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A Systematic Review Examining the Added Value of Water, Sanitation, and Hygiene Interventions for Preventive Chemotherapy Programs on Reducing the Prevalence of Trachoma

Anyess R. Travers
Georgia State University

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By Anyess Travers

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By

Anyess Travers

Approved:

Committee Chair

Committee Member

Committee Member

Date

ABSTRACT

BACKGROUND: Trachoma is a leading cause of avoidable blindness. Currently, trachoma is endemic in 57 countries, infects approximately 84 million people globally, and continues to threaten over 10 % of the world's population with the risk of blindness. Caused by the bacteria *Chlamydia trachomatis*, blindness due to trachoma is caused by repeated eye infection resulting in the inflammation of the upper eyelid eventually leading the upper lid to pull inward scratching and tearing the cornea causing it to become opaque resulting in loss of vision. The World Health Organization recommends eliminating trachoma as a public health problem using the SAFE strategy: Surgery, Antibiotic, Face washing and Environmental control.

OBJECTIVES: This review examined the benefits of the added value of water, sanitation, and hygiene education interventions on preventive mass drug administration for trachoma.

METHODS: Trials were identified from MEDLINE, PubMed, and LISTA EBSCO databases using a series of search terms. No restrictions were put on study date, location, design, or language of publication. The abstracts were examined from each of the searches, and any abstract describing risk factors, survey results of mass drug administration (MDA), or providing a general overview of trachoma were automatically discarded. Full text of papers including the combined use of key words including SAFE, WASH, intervention, impact, added value, MDA, azithromycin/ Zithromax® were obtained for review. Twelve full texts articles were retrieved all relevant information were placed in a standardized data extraction form.

MAIN RESULTS: Three studies met the complete criteria for inclusion. All studies found a significant change in reduction of active trachoma prevalence. One study focused on the added benefit of antibiotic and environmental components on hygiene education delivered by radio. Another trial compared two villages; the control community performed MDA and the surgery while the intervention village added the F and E components. The final study as well focused the added benefit of 'F' and 'E' on 'A'. Two of the three studies found this reduction was from the added benefit of face washing 'F' and environmental control 'E' to antibiotic use.

CONCLUSIONS: In order to eliminate blinding trachoma as a public health problem, recurrence of the active form of the disease must be interrupted before repeated scarring leads to trichiasis. The antibiotic component of the SAFE strategy is a quick fix to the immediate problem. The 'F' and 'E' components are the more sustainable interventions, yet little research has been done on the actual amount of added value the individual 'A''F'&'E' components have to one another. After thorough review of the articles, articles were found which documented the 'F' and 'E' components provide significant value to the overall decrease of prevalence of active. However, the limited results of the search suggest more research can better elucidate the ability of the 'F' and 'E' components to reduce trachoma prevalence and ultimately impact blinding.

Acknowledgements

Thank you Scott

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INTRODUCTION

1.1 Overview

Trachoma

Caused by the bacteria *Chlamydia trachomatis*, trachoma is the world's leading cause of preventable blindness, debilitating some of the world's most marginalized peoples (2006). Currently, trachoma is endemic in 57 countries, infects approximately 84 million people globally, and continues to threaten over 10% of the world's population with the risk of blindness (Mariotti, Pascolini et al. 2009; ITI 2010). Blindness due to trachoma is caused by repeated eye infection resulting in the inflammation of the upper eyelid eventually leading to scarring. Scarring, over time, shortens the upper lid causing the eye lashes to pull inward scratching and tearing the cornea and causing it to become opaque resulting in loss of vision (Pruss and Mariotti 2000; Solomon and Mabey 2007). To date, eight million people are blind or visually impaired due to the reoccurrence of trachoma infection (ITI 2010).

Transmission

After over 50 years of studies, consensus on the routes of trachoma transmission remains unchanged (Emerson, Cairncross et al. 2000). T The routes of transmission, all of which are hygiene-related, include indirect infection by the fly vector, *Musca sorben,* which breeds in nearby exposed feces (Mecaskey, Knirsch et al. 2003). The flies spread the disease person to person by landing on dirty faces of infected individuals and transporting the infection to others (Pruss-Ustun, Bonjour et al. 2008). Direct person-to-person contact, as well as indirect contact

via clothing, towels, handkerchiefs, bed sheets, and pillows causes the trachoma bacteria to spread among families, schools, and other groups (TCC 2010).

