraser-Hurt, 2003). Scarring trachoma also impairs the function of meibomian glands to protect the tear film which, in combination with abrading lashes create opportunity for other bacterial and fungal infections of the cornea, leading to ulcers and fibrosis as infections resolve resulting in corneal opacities which impair vision and ultimately lead to blindness (al-Rajhi et al., 1993; Guzey et al., 2000).

Ocular infection and inflammation due to *C. trachomatis* are most prevalent in children, most probably because children have copious contact with infectious material; via ocular and nasal discharge on fingers, fomites and flies (Dawson et al., 1976; West et al., 1991; Taylor, 2008). Less severe infection is observed with increasing age, due to immunity or reduced exposure to *C. trachomatis* (Bailey et al., 1999; Wright et al., 2008). Trachomatous scarring (TS) and TT increase with age, and hence are more often observed in adults (Dawson et al., 1976; Schemann et al., 1998). However TS has been observed in 6% to 19% of children below the age of 11 years in trachoma hyper-endemic areas of Tanzania and the Republic of South Sudan (Wolle et al., 2009a; Ngondi et al., 2005, 2006a; King et al., 2008). Moreover, incidence of TS in children has been shown to be as high as that in adults in hyper-endemic communities of Tanzania (Wolle et al., 2009a). Preventing scar development in childhood is perhaps the most effective target for preventing future blindness in at-risk populations.

Trachoma is targeted for elimination as a public health problem by 2020 through an integrated package of interventions to treat, control, and ultimately prevent new cases of blinding trachoma, known as the SAFE strategy: surgery (S), antibiotic distribution (A), facial cleanliness (F) and environmental improvements (E) (WHO, 1997a; Bailey and Lietman, 2001). Although widely propagated for eliminating blinding disease, evidence on the impact has been demonstrated mostly on reducing infection and inflammation due to *C. trachomatis*. In this study we assessed the impact of at least five years of region-wide implementation of the SAFE

strategy on the presence of TS in children in a hyper-endemic area in Ethiopia. Specifically we aimed to determine whether young children born into an environment of trachoma control interventions were at lower odds of TS compared to young children with no exposure to control interventions, and whether any impact observed was cumulative over the years of life lived since the concerted control efforts were implemented.

6.3. Methods

6.3.1. Study design and participants

Data for the study were obtained from four cross-sectional population-based cluster surveys conducted in 2000, 2003, 2007, and 2011 in the South Gondar zone of the Amhara Regional State in Ethiopia. Details of the sampling methodologies of each survey are described elsewhere.(Ngondi et al., 2009a, King et al., *at review*) In brief, probability sampling was used to randomly select communities (clusters) and households within selected communities. All residents within selected households were examined for clinical signs of trachoma. Surveys in 2000 and 2003 determined the baseline, district-level prevalence of clinical signs of trachoma for all 10 districts in the zone prior to any SAFE interventions. Four districts in 2000 were prioritised for assessment due to historical data suggesting these had the highest burden of trachoma (Assefa et al., 2001). These four districts were drought-prone areas and considered the least developed of all 10 districts. The remaining six districts were surveyed for the first time in 2003.

The SAFE strategy was fully implemented in the first four districts surveyed starting in 2005 and by 2006 the strategy was being implemented at scale in all districts. Implementation of SAFE activities included outreach camps to provide surgery in addition to the existing static service; annual, community-wide mass drug administration (MDA) with antibiotics; promotion of facial cleanliness and hygiene in schools and communities by health extension workers; and community-level promotion of latrine construction and use through the health extension workers and environmental health officers. Provision of improved water sources was simultaneously supported by the development sector. The 2007 survey aimed to estimate impact of the SAFE strategy on trachoma infection and clinical signs in three of the four districts surveyed in 2000 after three rounds of MDA in those districts (Ngondi et al., 2009a). Finally, a large-scale impact assessment was conducted in 2011 to estimate the prevalence of trachoma at sub-district level after all 10 districts had received five annual rounds of MDA (King et al., *at review*).

The study protocols were reviewed and approved by the ethical review committee of the Amhara Regional State Health Bureau. Additionally, the trachoma surveys in 2007 and 2011

were approved by Emory University Institutional Review Board (protocol #079-2006). Verbal informed consent in these surveys was approved and recorded prior to data collection rather than written information and a signed statement due to the high level of illiteracy. Consent for trachoma examination and household interview was obtained from heads of households, individuals, and parents of minors.

6.3.2. Procedures

In each survey a brief interview was conducted with the head of household or designated respondent and all household residents were examined for the presence or absence of all five clinical signs of the simplified trachoma grading system in both eyes using a 2.5x binocular loupe and adequate light (Thylefors et al., 1987). If multiple signs were present in either or both eyes, all were recorded. Training prior to each survey followed guidelines put forth by the World Health Organization (WHO), which included a rigorous selection process of trachoma graders based on ability of graders to apply the trachoma grading system (WHO, 1993a, 2006b). In each survey an inter-observer reliability study was conducted among trachoma patients where all signs were recorded. The best performers, defined as achieving agreement with a “gold” standard of ≥80% (2000 and 2003 surveys) or a kappa ≥0·7 (2007 and 2011 surveys), were selected for clinical grading during the survey.

For this study, we included the outcome measure of the presence or absence of WHO simplified trachoma clinical sign TS only among children 1-10 years of age inclusive. Scarring once developed may not resolve, thus differences in prevalence rates of TS in adolescents and adults may be difficult to interpret. Limiting the analysis to children allows a clinical description of the population with various length of life exposure to the SAFE strategy. For example in the 2011 data set, children less than six years of age represent a cohort of children who have grown up in the context of ongoing concerted efforts to implement the SAFE strategy. Children aged 6-10 years have lived part of their life in the absence of trachoma control interventions and part of their life in an environment where SAFE interventions were being promoted.

6.3.3. Statistical analysis

Data were analysed in Stata version 12.0 (Stata Corp.; College Station, TX, USA). First we plotted TS prevalence by age, based on survey-specific multilevel logistic regression models adjusting for clustering within communities and involving a fractional polynomial function of age, stratified by district groups 1-3 (baseline survey in 2000) and 4-10 (baseline survey in 2003) to control for any systematic difference at baseline. Robust variance estimation for proportions and

means was used to adjust for clustering at the household and community level through the *survey data* commands in Stata. Statistical comparisons between proportions were adjusted also for the cluster design utilising the second-order corrected Pearson statistic (Rao and Scott, 1984). We then determined the relationship between TS and exposure to SAFE interventions in a multi-level, logistic regression model adjusted for the survey year, covariates, district, and clustering at both the household and community level. The covariates in the models included age, sex, presence or absence of trachomatous inflammation intense (TI) in the child, number of children 1-10 years of age in the household, the presence of a TT case in the household and educational attainment of the head of household (any school attended *versus* none). We defined exposure as the number of years lived during which the SAFE strategy was implemented. To determine any cumulative effect of exposure, we weighted each year of exposure with a factor *w* determined by the age of the child in the respective year. This factor was modeled as a cubic function of age, i.e. $w\,(\text{age}) = c_0 + c_1*\text{age} + c_2*\text{age}^2 + c_3*\text{age}^3$. We combined survey data for the exposure analysis giving all exposure terms a value of zero for surveys in 2000 and 2003 prior to any implementation of SAFE activities. Children surveyed in 2007 were exposed for a maximum of three years and in 2011, children had a maximum of seven and at least five years exposure respectively due to the different onset of interventions in each district.

Finally, potential associations between TS and indicators of the antibiotic distribution, facial cleanliness and environmental improvement components were assessed using the 2011 data for children 1-5 and 6-10 years of age separately controlling for covariates and clustering at household and community level. The following indicators were used: (i) individual antibiotic compliance calculated as the ratio between the number of years for which taking antibiotics during the MDA was reported (number of times taken) and the number of years with such MDA; (ii) the mean of individual compliance of household members; (iii) frequency of washing the faces of children less than six years of age as reported by the caregiver at the time of the survey; (iv) an observed household latrine with evidence of use at the time of the survey; (v) an improved primary source of water as reported by household interview respondent defined as water from a borehole or capped protected well, protected natural spring, or piped water; and (vi) ability to depart the household, collect and return with water within an estimated time of 30 min. Age-group-specific interaction terms with the above indicators of interest were generated and introduced in separate models including all covariates and other indicators. The coefficient estimates and confidence limits of each interaction term were extracted and odds ratios were plotted.

6.3.4. Role of the funding source

Funds for implementing the surveys were provided by an ongoing collaboration between Lions Club International Foundation, Lions Club Ethiopia, The Carter Center and the Amhara National Regional State Health Bureau which also provide necessary support for implementation of the SAFE interventions in the region. The statistical analysis and interpretation of the data was supported by the Swiss Tropical and Public Health Institute, which has no affiliation with the ongoing trachoma control activities in Ethiopia.

6.4. Results

6.4.1. Survey data sets

The data sets included in the analysis are characterised by each survey in Table 6.1. Data were collected from 589 communities and 12,285 households with child residents 1-10 years of age. A total of 25,221 children were examined for clinical signs of trachoma in the combined surveys. The surveyed children were of the same sex distribution. Children surveyed in 2007 were slightly younger than those in baseline surveys as data from children aged 10 years were not available ($t=-3.64$, $p<0.001$). The prevalence of TS was higher among the children in the first three districts surveyed in 2000 compared to districts surveyed in 2003 at baseline ($F=79.12$, $p<0{\cdot}001$).

The description of the household conditions under which the sampled children lived is presented in Table 6.2. From baseline studies to 2011 there was an increase in the proportion of children living in a household whose head of household had received some school education ($F=15.75$, $p<0.001$ districts 1-3; $F=55.80$, $p<0.001$ districts 4-10) and where there was a household latrine ($F=656.86$, $p<0.001$ districts 1-3; $F=99.35$, $p<0.001$ districts 4-10). After the introduction of MDA, the proportion of children living in a household where every resident reported taking antibiotics at least once during an MDA increased from 56·6% in 2007 to 83·2% in 2011 in districts 1-3 ($F=53.35$, $p<0.001$). In districts 4-10, 63.2% of the children lived in a household where all residents reported taking antibiotics at least once. Mean individual compliance in MDA among children aged 1-10 years was 67.2% (95%Confidence Interval (CI) 61.7-72.6%) in 2007 and decreased to 48.8% (95%CI 46.7-50.9%) in districts 1-3 ($t=-6.19$, $p<0.001$). Mean household compliance increased from 38.1% (95%CI 35.0-41.2%) in 2007 to 51.2% (95%CI 49.1-53.0%) in 2011 after two additional rounds of MDA ($t=7.03$, $p<0.001$).

Table 6.1. Description of trachoma cluster random surveys from 2000 to 2011 in South Gondar Zone, Ethiopia

Survey	Survey type	Districts covered	Clusters	Households with children 1-10 years of age	Children 1-10 years of age	Mean age of children 1-10 years of age (SD)	Percent girls	%Trachomatous scarring* (95% CI)
2000	Baseline mapping	1-4	119	1009	2339	5.4 (2.8)	50.1	24.9 (21.2-29.1)
2003	Baseline mapping	5-10	89	1482	3109	5.2 (2.9)	51.7	6.0 (4.4-8.1)
2007**	3-year outcome	1-3	27	619	1381	5.1 (2.7)	51.2	6.9 (5.2-9.0)
2011	5-year outcome	1-10	354	9273	18392	5.5 (2.6)	51.6	2.2 (1.9-2.6)

*estimates adjusted for correlation in the data due to clustering; CI, confidence interval; **data not available for children aged 10 years

Table 6.2. Description of household conditions of children 1-10 years of age from 2000, 2003, 2007 and 2011 by district cohort in South Gondar Zone, Ethiopia

Indicator*	Districts 1-3			Districts 4-10		
	2000 (%, 95% CI)	**2007** (%, 95% CI)	**2011** (%, 95% CI)	**2000**** (%, 95% CI)	**2003** (%, 95% CI)	**2011** (%, 95% CI)
Proportion of children whose head of household had some education	6.5 (4.2-9.9)	13.7 (9.2-20.0)	15.5 (13.2-18.1)	2.3 (0.8-6.2)	10.3 (7.0-14.9)	25.6 (22.9-28.6)
All household residents report taking antibiotic at least once during MDA	Nil	56.6 (49.1-63.7)	83.2 (79.6-86.2)	Nil	Nil	63.2 (58.7-67.5)
Mean household compliance in taking antibiotics during trachoma MDA	Nil	38.1 (35.0-41.2)	51.2 (49.4-53.0)	Nil	Nil	47.5 (45.1-49.8)
Proportion of children in households where young children's faces were reported washed at least once per day	NA	96.9 (93.4-98.6)	87.0 (82.3-90.6)	NA	48.3 (39.5-57.2)	91.5 (88.7-93.6)
Proportion living in a household with a latrine	0.3 (0.0-1.0)	39.2 (28.4-51.2)	50.1 (44.8-55.4)	0	7.1 (3.9-12.8)	40.7 (36.3-45.2)
Proportion in household using an improved water source	16.6 (10.9-24.3)	30.0 (17.7-46.2)	35.6 (28.4-43.6)	23.2 (13.9-36.0)	31.6 (23.5-41.1)	39.5 (33.7-45.6)
Proportion living in a household within 30 min access for round-trip collection of water	30.9 (24.2-38.6)	82.1 (68.5-90.6)	78.2 (71.4-83.7)	42.3 (27.9-58.2)	73.0 (64.7-80.0)	76.5 (71.8-80.6)

*estimates adjusted for correlation in the data due to clustering; CI, confidence interval; **District 4 only; NA-not assessed

Mean compliance among children in districts 4-10 in 2011 was 44.3% (95%CI 41.5-47.0%). Nearly a two-fold increase (48·3-91·5%) in the proportion of children living in households reporting washing the faces of young children at least once per day occurred since 2003 in districts 4-10 ($F=140.29$, $p<0.001$). A statistically significant increase was observed in the proportion of children living in households reporting the use of an improved water source in both district cohorts ($F=12.66$, $p<0.001$ districts 1-3, $F=5.11$, $p=0.024$ districts 4-10). Also, more children lived in households reporting access to water within 30 min of collection in 2011 than at baseline in the three least developed districts ($F=81.26$, $p<0.001$). At baseline, the proportion of surveyed households in districts 4-10 had less TT cases ($F=11.83$, $p<0.001$), more educated heads of household ($F=5.31$, $p=0.022$), higher latrine coverage ($F=59.01$, $p<0.001$), higher reported improved water sources ($F=6.76$, $p=0.010$), and greater access to water within 30 min ($F=48.84$, $p<0.001$) as households in the districts 1-3.

6.4.2. TS in children

The prevalence of TS by age is plotted in Figures 6.2 and 6.3 for each survey according to the respective districts surveyed. TS was less prevalent in the 2007 and 2011 surveys compared to the baseline surveys. In all surveys, TS increased with age; however, the increase appears slower in the two impact assessment surveys conducted after three and five years of SAFE implementation than observed in baseline surveys. Odds ratios of TS for exposed and unexposed children are predicted by each year of age at the time of survey in Figure 6.4 based on the age-dependent exposure weight terms in the multivariable random effects model. The odds of TS with SAFE exposure are significantly lower than the odds of TS at baseline for each year of age except for 10-year-old children. The odds ratio decreased with each additional year of age among children aged 1-5 years. Children aged five years after the intervention *versus* children aged five years prior to any intervention had the lowest odds ratio point estimate (odds ratio=0.27, 95% CI 0.18-0.40). The odds ratio of TS between children having lived under the implementation of SAFE and children without this exposure increased again after the age of five years but remained significantly lower than 1.0 up to the age of nine years.

Older children 6-10 years were much more likely to have TS than their younger counterparts (odds ratio=6.6, 95% CI 4.8-9.0, $p<0.001$) examined in 2011. Odds ratios of TS for each intervention factor are plotted in Figure 6.5 for children 1-5 and 6-10 years of age in 2011. TS was not significantly associated with individual or household-level compliance in MDA.

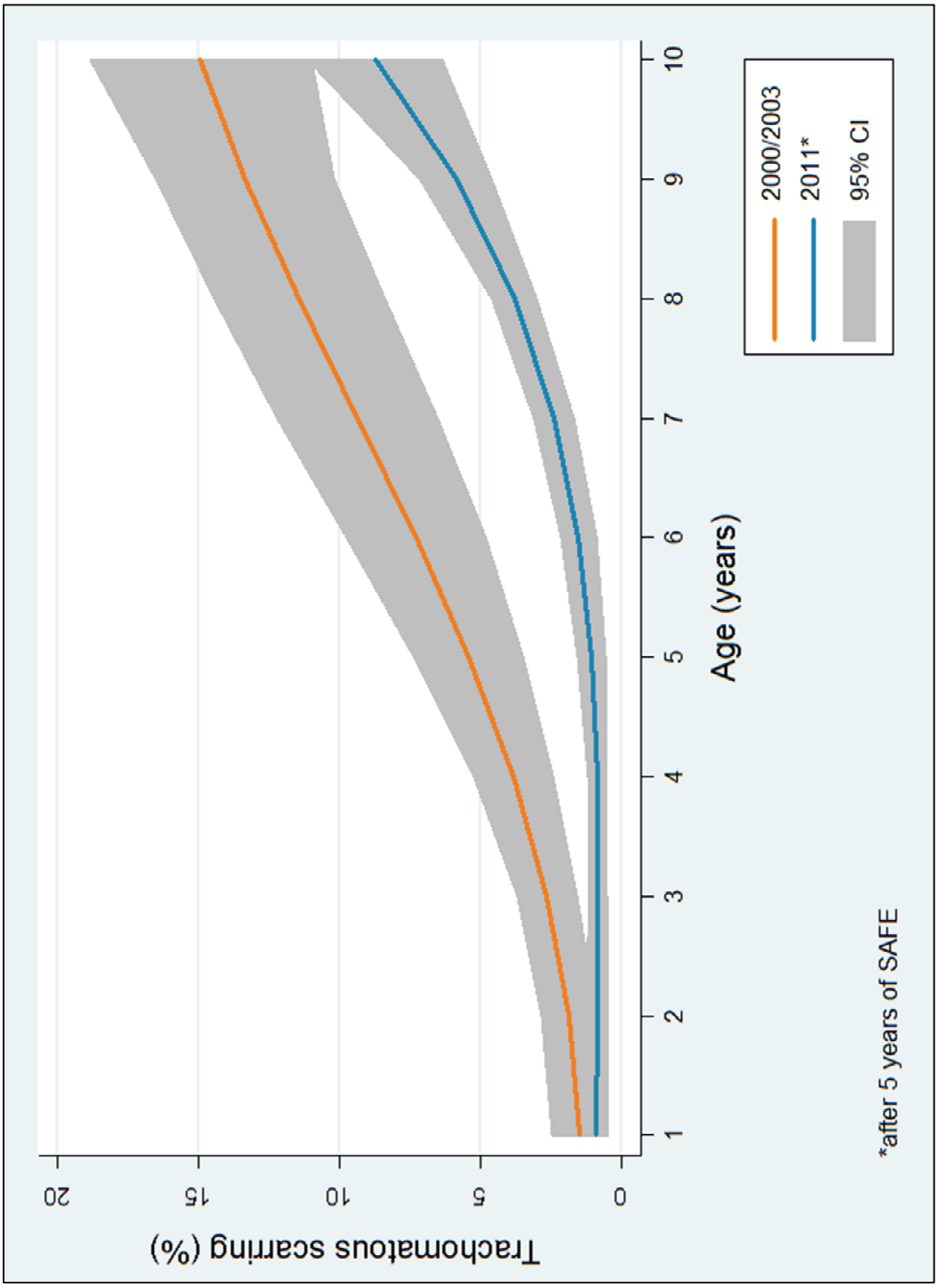

Figure 6.2. TS prevalence by age 2000/2003 and 2011 in districts 4-10

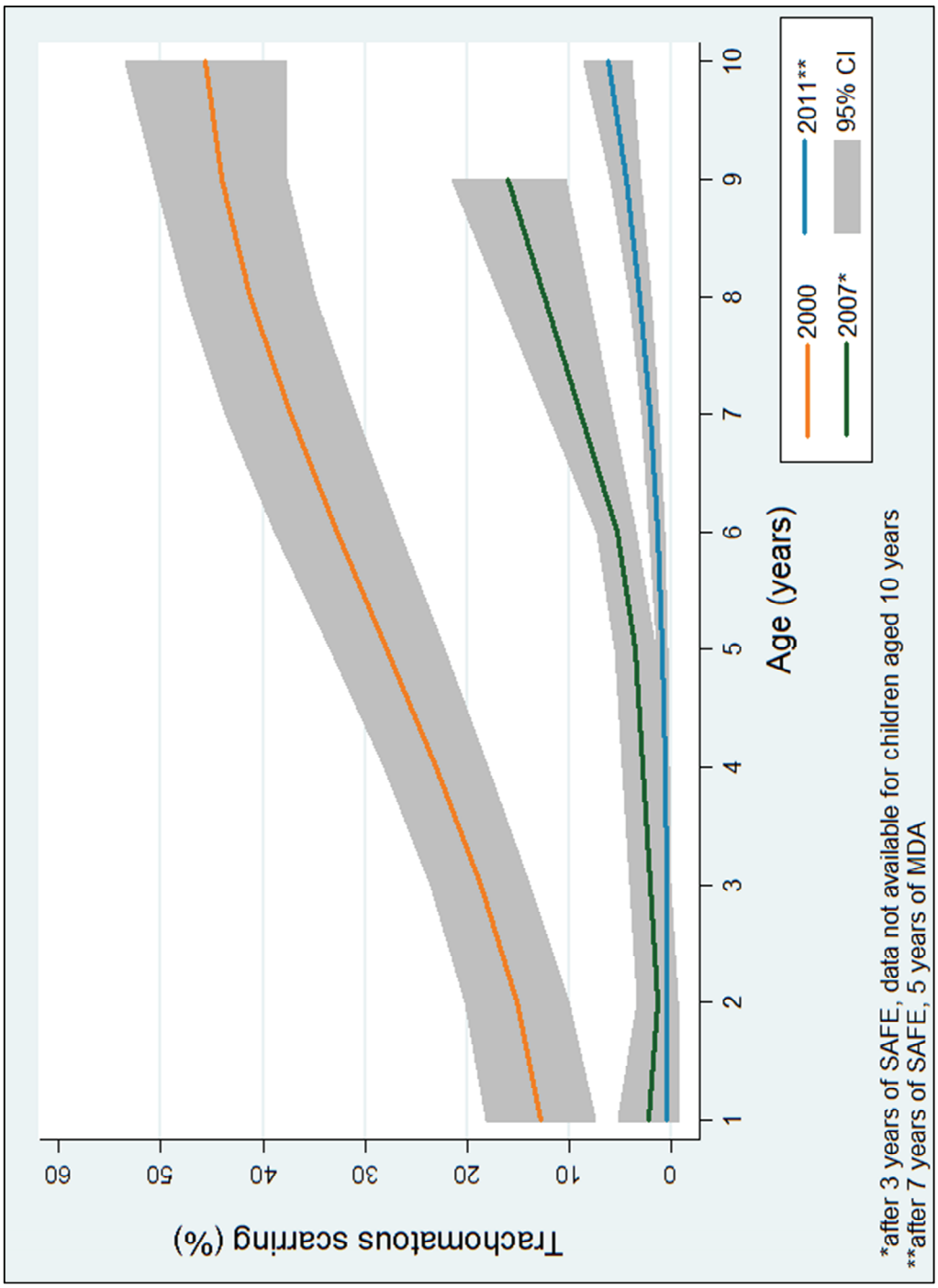

Figure 6.3. TS prevalence by age 2000, 2007 and 2011 in districts 1-3

Children aged 1-5 years living in a household where the respondent reported washing children's faces at least once per day compared to <1 time per day had lower odds of TS (odds ratio=0.47, 95% CI 0.23-0.97, p=0.041). TS was less likely among 6-10 year-old children living in houses where respondents reported washing children's faces twice or more compared to other households (odds ratio=0.62, 95% CI 0.42-0.90, p=0.012). The odds of TS did not differ between children living in a household with and without a latrine. A lower odds of TS was observed for children living in a household reporting use of an improved source of water and with round-trip collection of water within 30 min, but the effect was not statistically significant for either age group specifically. TS was less likely among children aged 1-10 years combined when living in a household with round-trip collection of water within 30 min (odds ratio=0.70, 95% CI 0.51-0.95, p=0.024). In these age-group specific effect models, living in a house with a case of TT (odds ratio=1.8, 95% CI 1.2-2.9, p=0.008) and having TI (2.7, 95% CI 2.0-3.7) were associated with higher risk of TS.

