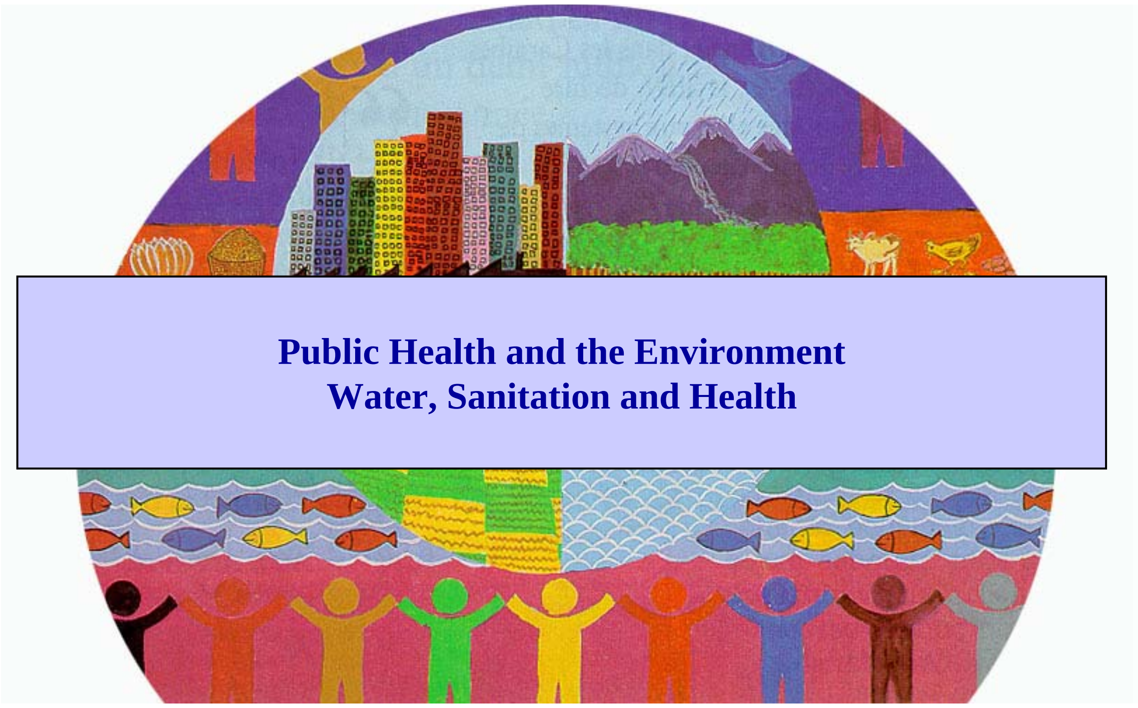
World Health Organization

Sustaining Trachoma Control and Elimination

The basis for environmental indicators in the certification of the elimination of blinding Trachoma



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The Basis for Environmental Indicators in the Certification of the Elimination of Blinding Trachoma

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Water, Sanitation and Health
World Health Organization
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Section 1: Introduction

The devastating consequences of the blinding disease trachoma are often underestimated. The impacts are especially unforgiving in developing countries where there is a lack of technology, health care services, and support structures to assist those at risk and those infected. The loss of sight engenders a corresponding loss of ability to engage in productive work, conduct basic household tasks and care for oneself and family. Trachoma related morbidity includes direct consequences, as well as impacts from secondary opportunistic infections commonly associated with trachoma. Furthermore, trachoma can even lead to increased mortality rates in children (1). This translates into significant economic losses that can cripple communities where the disease is endemic and inhibit development.

Trachoma is completely preventable. The disease was once widespread throughout the globe, but improved sanitation, greater access to water and economic development led to the elimination of the disease in Europe and the United States (2). Many of the poorest countries in the world continue to suffer from trachoma. Trachoma is endemic in the poorest and most remote areas of 56 countries, most of which are located in Sub-Saharan Africa and Southeast Asia, as illustrated in **Figure 1** (3). It is estimated that 92 million people suffer from some stage of trachoma and eight million are visually impaired or blind as a result of the disease (4). In addition, up to 600 million individuals live in endemic areas and are at risk for contracting the disease (5).

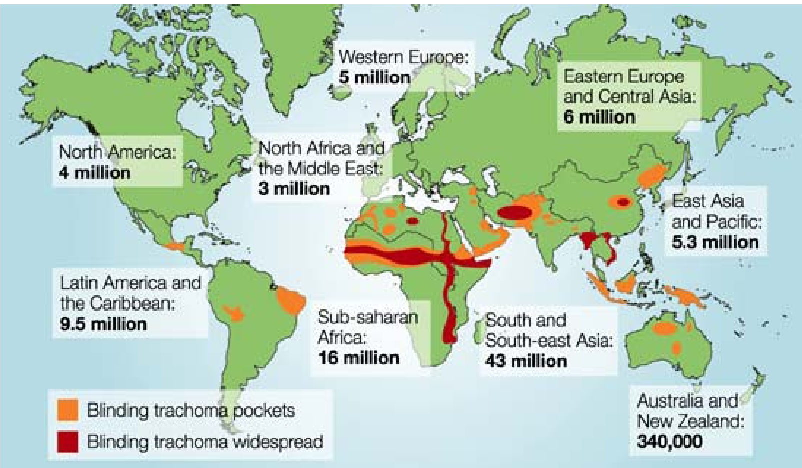


Figure 1: Global Distribution of Trachoma (source: WHO, 2002)

Historical evidence and current research demonstrate that with improved environmental sanitation, access to water and economic development trachoma can be eliminated. The WHO is leading a multi-faceted campaign with collaborators from the public and private sector to eliminate blinding trachoma by 2020 (GET 2020). A critical marker in determining the success of this campaign is formal certification of elimination. Eliminating trachoma will result in significant benefits to millions of individuals who currently suffer from the disease. From a policy perspective it will also allow Member States and GET 2020 collaborating partners to devote scarce resources to other important public health and development related problems. Given the importance of maximizing the benefit of trachoma control investments and the significant costs of campaign failure, deliberate care must be taken to develop certification indicators and procedures.

GET 2020 is in the process of developing indicators and specific standards which will be used to certify elimination of blinding trachoma. The identified indicators and efforts place greater emphasis on treatment, rather than the prevention. Although chemotherapy based treatment initially reduces disease prevalence, it may not be sufficient to sustain the elimination of blinding trachoma and even less likely to sustain elimination of all forms of the disease. Clearly, past lessons from trachoma control efforts demonstrate that the key to sustainable elimination of trachoma as a blinding disease rests not only on medical and surgical interventions, but on addressing the behavioral and environmental aspects of the disease (6). Preventing trachoma transmission through environmental interventions, such as providing improved sanitation, is cost effective, especially when done in collaboration with existing international initiatives, such those being carried out to meet the United Nations Millennium Development Goals (U.N. MDGs). Furthermore, relying primarily on treatment through antibiotics is not cost-effective as the benefits from resolving the infection are only temporary and individuals may become re-infected. The preferred antibiotic, azithromycin, is donated free of charge by Pfizer, but considerable costs are still involved in distributing and administering the drug to those in need. These costs will only rise as prevalence falls and those infected must be detected and treated on an individual basis, rather than the current practice of mass distribution in endemic areas.

Parallel efforts to improve, maintain and monitor environmental conditions have demonstrated effectiveness in preventing trachoma transmission. The formal requirement of such measures within the certification process documents is necessary to strengthen and ensure sustained success of both prevention and treatment efforts. Therefore, the certification process is in need of simple, straightforward prevention based environmental indicators that will give credibility and assurance to initial treatment related disease reductions.

This report is not an official document of the trachoma certification process and the proposals for indicators are not definitive. Rather, this report provides the basis for concluding that a substantial weight of evidence exists to include environmental indicators in certification and more generally to place greater focus on prevention through the environment. Section 4 does propose environmental indicators as a starting point for further evaluation and analysis by experts and program managers tasked with developing and measuring indicators for certification of the elimination of blinding trachoma. The report complements, rather than replicates existing environmentally related trachoma documents and reports, by examining the key factors that underpin the effectiveness of environmental interventions in preventing and controlling trachoma. The analysis presented draws upon disease theory and principles, academic research, and field reports to create a framework from which to develop and propose specific environmental indicators for use at the country and district level.

The body of this report is organized in three sections that address the following fundamental questions:

- **Section 2: Basis for Disease Elimination**
  According to principles of epidemiology and pathology and experiences of other infectious disease control efforts, what elements are necessary to reduce and sustain elimination of trachoma?

- **Section 3: Preliminary Analysis of Environmental Indicators and Trachoma**
  What is the extent of links between environmental indicators and trachoma prevalence? How might outliers from these trends be explained?

- **Section 4: Use of Environmental Indicators in Trachoma Campaign**
  From the current body of literature on environmental indicators and the statistical analysis, which indicators would be most effective and under what framework could such indicators be implemented within the current trachoma elimination campaign?

The main section is followed by conclusions, references and appendix where environmental indicator definitions, additional statistic plots and further resources for measuring indicators and promoting environmental change are located.

Section 2: Basis for Disease Elimination

Section 2 provides a framework for understanding the process of elimination of infectious disease and the basis for certification of disease elimination. It begins by describing the principles of disease elimination, transmission and prevention and how they apply to trachoma. This is followed by lessons learned from other water-related infectious disease control efforts. The final section highlights the driving forces for expanding the current blinding trachoma elimination certification standards to include measures of hygiene and environmental health in order to permanently sustain elimination once achieved.

2.1 Conceptual Framework

The conceptual framework is for understanding the major factors influencing trachoma elimination is built upon four main areas of investigation. These include disease elimination, the infectious agent of trachoma, disease transmission pathways, and disease recurrence. Two important terms to note in this section are the elimination of blinding trachoma and the elimination of trachoma. The GET 2020 campaign is focused on the former, but the latter is important to discuss as even non-blinding forms of trachoma can cause visual impairment and also could escalate to blindness if proper prevention measures are not taken.

2.1.1 Disease Elimination

The Dahlem Conference, held in 1998, provided a forum for disease experts to develop consensus on how to define and describe disease control efforts. A disease elimination campaign is specifically developed according to defined goals. For disease elimination this is "the reduction to zero of the incidence of infection caused by a specific agent in a defined geographical area as a result of deliberate efforts" (7). Inherent to this definition is the need for ongoing efforts and interventions to prevent re-establishment of transmission. In contrast, disease eradication is the permanent reduction to zero of incidence of infection which means once eradication is achieved interventions are no longer necessary (7).

The GET 2020 aims to eliminate only the blinding stage of trachoma and not less intense forms of the disease. The decision to target specifically blinding trachoma is based on the work of the International Task Force for Disease Eradication (ITFDE), a group of scientists who convened from 1989-1992 to establish and apply systematic criteria in evaluating the potential to eradicate or eliminate infectious diseases. Specifically, the ITFDE concluded that "it is scientifically feasible to eliminate blindness caused by trachoma, but not the infection or agent itself" (8). This led to the World Health Assembly Resolution 51.11 which calls on Member States to implement as required the SAFE strategy (surgery, antibiotics, facial cleanliness, and environmental improvement) "for the elimination of blinding trachoma" (9).

It is important when making scientifically based policy decisions regarding disease elimination to differentiate between what is technically and logistically feasible. The ITFDE ruling is not based on an actual technical or scientific basis for trachoma elimination. Rather, the ruling is based on an assumption that attempting to eliminate all forms of trachoma by 2020 would be difficult to justify from a cost-effectiveness perspective, especially considering other global health priorities and the minuscule national budgets on which developing countries operate. The argument for limiting elimination to only blinding trachoma is that the burden of early stages of disease is less adverse and therefore the benefits gained would also be incrementally less. The costs, however, for prevention of trachoma would not be borne by the health sector alone. The water and sanitation as well as the education sectors have a vested interest in improving services and hygiene behavior to reduce the burden of trachoma along with multitude of other water-related infectious diseases. Other disease elimination campaigns, such as Guinea Worm discussed further later in the report, have proven that capitalizing on water and sanitation efforts, results in mutually beneficial environmental and health gains.

To meet the aim of eliminating blinding trachoma, three certification indicators have been proposed:

- Elimination of blinding cases or trachomatous trichiasis (TT) through surgery or at least offering surgical services to all cases (patient may refuse surgery)
- Reduction of trachomatous follicular (TF) to < 1/1000 in adults
- Reduction trachomatous follicular (TF) to < 5% prevalence in children (1-9 years)

Formal adoption of the indicators and standards is hoped to be achieved by the end of 2006. WHO is in the process of establishing two committees to assist in the development and implementation of certification standards. The first is a technical indicator committee that will advise on selecting, assessing and monitoring environmental indicators. The second is a certification advisory committee that will ratify the guidelines and carry out the actual evaluation of certification status.

Primary Conditions Necessary for Elimination

Several essential conditions are necessary for disease elimination. These conditions, which were discussed at the Dahlem Conference and by the IFTDE, are summarized into three main areas highlighted below.

- Minimized epidemiological vulnerability
    - Humans essential life cycle
    - Naturally induced immunity
    - Ease of clinical diagnosis
- Effective, practical intervention(s) to interrupt transmission
    - Curative treatment
    - Prevention and vector control measures
- Demonstrated feasibility of elimination

The second and third conditions have been met for trachoma. Curative treatment is available and has proven to reduce disease prevalence, although with varying results. A review of case controlled studies on the impact of antibiotic treatment found reductions from 14-36% in trachoma *infection* 12 months after use (10). However, in comparing the impact of antibiotics on *active* trachoma 12 months after use, the results were less promising and in some cases it was the control group that had less signs of active disease (10). This may be partially due to the difficultly in diagnosing trachoma which is discussed in further detail in subsequent section. Surgery is another form of treatment, but it can only assist in preventing blindness and does not cure the infection or prevent recurrence of the disease. Furthermore, even if the surgical procedure is done correctly, blindness may still occur either from reinfection with the disease agent, *Chlamydia trachomatis,* or from other opportunistic pathogens. In short, although treatment is important, it may not be sufficient to ensure that elimination of blinding trachoma is achieved and sustained. In fact, antibiotic programs for trachoma may only be relevant as interim measures until conditions for transmission have changed (11).

Historical Evidence of Elimination with Environmental Measures

Demonstrated feasibility of elimination, the third required condition, has been proven, largely based on environmental measures. Historical evidence from the U.S. and Europe demonstrates complete disease elimination is possible in the absence of treatment. In many cases improvements in sanitation, water supply, education, and hygiene combined with economic development were sufficient to eliminate trachoma (12, 13). In the United States, trachoma was especially prevalent in poorer regions and in marginalized, minority communities. In 1915 prevalence ranged from 10-92 % in various Native American populations (2).Yet in a single decade (1950-1960), blindness attributable to trachoma dropped 20-fold from 4.0 to 0.2% due largely to improved living standards, improved water and sanitation, and education (2).

More recently evidence of significant progress towards elimination through prevention measures has been documented in endemic countries. A survey comparing trachoma prevalence in 1983 to 1999 in Malawi found that a 50% reduction in active trachoma occurred in the absence of an antibiotic campaign and was largely due to health, water and hygiene programmes initiated in the endemic area during the 16 year period (14). In Marakissa, The Gambia, which did not have a formal, targeted trachoma control program, over a period of 37 years (1959-1996) trachoma prevalence in children fell from 65% to 2.4 % (15). Although lid surgery and some treatment was provided, most of the reductions of disease were attributed to improved sanitation, water supply, and housing, increased access to education and health care, and the construction of a paved road (15). Other countries such as Mexico and Morocco, which have nearly eliminated trachoma, have done so through a combination of treatment and prevention (4). These examples provide evidence that improved sanitation, water, and critical and often the most sustainable measures in eliminating trachoma.

Other Factors that Affect the Ability to Eliminate Trachoma

Other factors, both those that challenge and strengthen, the ability to eliminate trachoma. Many of these are described in *Future Approaches to Trachoma Control* and are highlighted in **Table 1** (16).

Table 1: Additional Trachoma Elimination Factors

Challenges	Strengths
Difficult to detect disease	Absence of another vertebrate host
Pathogenesis favors transmission	Committed global alliance
Poor patient compliance with antibiotic use	Prevention methods have proven effective
Lack of and reluctance to access surgical services	Repeated infections needed before disease occurs
Cost of providing services to isolated communities	

One of the most complicated challenges in eliminating trachoma is disease detection. Clinical detection is imprecise and is complicated by the non-linear relationship between infection and visual signs of disease (5). Signs of infection are highly dependent on the age of the individual, previous history of trachoma and other eye infections, and genetic response. In fact, the majority of infections are asymptomatic (17). Conversely, evidence of the disease may persist weeks after the infection has resolved itself.

2.1.2 Agent of Infection and Pathogenesis

The survival of any pathogen is dependent on two important factors. The first is the ability of a pathogen to utilize host resources for survival and replication. The second is the ability to spread from host to host. If the pathogen is prevented from replication within a host and spreading to other susceptibles, the pathogen load in the environment will decline leading to a decrease in disease prevalence (18).

To determine when such a decline will occur, it is first necessary to understand the lifecycle, transmission pathways, and pathology of *C. trachomatis,* the etiological agent of trachoma*. C. trachomatis* is an obligate, intracellular bacterium that only proliferates within a host eukaryote cell (13). It is one of three pathogenic *Chlamydia* species and causes both ocular and genital tract infections. Specifically, four serovars (*A*, *B*, *Bb*, and *C*) cause trachoma.