SAFE Strategy

Surgery (S), Antibiotic (A), Facial Cleanliness (F), Environmental Control (E)

The World Health Organization's (WHO) strategy to eliminate all avoidable blindness by the year 2020 is called VISION 2020: Right to Sight. Trachoma is specifically targeted in this initiative through an alliance of partners working with WHO called the *Global Elimination of Trachoma as a Cause of Blindness by the Year 2020* (GET 2020) (Pruss and Mariotti 2000). Elimination of trachoma-related blindness can be accomplished through the implementation of the complete SAFE strategy. The SAFE strategy includes the following: prevention of blindness by treating end stage trachoma through surgery; reduction of the reservoir of infection by distributing antibiotics such as azithromycin; and removal of risk factors that encourage transmission of infection through facial cleanliness and environmental changes (Mabey, Solomon et al. 2003).

Risk factors for trachoma are associated with lack of access to water, sanitation and hygiene (WASH) (Fewtrell 2004). Poverty creates a major barrier to gaining access to clean water, perpetuating the link between trachoma, lack of water, sanitation, and hygiene education, and economic development (UNDP 2006). According to the WHO, "the availability of clean water is a prerequisite to the sustainable growth and development of communities around the world" (Choffnes 2009). The conditions of poverty and inequality which perpetuate the prevalence of

trachoma and unsafe water and sanitation continue claiming lives, destroying livelihoods, and compromising prospects for economic growth (UNDP 2006).

WASH: Water, Sanitation and Hygiene

Globally approximately 10 % of the global burden of disease and 6.3 % of all deaths are due to unsafe water, inadequate sanitation, and insufficient hygiene (Pruss-Ustun, Bonjour et al. 2008). Over 1.1 billion people still defecate in the open and approximately 884 million people still do not get their drinking water from improved sources (UNICEF 2010). WASH interventions are programs specific to water, sanitation, and hygiene education and work to reduce the global burden of water and hygiene related diseases. WASH interventions, synonymous with the 'F' and 'E' components of SAFE, can be categorized into three groups:

1. Water supply, sanitation and hygiene
2. Water resources managements
3. Safety and environments

Trachoma is directly impacted by water supply, sanitation, and hygiene (Choffnes 2009). Water supply interventions at a public or household level include new or improved water supply source and distribution methods. The installation of hand pumps and household connections are often recognized as examples of water supply interventions. Sanitation interventions, such as construction of latrines, provide means of excreta disposal. Finally, hygiene interventions target specific behavior change, such as face washing, through hygiene and health education (Prüss-Üstün).

1.2 Purpose of Study

The 'A', 'F', and 'E' components of the SAFE strategy focus on the reduction of disease transmission and the impact on trachoma prevalence. Because active trachoma clusters in households or social groups, infection control should consist of community-based efforts to interrupt transmission (West 2003). This type of control is evident through annual mass drug administration (MDA) of azithromycin which is considered a safe, simple, and effective way to treat trachoma (Bailey and Lietman 2001). Through annual MDA, the 'A' component of SAFE becomes a preventive intervention as well as a treatment based intervention (WHO 2006). When regular treatment with antibiotics is complemented with the 'F' and 'E' components via improvements in water, sanitation, and hygiene education, transmission of trachoma can decrease to the point of elimination as a public health concern (Ngondi, Onsarigo et al. 2006).

The purpose of this review was to address the need for collaboration between organizations focused on different aspects of the SAFE strategy, i.e. WASH organizations and pharmaceutical donation programs. In order to reduce the burden of trachoma, and meet the targeted goal of elimination as a public health problem by the year 2020, there is a critical need to integrate the multifaceted approaches of trachoma control and prevention (Emerson, Lindsay et al. 2004). The review examined current evidence-based literature in an attempt to determine the added value of water, sanitation, and hygiene interventions on preventive chemotherapy programs described as MDA of azithromycin or Zithromax® donated by Pfizer. Change of prevalence within the context of the SAFE strategy is reviewed, revealing gaps in research and identifying the need for future studies.