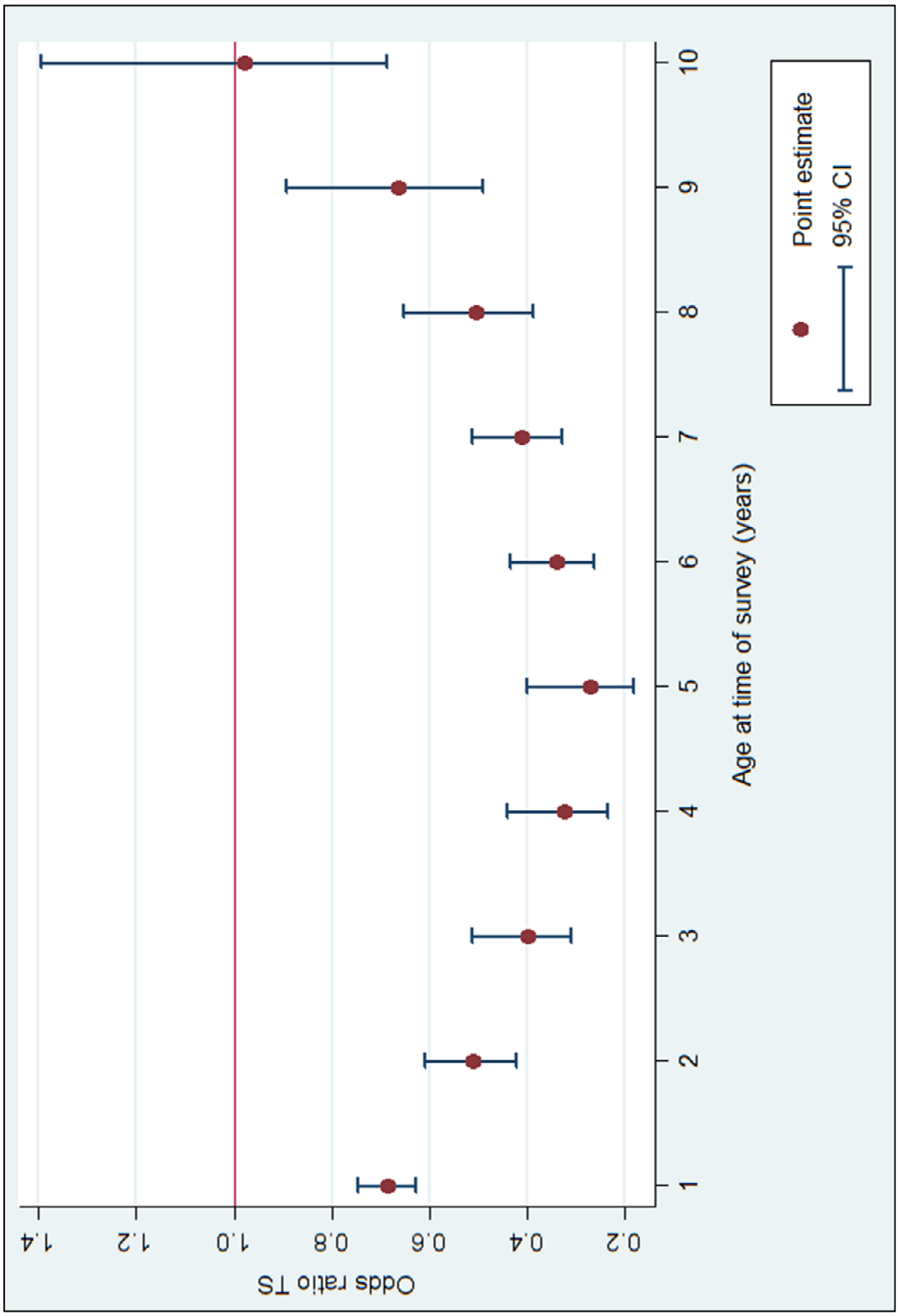

Figure 6.4. Age-specific odds ratios of TS after 5 years *versus* no years of life exposure during SAFE interventions

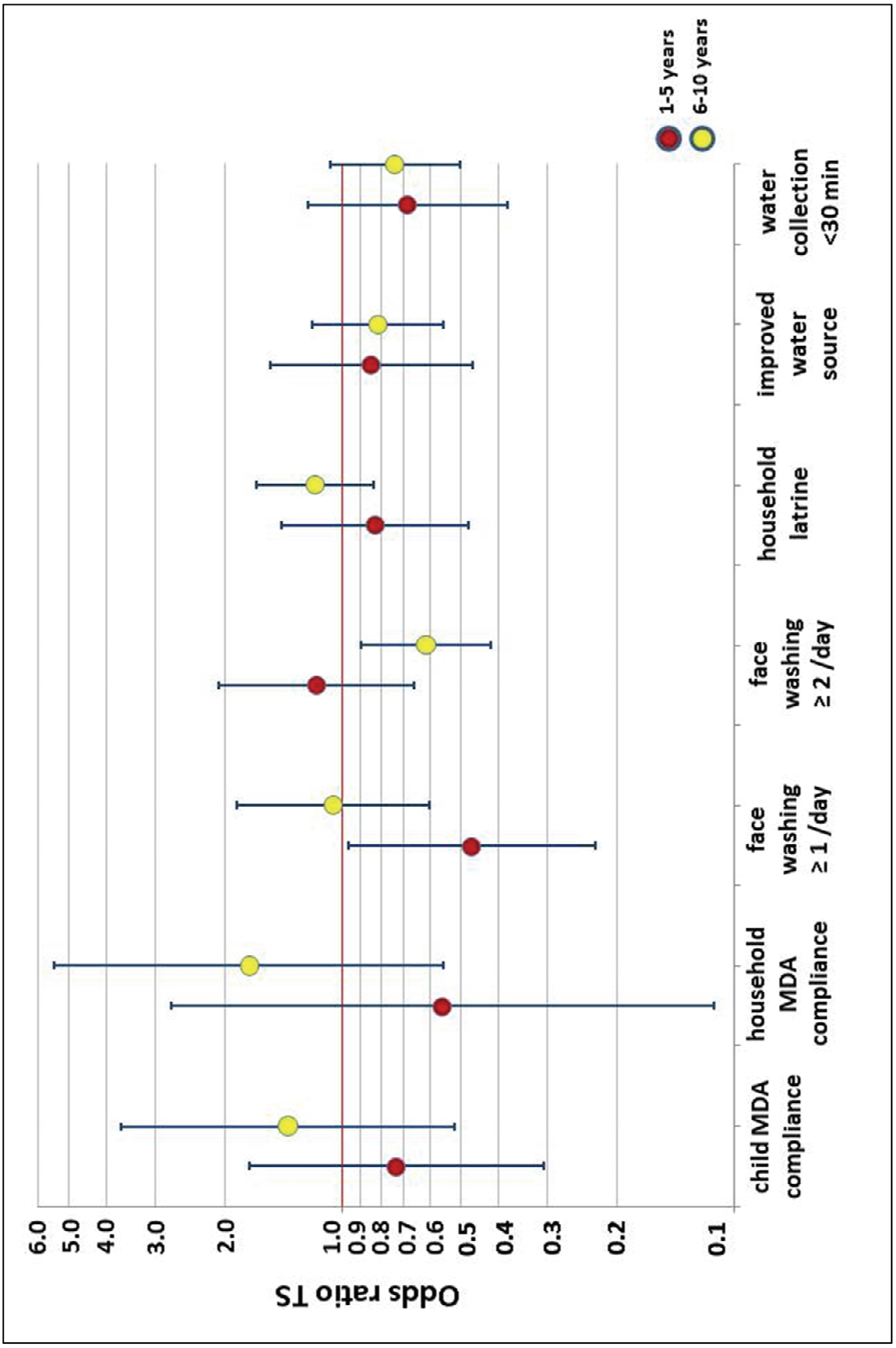

Figure 6.5. Odds ratio of TS by SAFE intervention indicator for children aged 1-5 and 6-10 years of age in 2011

6.5. Discussion

The prevalence of TS has significantly reduced among children aged 1-10 years since baseline survey in all districts of South Gondar, Ethiopia. This decline coincides with the implementation of the SAFE strategy, including five annual rounds of MDA with azithromycin. The exposure analysis, adjusted for secular variation, suggests a dose-response in children born since the start of interventions with the greatest impact seen in children born within the year the intervention activities were first implemented. This effect became less significant in those children having increased years lived prior to the introduction of interventions. This suggests that the children born since the interventions began have benefited the most from the integrated control measures and older children had not received the same benefits when they were younger. The apparent delay in presentation of TS in children moving out of the period of highest ocular promiscuity (under 10 years) predicts reduced or delayed presentation of cicatricial trachoma which may have the greatest impact in preventing blinding trachoma given that infection and intense inflammation occurs most frequently in that age group.

Chronic trachomatous inflammation which happens most frequently in childhood can persist among adults with repeated exposure to *C. trachomatis* or other bacterial pathogens leading to worsening of scarring (Bobo et al., 1997; Muñoz et al., 1999; Burton et al., 2011b; Hu et al., 2011). Considerably less inflammation was found in post-intervention surveys compared to baseline surveys suggesting less frequent and severe infection and scarring development (Ngondi et al., 2009a; Wolle et al., 2009b; King et al., *at review*). MDA using azithromycin has been shown to reduce *C. trachomatis* infection in hyper-endemic areas in a similar area in Ethiopia and low levels of infection were observed in the 2007 survey (Ngondi et al., 2009a; Gebre et al., 2012). This would suggest that distribution of antibiotics has had a similar effect in South Gondar. However, we found no linear association between the presence of scarring in children and individual or household indicators of antibiotic coverage. It is perhaps due to scarring being a chronic condition, rather than an acute indicator of transmission such as the presence or absence of infection which is directly susceptible to antibiotics. However, the lack of correlation to scarring might be explained by below-target compliance at the individual and household level. While 80% of the population may have taken at least one round of antibiotics, the children in these impact surveys reported taking azithromycin in less than 60% of the available distribution rounds. Despite the low coverage, the exposure effect on TS observed may well be measuring a herd effect of the MDA reducing *C. trachomatis* infection prevalence even in the untreated population as found with frequent azithromycin distribution in another part of Ethiopia, but we have no infection data currently available to support this hypothesis (Chidambaram et al., 2004; House et al.,

2009). What was certain is that children living in households within close proximity to water, regardless of time period and exposure, were less likely to have TS. Additionally, younger and older children were less likely to have scarring when living in households reporting the promoted behaviour of face washing at least once or twice daily, respectively. This finding further supports the presumption that using water for face washing (the F component enabled by access to water) has a persistent, independent effect of preventing trachoma (Emerson et al., 2000b).

Our study design does not allow us to infer causality. Trachoma was eliminated from Europe and the USA over time without antibiotic distribution or concerted interventions which is likely the result of social and economic development (Taylor, 2008). While we adjusted for the temporal variation between the surveys, we have collected only limited data at the household and community level. Hence we have no information on the socio-economic and development changes that might have occurred in the ten-year time span. However, we have reported elsewhere increases in household access to water and improved sanitation in South Gondar, changes that have paralleled secular declines in active trachoma observed in Malawi and a community in the Gambia in the absence of trachoma-control specific interventions (Dolin et al., 1997; Hoechsmann et al., 2001; King et al., *in press*). Secular declines in trachoma are not consistent within the literature and trachoma has been observed to remain unchanged in a more similar epidemiological setting of Tanzania with persistent, incident scarring development among children (House et al., 2007; Wolle et al., 2009a). Our study is also limited by the potential variation in inter-observer reliability in diagnosing TS between the different surveys. The assumption is that any measurement bias introduced was non-differential. Inter-observer agreement for the clinical sign of TS was high (kappa >0·7) in the development of the grading system (Thylefors et al., 1987). While the decision to select the best trachoma graders in each survey was based upon correct grading of trachomatous inflammation follicular (TF) and TT (clinical signs on which programmatic decisions are made according to WHO guidelines), all signs of the simplified grading system were taught and included in the reliability studies of both photographs and patients during the survey training.

Based on the following Bradford Hill criteria (Hill, 1965), we attribute the observed decrease in odds of TS with cumulative exposure to a non-specific combined effect of implementing the SAFE strategy. The model for the exposure analysis establishes temporality and included a term for the year of the survey which would have captured any unmeasured, secular variation over the time period. There was also clear observation of a dose-response for years lived under the intervention package. In addition to biologic plausibility, the association is coherent and analogous with the impact of the interventions on *C. trachomatis* infection and inflammation. Additional support for our conclusion might come

from repeating the analysis with temporal data from other areas under SAFE interventions. A question beyond causality is determining what impact stopping these concerted SAFE interventions, including MDA, will have on cicatricial trachoma.

To determine the need for SAFE interventions and measure programme success, the WHO recommends estimating the prevalence of TF in children aged 1-9 years. TF was suggested as a standardised indicator of transmission of *C. trachomatis* in the community, yet the presentation of follicles is known to persist for months in communities without demonstrable *C. trachomatis* infection (Muñoz et al., 2011; Gebre et al., 2012;, Keenan et al., 2012a). After implementing the SAFE strategy for years in this zone, including five annual rounds of MDA, TF has not been reduced to below recommended elimination thresholds (King et al., *at review*). Other studies have shown successful reduction of TF and infection with the introduction of SAFE interventions including three rounds of MDA indicating reduced transmission (Ngondi et al., 2006b; Roba et al., 2011). Our study demonstrates a decline in disease progression due to trachoma among children and suggests that TS provides additional evidence to measure programme impact. As designed, TS indicates the amount of cicatricial trachoma in the community (Thylefors et al., 1987). However, there has been no discussion of an elimination threshold as a measure of programme success based on prevalence of TS, but in the absence of cicatricial trachoma, there can be no risk of blinding trachoma.

Our method of using age-dependent exposure weights has been inspired by polynomial distributed lag models as they are frequently used to assess effects of cumulative exposure in environmental health studies (Zanobetti et al., 2000; Liu et al., 2011; Mehta et al., 2012). We applied this methodology for the first time to measure potential cumulative impact of years lived in an environment where the SAFE interventions were being implemented. By weighting each year of exposure with a cubic function of the age of the child in that year, we were able to observe a potential dose-response of decreased odds of TS with each year lived after the SAFE strategy was implemented. The observed patterns also suggest that the highest benefit of the intervention occurred in the first years of life. This method may have broader applications to other neglected tropical disease control programmes involving repeated interventions.

In this area of Ethiopia, a significant reduction of scarring has occurred in the most vulnerable age groups and likely has significantly prevented disability due to trachoma in the years to come. These data give great optimism that the implementation of the SAFE strategy is having the desired effect against the risk of blinding trachoma, even though the current indicator of programme success (TF) remains above prescribed elimination thresholds. Additionally, the environmental improvements promoted through SAFE have ancillary benefits such as reduced helminthiasis, which has also been observed in this zone recently

(Ziegelbauer et al., 2012, King et al., *in press*). Together, these results predict a long-term beneficial effect of a time-limited, intensive control programme.

6.6. Conflicts of interest

Several of the authors work for The Carter Center which provides support to the Amhara National Regional State Health Bureau for the implementation of the SAFE strategy to control trachoma

6.7. Acknowledgements

We are thankful for the collaboration of the Lions-Carter Sight-First Initiative and the Regional Health Bureau that provide funding for trachoma control in Amhara National Regional State, Ethiopia and provided funding for these surveys to evaluate the programme. We acknowledge the critical review and suggestions provided by Dr. Donald R. Hopkins in the formation of this manuscript. We are grateful to the data collection teams and their coordinators for each one of the randomised cross-sectional studies. Finally, we are most grateful to all the surveyed residents of South Gondar who volunteered their time for interview and examination.

Figure 7.1. School children in Ethiopia (courtesy Lisa Rotondo, The Carter Center)

7. Trachoma among children in community surveys from four African countries and implications of using school surveys for evaluating prevalence

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7.1. Abstract

***Background**:* School surveys provide a convenient platform to obtain large child cohorts from multiple communities and are widely used as a proxy to determine community prevalence of neglected tropical diseases. The purpose of this study was to compare trachoma prevalence between preschool- and school-aged children and children who attend and do not attend school.

***Methods**:* We analysed data from community-based trachoma surveys conducted from 2008–2011 in Ethiopia, Mali, Niger and Nigeria. The surveys utilised a cross-sectional, randomised cluster design. Individual-level data on school attendance was collected.

***Results**:* Overall, 75 864 children aged 1-15 years from 2100 communities were included in the analysis. The prevalence of trachomatous inflammation follicular (TF) among these children in surveyed districts was 19.1% (95% CI 17.9–20.2%) in Ethiopia, 6.2% (95% CI 5.4–6.9%) in Niger, 4.6% (95% CI 4.2–4.9%) in Mali and 4.2% (95% CI 3.5–4.9%) in Nigeria. Controlling for age, sex and clustering, the odds ratio of TF for school-attendees compared to non-attendees was 0.64 (95% CI 0.56–0.73) in Ethiopia, 0.67 (95% CI 0.56–0.80) in Mali, 1.03 (95% CI 0.81–1.16) in Niger and 1.06, (95% CI 0.65–1.73) in Nigeria.

***Conclusion**:* Estimating the prevalence of trachoma through examination of only school-going children risks underestimating the true prevalence.

7.2. Introduction

Surveys are required for mapping, monitoring, and the evaluation of neglected tropical diseases (NTDs) that are targeted for control and elimination by preventive chemotherapy and integrated intervention packages (WHO, 2006a; Brooker et al., 2009; Chammartin et al., *at review*). For example, the prevalence of clinical signs of trachoma is typically measured through cluster randomised household surveys to determine the need for, or monitor the impact of, control programmes (WHO, 2006b). Community-based household surveys generate prevalence estimates of trachomatous inflammation follicular (TF) based on a representative sample of the community on which programmatic decisions are based according to guidelines issued by the World Health Organization (WHO) (WHO, 2006b). This type of survey is recommended, as it is feasible to implement, requires reasonable financial input, but needs considerable human resources (Ngondi et al., 2009b; Chen et al., 2011; King et al., *at review*). Recent efforts to integrate mapping of multiple NTDs have utilised or suggest utilising school-based surveys (King et al., 2009; Baker et al., 2010; Koukounari et al., 2011; Pelletreau et al., 2011). Indeed, school-based surveys are often used as a proxy to determine community prevalence in NTD control programmes such as schistosomiasis, soil-transmitted helminthiasis, and lymphatic filariasis as they provide the convenience of a readily accessible and assembled cohort of children from multiple communities (Lengeler et al., 2002; WHO, 2002a, 2011).

In this study we utilise large-scale community-based survey data from trachoma control programmes in four African countries to determine whether trachoma prevalence differed among preschool-aged and school-aged children and, among the latter, to determine whether the prevalence differs between those who attend school and those who do not. Additionally, we explore whether school-attendees and non-attendees differ in gender, having a clean face and participation in mass distribution of antibiotics for trachoma control. The implications of our findings are discussed concerning estimating the true prevalence of trachoma for starting, implementing, and evaluating control or elimination efforts.

7.3. Materials and methods

7.3.1. Ethics statement

The study protocols were reviewed and approved by Emory University Institutional Review Board (IRB protocol #079-2006). Additionally, the surveys were approved by the local ethical review committee from the health administrations in each country. Verbal informed consent in these surveys was approved in the protocol and recorded prior to data collection rather than written information and a signed statement due to the high level of illiteracy in the surveyed populations. Consent for trachoma examination and interview was obtained from

heads of households, individuals, and parents/guardians of minors. In addition to parental consent, oral assent for examination and interview was obtained from school-aged children.

7.3.2. Sampling methodology

Box 7.0 defines several terms utilised in this paper to help clarify our methods. We analysed data from cross-sectional, community-based surveys conducted in 2008-2011 in Ethiopia, Mali, Niger, and Nigeria. The surveys were designed to measure the prevalence of trachoma clinical signs at the district or other implementation units, as part of ongoing trachoma control programmes. Details of the sampling methodology of each survey have been described elsewhere (Bamani et al., 2010b, Bamani et al., 2010a, King et al., 2010, King et al., *at review*). In brief, probability sampling was used to randomly select communities (clusters) and households within selected communities aligning with other standardised household survey protocols (Turner et al., 1996, UNICEF, 2006a). At each household an interview was conducted with the head of household or designated respondent. All household residents were examined for the presence or absence of all five clinical signs (TF, trachomatous inflammation follicular; TI, trachomatous inflammation intense; TS, trachomatous scarring; TT, trachomatous trichiasis; and CO, corneal opacity) of the simplified trachoma grading system in both eyes, using 2.5x binocular loupes and adequate light (Thylefors et al., 1987). Training prior to each survey followed WHO guidelines, which included a rigorous selection process for trachoma graders based on the ability of graders to apply the trachoma grading system (WHO, 2006b). Graders achieving agreement with a 'gold' standard of ≥80% (Nigeria) or a kappa ≥0.7 (Ethiopia, Mali, and Niger) specifically on the clinical sign TF were selected for clinical grading during the survey.

All residents of selected households present at the time of the interview, including all children were enrolled in the surveys. Prior to examination, each child was asked whether he/she attended school. The definition of school was clarified to exclude religious or informal schools. The face of children aged 1-9 years was observed for the presence or absence of ocular and nasal discharge. Those children with no ocular and nasal discharge were recorded as having a clean face. In districts where the primary purpose of the survey was to measure impact after control interventions (Ethiopia, some districts in Mali and Niger), children were asked whether they took antibiotics during mass drug administration (MDA) campaigns for trachoma. To improve recall, antibiotics distributed in MDA were shown to the children (tablets or suspension bottle with description of the suspension). For preschool-aged children, the responses of their parents/guardians were accepted.

Box 7.1. Definitions of common terms referenced

- **Community-based survey**: epidemiological study where people in their households represent the sample population
- **School-based survey**: epidemiological study where children attending school represent the sample population
- **School attendance**: "yes" response when asked "do you attend school regularly?" during community-based surveys
- **Preschool-aged**: children aged 1-5 years
- **School-aged**: children aged 6-15 years
- **TF**: trachomatous inflammation follicular
- **TI**: trachomatous inflammation intense
- **Clean face**: absence of ocular and nasal discharge on the face of children aged 1-9 years
- **WHO recommended indicators for trachoma control intervention decisions**: TF among children aged 1-9 years (4)
- **MDA**: mass drug administration

7.3.3. Statistical analysis

To assess age-specific TF prevalence and reported school attendance, stratified by country, we modeled the relationship between age and TF with a polynomial term of age to fit the observed estimates. Robust variance estimation for proportions and means was used to adjust for clustering at the household and community level through the *survey data* commands in Stata version 12.0 (Stata Corp.; College Station, TX, USA). Statistical comparisons between proportions were adjusted also for the cluster design utilising the second-order corrected Pearson statistic (Rao and Scott, 1984). We defined statistical significance as p-values < 0.05. Multilevel logistic regression was employed for analysis of the association between TF and reported school attendance expressed as prevalence odds ratio (OR), controlling for sex, and clustering at both the community and household level separately for each country. We adjusted for age by limiting the analysis to only school-aged children 6-15 years of age and including age as a continuous variable in the models. A fixed effect meta-analysis was then performed using the country-specific odds ratios and respective confidence intervals to obtain an overall summary odds ratio of TF between school attendees and non-attendees (Harris et al., 2008).

We simulated district-level prevalence of TF that might have been identified through school surveys by limiting the analysis to only school attendees and classified districts to either ≥10% or <10% TF. We then compared these classifications to our 'gold' standard classifications based on actual district-level prevalence of TF among children aged 1-9 years from the surveys as implemented. The following summary statistics and 95% confidence intervals (CIs) were calculated in Stata: sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). We chose the threshold of 10% as this is the prevalence at which the need for mass antibiotic distribution is determined when mapping and additional sub-district prevalence investigation is warranted after impact assessment surveys.

7.4. Results

7.4.1. Operational results

In total, 75,864 children were examined in 32,393 households from 2,100 communities across the four countries (Table 7.1). Highlighted in Figure 7.2 are 101 districts from where the data was collected during either baseline mapping or post-intervention trachoma prevalence surveys (impact). Among households with child residents, the mean number of children aged 1-15 years was 3.3 (standard deviation (SD) 2.6) in Nigeria; 2.5 (SD 1.6) in Mali; 2.2 (SD 1.4) in Niger; and 2.1 (standard deviation (SD) 1.1) in Ethiopia.

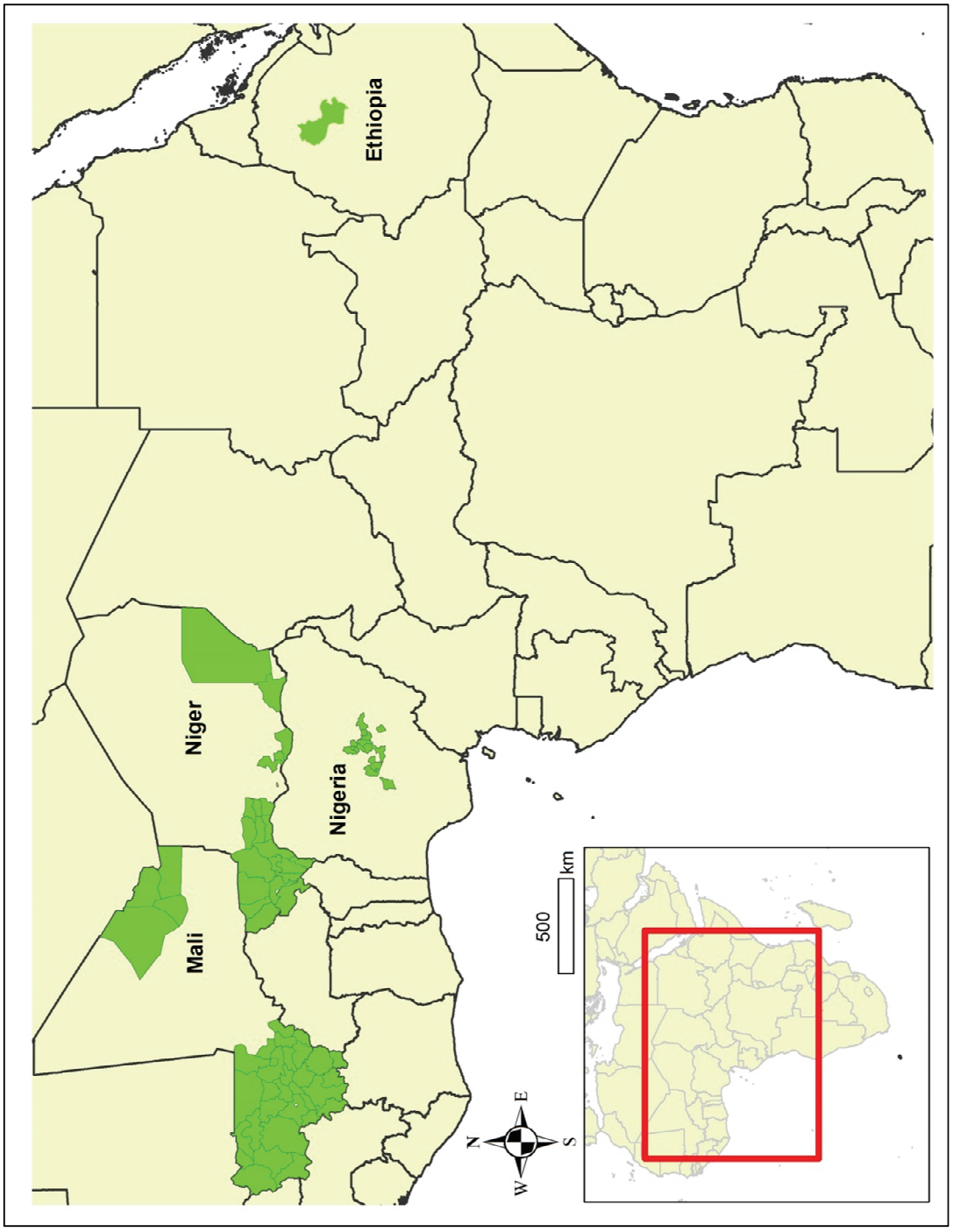


Figure 7.2. Map of surveyed districts included in analysis

Table 7.1. Description of data sets by country collected during cross-sectional cluster randomised surveys between 2008-2011

Country	Survey type	Districts	Clusters	Households*	Children examined**
Ethiopia	Impact	25	711	14,211	29,251
Mali	Mapping / impact	36	647	9,656	25,262
Niger	Mapping / impact	23	452	5,916	12,825
Nigeria	Mapping	17	290	2,610	8,526
Total		101	2,100	32,393	75,864

*Households surveyed with children aged 1-15 years; **Children aged 1-15 years

7.4.2. School attendance

School attendance varied by country. The proportion of school-aged children (6-15 years) attending school was 87.1% (5,023/5,766; 95% CI 85.2-89.0%), 64.3% (12,928/20,099; 95% CI 62.7-66.0%), 49.7% (9,627/19,381; 95% CI 47.7-51.6%), and 47.1% (5,066/10,764; 95% CI 44.9-49.2%) in Nigeria, Ethiopia, Mali, and Niger, respectively. The age-specific school attendance is shown in Figure 2 for school-aged children by country. Nigeria had the highest attendance rates with >80% of children above age 5 years reporting to attend school. Peak attendance was observed for the ages 10-14 years in Ethiopia, 8-13 years in Mali and 7-11 years in Niger (Figure 2). The proportion of communities surveyed where there were no children reporting school attendance was 9.1% (59/647) in Mali, 7.5% (34/452) in Niger, 1.0% (3/290) in Nigeria and 0.4% (3/711) in Ethiopia.