Outside the host cell, *C. trachomatis* exists as elementary bodies (EB), analogous to spores. Once inside the host cell, EB differentiate into reticulate bodies (RB) which are the non-infectious form of *Chlamydia* (13). While inside the cell, binary fusion replication occurs and RB differentiates back to EB. Eventually the EB occupy most of the cytoplasm within the cells and inclusions lyse at which point the EB are released into the environment.

Several important aspects of the pathogenesis of *C. trachomatis* are worth considering in relation to trachoma elimination. First, contrary to most pathogens, which typically regulate their own survival by limiting the amount of damage they incur on the host species, *C. trachomatis* has an incentive to exacerbate infection. Greater infection leads to increased ocular discharge which attracts flies and therefore increases the likelihood of transmission. Second, when infection occurs, the natural defense mechanism provided through tears washing away foreign objects, does not function properly. Without tears, *C. trachomatis* is more likely to attach to the conjunctival eye surface and subsequently cause infection (18). Finally, and perhaps most importantly, *C. trachomatis* is an extremely efficient and virulent, multiplying, producing infection and shedding all from the same epithelial surface site at which it enters the host (18). Even with such efficiency, tens if not hundreds of infections with *C. trachomatis* are necessary to result in the more advanced forms of trachoma that are of public health concern (13).

2.1.3 Disease Transmission and Progression

Understanding the transmission of infectious diseases forms a framework for determining how elimination of a specific disease, such as trachoma, may be achieved. Trachoma is transmitted when droplets containing *C. trachomatis* are spread through touching infected eyes, contact with contaminated pillows, clothes and towels, and feces breeding flies (*Musca sorbens* and *M. vestustissima*). These species of flies, for chemical and biological reasons, are preferentially attracted to eyes excreting mucus and the exudates of infectious discharge resulting from trachoma or other ocular bacteria (19). Crowded, unhygienic conditions with a lack of access to water and sanitation facilities are particularly conducive to transmission.

The progression of trachoma is dependent on a variety of interacting factors and many questions remain regarding the degenerative process that eventually leads to blindness. In general, three main periods describe the progression of infectious diseases: incubation, active disease, and recovery. **Figure 2** illustrates these periods for trachoma in both children (0-4 years) and adults (> 15 years).

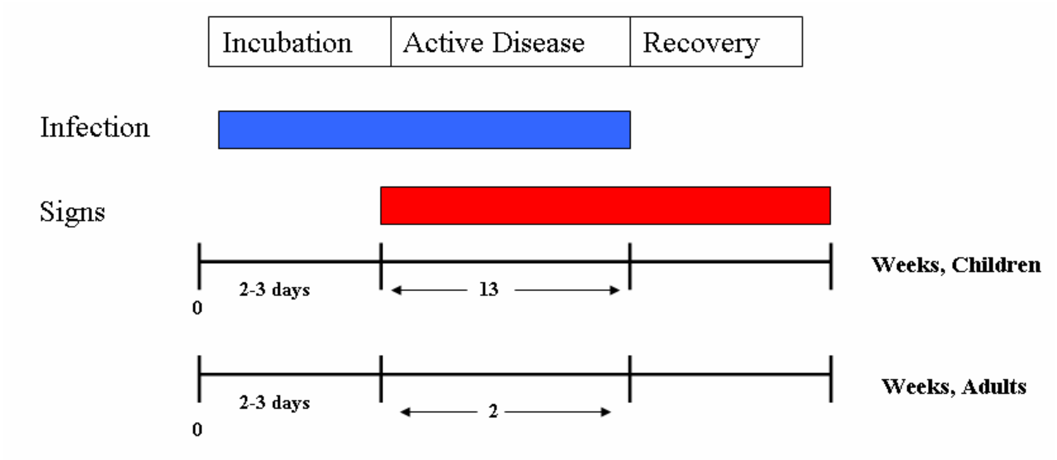


Figure 2: Main Stages of Trachoma (adapted from (17))

The duration of each stage of trachoma is poorly understood, but in general children suffer from longer periods of active disease compared to adults as illustrated in **Figure 2**. Incubation of the disease is relatively long as a result of the long bacterial growth cycle (2-3 days) of *C. trachomatis* (Schachter, 1990). During the incubation periods individuals do not usually show signs of the disease, which is one reason it may be difficult to detect through visual examination. The active disease period is highly variable both within and between subgroups. Children may harbor the active disease for up to 13 months. In extreme conditions found in highly endemic and unhygienic communities, children may never recover and instead suffer from persistent, ongoing infection for several years (17). Conversely, adults typically suffer from the active disease for two weeks. The final period, recovery, individuals continue to exhibit physical signs of trachoma even though they no longer are host to *C. trachomatis*.

Trachoma infection is greatest in children and therefore they serve as the main reservoirs of *C. trachomatis*. Children are more heavily infected both because they are more likely to engage in unhygienic practices and because they have not developed partial immunity that can possibly, but not necessarily, be gained through repeated exposure. The shorter disease period in adults indicates that with time partial immunity may develop through repeated exposure. This suggests trachoma is immunopathologic (20). However, studies have shown that repeated exposure can actually aggravate the disease due to antigens sensitized from prior infections that exacerbate tissue damage and the disease (21). Similarly, it has been suggested that persistent infection may alter cell-meditated immune responses and thus inhibit recovery (22). Although immune responses vary depending on various genetic and related factors, full immunity cannot be achieved.

Infection begins in childhood, but blinding consequences do not manifest until diseased individuals become adults. It is unclear how many infections, nor the length of these infections, required before the more advanced and debilitating forms of trachoma develop. It is known that repeated infections lead to vacuolization and scarring of the conjunctiva, eventually causing eyelashes to turn under and irreversibly damage the cornea. Individuals in highly endemic areas may become blind before they reach the age of 30, but generally blindness occurs 25-30 years after the peak of inflammatory processes (21). Interventions to halt the transmission of disease can be divided into treatment and prevention, both of which are described below.

Antibiotic Treatment Challenges

As opposed to other infectious diseases, treatment of trachoma is not straightforward. Treatment may either directly reduce the pathogen load in hosts or reduce the infectious period, thereby limiting the time and correspondingly the number of susceptibles an individual could infect. Two main treatment challenges, the difficulty in treating all infected individuals and the limited protective effect of antibiotics are discussed below. In endemic communities mass distribution of antibiotics improves the likelihood that all infected individuals will be treated. However, individuals may refuse treatment, especially those without signs of disease or who mistrust outsiders. Allowing even a few cases of the disease to go untreated, without blocking transmission pathways through environmental improvement, may lead to an eventual rise in trachoma prevalence. Even if near 100% coverage of antibiotics is achieved, because antibiotics only have a temporary protective effect, initial reductions in prevalence may be short-lived. Much of this is due to the fact that *C. trachomatis* is highly infectious and ubiquitous in the environment. An antibiotic study conducted in Nepal found that the effect of mass antibiotic treatment diminished rapidly. Between six and twelve months after antibiotics were initially administered, the impact on trachoma prevalence reduced from 36% to 14% (23). Meanwhile, 26% of the reduction twelve months after antibiotic distribution was linked to secular trends not linked to a specific trachoma control effort, such as improvements in access to water (23). It is unlikely that antibiotic treatment could be administered with enough frequency and coverage to effectively control and eliminate blinding trachoma long-term. The multiplicity of transmission pathways underscores the need for several types of concurrent interventions.

Need for Prevention

The aim of prevention is to interrupt transmission and eventually eliminate the spread of the pathogen and disease. With diseases such as trachoma, for which close associations between the environment and transmission exist, prevention efforts are likely highly effective in disease reduction. A recent WHO report concluded that trachoma is largely attributable to the environment (24). Given this conclusion and that treatment does not provide a lasting cure, prevention is essential to maintain disease reduction and elimination.

As evident from Figure 2, children suffer from infection for significantly longer periods and consequently they are the main reservoirs of the bacterium. Therefore, particular effort must be placed on child health and improving the environment in which they live. This poses an added challenge to the GET 2020 campaign efforts. First, it is extremely difficult to condition children's behavior. Second, in the conditions of poverty in which most trachoma infected individuals live, the lack of a clean environment may result in faces remaining dirty, or due to lack of resources, multiple children are forced to sleep in one bed, enabling the transmission of trachoma. Third, even though most prevention measures, such as encouraging children to use latrines by modifying the drop hole to preclude small children from falling in, require few resources, many families lack knowledge about their importance in relation to disease transmission and prevention.

Field research supports the notion that prevention is effective in reducing trachoma. Studies have shown that reducing fly population densities through latrines or insecticide can reduce trachoma prevalence 30% and 61%, respectively (25). However, the relative importance of transmission through mechanical vectors, such as flies, and other pathways remains unclear. For example, even though controlling flies has demonstrated significant disease reductions, molecular testing detected *C. trachomatis* on only 0.5% of face flies (26).

2.1.4 Disease Recurrence: Reproduction Number

The standard approach for determining whether or not a disease will re-emerge is to consider the reproduction number, R_o. The reproduction number is important because it provides a threshold for disease takeoff and re-emergence (27). R_o represents the number of disease transmitting contacts by an average infective person during the course of his or her infection in a population of completely susceptible individuals (27). If $R_o < 1$, the disease will eventually die out and disease elimination will be achieved. The value of disease die-off varies for different infectious diseases, and even the same disease may have different reproduction numbers for subsets of the population. The simple expression for R_o is presented below.

$$R_o = c * \beta * D$$

In the equation, *c* is the number of contacts per person per period, β is the probability that a contact transmits infection, and *D* is the average length of the infectious period. The difficult question then becomes how to select values for each of these variables, especially with a disease such as trachoma where there are multiple routes of transmission, different segments of the population who are more likely to be exposed (mothers and children), and extent of immunity to infection also varies depending on previous exposure and genetics. The acquired partial immunity gained by many individuals through repeated exposure indicates that to eliminate the most severe forms of trachoma it may not be necessary to achieve an $R_o < 1$. Rather recognizing asymptomatic individuals may harbor the pathogen, R_o may need to be a value small enough to reduce exposure to limited periods, such that the disease, which requires repeated exposure, does not develop.

Qualitatively, it is possible to further describe the inputs into R_o for trachoma. The number of contacts per person per period, *c*, is greatest for children and mothers, whereas men are likely to have the least amount of contacts. Women account for 60% to 85% of all cases of trichiasis, the stage of trachoma before blindness occurs, and the highest prevalence of active trachoma is found among children (28). The number of contacts is also highly dependent on the prevalence of trachoma in a community with individuals living in endemic areas having greater values of *c*, controlling for other factors. Thus, if *c* is calculated as the number of contacts in one week, it may vary from 10-1,000 or more depending on contact between uninfected and infected individuals and behavior of both groups. The value of β is likely to be large for reasons described above concerning pathogenesis. It may be difficult to modify β due to intrinsic biological and pathological characteristics of *C. trachomatis.* Finally, *D* varies as stated above from approximately 2 to 13 weeks. Although *D* can be slightly modified by antibiotic treatment, the largest impact on R_o will most likely come from reducing the number of contacts through reducing transmission pathways.

Through further analysis it may be possible to describe R_o quantitatively in a mathematical model. Models and the ability to mathematically determine R_o are highly dependent on the level of knowledge and information about a disease. The lack of epidemiological data concerning trachoma and variations in disease pathology and immunology may prohibit the creation of a precision-based model that accounts for heterogeneities. However, utilizing existing epidemiological data it may be possible to create a general deterministic model (29). Recently such a model was proposed for trachoma and is based on the basic transmission model below (30).

$$\frac{dP}{dt} = \beta(1 - P)P - \gamma P$$

Here, *P*, prevalence, changes over time according to the number of individuals who become infected, $\beta(1-P)P$, subtracted by the number who recover, γP. Specifically, $(1-P)$ are the susceptibles multiplied the diseased, *P*, times the likelihood that an interaction between the two will result in infection, β. Similarly, γ is the rate at which recovery occurs. The authors of the model assume that trachoma prevalence will decrease by an amount equal to the WHO target for mass antibiotic coverage of 80% times the drug efficacy of 95%. Recurrence of infection after treatment was assumed 10% per month based on a study in Ethiopia and therefore γ, was assigned the value of 0.10 (30). The authors conclude that the deterministic model above demonstrates that repeated administration of antibiotics can reduce infection to near elimination levels (30).

The model has several limitations. First, is that it does not account for specific environmental pathways of transmission that may permit for disease recurrence. Recurrence is highly dependent on existing environmental conditions and in the long-term disease prevalence could return to similar to pre-antibiotic distribution levels. Second, the model does not consider prevalence after antibiotic treatment ceases. Antibiotics cannot eliminate all cases and without ongoing interventions it is highly questionable whether elimination can be sustained. Therefore although the conclusion gained from the model, that elimination can be nearly reached through antibiotics, may hold validity, it cannot be concluded that such elimination can be sustained. Sustaining elimination is a more critical marker of a successful disease control effort and cost-effective use of investment.

A model that integrates all measures of the SAFE strategy and is able to predict prevalence both immediately and several years after interventions have been introduced currently does not exist. It is especially important to consider the period after antibiotic treatment ceases. Such a model could provide new insights into understanding how a single or a combination of treatment and prevention measures impact trachoma prevalence and the most cost-effective means to implement these interventions to sustain elimination.

2.2 Infectious Disease Control Case Studies

Controlling infectious diseases that are linked to poor water, sanitation or hygiene is difficult and perhaps even impossible to sustain with chemotherapy alone. Consequently, many disease control strategies acknowledge the role of water and sanitation in achieving long-term disease elimination targets. However, these same programs often have limited funds and often decide to invest in treatment to quickly reduce mortality and morbidity rather than implement prevention measure such as wells or latrines where it many take several years before a significant effect on disease is realized. Likewise, the decision making concerning environmental determinants directly and indirectly linked to health frequently occurs outside the health sector. Health may not be an overriding or even an important criterion in such decisions. As a result, the allocation of non-health sector resources, such as improving access to drinking water and sanitation or expanding irrigation, may not be made with consideration of the health benefits or consequences.

Reducing the burden of water-related diseases requires all sectors with a potential impact on health to consider how pooled resources may be used to most effectively achieve disease elimination. Two examples of disease control programs that provide insights into the trachoma elimination campaign are presented below. The first, dracunculiasis, is an example of how successful disease eradication can be achieved through focusing on the most effective interventions, conducting extensive monitoring, and collaborating with parallel water and sanitation efforts. The second, schistosomiasis, is an example of how a decrease in global control efforts and investment can lead to disease recurrence and emergence in new areas, demonstrating a poor use of original resources and requiring even further investment.

2.2.1 Dracunculiasis

Dracunculiasis, or guinea worm infection, is on track to be the next infectious disease to be eradicated. The disease has been reduced from 9 million cases in the late 1980's to 10,000 cases currently found in localized areas in the Sudan, Ghana, and Niger (31). Guinea worm is likely to be the first disease eradicated without a vaccine or treatment. The certification of the eradication of guinea worm is significantly more straightforward than trachoma. The disease is certified as being eradicated once there are no cases detected for three consecutive years. Detection through visual observation is simple and because no remaining cases are allowed, contrary to trachoma, recurrence is nearly impossible after eradication has been achieved.

Several important lessons can be gained from the success of the guinea worm eradication campaign. The first is that the intervention that has had the greatest impact is health education. As opposed to water supply and vector control measures which take time to establish and may require significant capital investments, health education was implemented quickly at a minimal cost (32). Networks of village volunteers were established and proved to be effective hygiene promoters. They also assisted in collecting data for disease and environmental indicator surveillance.

A second lesson is that integrated data collection and analysis on disease prevalence and environmental and hygiene indicators can be conducted effectively at a local and national level. Such data collection is ongoing and continues to provide important information that is used policy and investment decisions (32). The guinea worm campaign leaders pioneered the use of geographic information systems (GIS) to store and analyse data in the early 1990s. The software allowed for data to be easily uploaded into national databases to share data among regions. In addition to assisting in risk analysis and planning, the use of GIS and a centralized, easy to use database, helped NGOs and governments to target areas of campaign activities, in order to prevent overlap or neglect of specific regions.

The final lesson from guinea worm is the importance of obtaining cross sectoral support for water, sanitation and hygiene interventions at multiple levels. The guinea worm campaign was able to capitalize on the U.N. International Drinking Water Supply and Sanitation Decade (1980-1990) to help implement improvements in water, sanitation, and hygiene (32). This provided an incentive international support for preventive measures and perhaps more importantly assisted in effectively engaging stakeholders at the local level in decision making, educating and monitoring. It is important, however, to recognize that water and sanitation improvements are only effective if they are properly maintained and utilized.

2.2.2 Schistosomiasis

Schistosomiasis is an ancient water-related disease that continues to burden communities due in large part to ineffective control measures and a lack of collaboration between the water and health sector. Recent re-emergence in areas that had previously contained schistosomiasis and the spread to formerly disease-free regions has brought renewed attention to the disease. It is estimated that the disease is endemic in 76 developing countries with 600 million people at risk and 200 million individuals infected (33). Shistosomiasis shares similarities with trachoma in that it has a low mortality rate, but a potentially high morbidity rate, is spread by multiple transmission pathways, including a vector, is relatively expensive to treat with chemotherapy and improved sanitation and hygiene can markedly reduce disease prevalence.