CHAPTER II
REVIEW OF THE LITERATURE

2.1 History

The *Chlamydia trachomatis* bacterium has been around since the Jurassic period (Mathew, Turner et al. 2009). However, it did not manifest into what is known today as blinding trachoma until humans began living in clusters, creating optimal places for bacteria to spread from crowding and poor hygiene (Taylor 2008). Reports of this disease date as far back as the ancient Egyptians, Chinese, and Greeks (Taylor 2008; Taylor 2009).

Trachoma's effect on ancient Egyptians was evidenced through artifacts found in tombs including epilation devices for pulling out lashes and depictions of treatments for eye diseases written on papyrus called the Ebers' papyrus (West 2004). In ancient China mention of surgery, for what Hippocrates (460-377 BC) termed 'trichiosis' (in-turned eye lashes), dates back to the 27th century BC (Taylor 2008). It was not until the Greek physician Galen (126-216 AD) that trachoma was defined as hardness and roughness of the inner surface of the eye. His description of trachoma's various forms are similar to the ones still used today (Trompoukis and Kourkoutas 2007). The association between repeated trachoma infection leading to blinding trichiasis was not made until the 11th century, by the Arab physician Ibn 'Isa (Mecaskey, Knirsch et al. 2003).

Europe first noted trachoma after the Napoleonic wars (Hu, Harding-Esch et al. 2010). Trachoma initiated in the crowded barracks of British and French soldiers in Egypt, and

continued to spread to the general population once the troops returned home (Kumaresan 2005). From Europe the disease spread to the United States by immigrants (Mecaskey, Knirsch et al. 2003). Regulations were established and points of entry, including Ellis Island, were screened for signs of trachoma. If signs of the trachoma were detected the individual was offered treatment and then returned to their native land (Yew 1980).

The infection has disappeared from most developed countries (Taylor 1990). Places like the United States, Japan, the United Kingdom, and USSR were all endemic for trachoma at one point in their history but after years of treatment and development, blinding trachoma was eliminated (Taylor 2008). The difference between these countries and the countries where trachoma is still endemic is the amount of effort and money available for elimination programs. If all associated factors important to transmission of trachoma are not addressed, then a sustainable program cannot be created and the disease is likely to recur (Taylor 2008).

2.2 Clinical diagnosis

Throughout the years various grading systems for trachoma have been proposed (Hu, Harding-Esch et al. 2010). These forms have continued to follow the same form as Galen's initial observations (Trompoukis and Kourkoutas 2007). Most recently, WHO created a simplified trachoma grading scale to utilize non-specialized personnel and to report signs of trachoma simply and consistently. This system is now the most commonly used by program managers globally (Solomon and Mabey 2007). The WHO simplified system divides trachoma into five signs:

1. **Trachomatous inflammation (TF) - (follicles):** The presence of five or more follicles, at least 0.5mm in size, on the 'flat' surface of the upper tarsal conjunctiva.

2. **Trachomatous inflammation (TI) - (intense):** inflammatory thickening of the upper tarsal conjunctiva with more than half of the normal deep tarsal vessels obscured.

3. **Trachomatous scarring (TS):** scarring of the tarsal conjunctiva (fibrosis).

4. **Trachomatous trichiasis (TT):** at least one eyelash rubbing on the eyeball or evidence of eyelash removal.

5. **Corneal Opacity (CO):** where at least part of the pupil is blurred or obscured.
(WHO trachoma grading card)

TF and TI are described as active trachoma and TS, TT, and CO are considered cicatricial forms of trachoma (Thylefors, Dawson et al. 1987; Landers, Kleinschmidt et al. 2005) . Individuals, usually children, are infected with TF or TI and may be asymptomatic and therefore do not seek treatment (Kuper, Solomon et al. 2003) (Mabey, Bailey et al. 1991). The lack of immediate care can lead to repeated infection and increase the severity of symptoms by developing scars on the upper eyelid which shift the diagnosis from active to cicatricial trachoma (Munoz and West 1997).