7.4.3. Description by school attendance

A description of school-aged children is presented in Table 7.2 for each country by school attendance. School attendees were older than non-attendees in Ethiopia ($t=37.55$, $p<0.001$) and Mali ($t=8.78$, $p<0.001$) and younger than non-attendees in Niger ($t=-3.23$, $p=0.001$). Girls were more likely to report going to school than boys in Ethiopia ($F=15.04$, $p<0.001$). The opposite was found in Mali ($F=48.25$, $p<0.001$) and Niger ($F=144.98$, $p<0.001$) with significantly more boys attending school than girls. There was no statistically significant difference between girls' and boys' school attendance in Nigeria ($F=1.98$, $p=0.160$).

Children attending school had cleaner faces than those not attending in Ethiopia ($F=14.77$, $p<0.001$) and Niger ($F=5.44$, $p=0.020$). This difference in facial cleanliness was not observed in Mali ($F=0.58$, $p=0.447$) and Nigeria ($F=3.28$, $p=0.071$). In areas where MDA

had been implemented for trachoma control, children attending school in Ethiopia (F=246.70, p<0.001) and Niger (F=61.12, p<0.001) were more likely to have ever taken antibiotics than children not attending school. School-attending children were more compliant in MDA than children not attending school in Ethiopia (t=10.27, p<0.001), but not in Niger (t=0.96, p=0.336).

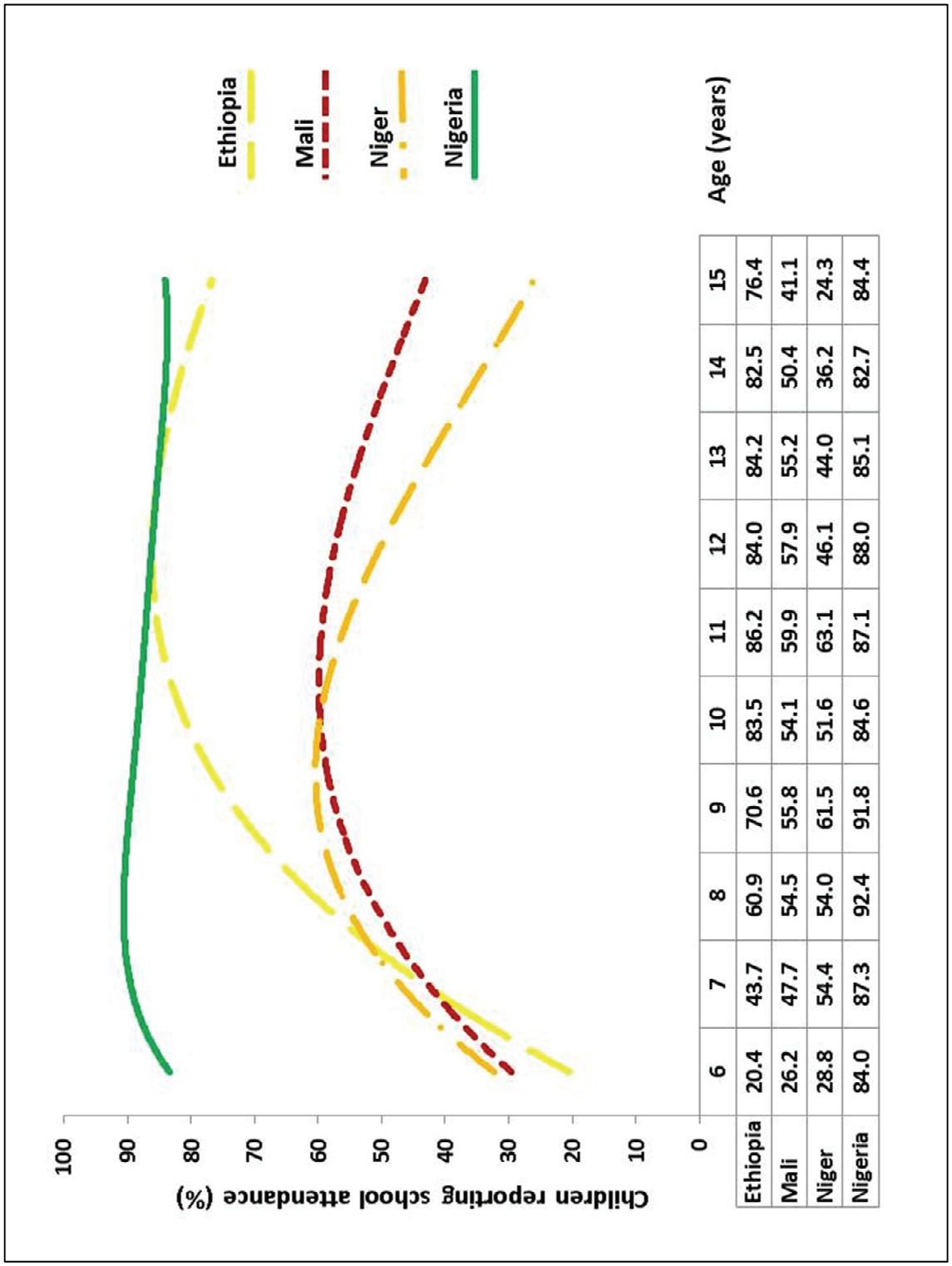
7.4.4. Prevalence of trachoma clinical signs

Among children aged 1-9 years the prevalence of TF was 23.4% (4,870/20,835; 95% CI 22.0-24.7%) in Ethiopia, 8.7% (681/7,858; 95% CI 7.7-9.7%) in Niger, 5.7% (889/1,5725; 95% CI 5.2-6.1) in Mali and 5.0% (292/5,865; 95% CI 4.1-5.9%) in Nigeria. Age-specific prevalence of TF is plotted in Figure 7.4 for each country. The prevalence of TF was highest among children aged 2-5 years in Ethiopia and Niger. The same pattern was not as pronounced in Mali and Nigeria. Adjusted for clustering and female gender, TF was more common in preschool-aged children than school-aged children in all countries (OR=4.34, 95% CI 3.99-4.71 in Ethiopia; OR=1.18, 95% CI 1.02-1.37 in Mali; OR=4.48, 95% CI 3.64-5.51 in Niger; OR=1.30, 95% CI 1.01-1.67 in Nigeria). TI was also more common among preschool-aged children than school-aged children in Ethiopia (OR=1.84, 95% CI 1.63-2.08), Mali (OR=1.52, 95% CI 1.06-2.16), and Niger (OR=3.06, 95% CI 1.96-4.79), but not significantly so in Nigeria (OR=2.03, 95% CI 0.83-4.98). Among school-aged children, the prevalence of TF was lower among school attendees (Table 2) in Ethiopia (F=69.51, p<0.001) and Mali (F=40.88, p<0.001). No difference in TF prevalence was observed in Niger (F=0.06, p=0.802) or Nigeria (F=0.04, p=0.835) between school-aged children attending and not attending school. TI also differed among school-aged children by school attendance in Ethiopia (F=57.48, p<0.001) and Mali (F=4.90, p=0.027). Adjusting for age, sex and clustering at the community and household level, the odds of TF among school-aged children attending *versus* not attending school are plotted in Figure 7.5. School attendees were less likely to have TF than those not attending school in Ethiopia (OR=0.64, 95% CI 0.56-0.73) and Mali (OR=0.67, 95% CI 0.56-0.80). In Nigeria (OR=1.06, 95% CI 0.65-1.73) and Niger (OR=1.03, 95% CI 0.81-1.16) there was no statistically significant difference in having TF between children who attend and do not attend school. The summary odds ratio of TF between school attendees and non-attendees was 0.71 (95% CI 0.65-0.78).

Table 7.2. Description of school-aged children (6-15 years) surveyed by reported school attendance by country

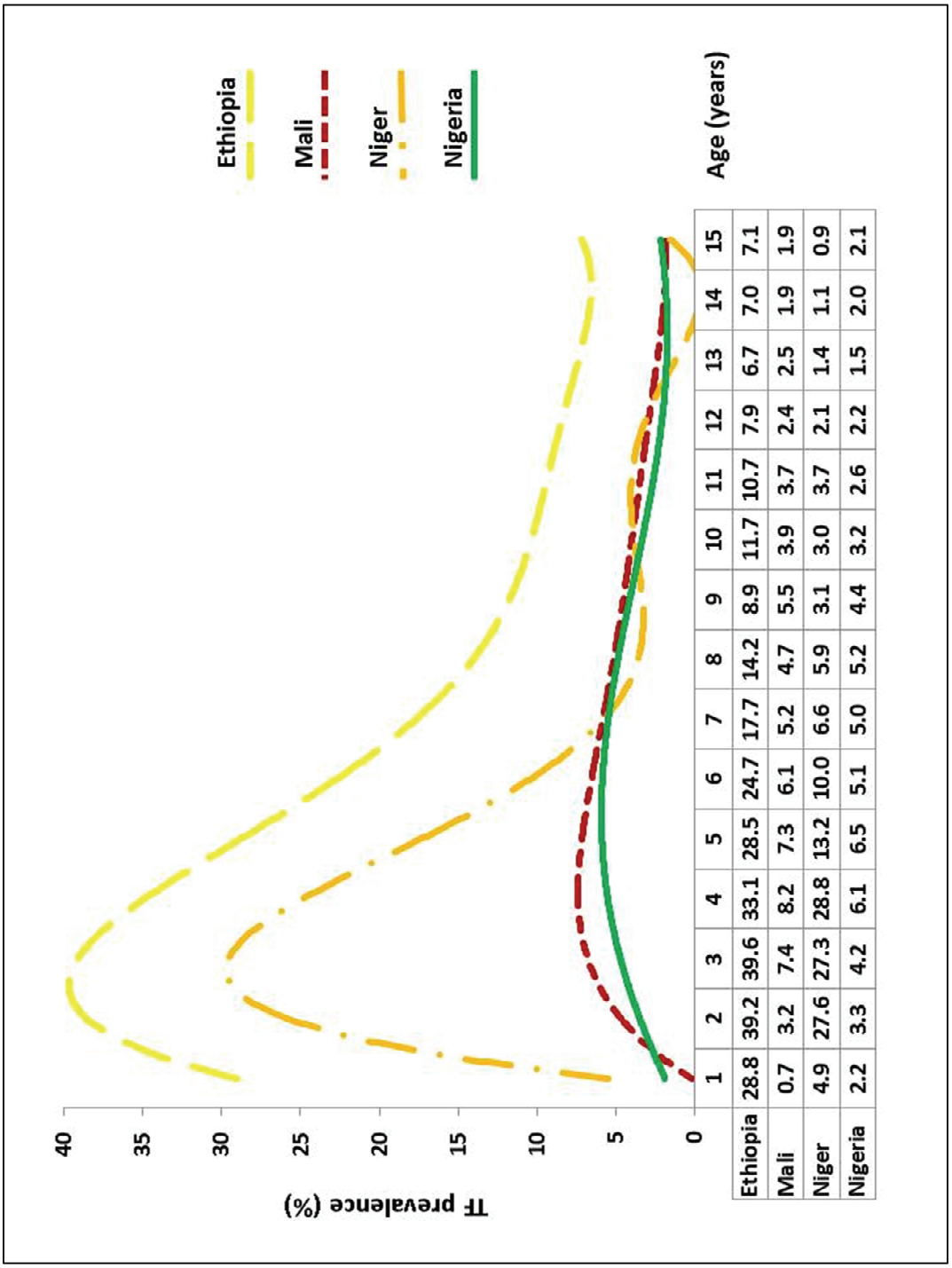
	Ethiopia		Mali		Niger		Nigeria	
	Attend	**Do not attend**	**Attend**	**Do not attend**	**Attend**	**Do not attend**	**Attend**	**Do not attend**
Mean age (SD, IQR)	10.4 (2.6, 8-13)	8.4 (2.6, 6-9)	10.0 (2.6, 8-12)	9.6 (2.9, 7-12)	9.4 (2.5, 7-11)	9.6 (3.0, 7-12)	9.6 (2.8, 7-12)	9.8 (3.0, 7-12)
Percentage girls (95% CI)	53.9 (53.0-54.9)	50.8 (49.5-52.2)	45.7 (44.6-46.8)	51.4 (50.3-52.5)	46.3 (44.6-47.9)	60.0 (58.4-61.5)	49.3 (47.0-51.6)	52.6 (48.7-56.6)
Proportion with clean face (95% CI)	89.8 (87.6-91.5)	84.8 (82.8-86.7)	78.4 (76.7-80.1)	79.3 (77.7-80.9)	62.7 (60.6-64.9)	59.0 (56.8-61.1)	57.2 (54.1-60.2)	64.5 (57.1-71.3)
Proportion taken antibiotics (95% CI)	97.8 (97.3-98.2)	87.8 (85.2-90.0)	91.7 (89.4-93.6)	90.6 (88.1-92.5)	95.9 (94.5-96.9)	87.6 (84.3-90.3)	NA	NA
Mean compliance in MDA* (95% CI)	85.8 (84.9-86.8)	73.8 (71.3-76.3)	NA	NA	52.3 (49.9-54.7)	50.7 (48.3-53.0)	NA	NA
Proportion with TF (95% CI)	10.4 (9.5-11.5)	16.6 (15.2-18.1)	3.0 (2.6-3.4)	5.2 (4.7-5.8)	4.6 (3.9-5.4)	4.7 (4.0-5.5)	3.8 (3.1-4.6)	3.6 (2.4-5.4)
Proportion with TI (95% CI)	3.2 (2.8-3.7)	6.0 (5.3-6.8)	0.4 (0.3-0.6)	0.7 (0.5-0.8)	1.0 (0.7-1.5)	1.1 (0.9-1.5)	0.2 (0.0-0.5)	0.3 (0.0-1.1)

CI, confidence limits; MDA, mass drug administration with antibiotics; NA, not applicable, either no MDA had occurred or number of times taken antibiotic in MDA was not recorded; *proportion of possible annual MDA campaigns in which antibiotics were reported taken (up to 3 campaigns)



	6	7	8	9	10	11	12	13	14	15
Ethiopia	20.4	43.7	60.9	70.6	83.5	86.2	84.0	84.2	82.5	76.4
Mali	26.2	47.7	54.5	55.8	54.1	59.9	57.9	55.2	50.4	41.1
Niger	28.8	54.4	54.0	61.5	51.6	63.1	46.1	44.0	36.2	24.3
Nigeria	84.0	87.3	92.4	91.8	84.6	87.1	88.0	85.1	82.7	84.4

Figure 7.3. Reported school attendance among school-aged children in surveyed areas



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Ethiopia	28.8	39.2	39.6	33.1	28.5	24.7	17.7	14.2	8.9	11.7	10.7	7.9	6.7	7.0	7.1
Mali	0.7	3.2	7.4	8.2	7.3	6.1	5.2	4.7	5.5	3.9	3.7	2.4	2.5	1.9	1.9
Niger	4.9	27.6	27.3	28.8	13.2	10.0	6.6	5.9	3.1	3.0	3.7	2.1	1.4	1.1	0.9
Nigeria	2.2	3.3	4.2	6.1	6.5	5.1	5.0	5.2	4.4	3.2	2.6	2.2	1.5	2.0	2.1

Figure 7.4. Age-specific prevalence of TF by country among children aged 1-15 years

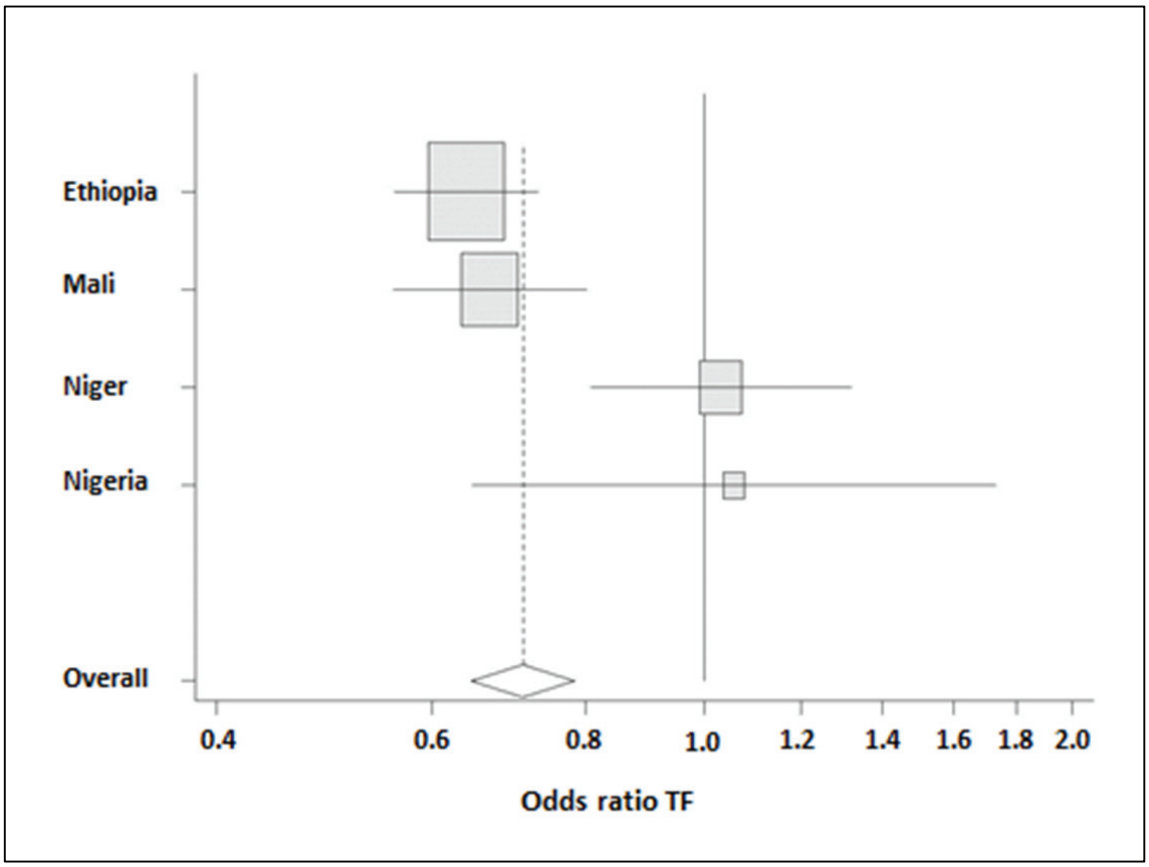


Figure 7.5. Country specific and overall adjusted prevalence odds ratios of TF among school-aged children attending *versus* not attending school

7.4.5. Simulated diagnostic comparison

Table 7.3 presents the summary findings of the classification of the 101 surveyed districts according to TF prevalence as defined by analysis of only school-attendees *versus* classification based on the actual survey findings. The proportion of districts correctly classified as ≥10% TF from analysis of only school-attendees had a sensitivity of 52.8% (19/36). The proportion of districts classified as ≥10% TF by school-attendee analysis that were also identified as ≥10%TF in the surveys had a PPV of 95.0% (19/20).

Table 7.3. Diagnostic summary statistics for the classification of surveyed districts (N=101) to ≥10% or <10% trachomatous inflammation follicular (TF) as estimated from analysis of school attendees only compared to classification from the true prevalence of TF among children aged 1-9 years as determined during community-based surveys

Districts classified based on all children aged 1-9 years as surveyed	Districts classified based on school attendees only	
	≥10% TF	<10% TF
≥10% TF	19	17
<10% TF	1	64
Summary		
Sensitivity	52.8%	(35.5 – 69.6%)
Specificity	98.5%	(91.7 – 99.9%)
Positive predictive value	95.0%	(75.1 – 99.9%)
Negative predictive value	79.0%	(68.5 – 87.3%)

7.5. Discussion

Consistent across three of the four study areas, school-attending children differed from their non-school-attending counterparts in sex and age. More school-attending than non-attending children in two of the three countries where trachoma interventions had been implemented had ever taken antibiotics during the community-based MDA. In Ethiopia and Niger, the faces of children attending school were observed to be cleaner than children not attending. The obvious difference observed between countries was the ratio of reported school attendance. We did not observe differences between the school-aged children attending and not attending school in Nigeria, as reported attendance in the surveyed areas was uniquely high, which is consistent with the findings from a previous study determining no difference in TF prevalence estimates between school-based and community-based integrated surveys (King et al., 2009).

Schools are often targeted for disease assessment and interventions due to the ease of accessibility and availability of children from multiple communities (Lengeler et al., 2002; Brooker et al., 2009; Kihara et al., 2011). School-based survey methodology is also being promoted in integrated NTD mapping methodology as operationally more feasible than traditional community-based cluster surveys (Pelletreau et al., 2011). However, of immediate importance to trachoma is that school-based surveys exclude adults who are also necessary for determining whether blinding trachoma is a public health problem and upon which to plan sight-saving surgeries.

Our findings raise important questions that warrant consideration by trachoma and perhaps other NTD control and elimination programmes and these are offered for consideration. A first issue is whether school-based surveys provide valid estimates of prevalence in the communities. We simulated a school-based sample by limiting analysis to only school-attendees and estimating TF prevalence. By doing so, we determined a school-based survey strategy would have misclassified nearly half of the districts as not warranting control interventions when actual TF prevalence among children aged 1-9 years indicated control measures were warranted according to WHO guidelines. While school attendance likely influenced this outcome, age also plays a factor. Children attending school are not always the target age group recommended for prevalence assessment. For example, trachoma programme decisions are based on estimates of TF prevalence in children aged 1-9 years (WHO, 2006b). In this study, the age group with the highest frequency of TF (1-5 year-olds) is considered too young to attend school. A prevalence estimate based on children in school would not provide an estimate of prevalence in the recommended age group and more importantly would then underestimate it and perhaps misclassify communities as areas not needing control interventions as our analysis suggests. Controlling for age-prevalence differences, children attending school in two of the countries included in this study were 33-36% less likely to have TF than children not attending. Our data are not generalisable to other NTDs as the transmission dynamics and infection patterns are often unique for each disease. However, a study in Zanzibar found higher prevalence and twice as many intense soil-transmitted helminth infections among younger children not in school compared to older children attending school (Montresor et al., 2001b). These findings should be taken into consideration so as not to exclude endemic areas from interventions when initiating or scaling down disease control programmes.

Other crucial questions brought to our attention from the secondary data analysis presented here, are whether children not in school are benefiting as much as school-going children from disease control interventions and whether these control efforts are indeed reaching all children in the community. The higher proportion of clean faces observed in children reporting to attend school may suggest that the desired behaviour of face washing is being practiced more often than among children not in school. In Ethiopia, Mali, and Niger, behaviour change communication for trachoma control is being delivered in primary schools as well as through health extension workers and volunteers in the community. MDA for trachoma is community-based from central distribution points, rather than school-based distribution, yet we found higher reported drug coverage among reported school attendees. While it is encouraging to know school-going children may be benefiting from disease control interventions, it is discouraging to observe a disparity between children who do not attend school. Recent monitoring of another MDA programme targeted to control intestinal

helminths in Cambodia similarly found that children who were not enrolled or who did not attend school were less likely to receive the drug treatments in a school-based distribution strategy (Chesnaye et al., 2011). While school-based MDA strategies in Sierra Leone have shown success in reducing intestinal helminth infections among school children, no community-based assessment was conducted in parallel to determine whether similar impact was observed in children not attending school (Hodges et al., 2012a). Of note, we observed a small proportion of surveyed communities in each country that had no children reporting school attendance. Hence, school-based disease control programmes must identify additional means to ensure that all children benefit as has been discussed in the literature and warrants renewed attention (Montresor et al., 2001a; Olsen, 2003; Massa et al., 2009) .

The analysis presented in this study was not the primary purpose of the surveys and we were not able to compare results from actual school-based and community-based surveys as has been done previously (King et al., 2009). We used community-based prevalence data from epidemiological rigorous household surveys employing standardised methods basing the analysis on the responses of children and their caretakers of whether the child attended school. The purpose of our study was not to quantify in detail the scholarship of school-aged children and we did not attempt to verify school attendance with enrolment records at schools, but enrollment rates reported by household surveys are often significantly lower than school reports (UNESCO, 2010). Inquiring about the school-aged child's attendance allowed us to make simple comparisons of prevalence, but also to provide a quick evaluation of school-based behaviour change communication in some of the countries. The response of the child and/or guardian may have introduced bias, but school attendance status collected in household surveys aiming to measure health conditions is not uncommon and used by standardised household surveys such as Demographic and Health Survey (Montressor et al.,2001; Fentiman et al., 2001; USAID, 2012). The amount and type of data collected at the household was limited and varied across surveys. Therefore, we are unable to control for other potential confounding or modifying factors that may account for the differences observed. Although we cannot generalise our findings to other NTDs, we encourage the scientific community and disease control managers to investigate potential disparities among children to ensure disease control/elimination interventions are reaching and benefiting all those in need.

7.6. Conclusions

In some areas under community-based trachoma control interventions, school attendees had cleaner faces, less trachoma and reported higher coverage of MDA. The summary odds ratio from our meta-analysis suggests that using a school-based approach to monitor

prevalence of trachoma will underestimate true community prevalence, which may result in misclassifying trachoma endemic communities as not warranting control interventions, which is supported by our diagnostic comparison of simulated school-based surveys. The exception was where school attendance is very high and where there is no difference in age-specific prevalence between preschool- and school-aged children. Similar investigations should be conducted to determine whether the finding is consistent across other NTD control programmes.

7.7. Acknowledgements

We are grateful to the National Trachoma Control Programmes in each of the countries, regions, states and districts from which the data were collected in these surveys. We thank the data collection teams and their coordinators for each one of the cross-sectional surveys. Finally, we are most grateful to all the surveyed residents of the communities who volunteered their time for interview and examination.