The resurgence of schistosomiasis corresponds to poor rapid increase in water resources development and irrigated farmland in developing countries. This has increased both snail habitat, a vector for the disease parasites *S. heamatobium* and *S mansoni*, and the likelihood of exposure with additional individuals working in irrigated fields where the snail breeds. A recent meta-analysis concluded that since the 1990s the risk of becoming infected with schistosomiasis has increased 10.9% and actual infections have increased by 7.3% worldwide (34). In particular regions the increase is much greater. For example, after the construction of a large dam and reservoir, Lake Taabo, in central Cote d'Ivoire, schistosomiasis prevalence reached 73% compared to levels near zero prior to construction of the dam (34). Even in areas where the disease had existed and been eliminated, re-emergence is occurring. A recent study in rural China documents re-emergence in over 30% of the districts on average, eight years after the disease had been eliminated (35). The authors cite changes in sociopolitical, local economic and local physical environment as the main reasons for disease re-emergence (35).

The difficulty in controlling schistosomiasis highlights the need to increase intersectoral planning and maintain initial disease interventions and awareness. A prerequisite for the development of water resources in high risk areas must be the integration of schistosomiasis control measures into project planning. In water development schemes there is a general lack of means for identifying priority parasitic diseases (36). Furthermore, even if diseases are addressed, after projects are completed health care services, vector control and sanitation measures are typically not maintained and irreversibly deteriorate (36). To overcome these pitfalls, improved coordination between health officials, water resource developers and local communities who will use and maintain the new systems is essential. Control though, must encompass more than integrated planning and measures that firmly root awareness and behavior change in a community, in addition to include long-term monitoring. As demonstrated in China, in addition to lack of coordination, re-emergence corresponded with decreasing awareness about the disease in the community and increased human mobility at local and regional levels (35). These lessons offer important considerations in developing guidelines and strategies for sustaining trachoma elimination.

2.3 Trachoma Elimination and Risk of Recurrence

The trachoma control strategy aims to eliminate blinding trachoma. To achieve this goal, all forms of the disease will need to be sufficiently reduced to levels where the risk of the disease progressing to the blinding stage is close to zero. Depending on trachoma prevalence, communities must follow a particular strategy that provides specific instructions for treatment but does not provide such guidance for prevention. The current eliminate on requirements only concern clinical indicators. Such indicators are highly dependent on both sensitive and specific disease detection. Detection is limited by ambiguity in visual examination, seasonality and clustering of the disease and lack of affordable and accessible molecular tests.

The greatest weakness in the elimination requirements is the absence of environmental and hygiene related indicators. Without requirements for achieving a particular level of environmental health, even if countries achieve the treatment and clinical indicators for elimination, the disease may re-emerge because transmission pathways exist. Conversely, if a sufficiently high level of environmental and hygiene health is achieved it is highly unlikely that trachoma could become re-emerge or establish itself in a new area. If the disease cannot be transmitted it will not infect suceptibles. A description and analysis of the current elimination indicators and strategy is provided below. This is followed by further analysis on the potential of trachoma recurrence.

2.3.1 Current Indicators and Assessment

The public health significance of trachoma is evaluated by the grade of the disease. The grade also is used to determine overall prevalence and control strategy. Early stages of the disease are often self-healing and have little impact on overall health. Later stages of the disease can lead to serious consequences both for the individual infected and for those they come into contact with as shedding of *C. trachomatis* increases with increasing disease intensity. The diagnostic tools available, especially in remote, impoverished areas where trachoma is most prevalent, are imprecise at best. Detection is either conducted by assessing clinical signs or by confirming evidence of the bacterium itself. Ideally, both approaches would be used as neither one alone will provide the accurate description of the disease in a community. The clinical signs of trachoma are often assessed through the presence of follicles, but thesea are not necessarily paothognomonic for trachoma (5). In addition, sampling errors, inappropriate methodology and inadequate reporting can further decrease the accuracy of detection.

In order to assess and standardize the grade of trachoma in the field several schemes have been devised starting as early at the sixth century (5). The most widely used and accepted is the WHO Simplified Trachoma Grading Scheme (5). The Scheme defines trachoma through five progressively worsening stages and is presented in **Table 2**. The first three columns present the grading scheme and the fourth column, impact, provides a measure of the affect on the diseased individual. Active trachoma is defined as TF, TI or TF/TI because it may be difficult to differentiate between two grades. The two important indicators that are often recorded are TF/TI in children, indicating the extent of the disease reservoir, and TT in adults, which signifies the number of individuals most at risk for developing the next stage of the disease which leads to visual impairment and/or blindness.

Table 2: WHO Simplified Trachoma Grading Scheme (based on (37))

Grade	Full Name	Condition	Impact	
			Immediate	Long-Term
TF	*Trachomatous inflammation follicular*	Presence of five or more follicles at least 0.5 mm in diameter	Pain, but no effect on vision	Potential to develop more intense forms
TI	*Trachomatous inflammation intense*	Pronounced inflammatory thickening of the tarsal conjunctiva that obscures more than half of the normal deep tarsal vessels	Pain, but no effect on vision	Potential to develop more intense forms; poses risk of developing secondary infections
TS	*Trachomatous scarring*	Presence easily visible scarring in the tarsal conjunctiva	Pain and reduction of vision	Potential to develop CO and blindness
TT	*Trachomatous trichiasis*	At least one eyelash rubs on the eyeball	Severe pain and large reduction of vision	If not operated on, could develop CO and blindness
CO	*Corneal opacity*	Easily visible corneal opacity over the pupil	Nearly blind	Irreversible blindness highly likely

The advantage of the scheme is that it is meant to be used in the field by observers with little medical background. Inter-observer agreement between local individuals following three hours of training and experienced ophthalmologists is fairly high, kappa statistic 0.45-0.76, based on studies conducted in Tanzania (5). Although the test is not a perfect measure and inter-observer agreement does not confirm that an individual is actually infected with *C. trachomatis* (only exhibiting signs), it can be used as a rough measure of grade of illness.

Trachoma prevalence and grade form the basis for implementing the four main components of SAFE strategy. As a result, determining prevalence and grade, which is not a straightforward task, is extremely important as it drives decisions on how resources will be invested for trachoma control in specific districts or communities. Manuals have been developed that provide field practitioners with simple but cost-effective tools to identify communities where trachoma is endemic, determine whether or not trachoma is blinding and to assist in planning and implementing control measures (38). **Table 3** outlines the prevention and treatment recommendations based on three categories of prevalence as currently promoted through the SAFE strategy.

Table 3: SAFE Strategy (based on (39))

Prevalence	**S**urgery	**A**ntibiotics		**F**ace Washing		**E**nvironment	
	(bilamellar tarsal rotation)	*Coverage*	*Period*	*Action*	*Period*	*Action*	*Period*
>10%	All TT cases	At least 80% of community	Annual dose, for 3 yrs	Education	3 yrs	Encourage latrine building	3 yrs
5-10%	All TT cases	At least 80% of community	Annual dose until < 5% prevalence	Education	3 yrs	Encourage latrine building	3 yrs
<5%	All TT cases	None	N/A	Education	Ongoing	Encourage latrine building	Ongoing

The lack of specific and quantifiable actions recommended for environmental interventions is a limiting factor in the current SAFE strategy. It is not clear what is meant by "education" or "encouraging latrine building". In contrast, the *S* and *A* components are outlined clearly, with quantifiable estimates. One role of environmental indicators will be to improve the rigor by which prevention efforts are measured to allow for straightforward recommendations for action on parity with those already prescribed for treatment efforts.

Field Visual Assessment

The GET 2020 has proposed two methodologies for assessing trachoma prevalence, both of which rely on the WHO Simplified Trachoma Grading Scheme. The first is the trachoma rapid assessment (TRA). Program managers are encouraged to base TRA on disease information collected from reports and through conducting actual field assessments of trachoma using the WHO Simplified Trachoma Grading Scheme. The methods for identifying individuals to screen are not based on statistical epidemiological methods, but rather through a deliberately biased approach that targets those most at risk based on socioeconomic conditions such lack of water, sanitation, and evidence of crowding (Negrel, et al., 2001). The second, are based on recommendations released in 2006 by the WHO, and encourage the current the use the standard epidemiology sample size equation based on a 95% confidence interval to randomly select households to survey (39). Clinical grading is the least expensive and most accessible to many communities, but has a specificity of 80.2% and a sensitivity of only 64.1% (40). Therefore, on average, 35.9% of those who are actually harbor *C. trachomatis* pathogen and serve as a potential source for future infections are identified as not harboring the disease.

Molecular Detection

Molecular detection is a more accurate measure of actual infection by *C. trachomatis*. Such detection is important for determining risks for future transmission, but less so for assessing the public health significance, which is more dependent on genetic and immunopathologic response to *C. trachomatis*. Molecular detection of *C. trachomatis* using polymerase chain reactions (PCR) or related techniques results in specificities and sensitivities > 99% (13). However, these tests do not determine pathogen viability and most endemic countries do not have the technical capability to conduct quantitative PCR (q-PCR) especially in neglected, rural areas where burden of trachoma is greatest. A new point of care dipstick (POC) which detects *C. trachomatis* lipopolysaccheride has demonstrated significant improvements on sensitivity and specificity, 83.6% and 99.4%, based on an initial study in Tanzania (40). Currently, the POC is neither available nor affordable for widespread use and further product development is required.

The limitations in trachoma detection are due to several inter-related causes. Clinical field detection provides a general idea of the public health significance, but does not detect *C. trachomatis* and therefore may be inadequate for determining the risk of transmission. In addition, clinical grading is less accurate in low prevalence areas. Although these areas may be close to achieving elimination and no longer require mass antibiotic distribution, unless preventative measures are in place, they also may be most at risk for recurrence. Molecular detection is important for estimating the prevalence of *C. trachomatis* which is important in calculating the R_o, but it is expensive and impractical for use on the scale necessary to effectively monitor and control trachoma. Rather than put forth extensive effort and investment in more complicated and scientifically accurate detection methods in order to gain incremental improvements in detection, focusing on prevention measures and monitoring may be a more effective use of resources. Utilizing environmental indicators in the certification of elimination will provide a safety measure for any inaccuracies or cases of trachoma that detection may have overlooked and thus prevent recurrence. Recurrence of trachoma, without prevention, is highly probable and is discussed further in the following paragraphs.

2.3.2 High Risk of Disease Recurrence

The current proposed certification standards allow for the existence of some active trachoma in a community and thus recurrence remains a possibility. Various studies have documented recurrence of TT after surgery varying from 25-75% (41). Recurrence is even a concern in low endemic communities. For example, a long-term study in the Gambia documented progression of trachoma from the early to more severe stages in low prevalence communities where a limited number of individuals with TT had refused surgery (42). Even in Oman where control measures have resulted in large reductions in prevalence, recurrence of TT three years after surgery was recently estimated at 56% (43). The proportion of individuals who require, but to not undergo surgery, may also have an impact on recurrence by continuing to serve as a host for *C. trachomatis*. In many endemic countries, especially those in Sub-Saharan Africa, the backlog of those needing surgery but without access is significant. Compounding the problem is that even when surgery is available, refusal rates may be high. In a Tanzanian study of individuals suffering from TT, only 18% of those offered surgery free of charge accepted (44). Thus unless trachoma is completely eliminated, which is not logistically feasible for reasons described earlier, or multiple prevention measures are in place, a small number of infected individuals could pose a large risk to an entire community.

The basis for disease elimination supports the need to incorporate preventative measures and indicators to monitor these measures and include them in the certification of the elimination of blinding trachoma guidelines. In summary:

- **Ongoing Interventions Required**
  - Explicit in definition of elimination
  - Ongoing, indefinite treatment is not effective nor practical
  - Environmental interventions have potential to be locally managed and sustained
  - Historical evidence confirms elimination possible through environmental measures alone

- **Complicated Clinical Aspects Underscore Need for Prevention**
  - Multiple pathways of transmission require multiple prevention measures
  - Prevalence assessment is undermined by disease pathology and limitations in grading
  - Improvements in diagnostic detection may provide only limited gains for widespread field applications and use in certification

- **Important Lessons Learned in Other Infectious Disease Control Efforts**
  - +: Collaboration with water sector provides opportunities for resource sharing
  - +: Effective community monitoring of environmental indicators is achievable
  - -: Lack of long-term planning and decrease in awareness are factors in reemergence
  - -: Weak inter-sectoral coordination may led to spread of infectious disease in new areas

- **Risk of Trachoma Recurrence High Without Environmental Interventions**
    - High rates of recurrence documented after surgery to treat TT
    - Even in low prevalence areas, evidence of recurrence exists
    - Small number of individuals can pose a large risk for entire community

Environmental indicators offer a means by which to measure the progress of implementing prevention measures and corresponding progress in achieving trachoma elimination. Appropriate selection of environmental indicators that are attributable to trachoma is therefore critical in order to monitor and assess elimination efforts. Section 3 examines hypotheses regarding the effect improvements in water, sanitation and hygiene have on trachoma prevalence at the global level. It also provides some analysis on noticeable trends in prevalence within and between countries in order to develop an improved understanding of the important role the environment can serve in controlling and sustaining elimination of blinding trachoma.

Section 3: Preliminary Analysis of Environmental Indicators and Trachoma

The following presents the preliminary analysis of the nature and magnitude of the links between environmental determinants of health and trachoma prevalence. The motivation is to determine, generally, which factors have a significant effect on trachoma and therefore may be viable indicators for use in the certification of elimination of blinding trachoma. It is important to recognize that statistical relevance does not necessarily prove causality and the results presented below can at best confirm hypotheses that environmental indicators impact and can be used to help predict trachoma. Section 3 is structured as follows: data, method, results, discussion, epidemiological risk factors and further analysis.

3.1 Data

The trachoma prevalence and environmental indicator data used is aggregated at the national level. District data would be preferred, but of the sets available questions arose in the reliability of the data. A total of 28 countries, the majority located in Sub-Saharan Africa, were used in the analysis. This represents those countries that provided the most recent trachoma data. Specifically the data sources include:

- Trachoma Prevalence
  - All countries besides Oman: Country data presented at the Tenth Meeting of the WHO Alliance for the Global Elimination of Blinding Trachoma, April 10-12, 2006
  - Oman: Data presented in Khandeka, et al., 2005
  - Missing Data from GET 2020 Member Countries: Djibouti, Guinea Bissau, Iraq, Libya, Mauritania, Mexico, Mozambique, Pakistan, Somalia, Malawi
- Rural and Urban Water and Sanitation Coverage: WHO/UNICEF JMP Database, 2002
- Population, Rural and Urban: WHO/UNICEF JMP Database, 2002 (confirmed with UNDP Development Report, 2004)
- Housing Durability and Crowdedness: World Resources Institute (WRI), Earth Trends, 2001
- Human Development Index (HDI), UNDP Development Report, 2005 (data from 2003)

Each indicator is defined according to specific terminology. Refer to the **Appendix I** for definitions of the indicators. For clarification, an index is a summary of several indicators used to represent an overall trend, or in the case of the UN HDI, achievement in human development (45). The WHO/UNICEF JMP data represents information collected in 2002 from both household surveys and national assessment questionnaires. The WRI Earth Trends database was developed to support UN-Habitat and is a compilation of a number of sources including Demographic Health Surveys (DHS), Multiple Indicator Cluster Surveys (MICS) and various other national census and survey reports. The DHS and World Bank LSMS databanks were reviewed but it was found that the data was either insufficient for most countries of interest (DHS) or too timely and complicated to gain permission to use and extract (World Bank LSMS).

3.2 Methods and Results

Both univariate and multivariate analyses were conducted using Minitab, Version 5 and SPSS, Version 12. The main methods used were regression, correlation, clustering and principal components analysis.

3.2.1 Univariate Analysis

Figures 3-7 present the relationship between trachoma prevalence (TI/TF as measured in children or TT in adults) and latrine coverage, water coverage and housing durability. The results for crowdedness and HDI demonstrated little if any relationship with trachoma and therefore they are presented. The R^2 value for each regression line is also listed. **Appendix II** contains additional plots of TI/TF and TT vs sanitation and water on the same chart for comparison.