2.3 SAFE strategy

As mentioned previously, the SAFE strategy is a multifaceted methodical initiative attempting to stop all levels of disease transmission and eliminate its reoccurrence (Emerson, Lindsay et al. 2004). The components of SAFE are implemented as both long and short term interventions of trachoma (West 2003). The prevalence of TF in children aged 1–9 years is the key index for determining whether an area needs intervention with the A, F and E components of SAFE. The prevalence of TT determines the probable need for surgical services (ITI 2010).

Surgery (S)

The final stage of the *Chlamydia trachomatis* infection, trichiasis (TT), poses the greatest risk for corneal ulcers leading to blindness (Bailey and Lietman 2001). As stated previously, corneal opacity and blindness are due to the continued occurrence of active trachoma as a child and can be stopped with surgery (West 2004). Surgery to correct in-turned lids is relatively short in time and can be performed by a general physician or trained ophthalmic nurses (ITI 2010). There are different types of TT surgery, all of which focus on turning the lid outward by 90 or more degrees (Schachter and Dawson 2002). According to Baltussen, Sylla et al. 2005, if 80% of coverage is obtained through trichiasis surgery 11 million disability adjusted life years (DALYs) per year would be averted globally (Baltussen, Sylla et al. 2005).

The impact of surgery is measured in terms of recurrence of trichiasis after surgery, including the position of one single lash touching the cornea (Kuper, Solomon et al. 2003). Recurrence may be considered to some degree inevitable due to the pathology of trachoma to continue scarring and the predisposition of a torn cornea to bacterial infection (Mathew, Turner et al. 2009). Several factors contribute to recurrent trichiasis such as the type of procedure used, the surgeon's experience, and infection status (Rajak, Makalo et al. 2010). However, long-term success rates for the procedure are approximately 80% (ITI 2010).

Another important factor affecting the impact of trichiasis surgery is the lack of accessibility to surgery (Hu, Harding-Esch et al. 2010). If the procedure was readily available at the community level, people with trichiasis would be more motivated to come forward for surgical correction

(Mecaskey, Knirsch et al. 2003). To help increase up-take of surgical services by patients, interventions such as mobile surgical camps provide communities access to surgery with little or no cost to the patient (Mabey, Solomon et al. 2003).

Antibiotic (A)

The 'A' component of the SAFE strategy is the current method of trachoma control for the active disease, TF or TI (ITI 2010). Active infection can be asymptomatic, influencing diagnosis and spot treatment (Kuper, Solomon et al. 2003) (Schachter and Dawson 2002). The WHO recommends mass antibiotic treatment of the entire district population annually for three years if active trachoma prevalence is above 10% (Hu, Harding-Esch et al. 2010). Due to the inclusive nature of MDA programs, they are successful in reducing the prevalence of infection below a certain threshold which slows trachoma transmission to the point of no longer being a public health problem. The disease becomes more manageable by other factors making re-emergence of diseases as a public-health problem unlikely (Smits 2009).

Before Pfizer began donating Zithromax®, an ingestible antibiotic, for trachoma control, tetracycline eye ointment was used as the antibiotic component of the SAFE strategy (ITI 2010). Tetracycline compliance, and therefore effectiveness, was affected by its tedious application process, twice a day for six weeks. Since the donation from Pfizer began in 1999, population coverage in the 'A' component reached more than 90% coverage at the WHO suggested district level (Kumaresan 2005). Additionally, azithromycin treatments are easily administered by community control programs through height-based dosing, and are considered by some to be the closest to the perfect antibacterial for MDA (Bailey and Lietman 2001) (Mathew, Turner et al.

2009). If azithromycin coverage achieves a 95% level, more than 4 million DALYs would be averted each year globally (Baltussen, Sylla et al. 2005).