Figure 8.1. Household latrines with hand washing containers as promoted in rural areas of the Amhara National Regional State, Ethiopia (courtesy The Carter Center)

8. Intestinal parasite prevalence in an area of Ethiopia after implementing the SAFE strategy, Enhanced Outreach Services, and Health Extension Programme

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8.1. Abstract

Background: The SAFE strategy aims to reduce transmission of *Chlamydia trachomatis* through antibiotics, improved hygiene and sanitation. We integrated assessment of intestinal parasites into large-scale trachoma impact surveys to determine whether documented environmental improvements promoted by a trachoma programme had collateral impact on intestinal parasites.

Methodology: We surveyed 99 communities for both trachoma and intestinal parasites (soil-transmitted helminths, *Schistosoma mansoni*, and intestinal protozoa) in South Gondar, Ethiopia. One child aged 2-15 years per household was randomly selected to provide a stool sample of which about 1 g was fixed in sodium acetate-acetic acid-formalin, concentrated with ether, and examined under a microscope by experienced laboratory technicians.

Principal Findings: A total of 2,338 stool specimens were provided, processed, and linked to survey data from 2,657 randomly selected children (88% response). The zonal-level prevalence of *Ascaris lumbricoides*, hookworm and *Trichuris trichiura* was 9.9% (95% confidence interval (CI) 7.2-12.7%), 9.7% (5.9-13.4%) and 2.6% (1.6-3.7%), respectively. The prevalence of *S. mansoni* was 2.9% (95% CI 0.2-5.5%) but infection was highly focal (range by community from 0-52.4%). The prevalence of any of these helminth infections was 24.2% (95% CI 17.6-30.9%) compared to 48.5% as found in a previous study in 1995. Pathogenic intestinal protozoa *Giardia intestinalis* and *Entamoeba histolytica / E. dispar* were found in 23.0% (95% CI 20.3-25.6%) and 11.1% (95% CI 8.9-13.2%) of the surveyed children, respectively. We found statistically significant increases in household latrine ownership, use of an improved water source, access to water, and face washing behaviour over the past seven years.

Conclusions: Improvements in hygiene and sanitation promoted both by the SAFE strategy for trachoma and health extension programme combined with preventive chemotherapy during enhanced outreach services are plausible explanations for the changing patterns of intestinal parasite prevalence. The extent of intestinal protozoa infections suggests poor water quality or unsanitary water collection and storage practices and warrants targeted intervention.

8.2. Author Summary

Part of the SAFE strategy (surgery, antibiotics, facial cleanliness, and environmental improvement) to eliminate blinding trachoma involves improving access to and use of water and sanitation. We combined the assessment of parasitic worm and intestinal protozoa infections with surveys of trachoma in an area of Ethiopia where the SAFE strategy together with enhanced outreach services and the health extension programme had been implemented for more than five years. We compared our findings with results from a survey conducted in the mid-1990s. We documented significant increases in household access and use of latrines and clean water: the F and E components of SAFE as promoted by the health extension programme. We found considerably lower levels of parasitic worm infections than that documented previously. We also documented-for the first time in this zone-pathogenic intestinal protozoa infections, which indicates poor water quality and unhygienic water collection and storage practices in the communities surveyed. A plausible hypothesis for the decline in parasitic worm infections might be the combined impact of ongoing simultaneous health programmes: SAFE strategy for trachoma control alongside the health extension programme and regular deworming of preschool-aged children.

8.3. Introduction

An integrated strategy of surgery, antibiotics, facial cleanliness and environmental improvement (SAFE in short) is recommended to eliminate blinding trachoma in endemic countries by the year 2020 (WHO, 1998). The F and E components aim to reduce the transmission of *Chlamydia trachomatis* via flies, fingers and fomites within the community (Emerson et al., 2000b). Face washing is promoted specifically to keep faces free of infectious ocular and nasal discharge, and make them less attractive to eye-seeking flies. The construction and use of latrines are promoted as a form of fly control to reduce fly-to-eye contact (Emerson et al., 2001; Emerson et al., 2004). Improved accessibility to clean water is also promoted, but whether or not water is used for hygiene is more important than absolute access to clean water in trachoma prevention. Where water is not readily accessible, household use of a limited supply of water may not be prioritised for bathing (West et al., 1989; Bailey et al., 1991; Polack et al., 2006). These aims of the F and E components go beyond trachoma control and align with other major initiatives, such as WASH programme of UNICEF and the Millennium Development Goal 7c which, by 2015, aim to provide access to clean water and sanitation to all children and to reduce by half the proportion of households without access to basic sanitation (UNICEF, 2006b; UN, 2010).

Improved hygiene, sanitation, and water have a positive and sustained impact on several diseases, including many of the neglected tropical diseases (Bartram and Cairncross, 2010, Ziegelbauer et al., 2012). Trachoma was eliminated from the United States of America (USA),primarily through sustained social and economic development (Taylor, 2008). The Rockerfeller Foundation noted the pivotal role sanitation played in the elimination of hookworm in the southern parts of the USA some 100 years ago (Stiles, 1939). Improving water supply and sanitation have been recommended after noting the reduction in the prevalence and incidence of parasitic worms such as dracunculiasis and soil-transmitted helminthiasis, and diarrhea and an increase in child survival (Esrey et al., 1991). A recent systematic review and meta-analysis of research studies reporting the effects of sanitation on soil-transmitted helminth infections (*Ascaris lumbricoides*, *Trichuris trichiura*, and hookworm) found that having access and using sanitation was associated with an approximately 50% lower odds of any soil-transmitted helminth infection even after accounting for random effects between studies (Ziegelbauer et al., 2012).

These are assumed ancillary benefits of the activities promoted by the F and E components of the SAFE strategy, yet these have not been fully documented in the context of an ongoing trachoma control programme. The purpose of this study was to determine prevalence of intestinal parasites (soil-transmitted helminths, *Schistosoma mansoni* and intestinal protozoa) among children aged 2-15 years to complement a large trachoma impact survey in 2011. Our data also allowed us to study changing patterns of parasitic worm

infections in the school-aged population by comparing our findings to those obtained in a survey conducted in the mid-1990s (Jemaneh, 2000). We aimed also to determine whether improvements in household-level access to water and sanitation have occurred in this zone of the Amhara National Regional state in Ethiopia after the SAFE strategy had been fully implemented for at least five years.

8.4. Methods

8.4.1. Ethics Statement

The study protocol was reviewed and approved by the ethical review committee of the Amhara Regional State Health Bureau. Additionally, the study activities, including oral consent, were approved by Emory University Institutional Review Board (protocol no. 079-2006). According to the principles of the Helsinki Declaration informed consent for the interview and for stool examinations was sought. Due to the high rate of illiteracy, oral informed consent was obtained from the parent or guardian and recorded in the electronic survey form. Additionally verbal assent was obtained from children aged 7 years and above and also recorded in the electronic survey form. Each selected child, regardless of participation, was offered a single dose of albendazole during the household visit (400 mg).

8.4.2. Study Area and Population

The study was conducted in South Gondar zone of the Amhara Regional state of Ethiopia in the rainy season from late June to early August 2011, covering all 10 rural *woredas* (districts) in the zone. The two semi-urban *woredas* excluded from the survey were the zonal capital, Debra Tabor Town and Woreta Town. The total population of South Gondar is approximately 2.05 million people with 1.86 million living in the 10 surveyed *woredas (Ethiopia, 2007)*. The elevation in the zone ranges from 600 to >4,000 m above sea level and is geographically diverse with areas of lake shore, lowlands, highland plateaus, rugged mountain peaks, and valleys. People are primarily engaged in subsistence agriculture; rice in the lake shore areas, wheat and teff in hill and mountain sides, and animal husbandry in all areas.

8.4.3. Sample Size and Sampling Methodology

We assumed a null hypothesis of no change in the prevalence of infection with any of the following helminths, *A. lumbricoides*, *T. trichiura*, hookworm, and *S. mansoni* as assessed in a cross-sectional survey of school-aged children of South Gondar in 1995, when it was estimated at 49% (Jemaneh, 2000). In order to detect at least a 20% decline in prevalence (from 49% to 29%) at the 5% level of significance and power of 90%, stool specimens from 800 school-aged children (7-15 years) needed to be examined assuming a design effect of

4 for the multi-stage cluster random sampling methodology implemented. We oversampled and included children 2-6 years of age to assess the prevalence of helminths and intestinal protozoa infections in this age group currently receiving preventive chemotherapy with albendazole during biannual campaigns known as enhanced outreach services (EOS) (Fiedler and Chuko, 2008). Additionally, given the focal nature of some helminths (e.g. *S. mansoni*); we aimed to select a geographically representative sample from each of 10 *woredas* by systematically selecting 10 *gotts* (communities) from a random starting *gott* from *woreda*-specific lists arranged geographically. In each *gott*, one child aged 2-15 years was selected randomly in each of 30 surveyed households and asked to provide a stool sample. Households were selected randomly using a modified segmentation design, and children were selected randomly by the electronic data collection device (see below) after enumerating all residents, both present and absent, of the selected household (UNICEF, 2006a).

8.4.4. Survey Tool and Stool Sample Processing

Household sanitation characteristics were determined and recorded at each consenting household by observing the presence of a used latrine and hand washing container noted with or without water. A used latrine was defined as directly observing faeces in the pit with the use of a torch if needed. The head of household or adult representative was interviewed about access to, and use, of water. The selected child and the parent/guardian were shown the albendazole tablets distributed during EOS campaigns and were asked whether the child had received and taken the drug.

Using small portable scales to measure submitted stool samples, field teams recorded the exact weight and fixed approximately 1 g of stool in 10 ml of sodium acetate-acetic acid-formalin (SAF) solution (Marti and Escher, 1990). Fixed specimens were labeled with unique identification numbers (IDs), transferred to a central storage area at room temperature and shielded from direct sunlight. Upon completion of the field data collection, all specimens were processed at the Amhara Regional Research Laboratory using an ether-concentration method that has shown good reliability among European reference laboratories (Utzinger et al., 2010). The entire sediment was assessed systematically for helminth eggs and intestinal protozoa cysts. For helminths, the number of eggs identified were counted and recorded as zero up to 100 eggs. Counting stopped above 100 eggs and was recorded as 100+. The frequency of intestinal protozoa cysts were recorded as none, rare (1-5 parasites per slide), frequent (1 parasite per observing field), and very frequent (>1 parasite per observing field).

8.4.5. Training and Quality Control

Prior to the field data collection, teams participated in a 7-day, applied training for data collectors (health facility-based laboratory technicians), which consisted of classroom instruction and field practice where the protocol and data collection tools were refined, and adapted to the local context. Technicians processing the specimens were trained in the methodology, reading slides, and identification of parasites at species level. Every tenth negative specimen and every specimen where a helminth was identified by a technician was reexamined by a senior laboratory technician.

8.4.6. Data Management and Statistical Analysis

Survey data were collected electronically using tablet computers operating on the Android™ (Google Inc.; Mountain View, CA, USA) platform, and were linked to results of processed specimens via the unique ID on each specimen. Laboratory results were recorded on paper forms by technicians and then double-entered in Microsoft Access by separate entry clerks, compared for discordance, and corrected with the original hard-copy.

Data were analysed using SAS version 9.3 (SAS Institute Inc.; Cary, NC, USA). Selection probabilities were calculated and used to weight the data in the analysis. Additionally, the variance of the estimates was adjusted to account for clustering. To measure differences in household-level access to, and use of, water and sanitation, the current survey data were compared to household survey data collected in 2000 and 2003 prior to any interventions, and 2006 after interventions in only three of 13 districts. All surveys were conducted by the Amhara Regional Health Bureau and The Carter Center using the same cluster, randomised survey methodology (Emerson et al., 2008; Ngondi et al., 2009a).

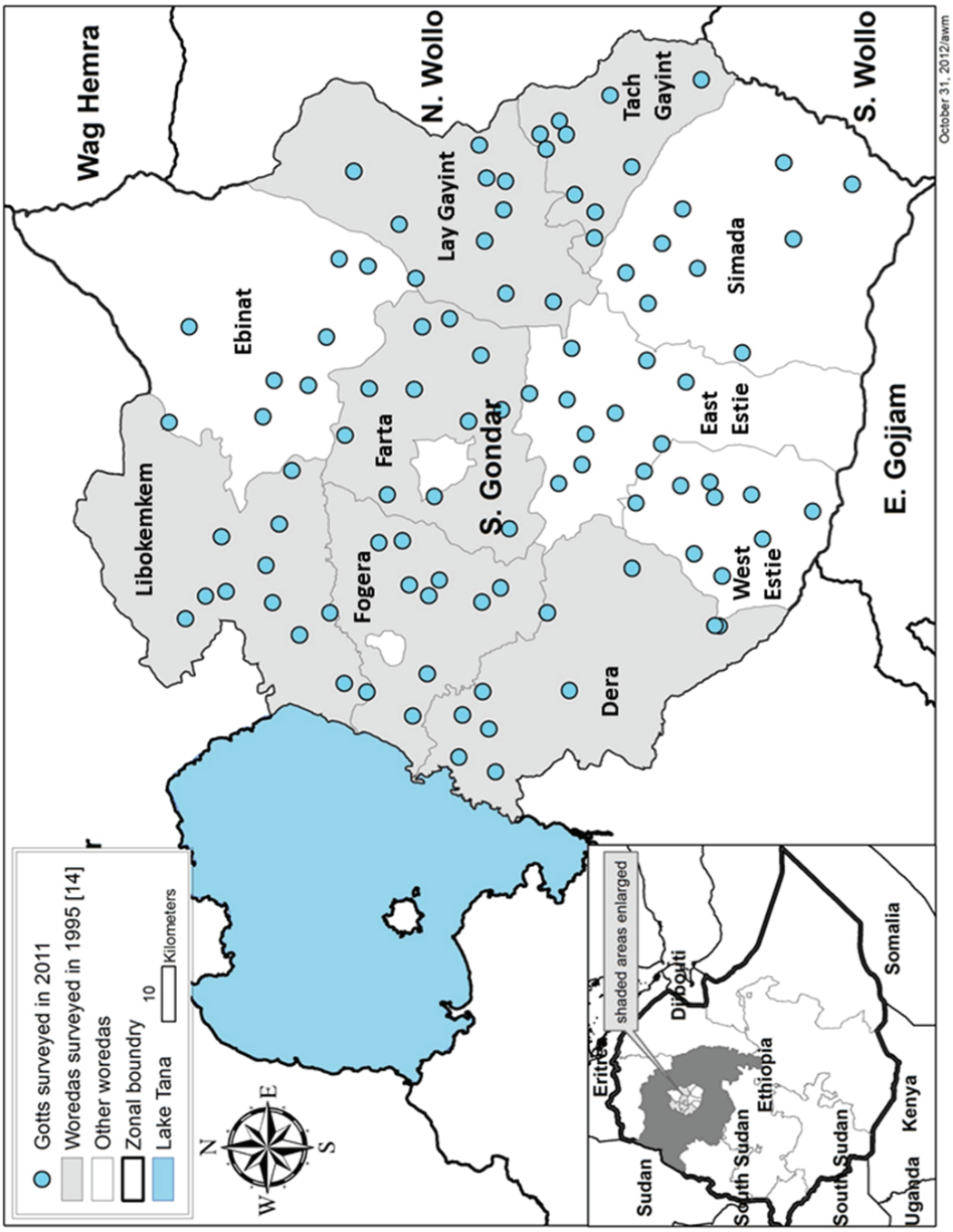


Figure 8.2. Location of *gotts* surveyed for both intestinal parasites and trachoma in South Gondar, Amhara Region, Ethiopia 2011

8.5. Results

8.5.1. Participation and Final Study Sample

Figure 8.2 shows the geographical distribution of the 99 surveyed communities across 10 *woredas* as well as the *woredas* where schools were surveyed in 1995. A total of 2,355 (88.6%) stool samples were provided and processed from 2,657 randomly selected children aged 2-15 years in surveyed households. Figure 8.3 shows the resulting sample sizes used in the analysis. Mean age of children submitting samples was 6.8 years (standard deviation (SD) 3.6 years) and 48.0% of specimens were from boys.

8.5.2. Helminth and Intestinal Protozoa Infection

Helminth eggs and intestinal protozoa cysts were examined in 2,338 processed stool specimens (Figure 8.4). The prevalence of any intestinal protozoa infection (76.8%; 95% confidence interval (CI) 73.2-80.4%) was higher than the prevalence of any helminth infection (23.0%; 95% CI 18.7-27.4%) in this study. The prevalence of the two intestinal protozoa *Giardia intestinalis* and *Entamoeba histolytica/E. dispar* was 23.4% (95% CI 20.7-26.1%) and 11.1% (95% CI 8.9-13.2%) respectively. The prevalence of infections where cysts of any intestinal protozoa were identified as very frequent was 11.0% (95% CI 9.5-12.6%) and the majority of these were *Entamoeba coli*.

Among the helminths, *A. lumbricoides* and hookworm were the most frequently observed with point prevalence of 9.9% (95% CI 7.2-12.7%) and 9.7% (95% CI 5.9-13.4%), respectively. Including *T. trichiura* and *Strongyloides stecoralis* (larvae), the prevalence of infection with any of these soil-transmitted helminths was 19.5% (95% CI 15.6-23.4%). At the *woreda* level, the prevalence of any soil-transmitted helminths ranged from 7.9% to 34.6% (Table 8.1). The prevalence of any soil-transmitted helminth among preschool-aged children (Table 8.2) was 17.4% (95% CI 13.0-21.7%) and was not significantly different from prevalence among school-aged children (21.4%, 95% CI 16.5-26.4%; p=0.106).The prevalence of *S. mansoni* was 2.9% (95% CI 0.2-5.5%; range by *woreda* 0-12.5%). In surveyed *gotts* the proportion of children with *S. mansoni* ranged from nil to 52.4%.

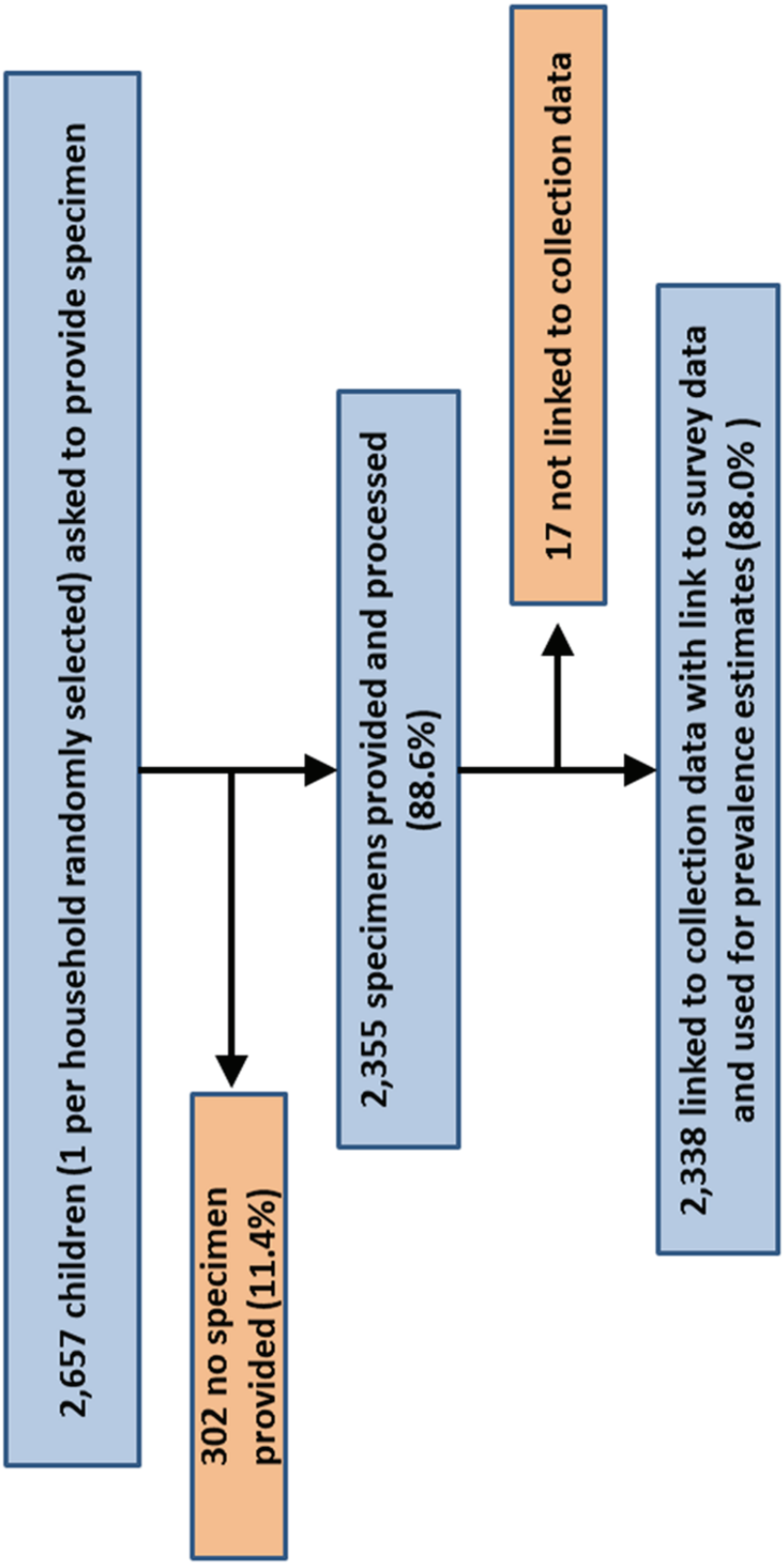


Figure 8.3. Flow chart of survey sample

Table 8.1. Prevalence* of soil-transmitted helminths (STH) and *Schistosoma mansoni* among children aged 2-15 years

	Any STH			*A. lumbricoides*			*T. trichiura*			Hookworm			*S. mansoni*		
Woreda	**(%)**	**95% CI**		**(%)**	**95% CI**		**(%)**	**95% CI**		**(%)**	**95% CI**		**(%)**	**95% CI**	
West estie (N=246)	34.6	22.0	47.2	22.2	11.9	32.5	5.8	0.4	11.2	13.4	1.1	25.7	1.3	0.0	3.2
Dera (N=248)	33.0	25.0	41.1	3.6	0.0	7.4	2.0	0.0	5.6	30.5	21.6	39.4	3.3	0.0	7.3
Fogera (N=227)	26.5	13.0	39.9	11.3	0.6	22.0	3.1	0.0	6.1	19.3	7.4	31.1	12.5	0.0	32.8
East Estie (N=212)	23.5	13.2	33.8	18.4	7.9	29.0	4.5	1.6	7.4	2.9	0.0	6.2	0.0	.	.
Ebinat (N=235)	17.5	7.0	28.0	11.1	0.1	22.1	1.8	0.2	3.5	6.3	1.1	11.5	0.2	0.0	0.5
Libokemkem (N=209)	17.2	12.4	21.9	9.7	6.6	12.8	3.7	1.3	6.0	6.5	0.9	12.0	7.7	0.7	14.7
Farta (N=249)	15.2	5.1	25.2	7.2	0.6	13.9	3.6	0.3	7.0	6.4	0.0	15.7	0.5	0.0	1.4
Lay gayint (N=243)	10.9	1.5	20.2	9.3	0.9	17.6	0.0	.	.	1.8	0.0	3.8	0.0	.	.
Simada (N=241)	8.2	5.1	11.3	5.2	2.5	8.0	1.8	0.3	3.2	2.0	0.2	3.8	0.2	0.0	0.5
Tach gayint (N=228)	7.9	0.1	15.7	7.3	0.0	14.7	0.7	0.0	2.1	0.2	0.0	0.7	0.7	0.0	2.0
Zone (N=2,338)	19.5	15.6	23.4	9.9	7.2	12.7	2.6	1.6	3.7	9.7	5.9	13.4	2.9	0.2	5.5

Results from a cross-sectional survey in South Gondar zone, Amhara Regional State, Ethiopia 2011
*Estimates weighted according to selection probabilities and adjusted for correlation in the data due to clustering

Table 8.2. Prevalence* of any soil-transmitted helminths (STH) among preschool-aged and school-aged children

	Preschool aged children (2-6 years)				School-aged children (7-15 years)			
	Any STH				Any STH			
Woreda	n	%	95% confidence interval		N	%	95% confidence interval	
West Estie	150	31.9	17.4	46.4	91	38.0	25.3	50.7
Dera	133	33.8	22.9	44.6	111	31.4	13.8	49.0
Fogera	112	23.4	7.0	39.8	112	28.9	14.1	43.7
East Estie	118	24.9	11.8	38.0	91	22.5	11.5	33.5
Ebinat	120	12.6	2.5	22.6	110	21.9	10.9	32.8
Libokemkem	112	12.9	3.3	22.5	90	19.4	8.9	29.9
Farta	138	13.5	1.9	25.1	106	17.0	5.6	28.3
Lay Gayint	126	6.6	0.8	12.4	111	15.5	0.3	30.8
Simada	162	11.3	5.8	16.7	73	1.3	0.0	3.0
Tach Gayint	138	7.1	0.0	15.4	87	9.0	0.0	18.2
Zone	1,309	17.4	13.0	21.7	982	21.4	16.5	26.4

Results from a cross-sectional survey in South Gondar zone, Amhara Regional State, Ethiopia 2011
*Estimates weighted according to selection probabilities and adjusted for correlation in the data due to clustering

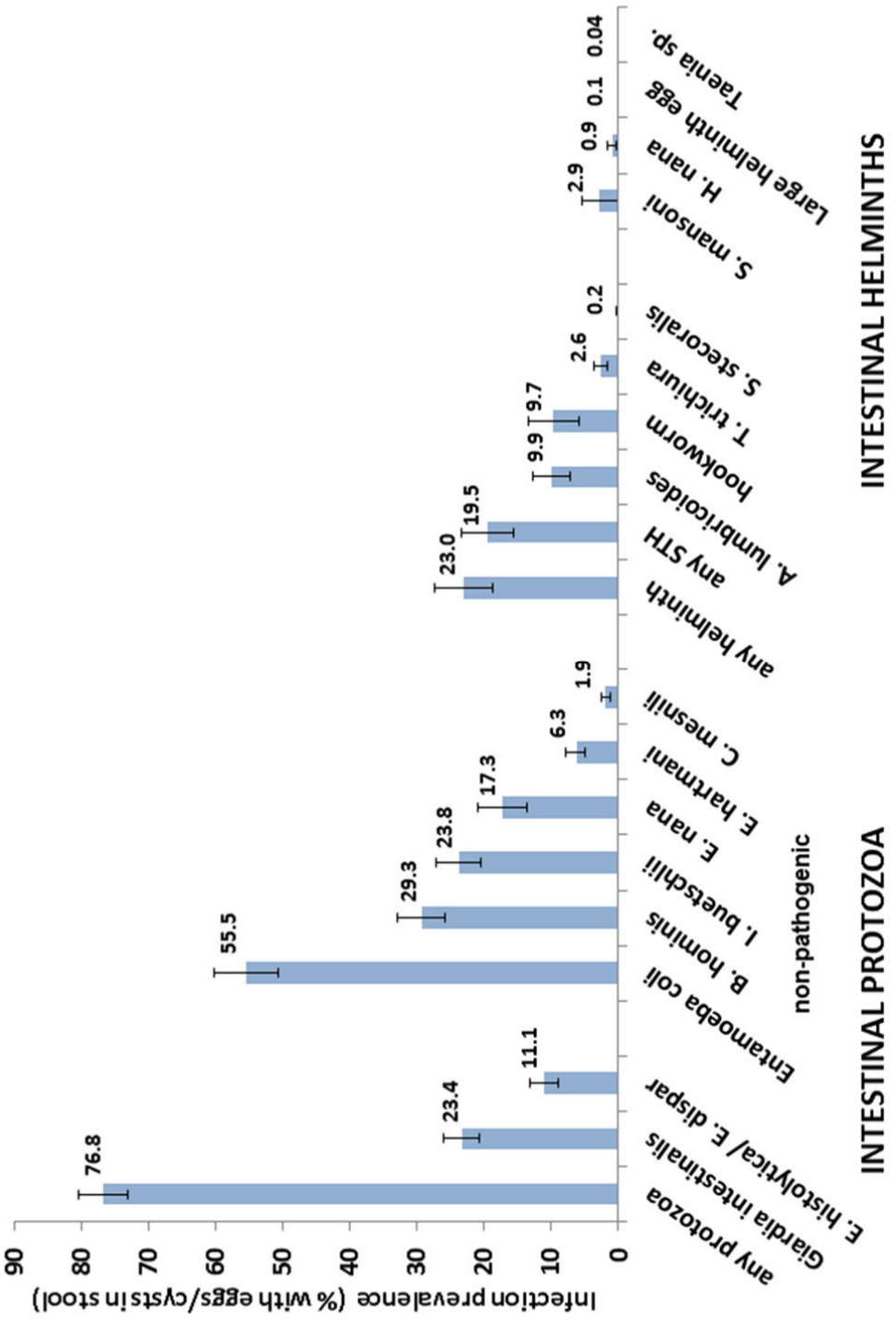


Figure 8.4. Prevalence of intestinal parasites among children aged 2-15 years in South Gondar, Amhara,Ethiopia 2011

8.5.3. Household Level Water, Sanitation and Hygiene

A comparison of household-level indicators revealed a statistically significant differences in household latrine ownership (X^2=32.47, p<0.001), use of an improved source of water for drinking (X^2=6.31, p=0.012), reported access to water within 30 min collection time (X^2=34.44, p<0.001), and reported frequency of washing faces of children under the age of 6 years (X^2=23.28, p<0.001) compared to the baseline household surveys for trachoma done in 2000 and 2003 (Figure 8.4). In 3.8% (95% CI 2.6-5.0%) of households, the presence of a container outside of the latrine to hold water for washing hands was observed in 2011, but this indicator was not assessed in prior surveys. There has been a 14-fold increase in household latrine ownership, a 69.4% increase in reported household use of an improved water source, and a 71.3% increase in household access to water as defined by the reported round-trip time of less than 30 min to collect water from the source. Among families with children younger than 6 years, the proportion reporting to wash the child's face at least once per day has increased by 81.2% since the implementation of the SAFE strategy.