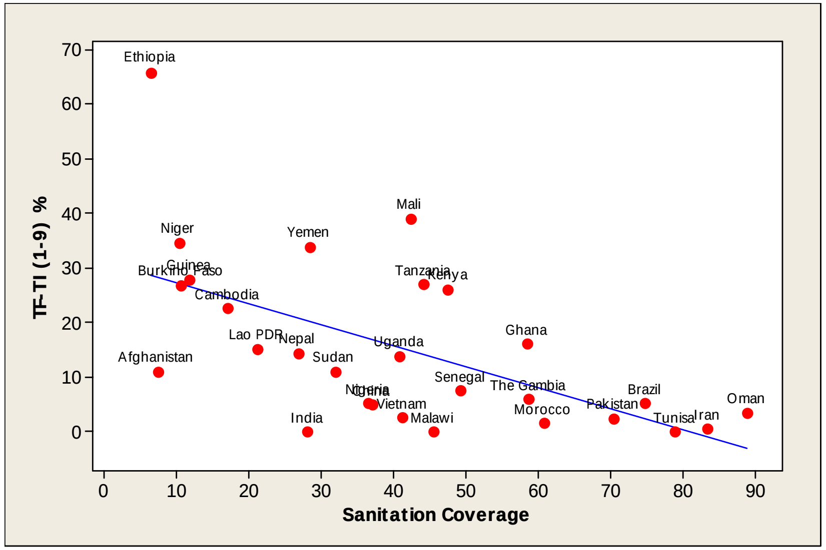


Figure 3: TF/TI vs. Sanitation Coverage, R^2=0.348

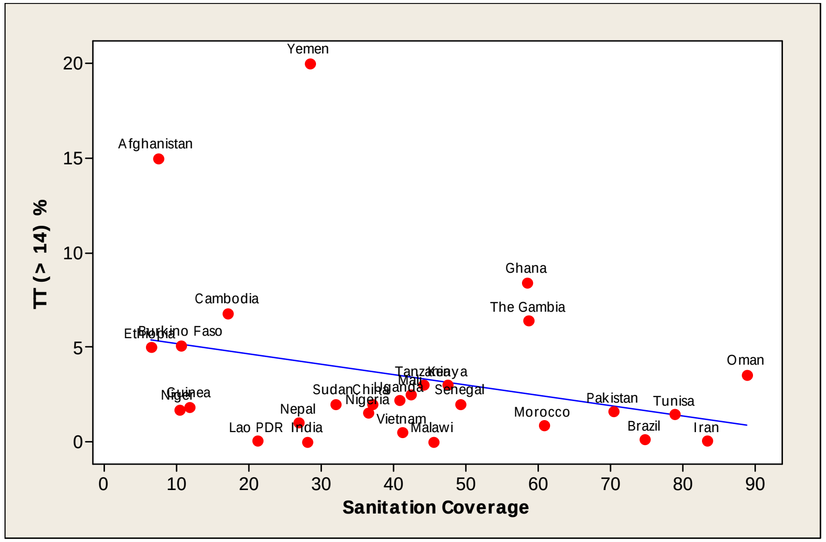


Figure 4: TT vs. Sanitation Coverage, R^2=0.08

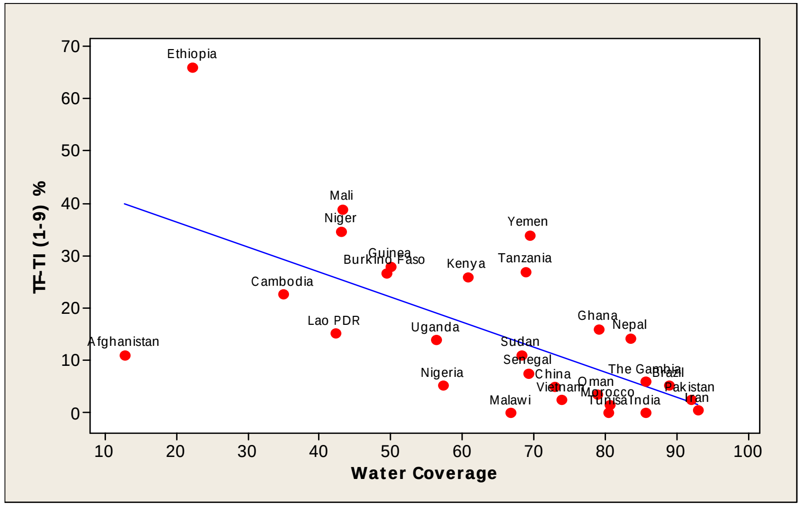


Figure 5: TF/TI vs. Water Coverage, R^2=0.418

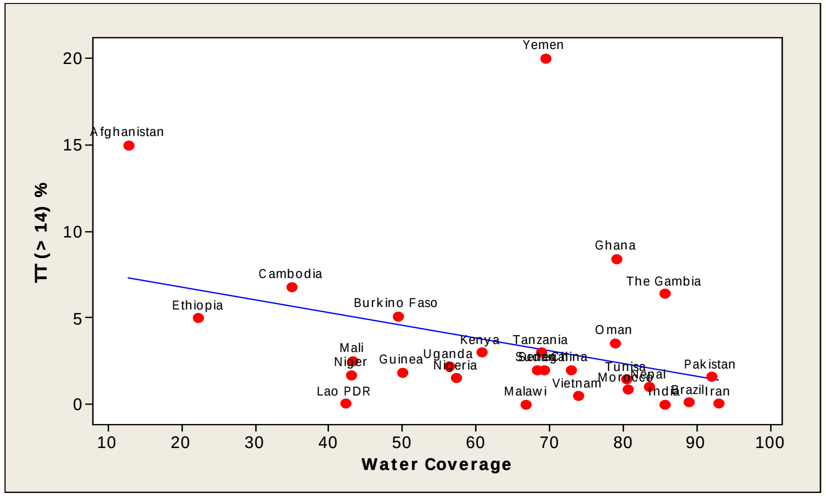


Figure 6: TT vs. Water Coverage, R^2=0.113

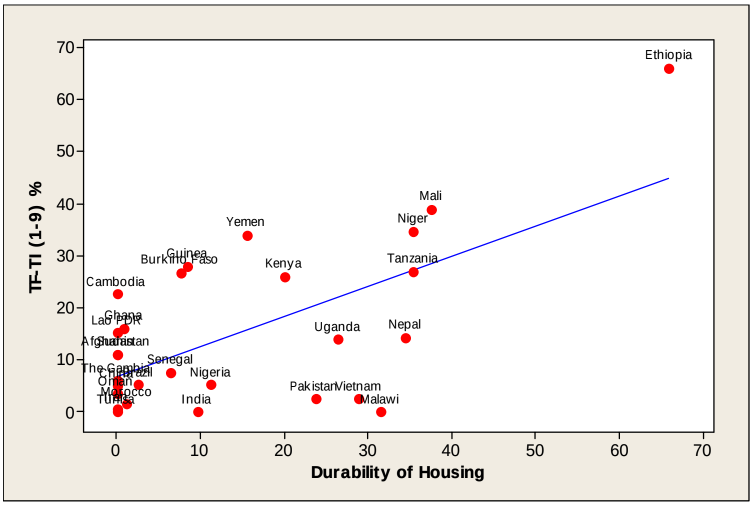


Figure 7: TF/TI vs. Durability of Housing, R^2=0.376

The final figure produced through univariate analysis, **Figure 8**, is a box plot of all the variables. As shown all the variables, except TT, have a univariate normal distribution. All indicators variables also exhibited normality as represented by a linear line in Q-Q plots. Outliers, such as Ethiopia for TF/TI or Yemen for TT are qualitatively explained later in the document.

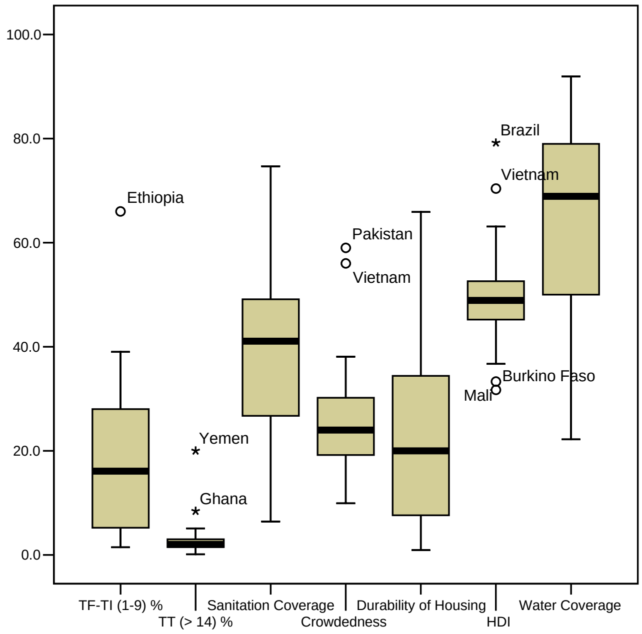


Figure 8: Box Plot of Normality of Variables

Correlation analysis was also conducted. In brief, the results confirm the regression analysis with durability of housing, water, and sanitation having the highest correlations to TF/TI (0.666, -0628, -0.611, respectively). The highest correlation between variables, not surprisingly, occurs between water and sanitation (0.765). The correlation between water and sanitation is meaningless because both are components, among several, used to determine HDI.

3.2.2 Multivariate Analysis

The regression of a combination of variables was preformed to assess whether or not a better fit of the data would be obtained. The analysis was only done with TF/TI data because the regression analysis of TT data with single indicators did not demonstrate a close correlation (as indicated by the R^2 value). Analysing water and sanitation coverage together resulted in a R^2=0.44 (P=.001) and water, sanitation and durability resulted in a R^2=0.639 (P=0).

Cluster analysis with the use of dendograms was performed to gain a general sense of which countries may be similar to each other based on the variables analysed. This could provide a basis for further case study investigation of similarities between clustered countries and allow for development of targeted trachoma prevention efforts. Due to the presence of outliers, single linkage and Euclidean distance were used. **Figure 9** displays the clustering of countries based on TF/TI and TT alone and **Figure 10** represents clustering based on all variables (TF/TI, TT, sanitation coverage, water coverage, durability of housing and crowdedness).

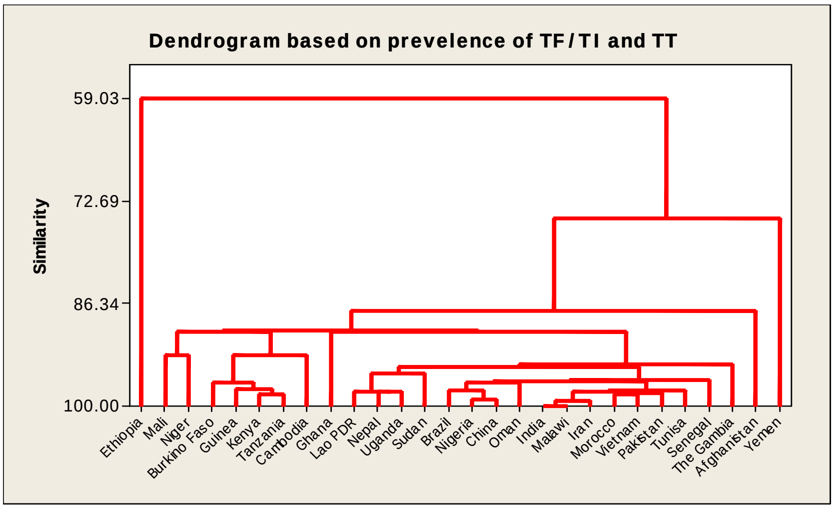


Figure 9: Dendogram based on TF/TI and TT

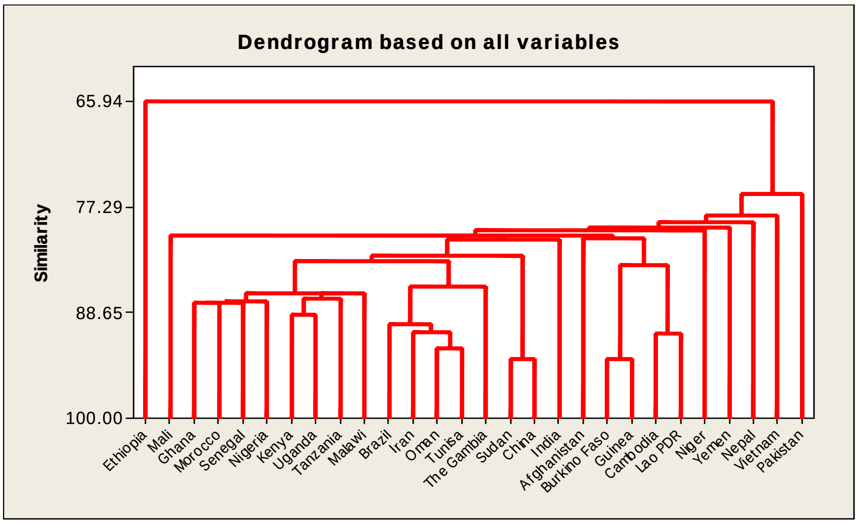


Figure 10: Dendogram based on all variables

The final statistical method utilized was principal components analysis. Principal component analysis is an interdependence method that considers all variables equally and determines which variables explain most of the variance in the data. **Table 4** presents the results from principal components.

Table 4: Principal Components of Trachoma Indicators

Component	Initial Eigenvalues		
	Total	% of Variance	Cumulative %
Water	2.76	55	55
Sanitation	1.10	22	77
Crowding	.505	10	87
Durable Housing	.374	8	95
HDI	.258	5	100

3.3 Discussion

A discussion of the main findings from both the univariate and multivariate plots and analysis is provided below.

3.3.1 Univariate Analysis of Water and Sanitation

The univariate regression plots support the hypothesis that trachoma prevalence decreases as water and sanitation coverage increases. This raises two main questions. How well can these indicators be used to predict trachoma prevalence? What percentage of coverage, or what degree of environmental health, is necessary to ensure trachoma remains below a determined threshold? Examining R^2, provides some insight into the first question. The R^2 of plotted data, which ranges from 0 to 1, gives an indication of a model's predictive power. The R^2 value represents the fraction of variance explained by the model and mathematically is represented as

$$R^2 = 1 - \frac{SS_{error}}{SS_{total}}$$

where SS_{error} is the sum of squares of the variance of the regression and SS_{total} is the sum of squares of the actual data about its mean. The values for R^2 appear quite low, considering the closer the value is to 1 the better the fit. However, because trachoma prevalence is dependent on a number of factors, rather than a single variable, some of the values may be considered to represent a relatively good fit (46).

The plots of TF/TI against water and sanitation coverage demonstrate the greatest correlation. For sanitation and water, the values obtained are 0.348 and 0.418, respectively. This suggests that water coverage is a slightly better predictor. However, in light of the Driver, Pressure, State, Impact, Response (DPSIR) model water availability is only a Pressure that may affect trachoma while sanitation is a State that directly impacts trachoma prevalence due to the effect it has on eye-seeking flies. For example, in study of 20 villages in Tanzania, although the risk of trachoma increased with distance to water source, there was no relationship between the amount of water brought home and the number of kids with clean faces (47). Consequently, improved access to water alone may be insufficient to alter trachoma without a concomitant effort to change perception of how water should be used at home.

The R^2 values for the TT plots are considerably lower, suggesting the indicators are less linked to prevalence. This may be reflective of mass antibiotic treatment regimes where the initial reduction of prevalence is dramatic. For example, a large reduction of cases of TF/TI to TT is seen in Mali where distribution of antibiotics has increased from virtually zero in 2000 to nearly 3.6 million doses distributed in 2005 (ITI, 2005). Comparatively, the trachoma cases in Yemen remain high even in adults, which is likely reflective of the fact the country lacks major international support for trachoma control.

Three main trends relating to water, sanitation and trachoma are observed from the univariate plots (Figures 3-7) and are highlighted below.

Trend 1: Countries with low sanitation or water coverage (< 50%) have high trachoma prevalence in children (30%>TF/TI > 10%)

- Mid-Range: Guinea, Burkina Faso, Cambodia, Afghanistan, Lao PDR, Nepal, Sudan, Uganda, Kenya, Tanzania
- High Outliers: Ethiopia, Niger, Mali
- Low Outliers: Nigeria, China, Vietnam, Senegal

One possible explanation for the high outliers is simply poverty and a lack of development. Ethiopia, Niger, and Mali are extremely poor and rank 170, 177, 174, respectively (out of 177) on the UN HDI scale (45). The low outliers may be due to greater development, centralized governments, and historical existence of trachoma control. China and Vietnam are substantially more developed (85 and 108) on the UN HDI scale and they also are ruled by centralized governments that are perhaps better at managing large, top-heavy trachoma control programs. In addition, Vietnam has had a trachoma program since 1975 while active trachoma (TT) has been reduced from 17.5 to 7% (48).

Trend 2: Countries with better sanitation and water coverage (> 60%) have lower trachoma prevalence in children (TF/TI < 5%)

- Mid-Range: Morocco, Pakistan
- High Outlier: Yemen
- Low Outliers: Iran, Brazil

The most plausible explanation for the outlier of Yemen is that none of the major supporters of the GET 2020 campaign (Carter Center, International Trachoma Initiative, SightSavers) are working in Yemen. The low outliers can be possible explained by the fact that countries such as Iran and Brazil are fairly well developed (99, 63) on UN HDI and although neither have a formal SAFE campaign, they have targeted construction of latrines and access to water in areas where trachoma is higher (45). In addition the data from both Iran and Brazil may have been homogenized due to the large populations of these countries, 67 and 186 million respectively (45). Therefore even if isolated, endemic areas of trachoma exist, they are diluted and not evident.

Trend 3: Countries with better sanitation and water coverage have lower trachoma prevalence in adults (TT)

- Mid-Range: Tanzania, Kenya, Sudan, Mali, Nigeria, Senegal
  - Reduction from TF/TI (Tanzania and Mali); indicative of successful and extensive mass antibiotic, trachoma research, and NGO investments
- High Outlier: Yemen, Afghanistan, Ghana, The Gambia, Oman
- Low Outliers: Laos PDR, Nepal, Vietnam, Niger, Guinea

One high outlier, which could still be considered a success story, is Oman. In the 1970s trachoma prevalence was nearly 80% and has been reduced to less than 5%. Ghana is another interesting outlier as it is better off than neighbouring countries with a HDI rank of 138 (45). Trachoma, however, is isolated in the economically depressed, arid north, an indication of how the disease clusters in underdeveloped areas.

Two of the notable low outliers, Nepal and Niger, demonstrate the effectiveness of interventions. In Nepal, the Department of Water Supply and Sewage manages the "F and E" strategies for trachoma where notable improvements in water and sanitation have been made. In Niger, 2004 marked the third year of the annual mass antibiotic treatment regime where 1.9 million individuals (15% of total population of country) received treatment (49).