A Cochrane review of antibiotics administration for reduction of trachoma prevalence was published in 2005. It concluded that antibiotic treatment for active trachoma seemed to reduce the relative risk of clinical disease and infection 3-12 months after treatment, however the results were inconclusive as to whether antibiotic treatment for active trachoma was effective (Mabey, Fraser-Hurt et al. 2005). Since the review, other cohort studies have been published with the same outcomes, in absence of the SAFE strategy, it was concluded that trachoma would return over a 24-month period (Taylor 2008).

Face washing and Environmental control (F & E)

The 'F' and 'E' components of the SAFE strategy are related and sometimes presented together. They are interventions which target water supply, sanitation, and hygiene education (Mecaskey, Knirsch et al. 2003). As discussed previously, trachoma is a disease prevalent in low socioeconomic countries and transmission of disease is due to lack of hygiene (Emerson, Cairncross et al. 2000). Unclean faces is a transmission route for the trachoma bacteria via direct person to person through ocular and nasal discharge and face washing decreases this potential source for the infection (Kuper, Solomon et al. 2003). It is difficult to achieve a behavioral change in face washing because of prolonged local involvement to implement, and the lack of appropriate monitoring measures (Taylor 2008) (King, Ngondi et al. 2010). However, West, Munoz et al. 1995 demonstrated the sustainability and long term benefits in the reduction of

prevalence severe trachoma and an increase in consistent face washing once it is implemented (West, Munoz et al. 1995) (Mathew, Turner et al. 2009).

Economic stability affects poor living conditions increasing the need for environmental interventions in trachoma control (Mathew, Turner et al. 2009). Trials suggest that interventions of the 'E' component including use of latrines, insecticide spray, and health education can reduce transmission of active trachoma (Pruss and Mariotti 2000). Due to the extended time needed to accurately interpret the effect the 'E' component interventions, additional studies are needed to understand the sustainability of these interventions (Rabiu, Alhassan et al. 2007). The scope of these components is so comprehensive that collaboration between country ministries' of sanitation, education, and health is needed (ITI 2010). Figure 1 represents trachoma The interventions include specific means of hygiene education which that communicate trachoma risk factors and prevention. Ohter interventions include water supply via wells, hand pumps, and storage, and sanitation through the use of latrines.