8.5.4. Reported Albendazole Coverage

The estimated drug coverage with albendazole is presented in Table 8.3. The proportion of children aged 2-6 years (preschool age) reported to have taken albendazole in the past year was 14.9% (95% CI 9.3-20.5%; range by *woreda* 0.8-33.0%) and 35.1% (95% CI 24.3-45.8%; range by *woreda* 10.3-68.4%) reported to have ever taken albendazole. The proportion of school-aged children reported to have ever taken albendazole was 33.2% (95% CI 22.9-43.5%; range by *woreda* 12.4-65.7%).

8.5.6. Comparison with Historical Helminth Data

The estimated prevalence of each, *A. lumbricoides*, *T. trichiura* and *S. mansoni,* infection was considerably lower than reported in 1995 (Figure 8.5). The prevalence of hookworm infection was not different from the previous estimate. Table 8.4 presents a comparison of the historical survey to data in the current study, restricted to children aged 7-15 years both within only the six *woredas* represented in the 1995 study (column 2) and within all 10 *woredas* covered in 2011 (column 3). For each of the helminths compared, infections were identified in a smaller proportion of communities in the current survey than observed in 1995. *A. lumbricoides* was the only helminth infection for which more than 100 eggs were counted per specimen, representing a prevalence of 1.9% (95% CI 0.8-2.9%). Without counting all the eggs identified in those specimens, a classification as moderate or high intensity using the standardised eggs per gram of stool (EPG) thresholds frequently employed when using the Kato-Katz thick smear method is not possible (WHO, 2002a). Even after adjusting for the

exact weight of stool preserved, all other infections identified would be classified as low intensity infections in contrast to the 1995 findings (Table 8.5.4).

8.6. Discussion

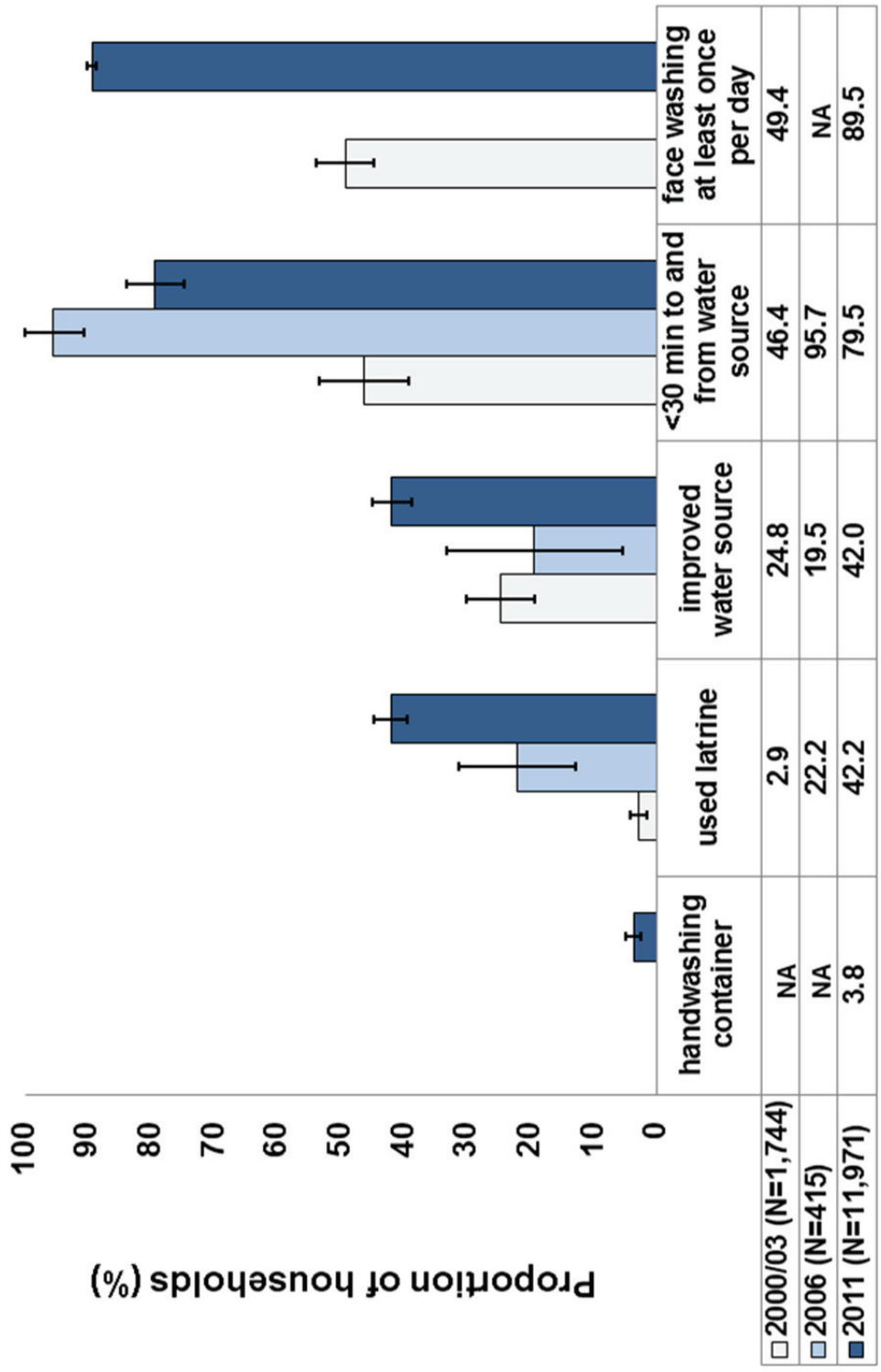
Our study done in 2011 revealed a considerably different epidemiological portrait of soil-transmitted helminths and *S. mansoni* in South Gondar zone of central Ethiopia than the one painted in 1995. Indeed, the infection prevalence of compared helminths has declined substantially, except for hookworm, and infection intensities have concurrently declined for all the identified helminths. These changes have occurred in the context of the health extension programme (HEP), the implementation of the SAFE strategy for the control of trachoma, and EOS. The HEP is a major undertaking since 2004 to provide access to preventive health services to the rural communities of Ethiopia and serves as the backbone of SAFE implementation in the communities (Ethiopia, 2012).

The SAFE strategy was implemented by the Amhara National Regional State Health Bureau in pilot areas of South Gondar starting in 2003 and, by 2006, the programme was operating at scale in all *woredas* due to simultaneous scale-up of HEP having in place at least one health extension worker in each *kebele* (village). In addition to the ongoing promotion of behaviour change communication in 337 *kebeles* of South Gondar, a total of 339,913 household latrines have been reported to be constructed since pilot interventions in 2003 (South Gondar Zonal Health Department reports, unpublished data). We have presented evidence (Figure 8.4) from a series of cross-sectional surveys indicating statistically significant improvements in reported hygiene behaviour (e.g., washing faces of young children), use of an improved water source, improved access to water, and household level access to basic sanitation (e.g., presence of a used latrine). If each of the 339,913 household latrines reported to be constructed were first latrines of households, then the estimated latrine coverage should be 72.6%, which is much higher than the 42.2% coverage identified in this study. There are several possible explanations for the discordance, which may contribute to the difference independently or in combination: health workers double-counted latrines or reported them as complete before they were, the reports from the districts were inflated to exaggerate progress, the collation of reports. at district level was not accurate, a proportion of the new latrines reported were actually new replacements for households that already had one and therefore would not add to the numerator of households with a latrine, or the number of household units and population has grown significantly so as to increase the denominator – as previously highlighted to be a challenge to meeting the MDG 7c target (Bartram et al., 2012). Whatever the reasons, the discordance outlines the importance of periodic household surveys to serve as an independent monitor of the uptake of promoted interventions.

Table 8.3. Proportion* of children reporting to have taken albendazole in South Gondar, Ethiopia 2011

	Preschool-aged children (2-6 years)							School-aged children (7-15 years)			
	Taken within the past year				Ever taken			Ever taken			
Woreda	n	%	95% Confidence Limits		%	95% Confidence Limits		n	%	95% Confidence Limits	
West Estie	148	8.8	1.0	16.7	17.3	4.3	30.2	88	16.0	3.1	28.8
Dera	130	31.9	17.1	46.7	68.4	41.9	94.8	110	63.1	35.6	90.6
Fogera	111	0.8	0.0	2.2	10.3	0.0	22.6	107	16.2	0.0	38.5
East Estie	114	12.4	2.9	22.0	22.0	9.2	34.9	84	12.4	1.6	23.1
Ebinat	118	33.0	4.5	61.4	42.4	14.3	70.6	106	28.8	2.6	55.0
Libokemkem	109	4.2	0.7	7.8	12.3	3.6	20.9	88	24.8	3.9	45.7
Farta	131	31.5	10.3	52.6	63.6	26.1	100.0	105	65.7	34.1	97.3
Lay Gayint	124	4.7	0.0	10.1	30.3	2.4	58.2	109	23.1	0.0	46.9
Simada	157	9.3	0.0	21.2	28.8	9.8	47.8	70	25.8	4.5	47.1
Tach Gayint	136	6.3	0.4	12.3	38.5	5.0	72.0	86	27.5	5.1	49.8
Zone	1,278	14.9	9.3	20.5	35.1	24.3	45.8	953	33.2	22.9	43.5

*Estimates weighted according to selection probabilities adjusted for correlation in the data due to clustering



*as assessed in cluster random household surveys of trachoma, N=total number of households surveyed, error bars represent 95% confidence limits; NA -indicator was not assessed

Figure 8.5. Proportion of households with basic sanitation and access to water in South Gondar, Amhara Region, Ethiopia 2000-2011*

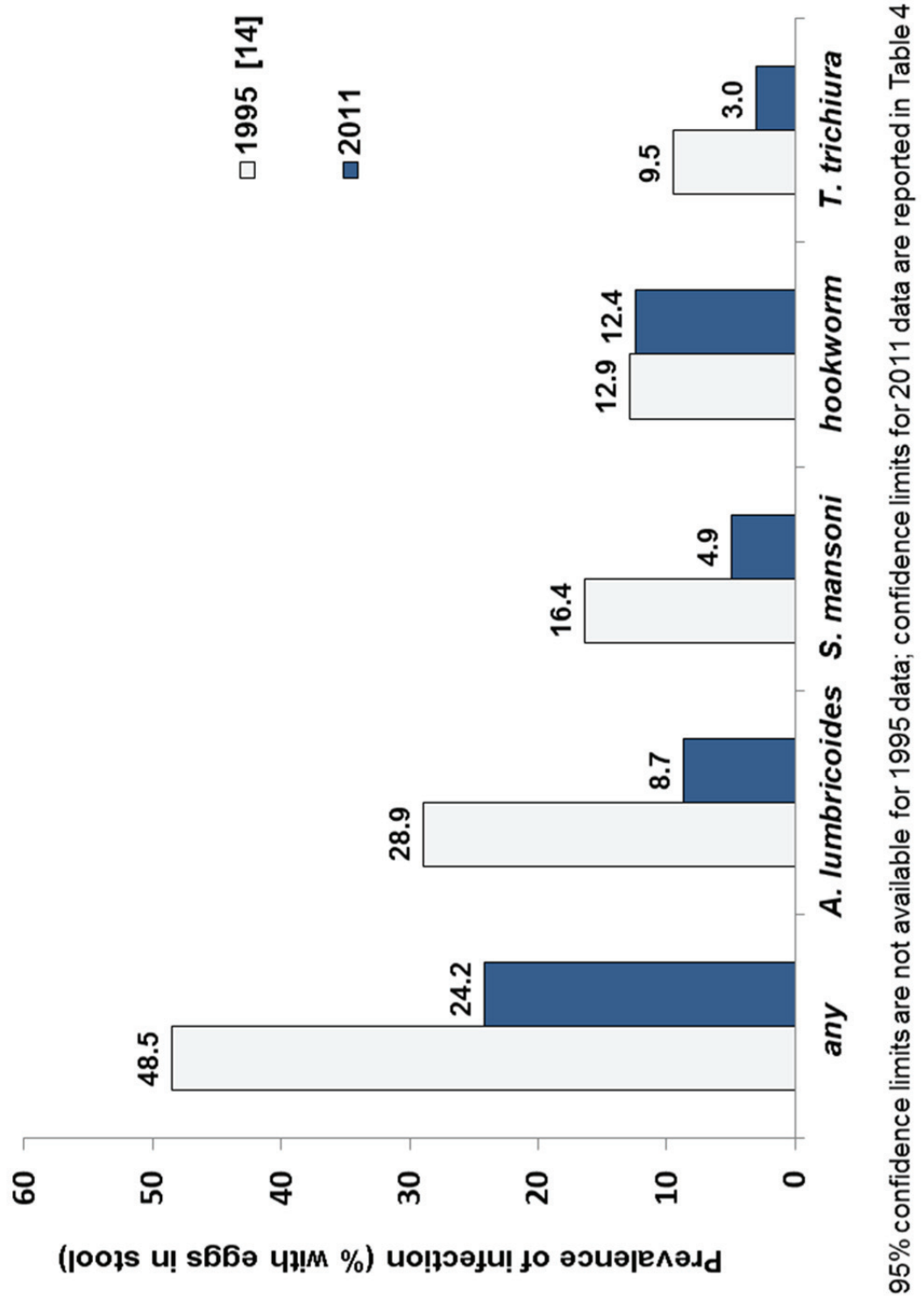


Figure 8.6. Prevalence of helminth infections among school-aged children in South Gondar 1995 (Jemaneh, 2000) and 2011 and Amhara Region 2006, Ethiopia

Table 8.4. Comparison of helminth prevalence data in South Gondar 1995 and 2011

Survey	Jemaneh 1995 [14]			Trachoma impact evaluation 2011*			Trachoma impact evaluation 2011		
Sample population	School children			Children in community			Children in community		
Woredas covered	6			same 6 as in 1995			all 10 rural *woredas*		
Communities	22			60			99		
Total children	2,279 (7-19 years of age)			617 (7-15 years of age)			982 (7-15 years of age)		
Median age	12			10			10		
Mean age	NA			11.0 (SD 2.4)			10.9 (SD 2.4)		
Specimens per child	Single			Single			Single		
Technique	Kato-Katz			SAF - ether concentration			SAF - ether concentration		
Clinical findings	Infection prevalence %	Positive schools	Intensity‡ >200 eggs/g	Prevalence** % (95% CI)	Positive *gotts*	Intensity‡ >100 eggs/g	Infection prevalence** % (95% CI)	Positive *gotts*	Intensity‡ >100 eggs/g
S. mansoni	16.4	63.6%	14.6	4.9 (0.5-9.2)	13.3%	0.0	3.6 (0.5-6.6)	16.2%	0.0
A. lumbricoides	28.9	90.9%	28.5	8.7 (4.8-12.6)	45.0%	0.9 (0.1-1.8)	10.8 (7.2-14.3)	66.7%	1.9 (0.8-2.9)
T. trichiura	9.5	86.4%	8.3	3.0 (1.1-4.8)	21.7%	0.0	3.2 (1.6-4.8)	35.4%	0.0
Hookworm	12.9	77.3%	12.1	12.4 (6.2-18.7)	43.3%	0.0	11.0 (6.5-15.5)	56.6%	0.0
Any above infection	48.5	100%	NA	24.2 (17.6-30.9)	73.3%	0.9 (0.1-1.8)	23.9 (18.8-29.0)	85.9%	1.9 (0.8-2.9)

*Data set limited to school-aged children from only the same 6 woredas included in 1995
‡ Prevalence of intense infection measured as proportion of total sampled population presenting with >200 eggs per gram of faeces (1995) or >100 (2011)
**Estimates weighted according to selection probabilities adjusted for correlation in the data due to clustering

Needless to say, despite improvements in access to sanitation (from 3% in 2003 to 42% in 2011), interventions are still needed, as more than half of households surveyed were without a toilet and using an unimproved source of water. While the presence of a water container for hand washing was observed outside a latrine in only a small proportion of households, some people are adopting a recently promoted health message even though there is a long way to go. These findings might explain the frequent intestinal protozoa infections identified. We have no background data to assess any change in protozoa infection prevalence, but presence of these infections suggests that the water being used for drinking is of poor quality. Whether contamination is occurring at the source, collection, or storage should be further investigated, so that adequate mitigation strategies can be implemented.

Albendazole was distributed to children aged 2-5 years every six months in EOS campaigns since 2004. At the national level, it has been reported that up to 9 million doses of albendazole have been distributed per round (Fiedler and Chuko, 2008). The programme was originally targeted to children in *woredas* labeled as “food insecure”, but has since been expanded. Coverage surveys to evaluate the EOS have reported achievement of 93.8% of targeted children for albendazole in 2006 and 92.1% for vitamin A in 2008 (Negash, 2011). Since 2009 in South Gondar, a cumulative 945,991 doses of albendazole have been distributed to approximately 213,000 preschool-aged children during such campaigns with a reported coverage of 100% (range by year 98.3-106%) (South Gondar Zonal Health Department, unpublished data). The reported coverage figures are in sharp contrast to our survey estimates. Coverage estimates of mass drug administration (MDA) programmes are commonly lower than administrative reports (Cromwell et al., 2012, Worrell and Mathieu, 2012). At the most, only 1 out of every 3 preschool-aged children reported taking the drug within the past year. From Table 3, it is evident that the food insecure *woredas* were likely to be Dera, Ebinat, and Farta, which had the highest proportions of children in both age groups reporting ever having taken albendazole. If the distribution decisions were determined at a level below the *woreda*, then we may have misrepresented albendazole coverage by aggregating the results from non-targeted communities with targeted communities. Nonetheless, the findings confirm the importance of independently assessing MDA coverage with household surveys.

Our survey has some limitations. First, the prevalence estimates of helminths and intestinal protozoa are based on a small amount of stool from a single specimen. Helminth egg output varies from one day to another and within each stool specimen, hence it is probable that we have underestimated the ‘true’ prevalence, although less likely intense infections (de Vlas and Gryseels, 1992, Knopp et al., 2008). However, this variation should be comparable to the single stool results presented by Jemenah in the mid-1990s which had the same limitation (Jemaneh, 2000). Second, we avoided calculating percent decreases in

prevalence due to the different diagnostic techniques used in 1995 (fresh stool samples using the Kato-Katz technique) and the current study (SAF-fixed stool samples subjected to an ether-concentration method) (Katz et al., 1972). Using the Kato-Katz technique may have allowed a more direct comparison to the baseline data and a more precise measure of infection intensity, but it was not feasible given the logistical challenges posed by community-based surveys in the remote settings surveyed here, as described elsewhere (King et al., *at review*). Our comparison of intensity of infection was limited, but in determining prevalence, fixing of stool samples in SAF and ether-concentration methods are as sensitive as the Kato-Katz technique (Glinz et al., 2010). The Kato-Katz technique has also been found to lack sensitivity in detecting low-intensity hookworm infections (Booth et al., 2003, Utzinger et al., 2008, Knopp et al., 2009b). Third, we did not assess the cleanliness of the observed latrines. While improved sanitation is protective against soil-transmitted helminthiasis, a latrine with faeces around the drop hole, in theory, may serve as a source of hookworm transmission (Stürchler et al., 1980, Cairncross et al., 1996). Fourth, our albendazole coverage estimates are subject to recall bias. However, we took steps to minimise recall bias by showing the albendazole tablets distributed during EOS campaigns and the most recent round of EOS was implemented less than one month prior to the survey. Additionally, other MDA participation studies reported that individuals are capable of recalling whether they have taken a drug during the distribution (Cromwell et al., 2009b, Budge et al., 2011). Albendazole coverage, even in targeted woredas, was very low, which we feel provides stronger support to the hypothesis that improvements in F and E were largely responsible for the decline in helminths. However, this study was cross-sectional and therefore inherently has the inability to link causal associations with improvements in the sanitation due to SAFE and preventive chemotherapy due to unmeasured confounding factors. An alternative hypothesis is that the recorded, significant improvements in latrines, water access, and face washing have had minimal impact on intestinal parasites and the decline is due to secular variation. The two surveys compared were conducted nearly 16 years apart. We cannot rule out a secular decline in the prevalence and intensity of helminth infections, but a national survey of school-aged children in 2006 reported a prevalence of *A. lumbricoides* of 28.0% and of any soil-transmitted helminth of 37.7%, perhaps indicating that from 1995 to 2006 there may have been little change in prevalence due to secular variation in South Gondar (Hall et al., 2007). Hence, further investigation of predictive factors of the observed infections is warranted.

This study demonstrates the feasibility and success of an integrated neglected tropical disease assessment for programmatic decision making. Despite the low intensity of identified helminth infections, infection with any of the helminths targeted for control was identified in over 80% of the communities surveyed. The *woreda*-level prevalence of any

soil-transmitted helminth exceeded 20% in East Estie, West Estie, Dera, and Fogera *woredas*, and hence, according to WHO guidelines, warrant preventive chemotherapy targeting school-aged children (WHO, 2006a). Additionally, preventive chemotherapy using praziquantel against schistosomiasis is warranted in Fogera *woreda* and other communities where the proportion of children infected with *S. mansoni* was greater than 10%. Through this assessment, we were able also to identify several intestinal protozoa infections, some of which contribute to morbidity (Becker et al., 2013). At the least, the high prevalence of these infections indicates contamination of water at the point of the source or use and warrants further investigation and setting specific interventions. It also suggests that there is much more work to be done in improving water quality, hygiene, and sanitation in these mostly rural areas of Ethiopia.

While we cannot directly attribute the decline in helminth prevalence and intensity directly to the SAFE strategy, the documented increase in hygiene and sanitation offer both a biologically plausible and parsimonious explanation for the decline which is consistent with our understanding of the epidemiology of helminth and intestinal protozoa infections. Preventive chemotherapy in national helminth control programmes has been shown to significantly reduce prevalence and intensity of helminth infections and has likely contributed to the observed decline (Sinuon et al., 2007; Keiser and Utzinger, 2008; Knopp et al., 2009a). However, without environmental changes, there is potential for rapid reinfection and continued transmission (Utzinger et al., 2009; Jia et al., 2012). Additionally, participation, defined as ever taking albendazole, among the targeted population as reported in this survey was much lower than administrative records suggest. Given the simultaneous scaling up of both F and E from the SAFE strategy and de-worming in EOP since 2006, one has to consider that there has been a synergistic effect of these ongoing interventions even though coverage (both household latrine ownership and preventive chemotherapy with albendazole) has been below target. There remain opportunities for integrated neglected tropical disease control throughout Ethiopia (Tadesse et al., 2008). These results are encouraging and present a portrait of what might be expected within an integrated, multi-sectoral package of interventions for neglected tropical disease control.