3.3.2 Univariate Analysis of Other Factors

The trends observed from durability of housing and crowdedness compared to trachoma are similar to those for water and sanitation. Durability and crowdedness were measured in the "negative" and therefore higher levels of durability represent less secure housing and therefore are correlated with increased prevalence of trachoma. The value of R^2 for TI/TF plotted against durability and crowdedness are again higher than for TT. Durability appears to be a significantly better predictor of TI/TF of with a $R^2 = 0.376$ compared to crowdedness with a $R^2 = 0.026$. It is expected that crowdedness might be a good indicator because trachoma is easily transmitted, especially where children share a bed. Several explanations can be offered for the lack of predicting power. First, it is unclear what percentage of crowdedness is attributable to urban compared to rural populations. It may be the case that urban dwellers live in more confined spaces, but because they have greater more access to water and sanitation they less likely to have trachoma. Second, durability of housing may be a better measure of marginalized individuals living in rural areas (who are more likely to have trachoma) as they are likely to have homes constructed completely of local materials (mud, sticks, thatch) compared to urban dwellers who may have access to improved building materials, such as corrugated iron roofing. Last, the data collection and reporting for these two measures may not be precise, especially because it represents an amalgamation of several sources which would require data standardization and/or transformation.

3.3.3 Multivariate Analysis

Due to the complexity of the disease and the multiple pathways of infection, no single indicator can be used to predict trachoma. Therefore, the first step in the multivariate analysis was to perform regressions on the three variables that have some significant correlation (sanitation coverage, water coverage, and durability of housing) with TI/TF. The results proved increasing levels of predicting power with water and sanitation producing a $R^2 = 0.56$ ($p = .001$) the combination of all three achieving a $R^2 = 0.639$ ($p = 0$). Further analysis is now required to determine which levels of each of the combination of these three would be most effective in predicting sustained elimination.

The dendograms confirm some of the observations seen in the univariate data. Figure 9 demonstrates a distinct difference between the outliers, Ethiopia and Yemen, and to a somewhat lesser extent Mali, Niger and Afghanistan, with the remaining countries. Figure 10, which is based on all the variables, shows more distinct clustering. This largely correlates to either geographic proximity (Kenya, Tanzania, Uganda and Malawi) or development status (Brazil, Oman, Iran and Tunisia).

3.3.4 Limitations

Several limitations exist in the data analysis presented. The first is the existence of confounding factors. Confounding occurs when the effects of two exposures have not been separated and it is incorrectly concluded that the effect is due to one rather than the other variable (50). Confounding factors commonly occur in water, sanitation and health observational studies and although multivariate analysis can help control for such factors, it may not be sufficient (51). Trachoma studies are especially prone to confounding due to the multiple pathways of the disease, difficulty in accurate detection, and the delayed onset, which could be several years, from exposure to the pathogen and manifestation of disease.

Ecological fallacy is a second limitation of the analysis of the global data set. In brief, statistical association does not necessarily prove causality (46). It is not known whether the proportion of the population without access to improved sanitation or water was the same proportion of the population that had trachoma. Therefore the analysis does not necessarily confirm that poor sanitation is a factor that will increase risk of trachoma, but rather that this is a possible hypothesis that could be proven true with through randomized interventions trials where cases of disease and risk factors are simultaneously measured at an individual, household or community level. Conducting a global intervention study of trachoma would be cost-effectively nearly impossible, but regional and community epidemiological studies have been conducted, many of which attribute large decreases in risk of transmission in the presence of environmental measures. These studies are summarized in **Section 3.4**.

The third limitation is the inability to capture population heterogeneity with aggregated data. Under heterogeneity it is still possible to measure risk as a cumulative incidence rate, but only if the risks are still somewhat homogeneous (52). Such heterogeneity in trachoma includes exposure groups (women and children have greater exposure), genetic variability (immunological responses can vary) and the duration of exposure due to the repetitive nature of contracting and shedding the pathogen. As shown, significant statistical differences exist between TF/TI and TT groups indicating that the use of aggregated total trachoma (all cases) data in environmental risk assessment is invalid. Furthermore, even the national prevalence data of TF/TI< 9 yrs may only be used a basic guide for possible trends and correlations or a confirmation of epidemiological risk studies conducted at the village or district level.

The fourth limitation involves the effect of time on disease progression and corresponding impact environmental improvements may have on reductions in trachoma prevalence. As described previously, the more advanced and debilitating forms of trachoma are the result of repeated exposure and infections over several years or decades. As such, when pathways of transmission are blocked through prevention measures, such as latrines, the effect on prevalence will be delayed. Individuals that are already highly diseased when prevention measures are implemented will likely continue to suffer from trachoma or related secondary infections. Also because trachoma does not directly cause death, infected individuals will remain in a population and serve as sources of *C. trachomatis.* However, for individuals who do not yet suffer from advanced trachoma, such as small children, when environmental interventions are put in place, they will be much less likely to develop the severe stages of disease that are seen in adults. Countries that have rapidly improved water and sanitation may have higher than expected prevalence for this reason. Such is the case with Tanzania and Ghana, two countries that increased water coverage in a 12 year period (1990-2002). The former increased coverage from 38% to 73% and the later from 54% to 79%.

The final major limitation concerns methods for measuring and defining indicators. Trachoma as explained in the previous section is difficult to detect and grade for a variety of reasons. The datasets for durable housing and crowdedness were drawn from a number of sources and the methodology for specific measurement of these is unclear in the literature (53). Finally, differences in the years in which trachoma prevalence data was collected (1998-2004, depending on when national surveys were completed) and environmental factors (2001-2003) complicate the analysis of correlation. The impacts of environmental interventions on prevalence are likely to result months and years after interventions are in place and therefore longitudinal monitoring and data is extremely important.

3.4 Evidence from Epidemiology Studies

A second means by which to gain an idea of the impact of environmental indicators on trachoma is through specific epidemiology studies. The lack of environmental indicator data and robust epidemiological "F and E" studies have led some researchers to conclude that the evidence for an effect of health education and environmental improvement is considerably weaker compared to surgery and antibiotic treatment (54). However, it is clear that the randomized, controlled studies have been conducted and demonstrate that prevalence of trachoma decreases as environmental sanitation and hygiene behavior improves.

One means by which to quantify the protective effect of prevention related indicators is through the odds ratio (OR). The OR estimates the likelihood of having trachoma if one is not exposed to the protective intervention. It is found by multiplying the ratio of those with trachoma who are exposed to the intervention over those that are not times the ratio of those without trachoma who are exposed to the intervention and those that are not. Usually OR of greater than two demonstrate a significant intervention impact (46). A total of five reviews have been published since 2000 documenting the impact of various environmental indicators on trachoma. Many of these reviews were extremely limited in scope or did not provide information on OR values. The WHO conducted a rigorous review that did provide information on OR values and the results of this study are presented in **Table 5** (55). The OR values presented in Table 5 were extracted from randomized studies, either observation or intervention, that utilized multivariate analysis to determine which environmental factors were most closely associated with trachoma.

Table 5: Summary of "F and E" Studies

Indicator	Range of OR	Number of Studies	Country Where Study Occurred
Water Availability	0.83-5.83	9	Morocco, Brazil, Malawi, Tanzania (3), Ethiopia, India, Review
Absence of toilet/latrine	1.2-6.07	5	Egypt, Brazil, Malawi, Ethiopia, Tanzania
Fly Density	0.25-1.87	5	Review (5)
Facial Cleanliness	0.4-1.74	5	Review (2), Tanzania (3)
Frequency of Face Washing	Not significant	3	Malawi, Brazil, Mexico
Hygiene Promotion	Negative-2.63	3	Review (2), South Africa
Garbage Collection	2.7-4.12	2	Ethiopia and Brazil
Animals	1.47	1	Ethiopia
Indoor Air Quality	1.24-1.48	3	Ethiopia, Tanzania (2)

All of the studies utilized multivariate analysis to determine effects. Caution should be taken in making clear comparisons between the range of OR because of the varying definitions used for both trachoma and the indicators themselves. In general, it is evident that water and latrine availability has a greater impact on disease while the evidence for facial cleanliness, fly density, and hygiene promotion is less convincing. The decrease in OR for these factors, especially hygiene education, may in part be due to the difficulty in measuring the quality and uptake of such education.

An update of this review would shed further understanding on the impact of prevention interventions on trachoma. Such an update was conducted in 2004, but was narrowly focused to only consider randomized studies that compared face washing to antibiotic treatment and concluded that face washing alone has no effect on trachoma (56). This may be expected because of the multiple routes of transmission and the importance of combing a suite of interventions. A cursory examination of studies published since 2000 and application of criteria used by Marriotti and Prüss indicates that prevention interventions continue to demonstrate OR similar or even greater than those presented in Table 5.

3.5 Need for Further Analysis

Further analysis is needed to systematically assess the impacts of environmental risks on trachoma. Current epidemiological studies offer some insight, but due to their specific nature, it is difficult and perhaps even invalid to extrapolate results from a single study to an entire country, let alone the globe. However, it may be extremely useful to compare epidemiological studies to indicator and prevalence data at the district and even national level to determine if similar trends and therefore support for causality links are found. Tanzania is one country which has data on both trachoma prevalence and some indicators at the district level, and could be used as a case-study. This would then offer further support for the use of indicator data in determining risks of trachoma prevalence.

Conducting a country or multi-country study to obtain direct data from the field could answer critical gaps in the current understanding of prevention and trachoma. Such a study would also help in the development of a model that considers both prevention and treatment. This model would allow trachoma program managers to make decisions on investment in prevention according to probabilities of risk reduction of disease transmission. The statistical analysis of the global data set, albeit a crude estimate, supports trends founds in specific epidemiology studies. Specific conclusions include:

- **Statistical Analysis Demonstrates Prevention Measures are Correlated to Trachoma**
  - Improved water, sanitation and housing closely correlated to trachoma prevalence
  - A combination of preventive measures can have an even greater impact on trachoma reduction than a single measure

- **Epidemiological Review Illustrates Significant Reductions of Trachoma With Environmental Improvements**
  - Water availability, sanitation, and garbage collection had highest OR
  - Facial cleanliness important, but difficulty in measurement may have led to lower OR

- **Large Need for More Reliable and District Level Data**
  - Current datasets are not inconsistent in measurement or reporting
  - District level data important for analysing disease clustering and areas of risk

- **Further Statistical Analysis Can Assist in Developing Range of Required Values for Environmental Indicators**
  - Use of mutually supportive indicators in combination can prevent confounding error
  - Level of environmental health needed to ensure endemic regions "on-track" to eliminate
  - Level of environmental health needed sustain active trachoma prevalence below 5%

It is clear that preventive measures can have an important impact on reducing trachoma and a combination of indicators are more closely correlated to trachoma than any single indicator. This supports the importance of implementing several prevention measures at once while measuring the impacts of such measures with multiple indicators. Even though the data needs are great, it should not derail efforts to select and implement indicators for use in certifying elimination of blinding trachoma. As more detailed and accurate data becomes available the indicators and how the indicators outcomes are used in decision making processes can be refined. The following section describes and proposes specific indicators that might be used for monitoring prevention in the campaign to eliminate trachoma.

Section 4: Use of Environmental Indicators in the Trachoma Campaign

Local communities are encouraged to improve "F", facial cleanliness, and "E", the environment as part of the trachoma SAFE campaign. To facilitate environmental improvement several manuals have been produced to explain the links between trachoma and the environment and provide suggestions on possible prevention methods (57), (58), (59). In addition, WHO has developed the Participatory, Hygiene, and Sanitation Transformation (PHAST) method to assist communities in implementing and maintaining water, sanitation and hygiene improvements. The PHAST method, along with the specific trachoma manuals offer important information, they do not provide a definitive framework for communities to assess risk and make decisions on how and to what degree to implement environmental interventions. This section begins the process of defining such a framework by proposing environmental indicators linked to trachoma control.

4.1 Environmental Indicators

Environmental indicators are increasingly becoming important in the field of public health. An environmental indicator is defined as "an expression of the link between environment and health, targeted at an issue of specific policy or management concern and presented in a form which facilitate interpretation for effective decision-making" (60). For purposes of this report, the term *environmental indicator* will be used to designate indicators related to preventing risk of trachoma transmission. The indicators presented focus on three (flies, fingers, fields/sanitation) of the five "Fs" identified as the transmission pathways for water related diseases. Fluids and foods are irrelevant to trachoma and are not considered. It is assumed the proposed treatment indicators for trachoma are better addressed by medical experts and therefore only environmental indicators of both exposure and contextual nature are discussed.

Environmental indicators can be used to measure risk of exposure. The Multiple Exposure-Multiple Effect (MEME) presented in **Figure 11** below provides a means to systematically understand the context in which exposure occurs and thus allow for development of specifically targeted indicators (61). The MEME model expands the more commonly referenced linear DPSEA (driving forces-pressures-state-exposures-health effects-actions) by acknowledging that context influences both exposure and health outcomes. The model also simplifies the DPSEA through grouping exposure and health outcomes into three main categories.

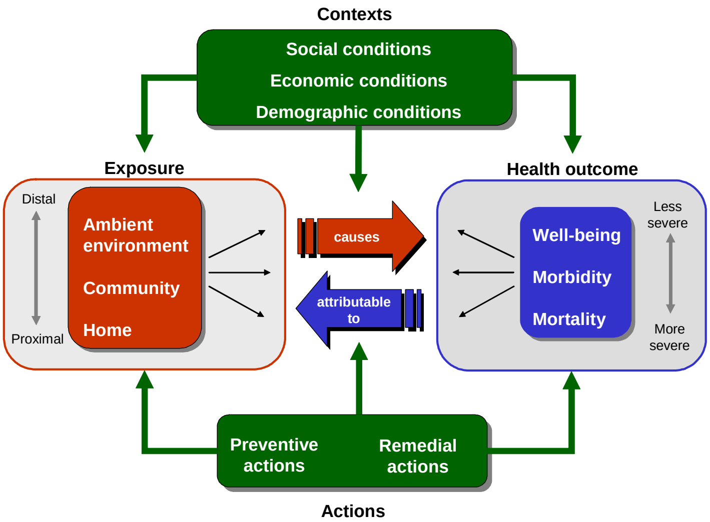


Figure 11: MEME Model (Extracted from (61))

The MEME model is especially relevant to trachoma because it was designed specifically to address children's environmental health indicators. The focus on the child, the reservoir of trachoma, is apparent by distinguishing the settings where children's exposure occurs, including the home, the community and the ambient environment. As shown in the MEME model, in addition to preventative and remedial actions, external ambient conditions, such as climate and economic, social, and political conditions impact both exposure and health outcomes. To ensure that all pathways of transmission are addressed and reduce risk of recurrence, it is important to select indicators for each of the three main influencing factors (exposure, remedial and context). **Figure 12** is based the studies reviewed for this report and further extends to the MEME model by specifically illustrating the factors, both prevention and treatment related, that influence trachoma transmission within a defined community.

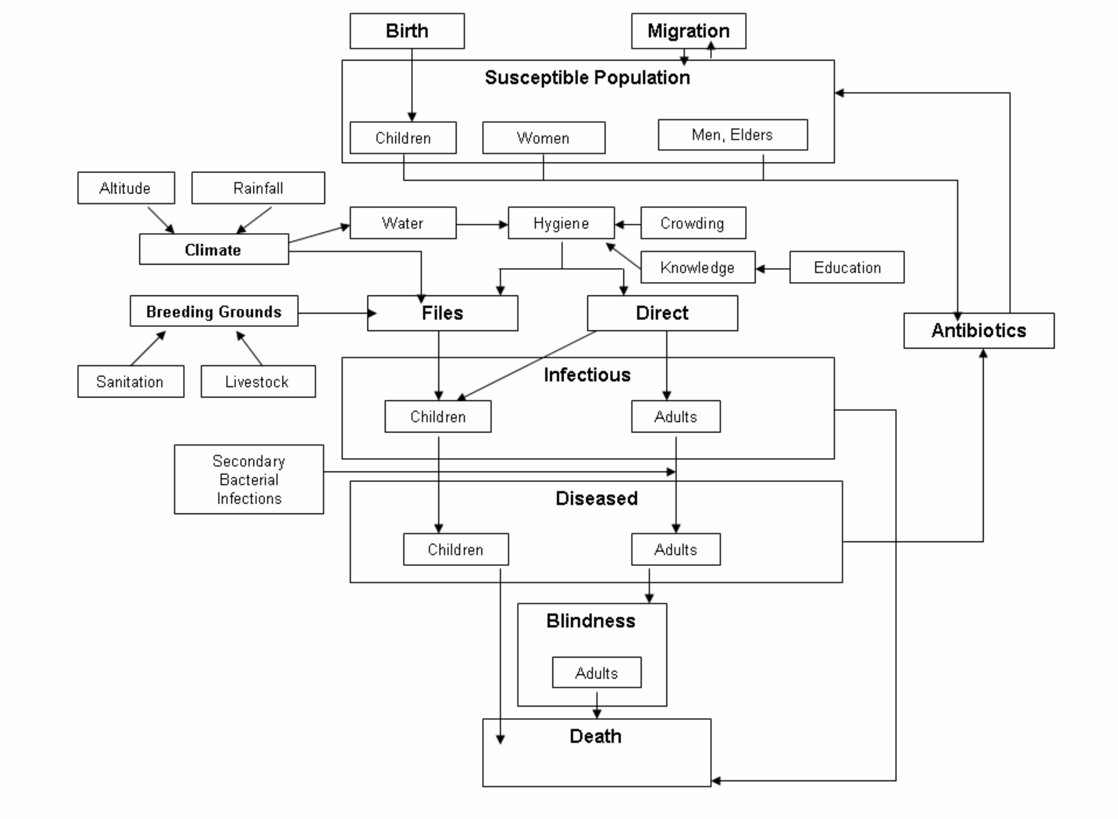


Figure 12: Trachoma Transmission Pathways and Disease Progression

Figure 12 illustrates several key elements of transmission. First, the population is divided into four main categories: susceptibles, infectious, diseased, and blind. These are bounded by births and migration (in and out) and death (out). In the absence of environmental prevention measures, migration could serve an important role in trachoma transmission. When infectious individuals migrate to areas where trachoma has not previously existed and thus local individuals have not had the opportunity to develop partial immunity, the new establishment of the disease may occur. Conversely, when individuals without any immunity migrate from areas where trachoma is not present to a region where it is endemic, such individuals may more easily contract the disease and require a longer period to resolve the infection. Such was the case in the early 20th Century, when Europeans traveling to Egypt where trachoma was endemic, more easily contracted trachoma and required longer periods to resolve the infection compared to their Egyptian counterparts(2). The longer infectious period may consequently increase risk of transmission to more susceptibles compared to a shorter infectious period.