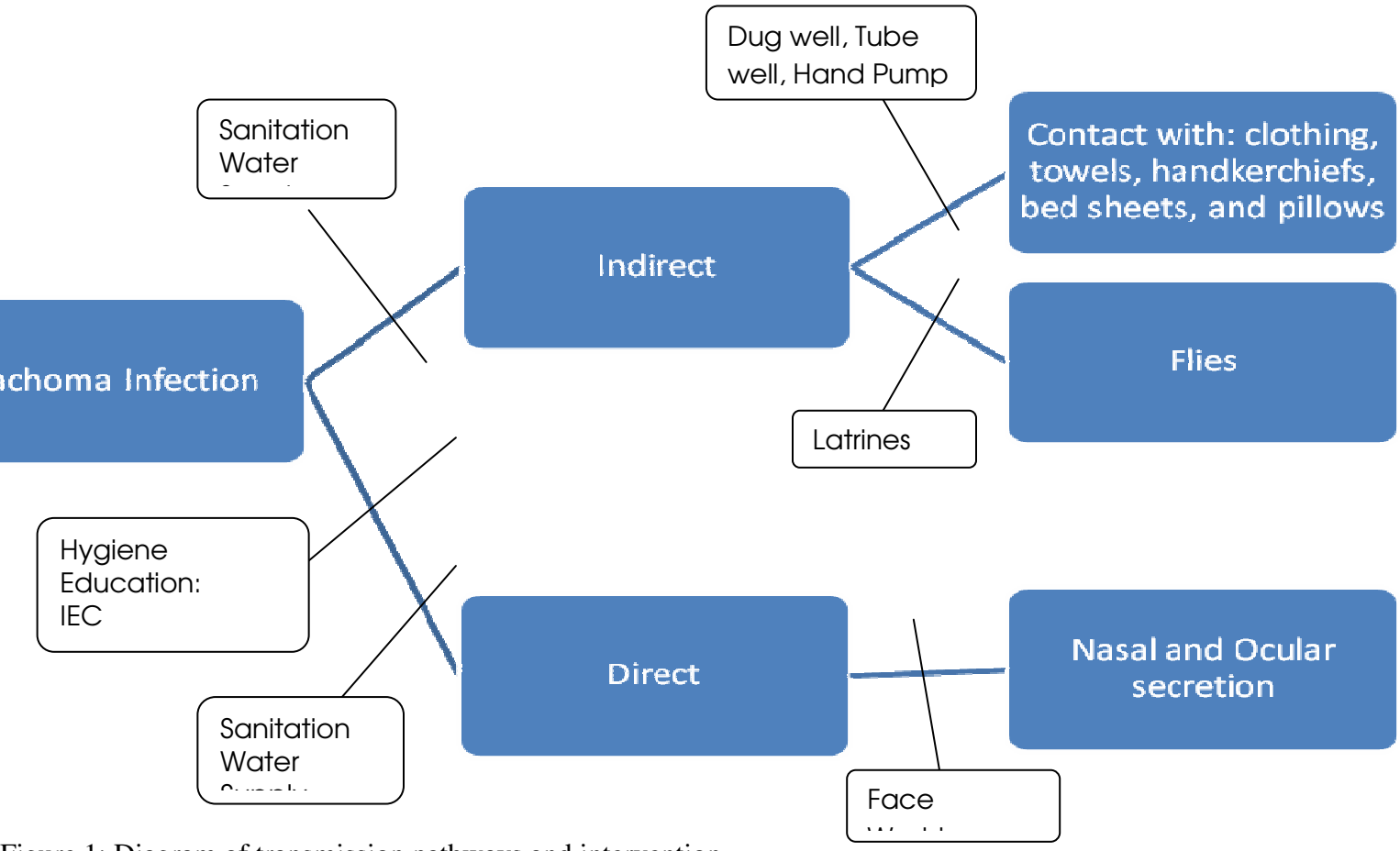

Figure 1: Diagram of transmission pathways and intervention

2.4 Impact of full SAFE

In order to receive Pfizer donated Zithromax® from the International Trachoma Initiative (ITI) a country is required to fill out an application including baseline prevalence survey results to illustrate endemicity. It is also recommended, in endemic areas, an impact survey be done three years after distribution (ITI 2010). Because of this requirement, several cross-sectional impact studies are now available describing the specific effects of antibiotics on prevalence of trachoma. Additionally, some researchers assessed the impact of the full SAFE strategy on prevalence of trachoma. In Roba et al. 2010, a study which included four regions across Ethiopia, the

prevalence of active trachoma (TF) was reduced from 36.7% to 18.4%, a significant 47% change in reduction (Roba, Wondimu et al. 2010).

A similar study looking at the impact of the 'A', 'F', and 'E' components was done by Ngondi et al. 2006. In this study the full SAFE strategy was being carried out in 4 different sites all having different amounts of control, but at different rates of uptake. The sites with the highest coverage of 'A', 'F', and 'E' interventions had the largest reduction of active trachoma (Ngondi, Onsarigo et al. 2006). Logistically, it is impractical to achieve sustainable results by individual interventions such as surgery and antibiotic therapy alone, the addition of the 'F' and 'E' components are needed to reduce transmission pathways (Emerson, Cairncross et al. 2000).

The prior studies confirmed that a comprehensive effort is needed to maximize results in decreasing the prevalence of active trachoma. In the following research, a systematic review was conducted to establish the added value of WASH interventions, the components 'F' and 'E' of the SAFE strategy, on the mass distribution of azithromycin the 'A' component. Knowing the added value of specific components will help advocate for further integration between trachoma programs and WASH organizations. This collaboration can occur through the selection of mutually beneficial intervention sites as well as identification of the most effective WASH indicators producing an impact on trachoma.