8.7. Acknowledgements

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9. Discussion

Trachoma caused by ocular *Chlamydia trachomatis* (*Ct*) is one of the oldest diseases known to man and remains a global health burden, accounting for 3% of blindness worldwide (Taylor, 2008; WHO, 2012a). The disease is targeted for global elimination by the year 2020, and while progress is being made, several countries have yet to identify endemic areas and initiate control efforts (WHO, 2012b). Ministries of Health in trachoma endemic countries are rolling out a recommended package of control interventions referred to as the SAFE strategy that includes: **S**urgery to alleviate suffering and prevent visual impairment in those currently burdened by the disease; **A**ntibiotics to reduce the load of *Ct* infections in a community; and both **F**acial cleanliness and **E**nvironmental improvements to reduce transmission and prevent new infections (WHO, 1997a). The GET 2020 (global elimination of blinding trachoma by 2020) alliance of trachoma endemic countries, academic partners, corporate sponsors, donors, government, and non-government organizations was formed to provide concerted advocacy for the elimination (WHO, 1997b). As a member of the alliance, The Carter Center directly supports Ministries of Health to implement the SAFE strategy in Ethiopia, Mali, Niger, Nigeria, Sudan, and South Sudan by the provision of resources to the existing public health programmes. The partnership between the Amhara National Regional State Health Bureau and The Carter Center has enabled the successful execution of this PhD project.

The principles of The Carter Center are not dissimilar from that of the Swiss Tropical and Public Health Institute (Swiss TPH). The Carter Center, based on careful research and analysis, aims to take action to address difficult problems to alleviate suffering and improve health of all people (TCC, 2013). A guiding principle of Swiss TPH is to seek solutions to challenges faced by international public health priorities through innovation, validation, and application (SwissTPH, 2013). Within both institutions there is mutual commitment to human rights, emphasis on taking action based on generated knowledge, and obtaining results, which ultimately lead to less disease and improved health of populations. This PhD thesis was conducted under the auspices and collaboration of these two institutions and aimed to address current, pressing issues within the global programme to eliminate blinding trachoma. Specifically, national Ministries of Health implementing the SAFE strategy need to know how best to determine whether the interventions are working and what further actions are required. The evaluation of performance of programmes is one of the greatest challenges for global health (Royston, 2011). We investigated novel approaches to evaluate the impact of the SAFE strategy on trachoma. However, given that part of the SAFE package of interventions involves improvement in hygiene, water, and sanitation, we explored the potential benefits of the strategy beyond trachoma. These foundations of public health clearly prevent other neglected tropical diseases, but the documentation of ancillary

benefits beyond trachoma has not been demonstrated in the context of the SAFE strategy (Esrey et al., 1991; Bartram and Cairncross, 2010). Therefore, we applied an integrated approach to the assessment of both trachoma and intestinal parasitic infections. Collaboratively, we wanted to validate what works in the field and interpret the findings into clear actions targeted to strengthening the ability of Ministries of Health to measure the full impact of interventions and identify areas to improve disease control efforts. Table 9.1 highlights how each of the individual objectives aligned with the joint principles of The Carter Center and Swiss TPH.

The ongoing trachoma elimination programme of the Amhara National Regional State Health Bureau served as a platform for conducting the operational research studies presented in this thesis. Operational research has been defined as the search for knowledge on interventions, strategies, or tools that can enhance the quality, effectiveness, or coverage of programmes in which the research is being done (Zachariah et al., 2009). The need for this type of research has been highlighted and specific operational research areas prioritised for neglected tropical disease control (Feasey et al., 2010; Boatin et al., 2012; Solomon et al., 2012). Figure 9.1 describes my proposal of an ideal process of such operational research. When research is conducted collaboratively within the ongoing provision of public health services (defined here as the health system), not only do the findings contribute to scientific knowledge, but are also directly applicable to meeting the needs of the system itself. Hypotheses are developed by identifying challenges through the ongoing activities and tested through the routine data collection activities or necessary periodic monitoring and evaluation. When conducted in such settings, the detailed analysis of the data generates evidence which can be discussed immediately with district, regional and national control coordinators for making health system decisions to improve programme strategies without having to wait for other important, but often delayed, venues of dissemination, such as presentations at conferences, publication in the scientific literature, or WHO guidelines. At the same time, the findings of the research contribute to the current scientific understanding of the subject under investigation. Hence, the knowledge generated is more applicable when derived within the dynamic and uncontrolled programmatic setting, rather than when limited to the laboratory or controlled research conditions. This process should be continuous, leading to the identification of additional challenges and hypotheses to be tested. After all, operational research led to the development of the SAFE strategy and how it is currently implemented (Emerson et al., 2006). Maybe this is what Professor Rudolf Geigy realized about extending laboratory research to the field and perhaps for all public health research, the guiding principle should be innovation transferred into action (Utzinger, 2013).

In the remainder of this final chapter, the findings of each of the research objectives presented in this thesis will be discussed in terms of the process in Figure 9.1, specifically

the evidence generated for programme decisions, the public health action recommended, the contribution to scientific knowledge and additional research issues identified.

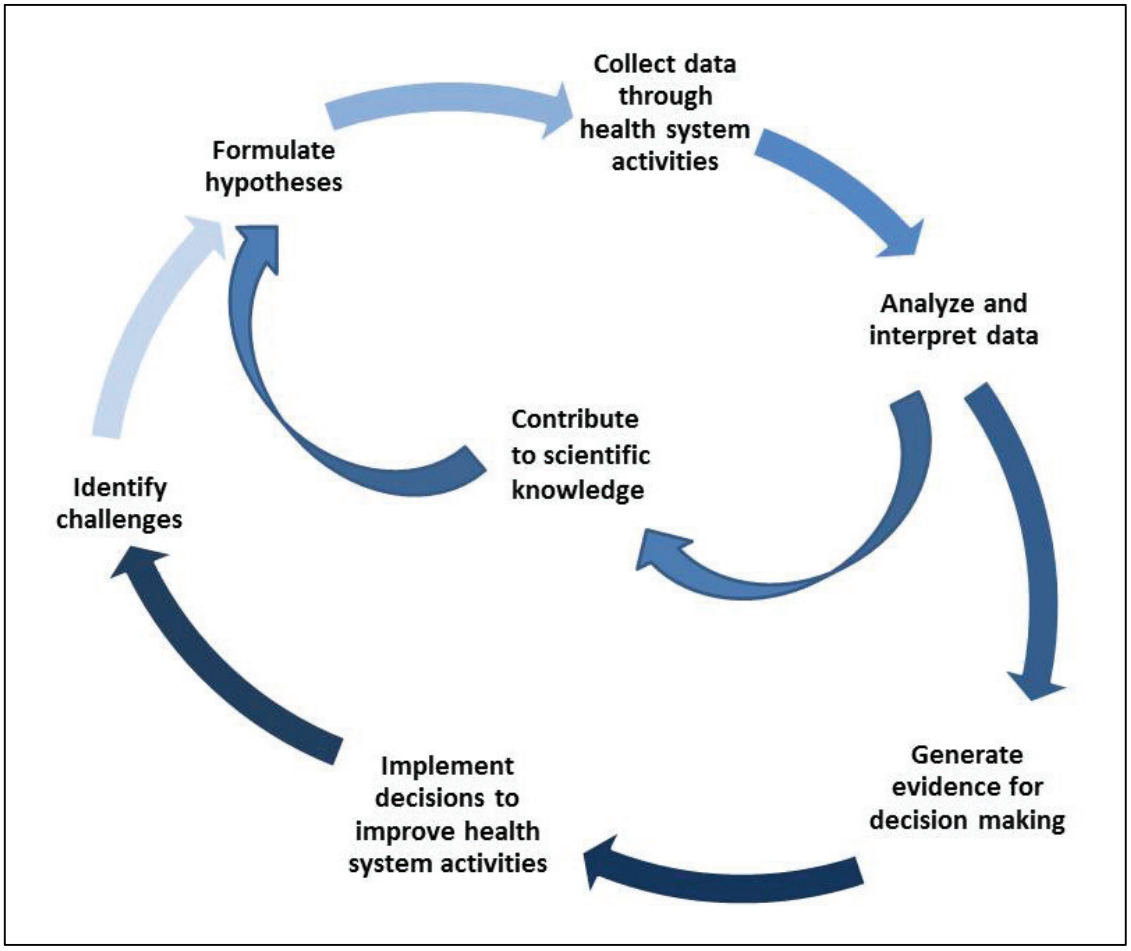

Figure 9.1. Proposed process of implementing operational research in the context of the health system

Table 9.1. Shared principles of The Carter Center and Swiss TPH addressed by the studies implemented within this PhD thesis.

Chapter	Study	Innovation	Validation	Application
4	Prevalence of trachoma at sub-district level in Ethiopia: determining when to stop mass azithromycin distribution	The first application of sub-district-level impact evaluation surveys of the SAFE strategy in the context of a national trachoma elimination programme	Determining that new WHO guidelines for estimating TF_{1-9} at the sub-district level on a large-scale is feasible, but requires considerable resources	Identification that most sub-districts warrant continued implementation of the full SAFE strategy In hyper-endemic areas, implementation of at least five years of SAFE did not reduce TF_{1-9} to below elimination criteria
5	A novel electronic data collection system for large-scale surveys of neglected tropical diseases	Utilisation of the latest advances in mobile technology to design an electronic data collection and management system specified to the needs of community-based household surveys	Field-testing the system in a pilot trial to further enhance the design Comparing the system to standard paper-based data collection	Applying the system in South Gondar sub-district-level surveys to assess the impact of the SAFE strategy on trachoma and intestinal parasites
6	Impact of the SAFE strategy on trachomatous scarring among children in Ethiopia: a repeated cluster randomised cross-sectional study	Assessing the prevalence of TS among children to evaluate the impact of SAFE interventions Utilising an environmental health approach of assessing the effect of cumulative exposure to years lived during SAFE interventions on TS	Current indicators used to evaluate the impact of the SAFE strategy, TF and TT, do not represent the full extent of disease reduction	Monitoring TS prevalence in children provides direct evidence of SAFE impact on averting blinding trachoma
7	Trachoma among children in community surveys from four African countries and implications of using school surveys for evaluating prevalence	Analysing data sets from multiple national trachoma elimination programmes to address a potential issue in NTD assessment and control strategies	Rebutted my recommendations from previous research by expanding the analysis of TF between children attending and not attending school in multiple countries	Identification that school attending children are less likely to have TF than children not attending school implies that evaluating impact of SAFE by assessing TF in school surveys may underestimate TF prevalence and thus overestimate programme success
8	Intestinal parasite prevalence in an area of Ethiopia after implementing the SAFE strategy, enhanced outreach services, and health extension programme	Integrated approach to community-based assessment of trachoma and intestinal parasites Intestinal parasite prevalence may serve as an additional indicator of evaluating public health impact of the E component of SAFE	SAF preserved stool collection and ether concentration are feasible methods for community-based surveys of intestinal parasite prevalence	The E component plus enhanced F to include hand hygiene should continue being promoted as control measures for intestinal parasitic infections Identification of districts where preventive chemotherapy among school-aged children might enhance intestinal helminth control

9.1. Evaluating the impact of the SAFE strategy on trachoma at the sub-district level

To meet this first objective we applied new guidelines from WHO on which the decision to stop MDA must be made on the basis of documented impact on trachomatous inflammation follicular among children aged 1-9 years (TF_{1-9}) after implementation of the SAFE strategy (WHO, 2010). The novel approach of the two cross-sectional impact evaluation studies conducted were that the prevalence estimates generated were powered to the district level, as standard practice, but also to the sub-district level simultaneously. By doing so, health system decisions could be made immediately, avoiding the need to conduct two separate surveys as suggested in the WHO guidelines (first at the district level, then at the sub-district level). The studies were conducted with the highest epidemiological rigor in regards to employing probability sampling at all levels, standardisation of trachoma grading, and quality assurance of data collection and management.

Evidence generated for health system decisions

The findings of the surveys provided sub-district-level prevalence estimates of TF_{1-9} on which to determine whether continuing MDA was warranted according to WHO guidelines. Additionally, the estimate of trichiasis (TT) prevalence in the total population allowed an updated estimate of the total backlog of persons with TT that the health system needs to reach and offer corrective surgery. These estimates were more precise than those established at the start of the programme based on zonal-level surveys and allow prioritising of high-prevalence districts for outreach. The proportion of households with basic sanitation (a household latrine), with access to water within 30 minutes of round-trip collection, and with an improved source of drinking water was also generated from the household surveys (reported in Chapter 8). The data allows measurement against Millennium Development Goal 7c, upon which the implementation targets can be made to determine what needs to be done to reduce by half the proportion of the population without access to safe drinking water and improved sanitation (UNDP, 2005).

The studies established the feasibility of conducting sub-district-level surveys on a large scale, but the resources required were substantial. While the health system has the human resource capacity to implement the field activities, extensive external financial and logistic resources were required and should be considered when planning similar impact assessments outside Amhara. Based on previous experience in Ghana and Mali, I had the assumption that where the baseline TF_{1-9} prevalence was <30%, a decline inTF_{1-9} to <5% was achievable after implementation of the SAFE strategy (Yayemain et al., 2009; Bamani et al., 2010b). Yet in South Wollo, where the baseline TF_{1-9} prevalence was 12% at the zonal level, only six of 36 sub-districts were <5% and the majority of sub-districts had TF_{1-9} prevalence higher than the baseline estimate after three years of implementing SAFE

activities, likely because these areas were hyper-endemic as in the rest of zones of Amhara Region (Berhane et al., 2006; Emerson et al., 2008). In South Gondar, after five years of SAFE activities, none of the 36 sub-districts had achieved TF_{1-9} prevalence of <5%. In this setting, only one (in Legambo woreda) of the 72 sub-district-level estimates provided any dissimilar evidence of impact from what was estimated at the district level. Within the remaining 71 sub-districts, the sub-district estimates varied little from the overall district-level estimates but required the assessment of at least 100 additional communities to obtain. These overall findings suggest that no other district in the Amhara region needs to be evaluated prior to receiving at least five years of SAFE interventions. Also, conducting trachoma impact evaluation surveys at the sub-district level are not warranted until further evidence of a decline in TF_{1-9} is noted. However, district-level surveys may still be of value in monitoring impact and refining programme targets.

Contribution to scientific knowledge

The observation that the prevalence of TF_{1-9} did not decline to prescribed elimination targets after five years of implementing the SAFE strategy contributes to the current scientific understanding concerning trachoma elimination. To meet current criteria of elimination in a similar hyper-endemic area, more than five years of the SAFE strategy as implemented in this programmatic setting will be required. Research from hyper-endemic communities in Tanzania has suggested that >7 years of MDA may be required before TF_{1-9} declines below the 5% target (West et al., 2011). However, these findings came from research communities where programmatic implementation of the SAFE strategy was not to scale, in contrast to Amhara, and perhaps less generalisable to a national programme. Research studies in other areas have demonstrated reduction of *Ct* infection from communities receiving only a few rounds of MDA (Gaynor et al., 2003; Burton et al., 2005b; Harding-Esch et al., 2009; Ngondi et al., 2009a; Gebre et al., 2012; Keenan et al., 2012a). In some of these studies, TF prevalence remained above 5% and, according to WHO guidelines, warranted continued MDA with antibiotics to treat infections which were rare or absent (Solomon et al., 2004a; Harding-Esch et al., 2009; Ngondi et al., 2009a; Gebre et al., 2012; Keenan et al., 2012a). Together these findings raise great concerns. Currently, the azithromycin is donated to national programmes for the elimination of trachoma. Forecasts of the amount of drug needed are based on the assumption that programmes might require a maximum of five annual rounds of MDA before the elimination targets are realised (ICTC, 2011). The drug donor might not be prepared to produce the amount of drug required for all areas to meet the target. Additionally, conducting an annual vertical MDA campaign requires significant planning and resources. Knowing that such campaigns are time-limited helps programmes and partners estimate the resources required in advance, but when elimination is uncertain,

it is much more difficult to obtain continued financial investments (personal communication Paul Emerson, Technical Director of The Carter Center Trachoma Control Program, Atlanta). More concerning is that if MDA continues with no evidence of *Ct* infection, there is additional risk of introducing antibiotic resistance among other community pathogens (Fry et al., 2002; Coles et al., 2013).

Research needs identified

Determining whether TF is the best indicator on which to measure impact should be a research priority for the global trachoma elimination programme. Recent studies from The Gambia and Tanzania suggest that the correlation between TF and *Ct* infection is variable across different settings (Harding-Esch et al., 2010). While we do not yet have *Ct* infection results to support the clinical data collected in these cross-sectional studies, once available, the correlation with TF prevalence will be assessed to determine whether TF in these study areas was indeed a sensitive sign on which to measure the impact of SAFE interventions on trachoma transmission. On the other hand, trachomatous inflammation intense (TI) in some studies has been more closely correlated to *Ct* infection and is highly associated with scarring development (West et al., 2001b; Burton et al., 2003; Solomon et al., 2003). Declines in TI were observed in both South Wollo and South Gondar zones, which, seems consistent with studies from different geographical settings (Ngondi et al., 2006b; Bamani et al., 2010b). The first WHO guidelines for assessing trachoma prevalence suggested that areas with >5% TI warranted antibiotic intervention (WHO, 1993b). What was the evidence supporting this guideline and could a reduction in TI to some other predetermined threshold below 5% serve as a better indicator of elimination? Additional investigation is warranted to determine whether TI might be a better indicator of controlling trachoma transmission. Regardless of whether TF or TI is the better clinical sign, clinical signs remain limited by the grader's subjective diagnosis. Only the development of a field-reliable, rapid diagnostic assay for detecting *Ct* infection would lead to direct evaluation of SAFE impact on transmission.

In regards to the methodology utilised for determining the achievement of elimination criteria, either the WHO guideline should be followed conducting district-level impact evaluations first, followed by the sub-district if TF_{1-9} <10% or the value of the additional sub-district-level survey should be challenged altogether. Support for the latter is more evident based on the programme decision that must be made at the sub-district level. The sub-districts utilised as evaluation units are not existing administrative areas. These were logically derived by joining existing health clusters (health catchment areas) by geographical orientation until the desired population size was met. If there were any mistakes in the geographical listing of health catchment areas in the creation of the survey sampling frame,

no distinction between areas would be possible. More importantly, implementation based on this created unit poses unique challenges. In both South Wollo and South Gondar, district health offices have proved to be resistant to the notion of non-uniform service delivery (personal communication Tesfaye Teferi, The Carter Center Trachoma Control Program Manager, Ethiopia). The argument stems from the survey results indicating trachoma remains a problem around the sub-districts that met the <5% TF_{1-9} criteria. Reintroduction of infection from neighbouring health clusters, as they fear, may increase transmission of trachoma if MDA stops in these sub-districts, thus losing any gains that were achieved. Previous research studies have postulated that travelers to and from neighbouring communities might be reason for the observed return of infection after successful MDA campaigns (Shah et al., 2010). Additionally, the ability of the health offices to reach and serve the community depends largely on the community's trust to provide the needed service where and to whoever is in need, one of the core functions of primary care (1978). Selectively stopping an appreciated service, i.e. the MDA with azithromycin, may jeopardise such trust.

With the exception of a few districts, estimates of TF_{1-9} varied little. It would be worthwhile to assess the usefulness of the sub-district approach in a different setting when limited to districts with <10% TF_{1-9} to determine whether the additional sampling provided any additional information beyond what a district-level survey might provide. A spatial analysis might be a further promising approach to identify areas likely requiring ongoing interventions, by sampling fewer areas and predicting based on spatial distribution as used frequently in other NTD control programmes and recently on a national scale for predicting trachoma in Southern Sudan (Raso et al., 2006a; Steinmann et al., 2007; Clements et al., 2010). However, this method might also be limited by the difficulty in distinguishing implementation units on which the health system would need to plan and carry out interventions. Application of spatial analysis to identify areas of trachoma clustering in Brazil was not successful (Schellini et al., 2010). The usefulness of this method has not been demonstrated in areas after interventions, but warrants additional investigation, particularly to determine whether the risk of trachoma resurgence might be predicted for sub-districts stopping MDA.

9.2. Applying new technology to facilitate data collection in impact evaluation surveys

Upon presenting the results from South Wollo sub-district-level surveys to the Amhara Regional Health Bureau, it was the Director of Public Health at the time, Dr. Asrat Genet, who said "This (paper questionnaire) methodology and the surveying of so many communities seems archaic; there has to be a better way." While I could not modify the

WHO recommended sub-district-level sampling strategy, I did realise that current mobile technology may be able to facilitate the completion of the surveys in South Gondar by electronic data capture. Within the six month period between field work in South Wollo and South Gondar, together with the volunteer assistance of computer scientist undergraduates at the Georgia Institute of Technology, we developed and field tested an innovative electronic data management and capture system, *Swift Insights*, which was deployed to evaluate the impact of the SAFE strategy in the South Gondar sub-district-level surveys. Both qualitative and quantitative methods were used to tailor the system to meet the needs of the survey methodology and scientifically document that the data collection was comparable to standard paper questionnaires.

Evidence generated for health system decisions

Results of the sub-district-level impact evaluation surveys were analysed and presented to the survey teams two days after the completion of field work and a formal summary report presented shortly thereafter to the Regional Health Bureau. Results from South Wollo, which used paper questionnaires, were not available for statistical analysis until two months after the completion of field work. Overall, the South Gondar surveys took 35% less time to complete, were implemented with less survey teams, and achieved a greater sample size than South Wollo surveys. Incremental costs of the electronic equipment for use in South Gondar were equivalent to costs incurred for double data entry of paper questionnaires in South Wollo and the electronic equipment can be used in multiple surveys. This evidence supports the conclusion that electronic data capture can facilitate large-scale community assessments required to evaluate health system programmes.

Contribution to scientific knowledge

Through the application of new, Android-based technology on tablet computers, we documented that such data collection and management adds efficiency to impact evaluation surveys on a programmatic scale. These advantages were similar as those advertised in recent applications of Android-based data collection applied to animal health and surveillance of zoonotic diseases (Karimuribo et al., 2012; Madder et al., 2012). To our knowledge, this is the first quantitative and qualitative comparison of Android-based and standard paper-based data collection within the context of an actual NTD control programme. Time savings, due to obviating the need for data entry, was the outstanding advantage of electronic data collection over standard paper-based questionnaires. There were no differences in time to completion of the household surveys between the methods, which was also reported in a comparison of smart-phone administrated interviews among attendees of maternal health clinics in China (Zhang et al., 2012). In Amhara, obtaining

immediate results on which to base health system decisions concerning MDA is crucial in trachoma programme management given the preparation required for coordinating two, sub-region-wide annual interventions targeting over eight million population each which includes meeting application deadlines for approval of the drug donation and shipment (Rotondo and Seligson, 2011).

Perhaps one of the more important contributions to the current scientific understanding concerning the application of electronic data capture using tablet computers was the qualitative feedback provided by the data recorders who had participated in the South Wollo sub-district-level surveys using the paper-based questionnaires. These experienced data recorders identified a concern that the use of the electronic devices disrupted the connection between interviewer and respondent. Quantitative research methods alone could not capture such an important issue potentially affecting the quality of responses provided by the interviewee (Creswell, 2003). Identifying the perceptions of the end-users allowed for these issues to be addressed in the training of data recorders for the South Gondar surveys. We were unable to assess the perceptions of the household interview respondents and perhaps how it may or may not have influenced their responses. We were, however, able to quantify a statistically significant difference in the increased proportion of individuals who refused participation in the surveys, but it is not clear that the use of the electronic device was influential in the decision. These findings highlight the importance of a mixed-methods approach to operational research.

Electronic data collection using the tablet computers led to fewer data recording errors compared to paper-based questionnaires in terms of blank entries and incorrect unique ID numbers of examined residents and resulted in more accurate recording of geographical coordinates. The upfront costs of the tablets and accessories were similar to double data entry and validation costs of paper-based questionnaires. Since the first deployment in South Gondar, the equipment and system has been reused for impact surveys in six other zones of Amhara, all leading to complete data analysis and reporting results back to the data collection teams and programme managers within two days. The findings of this study verify the continued importance of health informatics for monitoring and evaluating disease control programmes.

Research needs identified

One aspect identified through the qualitative work that warrants further research is the interface between the data recorder and the interview respondent. This may be particularly important in resource-poor settings where the devices are rare and have yet to reach the communities. What are the perceptions of the respondents concerning the novel devices utilised? Do the devices present barriers in communication and could programmes learn

how to mitigate any barriers by modified training agendas for data recorders? Additionally, the e-health field might be able to learn from the IT industry in terms of how best to train persons unfamiliar with the applied technology.

The area of e-health, particularly smart-mobile technology, is rapidly developing (Mertz, 2012). We integrated the use of a barcode scanning application with *Swift Insights* data collect application to link stool specimens to individual and household data collected during the survey through the use of an autofocus camera on the tablet. Given the problems identified with the simplified trachoma grading system, there have been recent efforts to enable such smart-phone cameras to take photographs of the tarsal conjunctivae for the confirmation of field grading (Bhosai et al., 2012). Currently, the resolution provided by smart-phone cameras has not been powerful enough for such a task and the add-on devices have been cost prohibitive for programmatic use. As the capacity of the devices increase, these applications should enable new ideas to be applied to field research like utilisation of a smart-phone for microscopy to diagnose helminth infections by our colleagues here at Swiss TPH (Bogoch et al., 2013). The ability to diagnose helminth eggs in a wet mount through a smart-adapted microscope shortly after collection might save significant resources currently expended in logistics of transporting specimens and processing in a laboratory. Perhaps the only limit to further applications of e-health is our own imagination.

9.3. Evaluating the impact of SAFE interventions on trachomatous scarring in children

Given the challenges discussed in interpreting TF prevalence after intervention, we assessed whether there was any demonstrable impact of SAFE interventions on trachomatous scarring (TS). TS at the development of the simplified grading system had very good inter- and intra-observer agreement and was intended to be an indicator of past trachoma severity within a community (Thylefors et al., 1987; WHO, 1993a). Yet, currently it is not a recommended indicator to be measured in prevalence assessments (WHO, 2006b), probably because of the assumption that TS develops over time and may not resolve, making prevalence difficult to interpret. Analogous to antibodies, once scars are present, they might remain and identified at any one point in time it would be difficult to determine when the scarring developed.

Currently in the global programme to eliminate lymphatic filariasis, one hypothesis under investigation is that demonstrating the absence of an antibody response to filarial antigens among young children born since the initiation of MDA indicates the interruption of filariasis transmission (Gass et al., 2012; Steel et al., 2012). Similarly, the absence of TS among children born since the implementation of the SAFE strategy would not only indicate reduced transmission, but also blinding disease averted. Therefore assessing TS among

children is a novel approach to the evaluation of the SAFE strategy. Also uniquely, we applied an approach commonly used in environmental epidemiology to assess any cumulative effect of exposure, defined as years lived since implementation of SAFE strategy, taking into consideration the age of the child at the start of the interventions.