Movement between the first three categories (susceptibles, infectious and diseased) is relatively fluid. Individuals may become infectious several times before they are diseased and even diseased individuals may be treated with antibiotics (or self-recover) and return to the susceptible population. Within the population categories, individuals are further separated into children, women, men/elders and/or adults. This recognizes that children are the reservoirs of the disease and therefore have a higher risk of contracting an infection, along with women who are typically the main child care-takers in trachoma endemic communities and therefore have greater exposure to *C. trachomatis* (28).

The two main transmission pathways are through flies or direct contact. The probability of flies transmitting trachoma is influenced by external environmental factors, such as climate and breeding grounds, as well as by individual characteristics such as facial cleanliness and presence of trachoma or another ocular disease. Direct contact is influenced by some of the same factors that influence flies, personal hygiene, as well as crowdedness and education. Modifications to the environment provide one means to stop transmission and antibiotics provide another. It is assumed that antibiotics are either distributed in mass to all susceptibles, or only to those that are diseased and display visible signs of infection. Antibiotics, however, do not provide a cure, and once treated individuals may become infected and diseased in the future. Once individuals become blind, the effects cannot be reversed. Finally, trachoma has been linked to premature death in children and therefore is represented separately.
With this model and understanding of disease transmission it is possible to define criteria for selecting indicators and establish possible indicators for use.

4.2 Criteria for Selecting Indicators

Criteria provide important guidance for selecting indicators. The commonly referenced group of five indicators, Specific, Measurable, Achievable, Realistic, and Time-bound (SMART), provides a comprehensive basis for selecting criteria. The following outlines each of these in further detail in relation to trachoma control and elimination.

Specific

A specific indicator is one that is directly attributable to trachoma. It is a necessary, but not always sufficient criterion. This requires that there is a basis, supported by conceptual and/or empirical evidence for linking the indicator to trachoma. Although this logic appears obvious, many environmental indicators fail to meet this criterion because as demonstrated by the MEME model, simple, univariate relationships between the environment and disease rarely exist (61). Specific indicators may not necessarily be causal indicators. An example of an indicator that does not meet the specific criterion for trachoma is safe water, as measured by absence of *E. coli*. This fails both because trachoma is not related to *E. coli* and ingestion of contaminated water is not one of the transmission pathways of the disease.

Measurable

A measurable indicator is one that clearly defines the indicator and process of assessment such that two individuals would be measured in the same way. This is especially important in the global elimination campaign as indicators must be interrupted universally within countries at the local, district and national level and between countries. A measurable indicator must be one that can be assessed and reported on to the greatest extent possible by local community members, such as is done in the guinea worm elimination program. For example, school teachers may select a committee of children to monitor face washing.

Accurate

An accurate indicator refers to how closely an indicator measures a desired effect. For example, if the aim is to measure the effect of crowding on disease transmission, it would be more accurate to record the number of individuals sleeping in one room rather than the number of individuals living in a household.

An even more accurate indicator would measure the number of children sleeping in one bed as children are the reservoir of the disease and are more likely to transmit *C. trachomatis*. Accuracy also refers to the methodology of measurement. In the example of crowding, it is not realistic to spend a night in every household to measure crowding, therefore one would have to rely on a verbal response, which may raise concern, especially for more contentious indicators. However, by utilizing several methods (spot-check visits, direct observation, and knowledge-action-questionnaires) threats to accuracy can be minimized.

Realistic

Selecting realistic indicators minimizes the burden of data collection on community health, education and sanitation workers. This is especially important considering that trachoma occurs in some of the most impoverished communities where resources are scarce. As opposed to observation and clinical studies which examine a suite of environmental factors, only the essential indicators for monitoring elimination of blinding trachoma should be selected. Furthermore, effort should be taken to utilize indicators that are already being collected regionally and globally through water and sanitation monitoring efforts such as the JMP and by specific environmentally-related infectious disease control programs including lymphatic filariasis and malaria.

Time-bound

The final SMART criterion is time-bound. Time-bound refers to the ability of indicators to measure an outcome or behaviour at both a particular moment and throughout time. Hygiene behaviours are intrinsically dynamic especially in developing countries where poverty impacts access to water and sanitation and ability to engage in safe hygiene behaviour. Therefore indicators may need to measure behaviour at key periods (according to climate, farming seasons, or even the holiday/religious calendar) to gain a reliable indicator data. A second consideration in the time-relevance of an indicator is that the time delay between the implementation of environmental improvements and the impact on trachoma. The construction and use of latrines must meet a specific threshold before fly populations are reduced in sufficient numbers to have a noticeable impact on trachoma transmission. This may take several months are more likely several years. In addition, the real measure of the effectiveness of prevention is the sustained, rather than immediate, reduction and elimination of trachoma. This can only be measured on a time-scale of several years and decades.

Specific, measurable and realistic are the three criteria that are most important for use in the certification of the elimination of blinding trachoma. Although accuracy is important, it may not always take precedence when time and resources are at a minimum. The aim of developing environmental indicators for certification is to more effectively encourage, control and eliminate trachoma with simple, locally-sustaining interventions.

4.3 Proposed Indicators

A review of the trachoma and environmental indicator literature led to the development of key indicators in four main categories. These categories, hygiene, access to hardware, knowledge and enabling environment, are described below along with the possible and proposed indicators. The description is followed by an indicator rating sheet that provides a means to quantify the environmental progress towards elimination in a specific community or district. The proposed indicators and rating sheet are meant to serve a basis for the GET 2020, program managers and field officers to discuss, refine and eventually select indicators.

4.3.1 Hygiene

Hygiene may be one of the most effective measures for preventing trachoma because of the direct links to transmission. The measurement of hygiene includes both behaviour and general living conditions.

The following provides a short-list of possible hygiene indicators that could be measured in trachoma control.

Possible Indicators
Behaviour
- Frequency of face washing
- Frequency washing clothes, bedding, and rags to wipe face after being used
- Proportion of households that dispose of child's faeces in a latrine

Condition
- Proportion of households with more than two children sleeping in one room
- Proportion of children with clean faces in or near their home and at school
- Fly density in and around households
- Livestock and domesticated animals within 10 m of households
- Presence of garbage pit within 10 m of households

Recommended Indicators
- Proportion of households with more than two children sleeping in one room
- Proportion of school children who wash their face on a daily basis at school

Selecting hygiene indicators to monitor is extremely challenging and a global consensus on which indicators are most relevant does not exist. The two largest difficulties lie in measurement and variability over time. Questionnaires are the most commonly used tool to measure indicators but they are subject to inaccuracies in recall and over-reporting of good behaviour. Several studies have found that the agreement between questionnaires and observations is little better than what would be expected by chance as calculated by a Kappa ratio close to zero (62) ,(63). In addition, recall questions only capture one moment in time, especially considering if recommendations to only ask about behaviour in the past 24 hours are followed (64). Structured and spot-check observations have been offered as an alternative or compliment to the traditional questionnaire (65). Although these may be more accurate they are either extremely time consuming and expensive (structured) or only capture one moment in time (spot-check). A second difficulty is defining and standardizing what is meant by good hygiene behaviour or conditions. For example, how does one define a clean face? Researchers continue to struggle over how to best answer the challenge of measuring and reporting good hygiene (66).

Due to the lack of proven methodology for measuring hygiene on a global scale, only two hygiene indicators are recommended. Both indicators specifically target children, because they are the reservoir of the disease and may shed copious amounts of *C. trachomatis* and thus increase risk of transmission to an entire community. The sleeping quarters indicator is limited to children because although it may be common for several children to sleep together, it is rare that more than two adults would sleep in one room. Two recent rigorous epidemiological studies conducted in Mali and Tanzania confirm that the risk of transmission of increases with greater numbers of people sleeping in one room (1), (67). The proportion of school children who wash their face on a daily basis provides a basis for determining the relative risk infected children pose to others at school. In some impoverished communities they may be up to 60 children packed into a single classroom thus increasing the likelihood of transmission. As long as children are required to bring a small amount of water with them to school, as it done in some communities in Tanzania, they would not need to necessarily have access to water at school in order to wash their face. Further review by those more intimately involved in monitoring of hygiene may provide a convincing argument to include additional indicators.

4.3.2 Access to Hardware
Access to hardware is more straightforward to measure than hygiene, but it is not necessarily a direct indicator of transmission. For example, even if individuals have access to water, they may not use the water to wash their face or engage in hygiene behaviour that demonstrates reduced risk of trachoma. It is important to note that access as used is this document, is based on the definition provided by the JMP Water and Sanitation Monitoring Program and is the proportion of the population using improved drinking water sources and sanitation facilities (68). However, as described earlier, statistical analysis and epidemiological studies, indicate that access to hardware is closely correlated to trachoma. The short list of access indicators and the proposed indicators are as follows:

Possible Indicators
- Proportion of households with access to improved water source throughout the year
- Proportion of school children with access to improved water source at school throughout the year
- Proportion of households where time to collect water is less than 30 min
- Proportion households and proportion in households that are children with access to improved sanitation
- Proportion of school children with access to improved, child-friendly sanitation at school
- Proportion of households and proportion in households that are children with access to face washing facilities
- Proportion of school children who wash their face on a daily basis at school

Recommended Indicators
- Proportion of households with access to improved water
- Proportion of households with access to improved sanitation
- Proportion of school children with access to improved sanitation at school

The first two indicators, access to water and sanitation within households are the most important. These two indicators were most closely associated with trachoma in the analysis presented in the previous section on global data and epidemiological studies have found OR as high as 5.83 and 6.07 where there is an absence of water and latrines, respectively(55). Access to sanitation at school is also important, but the degree of significance would depend on the actual proportion of children attending school in a given community. In neglected, underdeveloped areas where trachoma is often found, the attendance rate may be quite low and therefore these indicators would provide little insight into risk of disease transmission and progress towards elimination. At present, it can be assumed that measuring access is sufficient. If the interventions are incorporated as part of elimination efforts it may be inferred that some motivation exists to utilize water for hygiene purposes, especially because the amount required to wash one's face is small compared to the daily water requirement for a household.

4.3.3. Knowledge
Measuring and increasing knowledge is an important component in any effort to improve hygiene, including within the trachoma campaign. This is highlighted by the fact that trachoma has been endemic in some areas for centuries and as result strong cultural and religious beliefs concerning why certain individuals become afflicted with the disease have become established. For example, in rural areas in Mali, trachoma is thought to be caused by evil spirits or misfortune brought on by wrong-doing. Similar to access, knowledge does not necessary denote behaviour, but individuals are more likely to practice safe hygiene if they are aware of the benefits. Indicators to assess knowledge include:

Possible Indicators
- Proportion of household and school children that receive hygiene and trachoma education
- Frequency of hygiene and trachoma education seminars or instruction household visits per year

- Proportion of households and school children that find this education informative and useful
- Number of households and school children that are aware that trachoma is a blinding disease
- Proportion of households and school children that know at least one way to prevent trachoma
- Proportion of households and school children that can identify the danger signs of trachoma
- Proportion of households and school children that participate on social mobilization to encourage improved hygiene
- Proportion of households that participate in problem identification and problem-solving exercises relating to environment sanitation, trachoma, and health

Recommended Indicators

- Proportion of households and school children that are aware that trachoma is a blinding disease
- Proportion of households and school children that know at least one way to prevent trachoma

Only two main indicators are recommended, simply because it is difficult to measure knowledge without using a host of indicators, which is too time consuming and costly for the specific aim of trachoma elimination. Rather than select more distal indicators of knowledge, such as the proportion of households that receive education on trachoma, actually measuring the extent of knowledge regarding trachoma is a more accurate indication of an individual's likelihood of taking measures to prevent disease transmission. If other hygiene and behaviour programs are operating in the district, additional indicator information could be added to enhance the current indicators. Compared to the other indicators, knowledge may not be an essential indicator for use in certification of elimination. However, this should not underscore the need to improve knowledge about the scientific causes of the trachoma and means to prevent transmission. Such education should be done with consideration for respect of cultural beliefs concerning the disease to avoid alienating members of the community.

4.3.4. Enabling Environment

The enabling environment comprises a host of cultural, political, and social factors which serve to either support or weaken prevention measures. It is important to monitor the enabling environment because it is a critical indicator for the likelihood of sustaining interventions and by deduction sustaining the reduction in risk of transmission (64). Possible and proposed indicators that measure the enabling environment include:

Possible Indicators

- Close working links exist between government and non-government water/sanitation, health, and environment entities as demonstrated through agreements, meetings and joint projects
- Government maintains or increases investment in environmental sanitation on an annual basis
- Proportion of communities with trachoma control programs and local representatives
- A positive, equitable relationship exists between community members and trachoma control individuals as demonstrated for example by well attended seminars
- Local organisations are positive and productive contributors to community
- Local organisations commit to specific environmental sanitation promotion responsibilities and carry through with these responsibilities

Recommended Indicators:

- Local: Health, water and education committees collaborate on at least one trachoma control activity
- National: Government sustains and/or increases funding for water, sanitation and hygiene on an annual basis in areas where trachoma is present

The two indicators recommended for enabling environment aim to measure how effective trachoma programming and collaboration is at both a grassroots and national level. Together the two indicators will give at least a general idea of commitment to trachoma elimination and resource allocation devoted to carry out trachoma prevention activities. Also, it is likely that the indicators would be relatively simple to measure and require a review of government budgeting and reporting documents. This provides an additional reason to include them in the scorecard.

Environmental Indicator Scorecard
A proposed scorecard for quantifying environmental indicators of trachoma is provided in **Table 6** on the following page. The scorecard provides a starting point for developing a means to determine the progress being made by local communities or districts in meeting a level of environmental health that will effectively reduce sustain elimination of trachoma. For each of the four areas (hygiene, access to hardware, knowledge and support structures) communities receive a score, based on the level of environmental sanitation they have achieved. The four area scores are then summed to reach a total score. This score is what determines progress towards elimination which ranges from one (sustaining or will achieve elimination) to four (not on track). It is envisioned that the overall environmental score would be directly added to the surgery and antibiotic indicators that have already been proposed and were discussed in Section 2. Together the two sets of indicators, prevention and treatment, would determine whether or not a country has achieved elimination of blinding trachoma. The inter-related nature of the two sets of indicators will require coordination in measuring and reporting as it will be important that the trachoma prevalence data is compared directly to the environmental indicator data both spatially and longitudinally. In order to demonstrate sustained elimination countries would need to continue to submit information on indicators at regularly spaced intervals beginning on an annual basis and gradually increasing to every three or four years as levels of indicators and prevalence that signify elimination continue to be maintained.

Further modifications to the scorecard are required before it can be piloted and used in the elimination process. First, due to the high level of effort required to monitor several indicators, the recommended list may be need to be divided into essential and supporting indicators. The essential indicators would be those which countries would be required to monitor in order to apply for and maintain elimination status. Supporting indicators could be used in countries aiming to increase the rate at which they achieve elimination. Other modifications include providing clarification on the definition of each indicator and measurement methods. Also, the units and cut-off proportions, which were derived from the statistical analysis and epidemiological studies, require additional critical review. This is especially true of those for knowledge as the evidence base for such indicators is limited. In sum, refinement by experts and practitioners in the field of behaviour change, water supply and sanitation and community trachoma control would improve the rigor and utility of the proposed scorecard.