Chapter III

METHODOLOGY

3.1 CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Initial Selection Criteria

Eligible study designs included peer-reviewed studies evaluating the impact of WASH interventions on the antibiotic component of the SAFE strategy. All articles included in the review were required to report trachoma prevalence data pre- and post-program implementation. Any studies focused specifically on the outcomes of WASH interventions as an added value to Mass Drug Administration (MDA) of azithromycin treatments were included. Due to limitations of monitoring and lack of compliance with the use of tetracycline, studies distributing tetracycline and not azithromycin to people with active trachoma were excluded. All impact studies, totaling four from the keyword search, providing a complete assessment of the SAFE strategy and its impact on trachoma prevalence, rather than the added benefits of the interventions to one another were additionally excluded. Other excluded articles were those that focused on analyzing risk-factors for trachoma and providing descriptions of trachoma and SAFE strategy through literature-based review.

3.2 Types of outcome measures

Primary Outcome

The primary outcome measure for this review was prevalence of active trachoma measured as the number of participants with Trachoma Follicular (TF) and/ or Trachoma Inflammation (TI)

pre-and post-intervention. Active trachoma was identified by the WHO trachoma grading scale and/ or diagnostic swab testing.

Secondary Outcome

Secondary outcomes included changes in knowledge, attitudes, and practice specific to the risk factors associated with prevention of trachoma through antibiotics, face washing, and environmental control.

3.3 Search strategy

Electronic searches

The PubMed database searches were made with key word searches pairing aspects of water, sanitation and hygiene education against trachoma and either preventive chemotherapy, mass chemotherapy, or antibiotic. No restrictions were put on study date, location, design or language of publication. Similar searches were conducted using *LISTA EBSCO,* and *MEDLINE* which yielded no additional papers relating to WASH interventions on preventive chemotherapy interventions. A complete list of the key word search and results for each search are included below:

Table 1: Keyword search by name and results

SEARCH NAME	SEARCH RESULTS
Antibiotic and Water and Sanitation and Hygiene Education	11
Azithromycin and Water and Sanitation and Hygiene Education and trachoma	2
Hygiene Education and Antibiotic and trachoma	20

Hygiene Education and Preventive Chemotherapy and trachoma	2
Hygiene Education and Mass Chemotherapy and trachoma	5
Mass Chemotherapy and Water and Sanitation and Hygiene Education	6
Preventive Chemotherapy and Water and Sanitation and Hygiene Education	2
SAFE strategy and trachoma and intervention	27
Sanitation and Antibiotic and trachoma	17
Sanitation and Mass Chemotherapy and trachoma	5
Trachoma and Water and Sanitation and Hygiene Education	18
Water and Sanitation and Hygiene Education and Antibiotic and Trachoma	5
Water and Sanitation and Hygiene Education and Mass Chemotherapy and Trachoma	1
Water and Mass Chemotherapy and trachoma	5
Water and Antibiotic and trachoma	24

TOTAL NUMBER OF ARTICLES FROM SEARCH:	150
TOTAL NUMBER OF NON-REPEATED SEARCHES:	81
TOTAL NUMBER RELEVANT TO REVIEW (in non-repeated searches)	3

3.4 Data collection and analysis

Selection of studies

One author screened titles and abstracts found in the electronic databases. Any confusion about studies was resolved by an external source. The abstracts were examined from each of the searches, any abstract describing risk factors, survey results of MDA specifically, or providing a general overview of trachoma were automatically discarded. Full copies of papers including the

combined use of key words including SAFE, WASH, intervention, impact, added value, MDA, azithromycin/Zithromax® were obtained for review. As studies were identified for inclusion into the review their listed references, via abstracts, were examined for potential relevant studies.

Quality assessment

All studies meeting the initial selection criteria by reporting trachoma prevalence data pre- and post-program implementation and focusing specifically on the outcomes of WASH interventions as an added value to Mass Drug Administration (MDA) of azithromycin treatments were included were included.

Data collection

Specific data, including reduction of prevalence, was used to measure the effect of water, sanitation, and hygiene interventions for preventive chemotherapy programs on trachoma in relevant studies. The data analysis was contingent on the various study methods of the published articles determined by an initial reading of the abstracts from all studies retrieved and narrowed by previously mentioned keywords. Once titles were narrowed down, full texts were retrieved and relevant information was extracted onto a standardized form then pooled for summary estimates of the effectiveness of the interventions on the preventive chemotherapy programs specific to disease. The data fields included on the extraction form are presented in Table x.