We observed a decline in TS prevalence over time in each of the cross-sectional surveys. Either the observed decline has occurred because of inconsistent reliability of diagnosing TS across surveys, a secular trend, or the SAFE strategy has been successful in preventing disease progression. In each of the surveys, all potential trachoma graders participated in extensive training where all signs of the simplified trachoma grading system are taught. Prior to initiating data collection, the graders take practical exams where only graders with the best diagnostic skills (measured by agreement with instructor's diagnosis or standardised slide set) are selected. Field-testing of the simplified trachoma grading system shortly after development, showed very good inter-observer agreement for TS after extensive training (Taylor et al., 1987). Hence, variability in the grading of TS is not a strong argument for the observed decline. Adjusting for the year of the survey in the model measuring effect of cumulative exposure allowed us to control for any secular trend. Even after adjusting for the year of the surveys, there was a clear trend of declining odds of TS for every year exposed among the children born since the SAFE interventions began. Conversely, the reduced likelihood of TS explained by five years of SAFE exposure among the children 6-10 years of age became less pronounced for each year lived prior to the interventions and was not statistically significant for children aged 10 years. This should not be interpreted as children aged 10 years exposed to SAFE interventions are no more likely than children aged 10 years having never been exposed. All children aged 1-10 years after five years implementation of the SAFE strategy were significantly less likely to have scarring (range of decreased odds; OR=0.11 for children aged 5 years, OR=0.42 for children aged 10 years).

Evidence generated for health system decisions

The significant decline in TS provides evidence that the SAFE interventions implemented by the health system are reducing blinding disease and should continue according to WHO guidelines. Additionally, the study suggests that TS among children is a valuable indicator on which the programme may track progress towards eliminating blinding trachoma. Ideally, a TS prevalence of zero among children born since control interventions would indicate that blinding trachoma has been mitigated. Therefore, the health system should continue to record TS among all ages in impact evaluation surveys. Additionally, TS should be recorded in long-term surveillance activities among young children as a monitor of trachoma resurgence in the community once MDA has stopped.

Contribution to scientific knowledge

The findings indicate that SAFE interventions are averting the development of scarring in children which is likely to greatly reduce TT incidence in the future. The greatest impact has occurred among the children born the same year the interventions began, indicating a cumulative beneficial impact for children born after the implementation of SAFE in Amhara. The finding that the impact lessens for each year lived prior to the interventions indicates that the development of scarring may be influenced by factors occurring during the first years of life. This is consistent with the understanding that repeated reinfection and inflammation leads to scarring and that infection and inflammation is experienced most frequently, for the longest duration and with the highest bacterial loads during the ages 1-5 years (Dawson et al., 1976; West et al., 1991; Bailey et al., 1999; West et al., 2005). The findings of the study are also consistent with findings from Tanzania indicating that scarring develops at young ages and is significantly associated with the presence of intense inflammation (West et al., 2001b; Wolle et al., 2009a).

The lower occurrence of TS among children with close access to water (<30 min round-trip collection) in the exposure analysis model using all survey data is biologically plausible if those households prioritised the use of water for hygiene that has prevented transmission and inflammation due to trachoma in those children. Households in The Gambia that used a greater quantity of water for washing children were less likely to have a household member with active trachoma (Bailey et al., 1991). When a round-trip collection of water takes more than 30 min, the amount of water used in the household declines and perhaps along with it, washing *Ct* contaminated fingers, faces, and clothes (Cairncross, 1999). Improved access to water could also simply be correlated to an unmeasured factor of development that has led to the decline in *Ct* transmission. However, the additional finding of reduced odds of TS among both children aged 1-5 and 6-10 years with household-level face washing frequency contributes to the argument that water used for hygiene is, at least in part, responsible for the decline in TS. Together, these findings indicate long-term benefits of the F component in SAFE.

We did not find a significant association between reported individual or household participation in the MDA campaigns and TS, but several studies show that MDA with antibiotics is effective at reducing *Ct* infection in the community (Evans and Solomon, 2011). Additionally, the presence of a household latrine was not associated with TS among children. However, data from Southern Sudan suggested a combined, perhaps synergistic, impact of SAFE on active trachoma at the community level (Ngondi et al., 2006b).Therefore, the cumulative exposure analysis may have captured such a non-specific beneficial impact

of SAFE interventions in the environment on the progression of blinding disease in the individual.

Research needs identified

The cumulative exposure analysis influenced by studies of air pollution impact on health was useful in evaluating the impact of SAFE in this setting. Because this was the first application of the method within the trachoma programme, it should be validated in other longitudinal data sets from other trachoma endemic areas. The analysis could be repeated in areas with similar cross-sectional or longitudinal data where interventions have been implemented for multiple years. Substantiating this effect would provide great hope that blinding trachoma is indeed being prevented through the SAFE strategy.

While the current analysis provides evidence that the SAFE strategy reduces TS prevalence, additional analysis is warranted to address two important issues. First, the rates of increasing scarring prevalence and age for pre- and post-SAFE intervention determined in this setting should be extrapolated to determine an estimated magnitude of blinding trachoma averted. Different estimates of the rate of progression from scarring to trichiasis observed in other research could be applied to the current data to provide a range for such estimates (Muñoz et al., 1997, 1999; Bowman et al., 2001). The second, more important issue would be to apply the current rate of scarring with age to estimate the total number incident cases of TT which might be expected and over what period of time health systems would need the capacity to identify and provide surgery for these cases. Existing mathematical models could use estimates generated with this data set as parameters for simulations to answer this important programmatic question (Gambhir et al., 2009).

9.4. Exploring a school-based approach to evaluate impact of SAFE interventions

The utilisation of schools as a venue for preventive health programmes is not novel. Many national de-worming campaigns are conducted through the schools in a collaborative effort between Ministries of Health and Education as well as partner NGOs and corporate pharmaceutical donors (Schroeder et al., 2002; Monse et al., 2010; Kihara et al., 2011). The SAFE strategy is recommended for inclusion in the primary school curriculum and some trachoma endemic countries have already designed and applied such curricula (Mariotti and Prüss, 2001; Zondervan et al., 2004; WHO, 2006b; Lewallen et al., 2008). Additionally, surveys among children in schools are a commonly practiced method on which to determine the need for, monitor and evaluate such interventions and are currently recommended in helminth control programmes (Brooker et al., 2000; WHO, 2002a; Hodges et al., 2012b; Sherkhonov et al., 2013). Most recently, new guidelines on surveillance of trachoma suggest the assessment of active trachoma among school children (WHO, 2008). There have been few recent studies to determine whether school children are representative of the

communities in which they live and whether school-based interventions are reaching all children in the community. The novelty of the study conducted in this thesis was to challenge the school-based survey approach by assessing whether the prevalence of TF was the same between children attending and not attending school.

The best way to have tested this hypothesis would have been to actually conduct school-based surveys and compare the findings with community-based surveys in each of these cross-sectional assessments, similar to what was done in eight districts of Nigeria (King et al., 2009). Given the recommendation to incorporate the promotion of the SAFE strategy through school health curricula, I included a question concerning school attendance during community surveys of trachoma prevalence supported by The Carter Center since 2008, including the sub-district-level surveys from this thesis project. Therefore, data sets from large-scale, community-based trachoma surveys conducted in Mali, Niger, and Nigeria were included in this analysis. In each of the surveys a child was asked “Do you attend school regularly?” to assess school attendance.

Evidence generated for health system improvement

School attendance varied across surveyed areas in the four countries in terms of gender, school-entering age and age of highest frequency of attendance. Any school-based intervention could only expect to reach, at maximum, the proportion of children attending school, which in the case of Mali and Niger, would represent less than half of all school-aged children. The proportion of school-attending children participating in antibiotic distribution and who had clean faces was higher than that among children not attending school. Overall, school-attending children were less likely than children not attending school to have TF. This finding implies that school-based survey methods to assess prevalence of trachoma will likely underestimate the prevalence within the community. Additionally, school-based trachoma surveys will not provide estimates of TT prevalence on which to plan surgical programmes. While the health system might be encouraged that school children are learning and practicing prevention behaviour because of education received at the school, the observed disparities may mean that children not in school are not benefiting as much from the interventions as their peers attending school. The health system should ensure that additional strategies are implemented to reach all children according to their needs. Evaluating impact of interventions should not be limited to assessing only children in schools.

Contribution to scientific knowledge

Several issues relevant to the current practice of school-based surveys and interventions were addressed. First, the age cohort with peak prevalence of the disease to be assessed

may not be the same age cohort attending school. The community-based surveys confirmed that TF is most common in children aged 1-5 years who are too young to attend school and thus, school-based methods would inevitably underestimate TF prevalence, but the extent might vary according to the local epidemiology of the disease. Preschool-aged children were only about 30% more likely to have TF than school-aged children in Mali and Niger, which had the lowest community prevalence of TF_{1-9}, whereas preschool-aged children in Ethiopia and Niger were over 400% more likely to have TF than school-aged children. The finding suggests that the accuracy of school-based prevalence estimates might be influenced by the local age-specific prevalence of a disease.

Second, school children may be systematically different than children not attending school in respect to socio-economic status, gender, knowledge, behaviour, and disease prevalence. When limiting the analysis to school-aged children and controlling for age and gender, TF remained significantly less common among school attendees. The higher antibiotic coverage and percent clean faces in school attendees may suggest increased awareness and practice of preventive behaviours, but the factors responsible for the observed differences in TF cannot be determined with the data collected. A report from a WHO technical meeting on trachoma surveillance concluded that two sentinel communities per district per year should be assessed for TF among school-entrance-aged children (5-6 years) where the school attendance rate is >90% with no gender bias (WHO, 2008). According to the data observed in this analysis, none of the trachoma endemic locations surveyed would have qualified for surveillance activities as suggested by the report, due to low attendance, gender bias and a recommended age group that would not have been found in schools. Fortunately, an alternative suggestion was to conduct community-based surveys.

Finally, the low attendance rates reported by the students is concerning, especially if disease control strategies, such as preventive chemotherapy, are school-based because coverage of all school-aged children will not be attained. This issue has been addressed in the past regarding helminth control programmes by bringing siblings to school on school health days (Montresor et al., 2001a). But this strategy assumes that each family has at least one child who attends school and who remembers to inform his or her family. The same assumption applies to the theory of reaching the family unit with trachoma health education through the school child (personal communication Paul Emerson, Technical Director of The Carter Center Trachoma Control Program, Atlanta). I did not analyse the proportion of households in which no school-aged child attended school, but in several communities of the areas surveyed, none of the children among the surveyed households reported attending school. Such issues identified by this study warrant further investigation, discussion and renewed strategy development.

Research needs identified

Only trachoma data was assessed in this study, but since implementing the sub-district-level surveys of South Gondar, stool collection among school-aged children has continued in ongoing trachoma impact assessments in seven other zones of the Amhara National Regional State and over 7,000 samples have been processed for the identification of intestinal parasitic infections. This school analysis could simply be extended to the current data to determine whether school children are less likely to have intestinal helminth or protozoan infections compared to their counterparts not in school in these areas not under school-based helminth control. Furthermore, for current school-based NTD control programmes, a useful evaluation of programme impact would be to compare infection prevalence, knowledge and behaviour among school-aged children both attending and not attending school.

Additionally, the assumption that a child's knowledge of the SAFE strategy from school is being transferred to the household and other school-aged child residents should be tested. The findings of the current study suggest that children not in school may not be benefiting as much as school children from current interventions. Therefore, some community-based, mixed-methods research could help identify novel, preferred strategies to ensure the benefits of any disease control interventions reach children not attending school.

9.5. Determining the impact of SAFE interventions on intestinal helminths

Water and sanitation are the foundations of public health. The promotion of water use for personal hygiene and the construction and use of household latrines in this area of rural Ethiopia is most likely to have impacts beyond the targeted purpose of reducing trachoma transmission. Increased access to water is associated with increased use of water for hygiene practices, which prevent the spread of infectious faecal-oral, respiratory, and contact transmitted diseases (Cairncross, 1999; Prüss et al., 2002; Prüss-Üstün et al., 2008). Use of an improved, uncontaminated water source for drinking is clearly related to reduction in the burden of water-borne diseases (Prüss-Üstün et al., 2008; Hunter et al., 2010). Improved sanitation has been shown to decrease incidence of diarrhea and is significantly associated with a reduced odds of soil-transmitted helminth infections (Mara et al., 2010; Ziegelbauer et al., 2012). However, such ancillary impact in an area under SAFE interventions has not been demonstrated.

We applied a novel approach, integrating both the assessment of intestinal parasitic infections and trachoma through community-based surveys, to evaluate the impact of SAFE strategy on these infections in South Gondar where prevalence data on intestinal helminths prior to interventions existed in the scientific literature. The selection of a cross-sectional study design was influenced by the application of the new trachoma impact assessment

guidelines from WHO, but also the desire to demonstrate the feasibility of conducting integrated NTD surveys through a community-based methodology. While the cross-sectional design was useful in determining the current prevalence of trachoma and helminth infections establishing causal relationships between the F and E components and any observed differences in prevalence from baseline is limited.

Evidence generated for health system improvement

We documented a significant decline in the prevalence and intensity of *Ascaris lumbricoides*, *Trichuris trichiura* and *Schistosmoa mansoni* infections among school-aged children since the school-based cross-sectional survey conducted in 1995 (Jemaneh, 2000; King et al., 2013). Hookworm prevalence was the same as in 1995, but no high infection intensities of hookworm infections were identified. These changes in helminth prevalence occurred in the context of substantial improvements in household sanitation (14-fold increase in latrine ownership), access to water (71.3% increase), use of improved water source for drinking (69.4% increase) and reported face washing behaviour (81.2% increase) since the implementation of the SAFE strategy. Preventive chemotherapy with albendazole has also been targeted to preschool-aged children living in districts considered prone to drought and food insecurity through biannual interventions called Enhanced Outreach Services. Concurrently with these interventions, the Health Extension Programme has assigned and placed trained health extension workers (HEWs) in each *kebele* (cluster of communities). A core function of the HEWs is to provide behaviour change communication concerning sanitation and hygiene including the F and E components of the SAFE strategy.

The prevalence of any of the soil-transmitted infections exceeded 20% among school-aged children and, according to WHO guidelines, warrant preventive chemotherapy (PCT) among this age group (WHO, 2006a). District-specific prevalence estimates of soil-transmitted helminth and *S. mansoni* infections were generated on which the Regional Health Bureau can apply WHO guidelines. Additionally, nearly one of four children had *giardia intestinalis* infection and three of four children had some type of intestinal protozoan infection. Identification of these intestinal parasitic infections indicates the potential ongoing transmission of pathogenic faecal-oral infections such as *Cryptosporidium* and *Salmonella typhi* and demands strengthened interventions throughout the zone to improve quality of drinking water, sanitation and hygiene.

Figure 9.2 presents the current modes of transmission of intestinal parasitic infections in South Gondar along with the estimated indicators of household-level practice of control interventions. The bold dotted lines indicate points of effective interventions to block transmission, but are only partially being practiced. Parasite eggs and cysts via human faeces are still contaminating water and soil as only 42% of households in the zone were

observed to have a used latrine. Fingers and hands are still being contaminated because there is little evidence that residents are practicing hand washing after defecation. Overall, only 4% of households were observed to have a hand washing container outside of the latrine as promoted by the health services. The majority (89.5%) of households with children aged less than six years reported washing their children's faces at least once a day, indicating a high awareness of this promoted hygiene behaviour. In regards to water, 42% of households reported using an improved source of water for drinking, indicating that the majority of households may be drinking water from a contaminated source. Even in those households drinking from improved sources of water, contamination of the water can occur while in transport or storage within the household (Jensen et al., 2002). Additionally, the Regional Health Bureau should be concerned with the discrepancy between the doses of albendazole reported distributed, nearly 100% coverage of preschool-aged children over the last six distribution rounds, with surveyed coverage of 14.9% reported to have ever taken albendazole. All of these factors suggest transmission of intestinal parasites will continue unless improvements are made to fill the gaps within the interventions.

Contribution to scientific knowledge

The current study provided recent data on intestinal helminth infections that may be referenced in future surveys to evaluate impact of improved interventions. Additionally, the study documented a high prevalence of intestinal protozoan infections not commonly assessed. Whether or not these are locally considered a public health burden, they provide clear indication of faecal-oral disease transmission (Becker et al., 2013). Timely assessment of stool specimens required by the standard Kato-Katz method for diagnosing helminth infections would have not been possible in the rural, remote communities selected randomly in this study. Our methods confirmed the field applicability of preserving stool specimens in sodium acetate-acetic acid-formalin (SAF) during community-based surveys in such settings and assessing intestinal parasitic infections using ether concentration on a programmatic scale (Ouattara et al., 2008; Utzinger et al., 2010). Also, the technique provided the additional opportunity to detect the protozoan infections (Marti and Escher, 1990). The integrated methodology was feasible to implement in population-based surveys utilising probability sampling within communities. We have since continued these methods in seven other zones in Amhara demonstrating repeatability, which suggest these methods, can be used for ongoing monitoring and evaluation of control interventions. Finally, the reductions in helminth infections among school-aged children documented here either indicate an important secular decline or an ancillary impact of an integrated, multi-sectoral package of interventions to control NTDs.

Research needs identified

The cross-sectional design of this thesis study limits our conclusions concerning the effect of SAFE interventions on intestinal parasites. Stool samples have now been collected and processed from over 300 communities in 8 of the 10 zones of Amhara. A cluster randomised control trial could be established by utilising the 300 communities for which we now have data on trachoma clinical signs and ocular swabs; intestinal parasitic infections; and linked individual, household and community level characteristics. A subset of these 300 communities could be randomised to receive only the ongoing health system interventions as currently implemented or additional intensive interventions providing face washing and hand hygiene behaviour change communication; 100% household latrine coverage; 100% of households with hand washing containers; and 100% households with access to an improved water source within 30 minutes round-trip collection. Follow-up data collection and analysis could occur annually at the same time of the year for three years to align with the WHO recommended duration of SAFE implementation and impact assessment. Additionally, to make the most of the data collected during this thesis, a subset of the 300 sites could serve as integrated NTD sentinel surveillance sites to monitor progress of the ongoing control interventions.

Without any additional funding, the individual, household, and community-level factors associated with intestinal parasitic infections should be determined through multi-level random effects modeling. Identifying such factors along with the geospatial determinants of these infections might allow for the prediction of prevalence in areas not surveyed in need of enhanced control measures, particularly *S. mansoni* (Raso et al., 2006a, 2006b; Vounatsou et al., 2009; Schur et al., 2011). Additionally, an in-depth analysis of the current data for associations between combinations of indicators of water, sanitation and hygiene at the community level and individual parasitic infections is warranted in particular the intestinal protozoan infections.

While improvements in water access and sanitation were documented through the study, there was little indication of adoption of the promotion of hand washing immediately after defecation, evident by the low proportion of households with hand washing containers. Indeed, hand hygiene is one of the core objectives supposedly addressed by the HEWs. Understanding the factors associated with not adopting or adopting the promoted behaviour could lead to the modification of programme strategies to improve practice of the desired behaviour. Such operational research would require a mixed-methods approach as implemented in Kenya prior to a nationwide hand washing campaign (Schmidt et al., 2009).

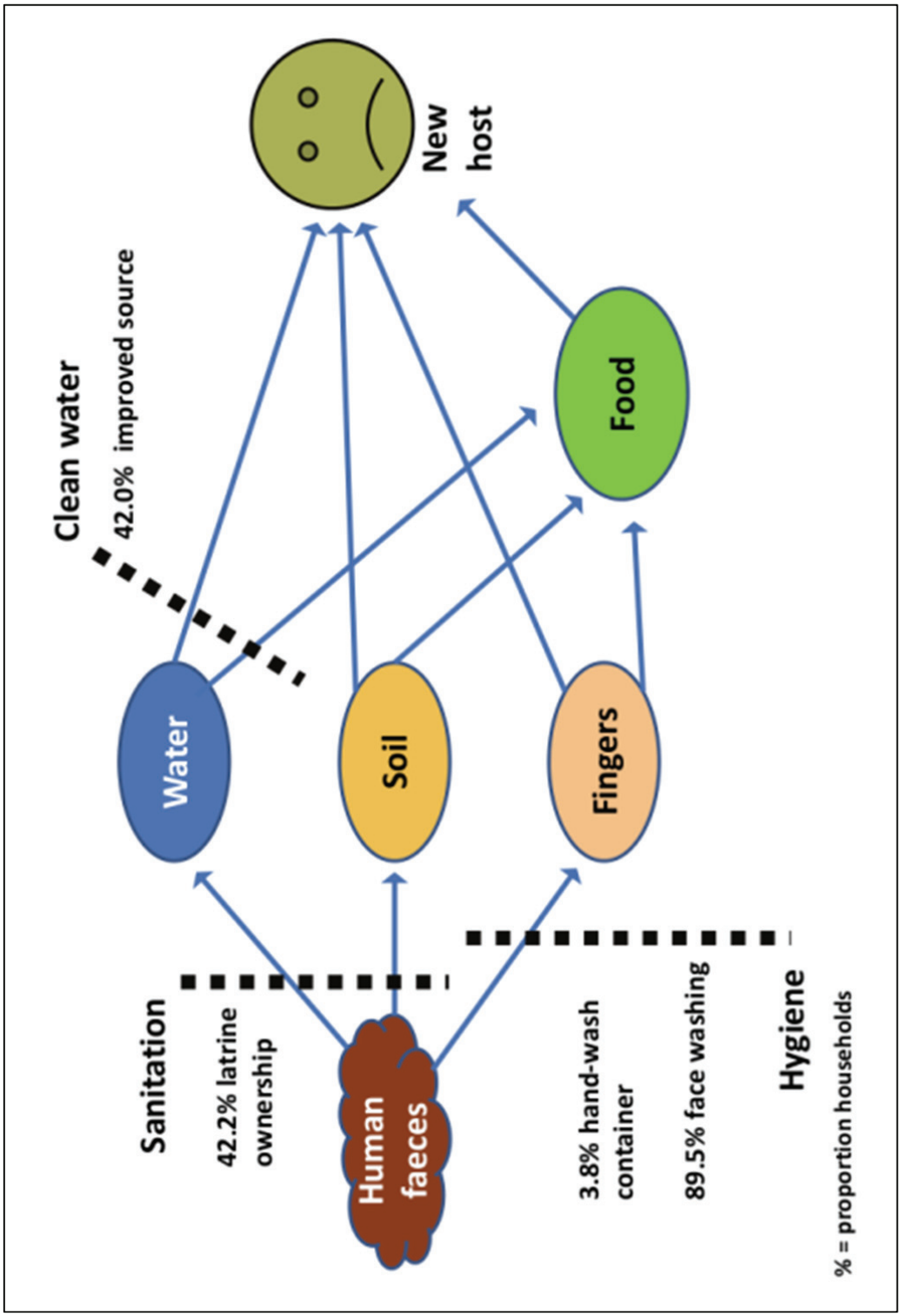

Figure 9.2. Intestinal parasite transmission routes and household level uptake of control interventions in South Gondar, Ethiopia 2011 (modified from Mara et al., 2010)

9.6. Future considerations

The work carried out for this PhD has highlighted additional opportunities and potential issues relevant to sustainable health services. The North-South collaboration between The Carter Center, Swiss TPH, and Amhara Regional Health Bureau worked well utilising the trachoma control programme activities as the platform for operational research. Efforts should be made to extend this partnership to improve the transfer of analytical skills locally and to build capacity, an essential ingredient to sustain ongoing operational research to improve the delivery of health services (Zachariah et al., 2009; Royston, 2011). Through the conduct of the field studies (activity mandated by WHO for trachoma programme evaluation) skills were transferred to over 40 integrated eye care workers, 20 lab technicians and 20 technology students at the local university. Additionally, the zonal-level health department programme managers played lead roles in coordinating the field work and participating in the training and supervision. However, to improve the capability of the Regional Health Bureau to monitor and evaluate the impact of NTD control programmes, key persons should be identified who could work with Carter Center staff and survey teams in the design, implementation, analysis and interpretation of such large-scale impact evaluations in the future. Evaluating the impact of the SAFE interventions would represent an applied training which could hence be extended to other health programmes. Such collaboration should also be extended to the local university system within Ethiopia with an aim to improve integration of the research conducted by the universities with the ongoing activities and needs of the Regional Health Bureau. Modules on operational research could be included within the health science schools and in existing applied training programmes such as The Ethiopian Field Epidemiology and Laboratory Training Program (Jima et al., 2011).

Finally, the decline in intestinal helminth infections in South Gondar suggests a combined beneficial impact of multiple health system interventions; the SAFE strategy, PCT through Expanded Outreach Services and the Health Extension Programme. There are opportunities for similar synergies between programmes and across sectors. Our study identified very low coverage of the targeted preschool population with albendazole and thus potential problems with the delivery strategy. It would be feasible to coordinate the community-based distribution of albendazole to preschool and school-aged children during the current integrated MalTra campaigns of antibiotic distribution for trachoma and fever screening, testing and subsequent treatment for malaria. However, these integrated, but vertical campaigns are time-limited and depend mostly on drug donations and external financing. While such programmes can be successful, long-term, sustainable solutions are required (Utzinger et al., 2009; Ruxin and Negin, 2012). We (speaking as an NGO) need to realise that the sustainable provision of health services comes through primary health care and sustainable disease prevention comes from changed behaviour enabled by an improved

environment. Trachoma was eliminated throughout Europe and the United States with improvements in development, as was hookworm from the southern United States (Stiles, 1939; Taylor, 2008). The hands and feet of the health services delivery system in Ethiopia are the health extension workers (HEW). They currently are involved in most community-based primary care and public health programmes, including immunisations, distribution of antibiotics during MDA for trachoma and behaviour change communication for the SAFE strategy. Their main focus is to achieve 100% of the households in their *kebele* with indicators of the 17 health "packages," including safe water containers, latrines, and hand washing stations (Ethiopia, 2012). Community led total sanitation (CLTS) has been adopted by the Amhara National Regional State Health Bureau and is implemented primarily through HEWs (Kar and Chambers, 2008). Improved coordination between the current CLTS, UNICEF WASH and the trachoma control programmes might provide additional synergies in controlling disease and improving health. This would require the joint planning, implementation, supervision, and operational research among Bureaus of Development, Education and Health. Improving water quality, sanitation, and hygiene would remove a certain dependence of NTD control efforts on drug donations and external resources and ultimately fulfill a core component of primary health care (1978).

10. Conclusions

Through this thesis, novel approaches to evaluate the impact of the SAFE strategy were applied in the context of the ongoing disease control programmes of the health system. Each objective was successfully addressed adhering to a proposed ideal process of implementing operational research. Each study provided the following: information upon which the Amhara National Regional State Health Bureau can base decisions to improve delivery of disease control interventions; generalisable knowledge concerning trachoma elimination, electronic data collection, community-based surveys, and integrated NTD survey methodology; and additional operational research issues to be addressed. Listed below are specific conclusions substantiated through the findings of the operational research studies presented in this thesis:

- The implementation of the SAFE strategy has reduced severe inflammation and scarring due to trachoma among children, which reduces their risk of blinding trachoma later in life. However, the WHO targets for elimination have not been achieved. Trachoma remains a public health problem in South Wollo and South Gondar zones of the Amhara National Regional State of Ethiopia and ongoing interventions are warranted to control transmission to prevent incident blinding disease and provide surgery for prevalent and incident cases of trichiasis.