Table 6: Environmental Indicator Scorecard

AREA	INDICATOR	MEASURE	METHOD	UNIT	SCORE
HYGIENE	Crowdedness*	Proportion of households with individuals sharing a bedroom	-spot observation -self reporting	0: 50% have more than 5 1: 50% have more than 2 2: 50% have 2 per bedroom	
	Daily face washing in schools	Proportion of school children	-spot observation -self reporting	0: Less than 50% 1:50-90% 2: More than 90%	
				TOTAL HYGIENE SCORE__________	
ACCESS TO HARDWARE	Access to Improved Sanitation*	Proportion of households	-spot observation -self reporting	0: less than 20% 1: 20-60% 2: greater than 60%	
		Proportion of school children			
	Access to Improved Water*	Proportion of households	-spot observation -self reporting	0: less than 20% 1: 20-60% 2: greater than 60%	
				TOTAL ACCESS TO HARDWARE SCORE__________	
KNOWLEDGE	Proportion of households and school children that are aware that trachoma is a blinding disease	Proportion of households	-self reporting -official documents	0: less than 5O% 1: between 50-75% 2: more than 75%	
		Proportion of school children			
	Proportion of households and school children that know at least one way to prevent trachoma	Proportion of households	-self reporting -official documents	0: less than 5O% 1: between 50-75% 2: more than 75%	
		Proportion of school children			
				TOTAL KNOWLEDGE SCORE__________	
ENABLING ENVIRONMENT	Local Government	Health, water and education committees implement trachoma control activities in collaboration	-committee, HH reporting	0: No collaboration 1: Have at least one, active joint project 2: Have more than one project	
	National Government	Sustains or increases funding to water, sanitation and hygiene in areas where trachoma is present	-self reporting -budget and policy review	0: Funding grossly insufficient or decreasing 1: Invests at least 5% of water-sanitation (wat-san) budget in districts where trachoma is endemic 2: Invests at least 10% of wat-san budget in districts where trachoma is endemic or 5% where present but not endemic	
				TOTAL SUPPORT STRUCTRE SCORE__________	
				TOTAL INDICATOR SCORE=HYGIENE+ACCESS+KNOWLEDGE+SUPPORT STRUCTURE_________	
ELIMINATION STATUS	1. Sustaining or will achieve elimination (20-22) 2. Likely to achieve in the next 5 years (18-19) 3. On track to achieve in next 10 years (16-17) 4. Not on track (<15)				

*Denotes indicators that are currently measured on a global or partial global basis and aggregated at a national level (see Section 3.1 for details)

4.4 Measurement and Monitoring

The measurement and monitoring of trachoma prevention interventions in theory does not require a large amount of resources or technology. Rather with proper planning, training of local enumerators and periodic quality assurance checks, a community may be able to conduct monitoring at a minimum cost. The monitoring of environmental indicators for trachoma prevention could be combined with other water-sanitation and diarrhoeal disease monitoring activities to minimize the burden of data collection burden and community survey fatigue while maximizing the utility of the information gathered (69).

4.4.1 Establishing and Sharing Responsibility

Effective monitoring will require stakeholders at the international, national and local level to share responsibilities. Stakeholders refers to all individuals allied with trachoma elimination, whether directly (health care providers, hygiene educators) or indirectly (community leaders, water and sanitation committees). **Table 7** provides starting point for defining responsibilities.

Table 7: Stakeholder Roles and Responsibilities

Level	Stakeholder	Role	Responsibilities
International	WHO	Coordinate Elimination Campaign	-Utilize effective science, institutional knowledge, and experience to guide development of certification and indicators -Annually publish and share results of treatment and prevention efforts (as measured with indicators) -Annually organize relevant workshops and meetings to discuss progress and adjustments
	Collaborating Partners	Provide funding and technical support	-Assist in training individuals to monitor indicators -Provide tools to assist communities in implementing and sustaining trachoma interventions
National	Health Ministry	Coordinate national trachoma campaigns	-Compile data gathered at district or state level and report -Effectively communicate policies and provide technical assistance
	Supporting Ministries (Water, Environment, Education)	Collaborate on integrated prevention efforts and monitoring	-Discuss linkages and importance of coordinating indicator monitoring to reflect interdisciplinary nature of trachoma -Report relevant indicator data to Health Ministry
	WHO Country Offices	Liaison with WHO and governments	-Verify data before it is sent to WHO headquarters -Clarify ambiguities in indicator monitoring
District	Water, Environment, Health Ministry	Assist in implementation of national policies	-Collect data from village level and report to national level -Adjust funding and program support depending on outcomes and local needs
Local	Health Officers	Treat and assist in preventing trachoma	-Ensure treatment also involves education on prevention -Work with water, education, and community officials on prevention efforts
	Water and Sanitation Technicians	Assist in provision of improved water and sanitation	-Assist in monitoring water and sanitation provision -Assist in maintaining facilities
	Primary Schools	Educate children on healthy practices and trachoma	-Provide eye-washing facilities -Provide learning opportunities to discuss and investigate trachoma -Monitor face washing
	Community Organizations	Assist in efforts to treat and prevent trachoma	-Participate in and help organize workshops, trainings, and trachoma campaigns
	Households	Practice good hygiene and health	-Assist in monitoring indicators in immediate surroundings -Contribute to problem and solution identification

Experience has shown that it is necessary to establish a structure from which partnership arrangements may operate (70). This structure may be informal, but may involve both verbal and written agreements between stakeholders. Final commitments to responsibilities will naturally require input from stakeholders and further discussion of the definition of indicators and how they can most effectively be monitored.

4.4.2 Monitoring Plan

The manner in which indicators are measured and monitored has a large effect on the validity of the data gathered. Therefore a clear monitoring plan is essential. The main components of such a plan include defining the study area and sample size, collecting data, verifying and reporting data, and analysing results. Methodology has been developed for monitoring trachoma prevalence and a similar format could be used in the monitoring of the environmental indicators (38).

The following provides a basis for understanding the important elements of monitoring, but does not intend to serve as specific a how-to-guide. Any monitoring plan should be include the use of a cross-sectional survey where trachoma prevalence is measured along with the prevalence of risk factors. Although cross-sectional surveys can lead to difficulties in determining temporal relationships and a potential Nyman bias, because trachoma is not fatal and is slow to progress, most cases are likely to be captured if surveying is done on an annual or semi-annual basis.

Defining the Study Area and Sample Size

Defining the population boundary is important due the clustering tendency of trachoma. Although ideally this would be done on a geographic basis to reflect different levels of prevalence, it is more realistic to rely on political boundaries because of the need to systematically gather and report data. A practical study boundary would be village and possibly even the sub-village depending on the country. For example in Tanzania villages may be spread across several kilometres with each sub-village having separate water, development, and environment committees. Sub-villages may differ considerably in development and extent of environmental sanitation and therefore risk for trachoma. Furthermore, careful consideration needs to be given to village or sub-village boundaries, as not to exclude households on the periphery where the infection may be most severe.

Calculating the sample size within the study area will depend on defining the required precision and design effect. Most statistically relevant surveys suggest a precision (e) of 0.05 representing a confidence interval of 0.95. The design effect (D) provides a measure for clustering that can be used to minimize risk of homogeneity and improve statistical relevance of data. The range of D used and suggested for indicator surveys is between 2 and 10 (71). Due to the clustering nature of trachoma and risks (if one household has trachoma, the neighbouring household may also at risk) a somewhat lower D could be used, such as 2. This will also minimize the amount of time spent collecting data. The general equation for sample size estimation derived from the statistical random sampling equation is (71):

$$n = \frac{4P(1-P)D}{e^2}$$

Assuming that P is the proportion of individuals without improved environmental conditions, the equation will allow for estimation of sample size. In the case of trachoma, it may be difficult to select one P, because rates of water, sanitation and hygiene behaviour all vary among each other and likely within areas of the village. To begin an estimate of 0.5 is sufficient and can be modified according to local conditions. Thus, for a village with a population of 1,000 individuals, approximately 400 individuals (or 80 households assuming an average household size of five) would need to be interviewed. In addition, it would be enlightening to combine this sampling methodology with targeted extreme case sampling to help understand unusual cases, such as areas with specific clustering of disease.

Data Collection
As with the indicators, the methodology for data collection should be defined carefully and with precision. The first step is defining those responsible for actually collecting data on the indicators. The frequency at which data should be collected also needs to be determined. Preferably data collection will occur at least biannually to account for the expected variations both in community members' available time to participate in and help conduct surveys and measured outcomes. The major influences on such variations were discussed previously in the indicator criteria.

The means by which data will be collected must be multi-faceted in order to capture behaviour or indicators that may be misrepresented through a single method. The three main methods include spot-check observations for hygiene, household questionnaires, and interviews to gather information from schools, community groups, and other stakeholder organizations. One community member should be in charge of coordinating such data collection. Although some additional details on methodology are provided in the Indicator Appraisal in the Appendix, a formal questionnaire and methodology has not been developed. A variety of international organizations have devoted considerable energy to the development of such questionnaires and clearly defining what is meant by a "clean face" or "access to improved sanitation". For an abbreviated list of references concerning this refer to the Indicator Monitoring Resources in **Appendix III.**

Use of Indicator Data in Certification
The environmental indicator data serves a key function in the certification process. As mentioned previously, countries will have to both demonstrate that they meet indicator requirements at a single point in time and continue to maintain these requirements for several years and even decades. This raises two issues. The first is the need for the expert committee which will evaluate and make determinations on elimination to verify indicator scores as reported by national governments. Medical professionals will obviously be required to check prevalence in selected communities, but water, sanitation and hygiene specialists are also needed to ensure that indicators are being measured and reported as prescribed in forthcoming certification protocol. Second, ongoing monitoring and reporting of indicators is critical to demonstrate sustained elimination. Thus, initially countries may be simply granted *provisional elimination* status of elimination and if after five years of continually achieving of environmental indicator requirements, the status may reach *elimination*. If after additional five or ten years countries continue to meet requirements the status may become *sustained elimination*. If at any point countries fail to meet indicator requirements they may be placed on temporary probation until conditions are once again achieved.

4.4.3 Translating Results into Action
Monitoring of indicators is not meant to be merely an exercise in the study of environmental risk or an academic exercise. The utility of indicator data is directly measured by how such data is analysed and used to make evidence-based policy decisions. This will require that the indicators are probed and tested sufficiently by the trachoma campaign stakeholders before they are adopted into use. It will also require that a standard methodology is agreed upon by which to analyse the data, as false interpretation can lead to potentially devastating consequences. Other less tangible indicators may also have considerable influence on the outcomes of efforts. In Tanzania, the phrase, "Mungu atupelekwa magonjwa", is often heard, even after individuals speak of how poor water and sanitation can lead to diarrhoea and other diseases. The literal translation from Kiswahili is "God is the one who brings disease". Perhaps this is less of a reflection of lack of knowledge concerning disease, and more of an indication that health cannot be addressed with standard science and medical evidence alone. Therefore any interpretation of data should take into account more qualitative measures and understanding. Finally, in order to help enable communities to actively participate and manage trachoma prevention, further guidance is needed on how to integrate such efforts with existing water, sanitation and hygiene efforts. Manuals do exist to this

regard, but require updating of evidence and further specific "how to" guidance with specific reference to trachoma.

4.5 Cost-Benefit Considerations

The GET 2020 Campaign has helped sparked interest and investment by governments, donors, and international organizations in controlling and eliminating trachoma. Such investments are especially pronounced in donor-friendly countries such as Tanzania, Ethiopia and Ghana. With increased investment it is important to assess how effectively these funds are being spent.

The current investment and therefore the examination of the cost-benefit of the elimination of blinding trachoma campaign focuses nearly exclusively on treatment. This is typical of many infectious disease elimination campaigns, but status quo should not provide the basis for continuing such action. One reason for the limited reach may be based on claims that the face washing and environment components are the most costly and challenging to implement may have led campaign officials to focus most of their energy on treatment (72). The lack of attention on analysing water and sanitation may also be entrenched in what is actually considered prevention. The term "prevention intervention" has been used erroneously to refer to antibiotic treatment and surgery (73). Both of these measures attempt to treat the symptoms of the disease but neither provides a lasting preventative effect.

The existing cost benefit estimates provide some starting point from which to assess the burden of the disease. According to a recent study the estimated productivity losses from trachoma are USD 2.9 billion (28). If social impacts were included the figure would likely rise considerably. In assessing trichiasis surgery it was found that the cost effectiveness ranges from USD 13 -78 per disability adjusted life years (DALYs) adverted depending on the region. Providing surgery to 80% of those who need it would avert over 11 million DALYs. This provides a strong case for the cost-benefit of surgery, which costs approximately USD 80. However, if individual willingness to pay (WTP) to examined, the effectiveness is less clear as individuals are only willing to forgo USD 1.4 for surgery for many of the reasons discussed previously (74). Therefore the policy is to provide such surgeries without charge.

In contrast, the cost of providing antibiotics compared to the benefits gained does not demonstrate a favorable ratio. Estimates of USD 9,000 to USD 211,000 per DALYs adverted have been suggested (73). The difficulty in obtaining and distributing antibiotics to affected individuals that live predominately in remote, rural areas, especially after mass distribution is discontinued, would likely significantly increase these figures. With little likelihood of a vaccine being developed, it is doubtful that the effectiveness of curative treatment will significantly improve in the future (13).

A cursory examination of the cost-effectiveness of water and sanitation interventions demonstrates significantly better returns. It is estimated that meeting the U.N. MDGs for Water and Sanitation would bring economic benefits of ranging from USD 3 -34 per single USD invested (75). The attention directed towards these measures provides valuable monitoring data and knowledge-based resources for the trachoma campaign. Collaborating with existing and new water and sanitation improvement efforts in trachoma endemic countries is essential in this regard. For example, in 2005 the World Bank provided a 60 million USD loan to the Moroccan Government for a rural water and sanitation project (76). By including a trachoma prevention component in this effort the funds could generate even greater benefits and help in eliminating trachoma.

Sanitation and hygiene measures are likely to have significant impacts in three main areas. The first two are on reducing trachoma and on reducing other adverse health effects from both secondary opportunistic ocular infections and other water-related diseases. A multi-faceted review study on the effects of improved water supply and sanitation on infectious diseases including dracunculiasis, schistosomiasis, and trachoma demonstrate significant reductions in both the severity and prevalence of disease. The reductions for the three aforementioned diseases based on examination of only rigorous studies were 77%, 78%, and 27% respectively (77). The third significant impact concerns the larger chronic health, economic, and social impacts of improving water, sanitation and hygiene.

Investing in water and sanitation does not necessarily require large sums of money as has been suggested. Simply improving hygiene and sanitation requires little infrastructure with basic latrines costing as little as USD 10 or less. Furthermore, the consumer willingness to pay for water and sanitation is likely much higher compared to trachoma treatment, as drivers such as improved status, less sustaining motivation to maintain infrastructure and continue to practice safe hygiene behavior. This requires such practice to be rooted in and managed by the community before external assistance withdraws support.

Section 5: Conclusions

WHO and GET 2020 collaborators are currently confronted with a novel opportunity to integrate disease control with environmental improvement to enhance and sustain trachoma elimination. Success in this endeavour would serve to advance other joint undertakings between the infectious disease control and environmental sanitation sectors. By providing a clear example of the effectiveness of prevention and the systematic inclusion of environmental indicators in certification of elimination, the trachoma campaign could usher in a new of inter-sectoral collaboration.

It is clear that the underlying causes of trachoma must be tackled in order to effectively sustain elimination. This will require greater attention on implementing environmental improvements and measuring their impact on trachoma prevention. Trachoma is especially well-suited to this venture because of broad support from over a dozen partners which annually contribute millions of dollars to trachoma and are directly involved in field activities. In addition, the current UN MDGs of reducing by half, the proportion of individuals without improved access to water and sanitation by 2015, align well with the 2020 date for elimination of blinding trachoma. Three main conclusions are drawn:

- **Sustaining elimination requires prevention through environmental measures**
    - Definition of elimination of infectious disease requires ongoing intervention
    - Environmental measures offer only realistic long-term prevention option
    - Complicated disease pathology and absence of vaccine gives further credence to need for ongoing prevention through environmental measures
- **Improving environmental sanitation is cost-effective**
    - Provides benefits to trachoma and control of other water and sanitation related diseases
    - Cost-sharing with existing water and sanitation efforts increases benefits of investments
- **Integrating environmental indicators into trachoma elimination certification is achievable**
    - Scorecard provides simple means to measure environmental impact on elimination
    - Measurement and monitoring possible at local or district level
    - Ongoing monitoring provides insight into future prevention investments

Requiring countries to meet specific environmental indicators in order to obtain elimination of blinding trachoma certification will help ensure that elimination is sustained. Sanitation and related environmental improvements are cost-effective especially with inter-sectoral resource sharing and the use of locally appropriate, inexpensive technologies. In order to measure the extent of improvements, environmental indicators are necessary. Local monitoring of such indicator is possible as proven by the guinea worm campaign. Furthermore, recent advances in promoting and measuring hygiene and behavior change offer additional resources to the trachoma elimination effort. The information provided by indicators is critical for making cost-effectiveness decisions about how and where to spend limited resources.

Evidence based policy is essential to maximize the benefits from current and future investments in trachoma control. The current research provides sufficient data for selecting and implementing core environmental indicators. Once implemented, operational research can provide information on fine-tuning indicators to more accurately measure prevention of trachoma prevention and to more effectively invest disease elimination funding. This is especially critical in an era where public health programs are increasingly being called upon to justify the use of funds. Demonstrating sustained disease elimination, along with a number of other benefits related to environmental improvement, is a more powerful marker of a successful elimination campaign. The need to abolish the devastating effects trachoma, a disease that can be completely prevented through environmental measures, is one that can no longer be ignored.

References

1. Hsieh Y, et al. Risk Factors for Trachoma: 6 Year Follow-up of Children Aged 1 and 2 Years. *American Journal of Epidemiology*, 2000, **152:** 204-211.
2. Allen S, Semba R. The trachoma "Menace" in the United States, 1897-1960. *Survey of Ophthalmology*, Sept-Oct 2002, **47:** 500-509.
3. WHO. *Prevention of Blindness and Visual Impairment Website*. Visited July 20, 2006. Geneva.
4. WHO. *Report of the Seventh Meeting of the WHO Alliance for the Global Elimination of Trachoma.* Geneva.
5. Solomon A, et al. Diagnosis and Assessment of Trachoma. *Clinical Microbiology Reviews*, Oct 2004, **17:** 982-1011.
6. Mariotti S, Pararajaseqaram R, Resnikoff S. Trachoma: looking forward to global elimination of trachoma by 2020 (GET 2020). *American Journal of Tropical Medicine and Hygiene*, Nov 2003, **69 (suppl 5):** 33-35.
7. Dowdle W. The principals of disease elimination and eradication. *Bulletin of the World Health Organization*, **76 (Suppl 2):** 22-25.
8. CDC. *Recommendations of the International Task Force for Disease Eradication*. Atlanta, Georgia.
9. *Resolution, WHA 51.11, Agenda Item 20 in Global Elimination of Blinding Trachoma*. Geneva.
10. Mabey D, Fraser-Hurt N, Powell C. Antibiotics for trachoma (Review). *The Cochrane Database of Systematic Reviews*, April 2005, 1-35.
11. Ewald D, Hall G, Franks C. An evaluation of a SAFE-style trachoma control program in Central Australia. *Medical Journal of Australia*, Jan 20, 2003, **178:** 65-68.
12. Grove D. *Operational Models for Prevention of Blindness*, in *Models for Infectious Human Diseases*. 1996. Cambridge University Press, Cambridge.
13. Mabey D, Soloman A, Foster A. Trachoma. *The Lancet*, July 19, 2003, **362:** 223-229.
14. Hoechsmann A, et al. Reduction of trachoma in the absence of antibiotic treatment: evidence from a population-based survey in Malawi. *Ophthalmic Epidemiology*, July 2001, **8:** 145-153.
15. Dolin P, et al. Reduction of trachoma in a sub-Saharan village in the absence of a disease control program. *The Lancet*, May 24, 1997, **349:** 1511-1513.
16. WHO. *Future Approaches to Trachoma Control*. Geneva.
17. Wright H, Keeffe J, Taylor H. Trachoma and the Need for a Coordinated Community-Wide Response: A Case-Based Study. *PLos Medicine*, Feb 2006, **3:**
18. Mims C. *The Pathogenesis of Infectious Disease*. 1982. Academic Press, London.
19. Scalon J. *Association of Diptera with Incidence of Trachoma and Conjunctivitis*. 1964. SEATO Medic Study, San Francisco.
20. Bailey R, et al. The duration of human ocular Chlamydia trachomatis infection is age dependent. *Epidemiology Infection.*, **3:** 479-486.
21. Schachter J. Chlamydial Infections. *Western Journal of Medicine*, **153:** 523-534.
22. Bailey R, et al. Subjects Recovering from Human Ocular Chlamydial Infection Have Enhanced Lymphoproliferative Responses to Chlamydial Antigens Compared with Those of Persistently Diseased Controls. *Infection and Immunity*, Feb 1995, **63:** 389-392.
23. Jha H, et al. Disappearance of Trachoma from Western Nepal. *Clinical Infectious Diseases*, 2002, **35:** 765-768.
24. Prüss-Ustun A, Corvalan C. *Preventing disease through healthy environments*. 2006. WHO, Geneva.
25. Emerson P, et al. Role of flies and provision of latrines in trachoma control: cluster-randomized controlled trial. *The Lancet*, April 3, 2004, **363:** 1093-1098.
26. Emerson P, et al. Transmission ecology of the fly Musca sorbens, a putative vector of trachoma. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Jan-Feb 2000, **94:** 28-32.

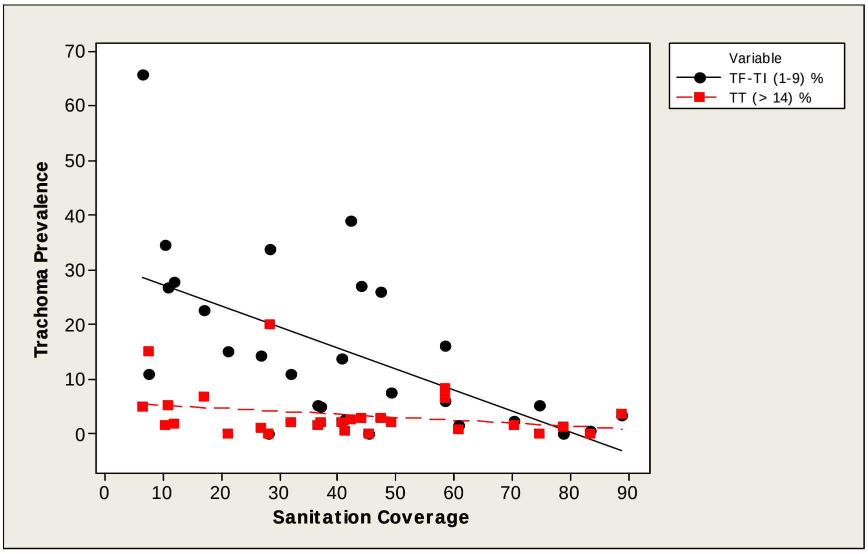
27. Simon C. *A Liapunov Function Approach to Computing Ro*, in *Models for Infectious Human Diseases*. 1996. Cambridge University Press, Cambridge.
28. Courtright P, West S. Contribution of sex-linked biology and gender roles to disparities with trachoma. *Emerging Infectious Diseases*, November 2004, **10:** 2012-2016.
29. Duerr H, Dietz K, Eichner M. Determinants of the eradicability of filarial infections: a conceptual approach. *Trends in Parasitology*, Feb 2005, **21:** 88-94.
30. Lee D, et al. Seasonal Effects of the Elimination of Trachoma. *American Journal of Tropical Medicine and Hygiene*, **72:** 468-470.
31. *Dracunculiasis eradication*. 2006. WHO, Geneva.
32. Cairncross S. Dracunculiasis (Guinea Worm Disease) and the Eradication Initiative. *Clinical Microbiology Reviews*, April 2002, **15:** 223-246.
33. *Fact Sheets on Water-related Diseases: Shistosomiasis*. 2004. WHO, Geneva.
34. Steinmann P, et al. Schistosomiasis and water resources development: systematic review, meta-analysis, and estimates of people at risk. *The Lancet*, July 2006, **6:** 411-425.
35. Liang S, et al. Re-emerging schistosomiasis in hilly and mountainous areas of Sichuan, China. *Bulletin of the World Health Organization*, Feb 2006, **84:** 139-144.
36. Hunter J, et al. *Parasitic diseases in water resources development*. 1993. WHO, Geneva.
37. Thylefors B, et al. A simple system for the assessment of trachoma and its complications. *Bulletin of the World Health Organization*, 1987, **65:** 477-483.
38. Négrel A, Taylor H, West S. *Guidelines for the Rapid Assessment of Blinding Trachoma*. 2001. WHO, Geneva.
39. WHO. *Trachoma Control, A Guide for Program Managers*. 2006. WHO, Geneva.
40. Michel C, et al. Field evaluation of a rapid point-of-care assay for targeting antibiotic treatment for trachoma control: a comparative study. *The Lancet*, May 13, 2006, **367:** 1585-1590.
41. Zhang H, et al. Prospective impact of oral azithromycin on postoperative recurrence of trachomatous trichiasis in Nepal over one year. *British Journal of Ophthalmology*, May 10, 2006,
42. Burton M, et al. The long-term natural history of trachomatous trichiasis in the Gambia. *Ophthalmology Vision Science*, March 2006, **47:** 847-852.
43. *Follow-up of Trichiasis Surgery*. 2000. Sultanate of Oman, Ministry of Health,
44. West S, et al. Predicting surgical compliance in a cohort of women with trichiasis. *International Opthalmology*, **18:** 105-109.
45. UN. *United Nations Human Development Report*. 2005. UNDP, New York.
46. Jeckle J, Elmore J, Katz D. *Epidemiology, Biostatistics, and Preventative Medicine*. 1996. W.B. Saunders Company, Philadelphia.
47. West S, et al. Water availability and trachoma. *Bulletin of the World Health Organization*, 1989, **67:** 71-76.
48. Myatt M, et al. Using lot quality-assurance sampling and area sampling to identify priority areas for Trachoma control: Vietnam. *Bulletin of the World Health Organization*, October 2005, **83:** 756-763.
49. Center C. *Summary Proceedings from 6th Annual Trachoma Control Program Review*. Atlanta, Georgia.
50. Beaglehole R, Bonita R, Kjellstrom T. *Basic Epidemiology*. 2000. WHO, Geneva.
51. Cairncross S. *Engineering for Public Health*. 1992. Ellis Horwood, England.
52. Nurminen M, Nurminen T, Corvalan C. Methodologic Issues in Epidemiologic Risk Assessment. *Epidemiology*, Sept 1999, **10:** 585-593.
53. UN Habitat. *Slums of the World: The face of urban poverty in the new millennium*. 2003. UN Habitat, Nairobi.
54. Kuper H, et al. A critical review of the SAFE strategy for the prevention of blinding trachoma. *The Lancet*, May 22, 2003, **30:** 373-381.

55. Prüss A, Mariotti S. Preventing trachoma through environmental sanitation: a review of the evidence base. *Bulletin of the World Health Organization*, 2000, **78:** 258-266.
56. Ejere H, Alhassan M, Rabiu M. Face washing promotion for preventing active trachoma (review). *The Cochrane Database of Systematic Reviews*, **3:** 1-12.
57. Francis V, Turner T. *Achieving Community Support for Trachoma Control*. 1995. WHO, Geneva.
58. Mariotti S, Prüss A. *Preventing Trachoma: A guide for environmental sanitation and improved hygiene*. 2000. WHO, Geneva.
59. Emerson P, et al. *Implementing the SAFE Strategy for Trachoma Control*. 2006. Center T C, Atlanta, Georgia.
60. Corvalan C, Briggs D, Kjellstrom T. *Linkage methods for environment and health analysis: general guidelines.*, in *Development of environmental health indicators*. 1996. Geneva. 19-53.
61. Briggs D. *Making a Difference: Indicators to Improve Children's Environmental Health*. 2003. WHO, Geneva.
62. Ebo M, et al. Measuring hygiene practices: a comparison of questionnaires with direct observations in rural Zaire. *Tropical Medicine and International Health*, Nov 1997, **2:** 1015-1021.
63. Stanton B, et al. Twenty-four hour recall, knowledge-attitude-practice questionnaires, and direct observations of sanitary practices:a comparative study. *Bulletin of the World Health Organization*, 1987, **65:** 217-222.
64. Kleinau E, et al. *Guidelines for Assessing Hygiene Improvement (unpublished)*. 2003. Environmental Health Project (EHP), Washington D.C.
65. Ruel M, Arimond M. Spot-check Observational Method for Assessing Hygiene Practices:Review of Experiences and Implications for Programs. *Journal of Health Population Nutrition*, March 2002, **20:** 65-76.
66. Emerson P, et al. Review of the evidence base for 'F' and 'E' components of the SAFE strategy for trachoma control. *Tropical Medicine and International Health*, August 2000, **5:** 515-527.
67. Shemann J, et al. Risk factors for trachoma in Mali. *International Journal of Epidemiology*, February 2002, **31:** 194-201.
68. WHO/UNICEF. *Meeting the MDG Drinking Water and Sanitation Target, A Mid-Term Assessment of Progress*. 2004. Geneva.
69. Almedon A, Blumenthal U, Manderson L. *Hygiene evaluation procedures: approaches and methods for assessing water and sanitation-related hygiene practices*. 1997. International Nutrition Foundation for Developing Countries (INFDC).
70. von Schirnding Y. *Health in Sustainable Developing Planning: The Role of Indicators*. 2002. WHO, Geneva.
71. Howard G, Ince M, Smith M. *Rapid assessment of drinking water quality*. 2003. UNICEF/WHO, Geneva.
72. Kumaresan J. What's new in trachoma control? *Community Eye Health Journal*, Dec 2004, **17:** 49-62.
73. Baltussen R, et al. Cost-effectiveness of trachoma control in seven world regions. *Ophthalmic Epidemiology*, April 12, 2005, **12:** 91-101.
74. Frick K, Hanson C, Jacobson G. Global Burden of Trachoma and the Economics of the Disease. *American Journal of Tropical Medicine*, **69:** 1-10.
75. *Evaluation of the costs and benefits of water and sanitation improvements at the global level.* 2004. Summary E, WHO, Geneva.
76. *Promoting Rural Sanitation and Hygiene in Morocco*. Mar 2006. World Bank, Washington D.C.
77. Esry S, et al. Effects of improved water supply and sanitation on ascarius, diarrhoea, dracunculiasis, hookworm infection, shistosomiasis, and trachoma. *Bulletin of the World Health Organization*, 1991, **69:** 609-621.

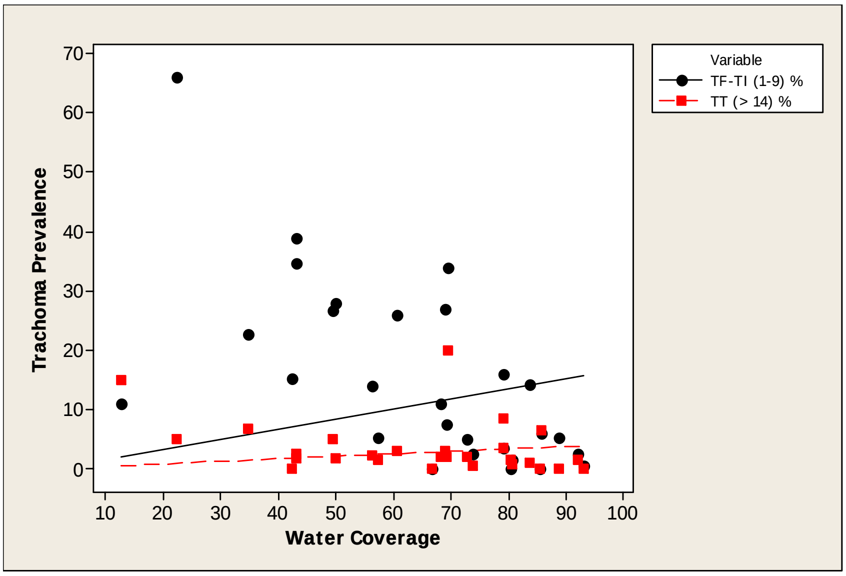
Appendix I. Definitions of Data

Term	**Definition**	**Source**
TF/TI	*Trachomatous inflammation follicular/ Trachomatous inflammation intense:* Presence of 5 or more follicles at least 0.5 mm in diameter and pronounced inflammatory thickening of the tarsal conjunctiva; for data collection purposes is measured in children from 1-9 years	WHO. *Trachoma Control, A Guide for Program Managers.* 2006. Geneva, Switzerland.
TT	*Trachomatous trichiasis* : At least one eyelash rubs on the eyeball; for data collection purposes measured in adults> 15 years	WHO. *Trachoma Control, A Guide for Program Managers.* 2006. Geneva, Switzerland.
Water Coverage	The percentage of the population using "improved" water sources, including access to a household connection, borehole or protected spring.	WHO/UNICEF. Joint Monitoring Program (JMP). http://www.wssinfo.org/en/watquery.html
Sanitation Coverage	The percentage of the population using "improved" sanitation, including connection to a sewer, septic system or latrine.	WHO/UNICEF. Joint Monitoring Program (JMP). http://www.wssinfo.org/en/watquery.html
Housing Durability	The percentage of dwellings built with permanent building materials on non-hazardous locations that have a structure adequate enough to protect inhabitants. Hazardous locations include flood plains, steep slopes, and dangerous right of ways.	World Resources Institute. Earth Trends Database. http://earthtrends.wri.org/searchable_db/index.php?theme=4, UN HABITAT. Sl*ums of the World: The face of urban poverty in the new millennium?* UN-HABITAT. 2003. Nairobi, Kenya.
Crowdedness	The percentage of dwellings that house less than three people per room, where the minimum size for a habitable room is four square meters.	World Resources Institute. Earth Trends Database. http://earthtrends.wri.org/searchable_db/index.php?theme=4. UN HABITAT. *Slums of the World: The face of urban poverty in the new millennium?* UN-HABITAT. 2003. Nairobi, Kenya.
Human Development Index (HDI)	Composite index that combines life expectancy, literacy rate, gross enrollment ratio for primary, secondary, and tertiary schools, and GDP per capita.	UNDP. Human Development Report. UN. 2005. New York.

Appendix II. Additional Statistic Plots



TF/TI and TT vs Sanitation



TF/TI and TT vs. Water

Appendix III: Selected Indicator Monitoring and Promotion Resources

Billing, P., et al. *Water and Sanitation Indicators Measurement Guide.* Food and Nutrition Technical Assistance. Series Indicator Guides. June 1999. Washington D.C.
Emerson, P., et al. *Implementing the SAFE Strategy for Trachoma Control*. January 2006. The Carter Center, Atlanta.
Global Public Private Partnership for Handwashing with Soap Website. http://www.globalhandwashing.org/
Kleinau, E., et al. *Guidelines for Assessing Hygiene Improvement.* 2003 (Unpublished) Environmental Health Project (EHP). Strategic Report.
Mariotti, S.P., Prüss, A. *Preventing Trachoma. A guide for environmental sanitation and improved hygiene*. 2000. World Health Organization. Geneva.
Narayan, D. *Participatory Evaluation*. World Bank Technical Paper, 207. 1993. World Bank, Washington D.C.
UNICEF. *A Manual for Hygiene Promotion. Technical Guidelines Series, No 6*. 1999. UNICEF, New York.
WHO/UNICEF. *Core questions on drinking water and sanitation household surveys.* April 2006 (unpublished). WHO, Geneva.
WHO/WASH. *Sanitation and Hygiene Promotion*. 2005. WHO, Geneva.
WHO. *PHAST step-by-step guide: A participatory approach for the control of diarrhoeal diseases.* 1998. WHO, Geneva.
WHO Environmental Sanitation and Hygiene Development Website. http://www.who.int/water_sanitation_health/hygiene/envsan/en/