- Determining the prevalence of trachoma at the sub-district level was feasible, but required significant resources. In the current application of these surveys, conducting surveys to estimate prevalence first at the district level would have required less field work.

- Large-scale community assessments required to evaluate health system programmes can be facilitated through electronic data capture. A mixed-methods research approach allowed the technology to be tailored to the functionality required by the survey methods, rather than the survey methods constrained by the capabilities of the technology.

- Children aged 1-10 years have a substantially, statistically significant, lower risk of scarring due to trachoma after having lived in an environment where the SAFE strategy has been implemented for five years. The benefit depends on both the number of years

lived prior to and during the interventions. Monitoring changes of TS among children offers an additional way to monitor impact of the SAFE strategy.

- Children who attend school do not represent the target age group recommended for assessment of trachoma prevalence and are less likely to have TF than children who do not attend school. Therefore, determining trachoma prevalence through school-based sampling methodologies risk underestimating prevalence in the community.

- The prevalence of intestinal helminths among school-aged children has declined alongside significant increases in household-level indicators of water, sanitation, and hygiene since the implementation of the SAFE strategy in South Gondar. However, there is ongoing transmission of intestinal parasitic infections, warranting improved control interventions. Community-based surveys integrating both the assessment of trachoma and intestinal parasitic infections are feasible.

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WORK EXPERIENCE

PROGRAM EPIDEMIOLOGIST Sep 2006 – present
THE CARTER CENTER
Health Programs

- Develop methodology, initiate field work, manage, analyze and interpret data for surveys assessing neglected tropical diseases in Ethiopia, Ghana, Mali, Niger, Nigeria, Sudan, South Sudan
- Design, apply and manage Android based electronic data collection in routine, large-scale disease monitoring surveys
- Provide written reports and presentations to Board of Counselors, donors of The Carter Center and former United States President Jimmy Carter and wife Rosalynn Carter
- Provide ongoing data analysis from field reports and surveys to monitor and evaluate progress towards meeting organizational output and disease elimination targets
- Present operational research findings from The Carter Center supported Neglected Tropical Disease programs at international scientific meetings

GUEST RESEARCHER Oct 2004 – Aug 2006
CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)
National Centers for Infectious Diseases
Parasitic Division

- Coordinated operational research activities to verify the absence of lymphatic filariasis (LF) in US affiliated Pacific Islands
- Developed recommendations for CDC support to the global program to eliminate blinding trachoma to be incorporated in the Parasitic Division's strategic plan and contribute to goal formation within the Office of Global Health
- Developed and implemented operational research studies on the integration of neglected tropical disease elimination programs
- Implemented sentinel surveillance activities to monitor the impact of mass drug distribution in American Samoa
- Developed and implemented surveys in American Samoa to validate reported community participation in mass treatment programs and determine reasons for compliance and non-compliance.
- Developed an operational research proposal for submission to the Bill and Melinda Gates Foundation to determine the feasibility and safety of integrated mass treatment to eliminate trachoma and LF (funded through a $5 million grant to International Trachoma Initiative in 2007)

GUEST RESEARCHER Oct 2002 – Sep 2004
CDC National Centers for Infectious Diseases
American Samoa Department of Health, Pago Pago

- Developed community surveys regarding LF and utilized the results to create new strategies that improved community participation in mass treatment from 49% to over 80% of the population
- Managed the program budget to acquire local services, supplies, equipment, transportation and methods of communication for filariasis elimination activities

- Developed a surveillance system to improve the capacity to detect and respond to outbreaks of infectious disease and investigated and controlled outbreaks of infectious diseases

PREVENTION SPECIALIST Sep 1999 – Sep 2002
CDC APPLIED PUBLIC HEALTH TRAINING PROGRAM

Hillsborough County Health Department Tampa, Florida
Tuberculosis Prevention and Control Program

- Analyzed and interpreted tuberculosis (TB) data and developed annual program reports
- Established partnerships with community organizations to improve TB services to rural farmworkers and the HIV co-infected
- Evaluated program effectiveness for contact investigations and treatment of latent TB infection
- Managed state funding for TB prevention programs targeting foreign-born populations
- Designed, implemented, and evaluated a program of directly observed therapy for refugees and recent immigrants with latent TB infection

Division of International Health CDC Atlanta, Georgia

- Provided technical assistance to the World Health Organization (WHO) and the Ministry of Health of Ghana during an assessment of Ghana's communicable disease surveillance system
- Contributed to the development of technical guidelines on analyzing and interpreting surveillance data for district level health workers a component of Integrated Disease Surveillance and Response (IDSR) implementation in member countries under the Africa Regional Office of WHO
- Developed proposals for supplemental funding in the areas of micronutrient malnutrition (MM) and Global AIDS prevention
- Facilitated discussions on MM programs with health workers from 11 different countries at an international conference

Division of Parasitic Diseases, Epidemiology Branch CDC Atlanta, Georgia

- Implemented a communication plan to reduce the transmission of waterborne diseases in recreational water facilities in the United States
- Developed, implemented, and evaluated several recreational water-borne disease prevention documents for the print media and the internet
- Designed content for the Division's web site
- Managed and analyzed data for a water contamination research study
- Developed a resource database concerning disease control in recreational water facilities

GRADUATE RESEARCH ASSISTANT Aug 1998 – Jul 1999
ROLLINS SCHOOL OF PUBLIC HEALTH EMORY UNIVERSITY
Department of Behavioral Science and Health Education

- Trained 38 data abstractors from Georgia health districts to collect data
- Completed a statistical analysis of the study database using EpiInfo and SAS
- Facilitated a focus group evaluation of the immunization study among data abstractors

OTHER QUALIFICATIONS

TEMPORARY ADVISOR WHO:

Western Pacific Regional Office

- Documented progress of the Pacific Program to Eliminate Lymphatic Filariasis from 1999-2005 for the 2006 WHO publication, *The PacELF Way*

Geneva, Department of Control of Neglected Tropical Diseases

- Present findings and recommendations of ongoing schistosomiasis control activities in central Nigeria at the Informal Consultation on Schistosomiasis Control Meeting 30 Mar-1 April 2011

TEAM MEMBER: US CDC EPI-AID Emergency Response to Bioterrorism
Washington, DC and Trenton, NJ Oct 23 - Dec 14, 2001

- Coordinated HAZMAT teams to collect surface wipe samples in identified mail rooms in DC
- Implemented a mass post-exposure prophylaxis (PEP) clinic for persons at risk of exposure to anthrax spores in NJ
- Created and managed a database of reported adverse events experienced by persons receiving PEP
- Implemented a communication initiative to promote adherence to persons receiving PEP

VOLUNTEER: Catholic Charities Mobile Medical Unit, International Mercy Missions Inc. and Mission to Haiti

- Worked with local medical providers to promote disease prevention in underserved communities in rural parts of United States, Honduras and Haiti

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EDUCATION

PHD CANDIDATE EPIDEMIOLOGY 2010-present
SWISS TROPICAL AND PUBLIC HEALTH INSTITUTE, UNIVERSITY OF BASEL

MSPH EPIDEMIOLOGY 1997-1999
EMORY UNIVERSITY, ROLLINS SCHOOL OF PUBLIC HEALTH

BS APPLIED BIOLOGY 1992-1996
GEORGIA INSTITUTE OF TECHNOLOGY

AWARDS

CDC PHPS 2002 Award for Distinguished Service and Achievement	June 13, 2002
Hillsborough County Health Department Director's Recognition Award	August 9, 2002

PUBLICATIONS

King JD, Schindler C, Ngondi J, Odermatt P, Utzinger J, Mulualem A, Amnie AG, Zerihun M, Tadesse Z, Teferi T, Gebre T, Emerson PM. (at review) Impact of the SAFE strategy on trachomatous scarring among children in Ethiopia: a repeated cluster randomised cross-sectional study. *Lancet*

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King JD, Odermatt P, Utzinger J, Ngondi J, Bamani S, Kamissoko Y, Boubicar K, Hassan AS, Nwobi BC, Jip N, Amnie AG, Teferi T, Mosher AW, Stewart AEP, Cromwell EA, Emerson PM. (2013) Trachoma among children in community surveys from four African countries and implications of using school surveys for evaluating prevalence. *International Health*

King JD, Buolamwini J, Cromwell EA, Panfel A, Teferi T, Zerihun M, Melak B, Watson J, Tadesse Z, Vienneau D, Ngondi J, Utzinger J, Odermatt P, Emerson PM. (2013) A novel electronic data collection system for large-scale surveys of neglected tropical diseases. *PLoS One*

King JD, Endeshaw T, Escher E, Alemtaye G, Melaku S, Worku A, Adugna M, Melak B, Teferi T, Zerihun M, Gesese D, Tadesse Z, Mosher AW, Odermatt P, Utzinger J, Marti H, Ngondi J, Hopkins DR, Emerson PM. (2013) Intestinal parasite prevalence in an area of Ethiopia after implementing the SAFE strategy, Enhanced Outreach Services, and Health Extension Program. *PLoS Neglected Tropical Diseases*

Cromwell EA, Amza A, Kadri B, Beidou N, **King JD**, Sankara D, Mosher AW, Hassan S, Kane S, Emerson PM. (in press) Trachoma prevalence in Niger: results of 31 district-level surveys. *Transactions of the Royal Society of Tropical Medicine and Hygiene*

Evans DS, **King JD**, Eigege A, Umaru J, Adamani W, Alphonsus K, Sambo Y, Miri ES, Goshit D, Ogah G, Richards FO. (2013) Assessing the WHO 50% prevalence threshold in school-aged children as indication for treatment of urogenital schistosomiasis in adults in central Nigeria. *American Journal of Tropical Medicine and Hygiene*

Cromwell EA, **King JD**, McPherson S, Jip FN, Patterson AE, Mosher AW, Evans DS, Emerson PM. (2013) Monitoring the mass distribution of interventions for trachoma in Plateau State, Nigeria. *PLoS Neglected Tropical Diseases*

Cromwell EA, Ngondi J, McFarland D, **King JD**, Emerson PM. (2012) Methods for estimating population coverage of mass distribution programmes: a review of practices in relation to trachoma control. *Transactions of the Royal Society of Tropical Medicine and Hygiene*

King JD, Eigege A, Umaru J, Jip N, Miri E, Jiya J, Alphonsus K, Sambo Y, Graves P, and Richards F Jr. (2012) Evidence for stopping mass drug administration for lymphatic filariasis in some, but not all local government areas of Plateau and Nasarawa States, Nigeria *American Journal of Tropical Medicine and Hygiene*

Hassan A, Ngondi JM, **King JD**, Elsanousi M, Abdalla Z, Aziz N, Elkhair B, Sankara D, Simms V, Cromwell E, Emerson PM, Osman KH. (2011) The prevalence of blinding trachoma in northern states of Sudan. *PLoS Neglected Tropical Diseases*

Chen C, Cromwell EA**, King JD**, Harding-Esch E, Ngondi JM, Emerson PM. (2011) Incremental cost of conducting population-based prevalence surveys for a neglected tropical disease: the example of trachoma in 8 national programs. *PLoS Neglected Tropical Diseases*

King JD, Ngondi J, Kasten J, Diallo M, Zhu H, Cromwell E, Emerson PM. (2010) Randomised trial of face-washing to develop a standard definition of a clean face for monitoring trachoma control programmes. *Transactions of the Royal Society of Tropical Medicine and Hygiene*

King JD, Zielinski-Gutierrez E, Pa'au M, Lammie PJ. (2010) Improving community participation to eliminate lymphatic filariasis in American Samoa. *Acta Tropica*

King JD, Nimzing J, Jugu YS, Othman A, Rodgers AF, Dajom DY, Miri E, Emerson PM. (2010) Mapping trachoma in Nasarawa and Plateau States, central Nigeria. *British Journal of Ophthalmology*

Bamani S, **King JD**, Dembele M, Coulibaly F, Sankara D, Kamissoko Y, Ting J, Rotondo LA, Emerson PM. (2010) Where do we go from here? Prevalence of trachoma three years after stopping mass distribution of antibiotics in the Regions of Kayes and Koulikoro, Mali. *PLoS Neglected Tropical Diseases*

Bamani S, Dembele M, Sankara D, Coulibaly F, Kamissoko Y, Ting J, Rotondo LA, Emerson PM, **King JD**. (2010) Evaluation of the prevalence of trachoma 12 years after baseline surveys in Kidal Region, Mali. *Tropical Medicine and International Health*

Baker MC, Mathieu E, Fleming FM, Deming M, **King JD**, Garba A, Koroma JB, Bockarie M, Kabore A, Sankara DP, Molyneux DH. (2010) Mapping, monitoring, and surveillance of neglected tropical diseases: towards a policy framework. *Lancet*

Cromwell EA, Ngondi J, Gatpan G, Becknell S, Kur L, McFarland D, **King JD**, Emerson PM. (2009) Estimation of population coverage for antibiotic distribution for trachoma control: a comparison of methods. *International Health*

Ngondi J, Gebre T, Shargie E, Adamu L, Teferi T, Zerihun M, Ayele B, **King JD**, Cromwell EA, Emerson PM. (2009) Estimation of effects of community intervention with Antibiotics, Facial cleanliness, and Environmental improvement (A,F,E) in five districts of Ethiopia hyper-endemic for trachoma. *British Journal of Ophthalmology*

Rotondo LA, Ngondi J, Rodgers AF, **King JD**, Kamissoko Y, Amadou A, Jip N, Cromwell EA, Emerson PM. (2009) Evaluation of community intervention with pit latrines for trachoma control in Ghana, Mali, Niger and Nigeria. *International Health*

Heggen AE, Valerio MA, Thoar GG, Rodgers AF, **King JD**, Kur LW, Becknell S, Emerson PM. (2009) Examining media habits: implications for health promotion programs among the Toposa in Southern Sudan. *International Health*

King JD, Eigege A, Richards F, Jip N, Umaru J, Deming M, Miri E, McFarland D, and Emerson PM. (2009) Integrating NTD mapping protocols. Can surveys for trachoma and urinary schistosomiasis be done simultaneously? *American Journal of Tropical Medicine and Hygiene*

Cromwell E, Courtright P, **King JD**, Rotondo L, Ngondi J, Emerson PM. (2009) The excess burden of trachomatous trichiasis in women: a systematic review and meta-analysis. *Transactions of the Royal Society of Tropical Medicine and Hygiene*

Yayemain D, **King JD**, Debrah O, Emerson PM, Aboe A, Ahorsu F, Wanye S, Ansah MO, Gyapong J, Hagan M. (2009) Achieving trachoma control in Ghana after implementing the SAFE strategy. *Transactions of the Royal Society of Tropical Medicine and Hygiene*

Ngondi JM, Matthews FE, Reacher MH, **King J**, Brayne C, Gouda H, Emerson PM. (2009) What will happen if we do nothing to control trachoma: health expectancies for blinding trachoma in southern Sudan. *PLoS Neglected Tropical Diseases*

Ngondi J, Gebre T, Shargie EB, Adamu L, Ejigsemahu Y, Teferi T, Zerihun M, Ayele B, Cevallos V, **King JD**, Emerson PM. (2009) Evaluation of three years of the SAFE strategy (Surgery, Antibiotics, Facial cleanliness and Environmental improvement) for trachoma control in five districts of Ethiopia hyper-endemic for trachoma. *Transactions of the Royal Society of Tropical Medicine and Hygiene*

Mladonicky JM, **King JD**, Liang JL, Chambers E, Pa'au M, Schmaedick MA, Burkot TR, Bradley MH, Lammie PJ. (2009) Assessing transmission of lymphatic filariasis using parasitologic, serologic and entomologic tools following mass drug administration in American Samoa. *American Journal of Tropical Medicine and Hygiene*

Chambers EW, McClintock SK, Avery MF, **King JD**, Bradley MH, Schmaedick MA, Lammie PJ, Burkot TR. (2009) An analysis of xenomonitoring of *Wuchereria bancrofti* and *Dirofilaria immitis* infections in mosquitoes from American Samoa: trapping considerations and a comparison of polymerase chain reaction assays with dissection. *American Journal of Tropical Medicine and Hygiene*

King JD, Ngondi J, Gatpan G, Lopidia B, Becknell S, Emerson PM. (2008) The burden of trachoma in Ayod county of Southern Sudan. *PLoS Neglected Tropical Diseases*

Jip NF, **King JD**, Diallo MO, Miri ES, Hamza AT, Ngondi J, Emerson PM. (2008) Blinding trachoma in Katsina State, Nigeria: population-based prevalence survey in ten local government areas. *Ophthalmic Epidemiology*

Liang JL, **King JD**, Ichimori K, Handzel T, Pa'au M, Lammie PJ. (2008) Impact of five annual rounds of mass drug administration with diethylcarbamazine and albendazole on *Wuchereria bancrofti* infection in American Samoa. *American Journal of Tropical Medicine and Hygiene*

Ngondi J, Reacher M, Matthews F, Brayne C, Gatpan G, Becknell S, Kur L, **King JD**, Callahan K, Emerson PM. (2008) Risk factors for trachomatous trichiasis in children: cross-sectional household surveys in Southern Sudan. *Transactions of the Royal Society of Tropical Medicine and Hygiene*

TECHNICAL TRAINING

Project Management
Focus Group Research Methods
Cultural Competency
Effective Presentations
Conflict Resolution
ArcGIS
HIV Pre/Post test counseling
STATA, SAS, SPSS, Epi Info
French (limited working proficiency plus)
Program Evaluation
Media Relations
Risk Communication
Negotiation Skills
Dale Carnegie Leadership
CDC Applied Epidemiology & Biostatistics
Tuberculosis Contact Investigation
Microsoft Access
Spanish (elementary proficiency)

13. Appendix

S1. South Gondar Trachoma Impact Evaluation Survey Questionnaire – Amhara, Ethiopia 2011

Team number:	|___|___|	Cluster Number (1-380):	|___|___|___|	Household number:	|___|___|
Serial Number:	|___|___||___|___|___||___|___| **Team Cluster Household**		Gott name:		
Woreda name:		Health Cluster Name:			
Kebele name:		Development team name:			

Survey Date (DD/MM/YYYY) |___|___|/|___|___|/|___|___|___|___|	GPS	Latitude: (N) |___|___| . |___|___|___|___|___|
Household interview consent given? No= 0 Yes= 1		Longitude: (E) |___|___|___| .|___|___|___|___| __|
Examination of children consent given? No= 0 Yes= 1		Elevation: |___|___|___|___| m

Respondents' demographics (Adult females: women and mothers of children are the preferred respondents)

RD1	Name of head of Household	*Write name* _____	
RD2	Description of Respondent	Head of household=1 Wife of head of household=2	
RD3	Gender of Respondent	Male= M Female= F	
RD4	How old are you? *(round months down)*	*(write age in years)* |___| __|	
RD5	What is the highest level of school you have attended? *(If "none," ask "have you had any non-formal education?")*	None=0 Religious=1 Primary school (grade 1-6)=2 Junior secondary=3 Senior secondary=4 College/University=5 Non-formal Education=6	

RD6	What is the HoH's primary occupation?	Farming and Cattle rearing = 1 Cattle rearing only = 2 Farming only = 3 Formal employment (monthly salary) = 4 Trade (business) = 5 Daily labourer = 6 Other *(write in)*_____ = 98	
RD7	Have you lived in this Gott for more than 4 years?	No=0; Yes=1	Yes go to ES1
RD8	If no, in which Woreda and Zone did you live recently?	(specify) _____	
Household Social Economic Status			
	Does your household have any of the following?		
ES1	Functioning radio set	No=0; Yes=1	
ES2	Functioning Television	No=0; Yes=1	
ES3	Working electricity	No=0 ; Yes=1	
ES4	Functioning telephone (landline)	No=0 ; Yes=1	
ES5	Functioning mobile phone	No=0 ; Yes=1	
ES6	**Observation:** what is the main construction material for the roof in this household? *(One response only)*	Corrugated Iron=1 Thatch =2 Stick and mud=3 Other=99 (*specify*)_____	
Knowledge			
K1	Have you ever seen anyone with this eye condition? *(link to show image TTwCO.jpeg)*	No=0; Yes=1	
K2	What is this condition called?	Trachoma=1 Cataract=2 I do not know=88 Other=99 (specify)_____	
K3	Do you know what trachoma is?	No=0; Yes=1	If No, go to HE1
K4	In the end, what can happen to a person who has trachoma? *(multiple response)* *(After each response ask 'anything else?' Do not read choices. Please mark all responses given.)*	K4.1 Nothing happens ☐ K4.2 Blindness ☐ K4.3 Reduced vision ☐ K4.88 I do not know ☐ K4.99 Other ☐ (specify)_____	
K5	How can someone protect him/herself from trachoma/trichiasis? *(multiple response)*	K5.1 Face washing/hygiene ☐ K5.2 Take antibiotics or medicine ☐ K5.3 Trichiasis surgery ☐ K5.4 Keeping environment clean ☐	

	(After each response ask 'anything else?' Do not read choices. Please mark all responses given.)	K5.5 Using pit latrines ☐ K5.88 I do not know ☐ K5.99 Other ☐ (specify)_____	
Health Education			
HE1	Have you ever heard health information on trachoma?	No=0 Yes=1	If No go to WS1
HE2	Where did you hear the trachoma information? *(multiple response)* *(After each response ask 'anything else?' Do not read choices. Please mark all responses given.)*	HE2.1 Trachoma volunteers ☐ HE2.2 Health extension worker ☐ HE2.3 Mass media (TV, radio, etc) ☐ HE2.4 Health facility ☐ HE2.5 Community gatherings ☐ HE2.6 School ☐ HE2.7 School child ☐ HE2.99 Other ☐ (*specify*)_____	
HE3	What information about trachoma did you hear? *(multiple response)* *(After each response ask 'anything else?' Do not read choices. Please mark all responses given.)*	HE3.1 Causes of trachoma ☐ HE3.2 Transmission of trachoma ☐ HE3.3 Latrine construction and use ☐ HE3.4 Face washing ☐ HE3.5 Antibiotics treatment ☐ HE3.6 Trichiasis surgery ☐ HE3.99 Other ☐ (*specify*)_____	
Water source and access (Ask person responsible for water collection)			
WS1	What is the main source of water your household uses for bathing?	Unprotected spring=1 Protected spring=2 Unprotected dug well=3 Hand pump/Tube well / borehole=4 Surface water (river, dam, lake, stream, canal)=5 Public piped water/ tap/standpipe=6 Private piped into Yard/dwelling=7 Rainwater collection=8 Other (*specify*)_____=99	
WS2	What is the main source of water your household uses for washing clothes?	Unprotected spring=1 Protected spring=2 Unprotected dug well=3 Hand pump/Tube well / borehole=4 Surface water (river, dam, lake, stream, canal)=5 Public piped water/ tap/standpipe=6 Private piped into Yard/dwelling=7 Rainwater collection=8 Other (*specify*)_____=99	

WS3	What is the main source of water your household uses for drinking?	Unprotected spring=1 Protected spring=2 Unprotected dug well=3 Hand pump/Tube well / borehole=4 Surface water (river, dam, lake, stream, canal)=5 Public piped water/ tap/standpipe=6 Private piped into Yard/dwelling=7 Rainwater collection=8 Other (*specify*)_____=99	
WS4	How long does a round-trip take to collect water from the source of water used for **bathing**?	<30 minutes=1 30 minutes to 1 hour=2 > 1 hour=3	
Face washing (Ask mothers or care givers of children)			
FW1	Do you have children under 5 years of age?	No=0; Yes=1	If No, go to PL1
FW2	How often are these children bathed? *(Indicate one answer)*	Never=0 Every other day=1 Once a day=2 Twice a day=3 Three or more times a day=4 Other (*specify*)_____=99	
FW3	How often are the faces of children washed? *(Indicate one answer)*	Never=0 Every other day=1 Once a day=2 Twice a day=3 Three or more times a day=4 Other (*specify*)_____=99	
Pit Latrines			
PL1	Have you ever had a latrine in this household?	No=0; Yes=1	
PL2	Currently, is there a latrine in this household (observed)?	No=0; Yes=1	If No go to LO2 (note there may still be a hand washing container in the HH)
PL3	Is this the first latrine in this household?	No=0; Yes=1	
PL4	How long ago was the most recent latrine built?	_____***YEARS*** _____***MONTHS ago***	
Latrine observations			
LO1	Evidence of latrine usage (*faeces in pit)?*	No=0; Yes=1	
LO2	Hand washing container present?	No=0; Yes=1	If no to LO2, END
LO3	Water in hand washing container?	No=0; Yes=1	
LO4	Location of hand washing container?	At latrine=1; At household=2	

Serial Number (same as HH quest.) |___|___|___|___|___|___|___|___| HH #: |___|___| Cluster #: |___|___|___|

				Absent	**School**	**Antibiotic treatment during MalTra (tablets, POS or TEO)**				**Use latrine**	**Discharge No=0; Yes=1**		**Right Eye No=0; Yes=1**					**Left Eye No=0; Yes=1**					**If TT**	**PCR or STH**
ID. #	**Name**	**Sex M/F**	**Age**	Present=0 Out=1 Travel=2 No consent=3 At school=4	No=0 Yes=1	**Ever taken** No=0 Yes=1	**# times taken**	**In register?** No=0 Yes=1	**Response Verified** No=0 Yes=1	Always=1 Some=2 Never=3	**Ocular**	**Nasal**	**TT**	**CO**	**TF**	**TI**	**TS**	**TT**	**CO**	**TF**	**TI**	**TS**	**Write # lashes on globe**	Write PCR, STH, or both if selected
1																								
2																								
3																								
4																								
5																								
6																								

S2. Questions to prompt group discussion concerning use of electronic and paper questionnaires

After using both paper and electronic questionnaire:

1. What are the advantages and disadvantages of each method?
2. Which data collection method do you prefer and for what reasons?
3. What problems did you have when collecting data using either method?
4. Which data collection method do you think took less time to complete during the survey and why?
5. With which tool do you think an interviewer will make fewer mistakes and why?
6. How did you feel about using the tablet computer to collect data?
7. What would you suggest adding or changing in order to make use of the tablet computers easier?
8. Which sections of the electronic questionnaire did you find difficult to use?
9. In what areas of electronic data collection do you feel you need more training?