Table X. Data Elements Extracted from Eligible Studies

- Author
- Title
- Journal
- Date
- Study Type
- Specific Intervention
- Specific antibiotic treatment
- Population group
- Age Range
- Number of Communities
- Sample size (n) at follow up
- Baseline prevalence
- Post intervention prevalence
- Effect measure
- Estimate

- Year of Baseline Survey
- Sample size (n) at baseline
- Trachoma Grading: WHO, Diagnostic, or both
- Country
- Region
- District
- Year of follow up
- 95% confidence interval
- P-value

Chapter IV

RESULTS

4.1 Results of the search

The initial electronic search, conducted on September 17, 2010, generated 123 studies. On October 1, 2010, an additional keyword search, including the key words SAFE strategy and trachoma and intervention, yielded 27 more studies. Of the 150 abstracts retrieved, a total of 81 were non-repeating. All non-repeating searches were screened by one author on two different occasions. After the screening, the full texts of 12 relevant articles were retrieved. These articles were assessed by one author; any questions arising from the assessment of these articles were answered by an external source specializing in NTDs.

From the 12 articles retrieved, one study (Edwards 2006) did not include antibiotic treatment due to limitations in distribution at the time of the study and therefore was excluded from the review. However, this study was followed up again two years later (Cumberland 2008) and those results were included in the review. Two studies following the impact of 'F' and 'E' on antibiotics (Reskinoff 1995 and West 1995) were excluded because the antibiotic distributed was tetracycline. As discussed previously the use of tetracycline is out-dated and compliance is difficult to measure. Two other articles (Astle 2006 and Khandekar 2005) were not included because the antibiotic distribution was not in the capacity of a MDA to the entire community and was only distributed to certain individuals during trachoma prevalence screening. Three more articles evaluating the comprehensive SAFE strategy turned out to be less rigorous cross-sectional surveys (Ngondi 2006, 2008 and 2010, and Roba 2010) and were excluded because the assessment did not specifically look at the added value of the SAFE components to each other.

The remaining three studies were considered and accepted for inclusion in the review (Cumberland 2008, Khandekar 2005, and Lansingh 2010). A full list of reviewed excluded studies is included below:

Table 2: Excluded studies and reason for exclusion

AUTHOR and YEAR	TITLE	REASON for EXCLUSION
Astle 2006	Trachoma control in Southern Zambia--an international team project employing the SAFE strategy	Spot treatment
Edwards 2006	Impact of health education on active trachoma in hyperendemic rural communities in Ethiopia	No MDA
Khandekar 2005	Active trachoma, face washing (F) and environmental improvement (E) in a high-risk population in Oman	Spot treatment
Ngondi 2006	Effect of 3 years of SAFE (surgery, antibiotics, facial cleanliness, and environmental change) strategy for trachoma control in southern Sudan: a cross-sectional study	Impact Survey
Ngondi 2008	Associations between active trachoma and community intervention with Antibiotics, Facial cleanliness, nd Environmental improvement (A,F,E).	Assessed Risk Factors
Ngondi 2010	Estimation of effects of community intervention with antibiotics, facial cleanliness, and environmental improvement (A,F,E) in five districts of Ethiopia hyperendemic for trachoma	Impact Survey
Reskinoff 1995	Health education and antibiotic therapy in trachoma control	Tetracycline only
Roba 2010	Effects of intervention with the SAFE strategy on trachoma across Ethiopia	Impact Survey
West 1995	Impact of face-washing on trachoma in Kongwa, Tanzania	Tetracycline only

4.2 Setting and participants by article

Including type of study, unit of randomization, place, number

The three eligible studies were diverse in population, region, study design, and intervention. The commonality was that they were all randomized control studies, with a specific intention to study the added value of SAFE components.

Types of Participants

Participants in these trials were residents in trachoma endemic communities, in Ethiopia, Vietnam, and Australia. No age restriction was placed on the studies, however because active trachoma is usually diagnosed in children under 15 years of age the studies self-limited themselves to children below the age of 15.

Ethiopia: Cumberland 2008 was a randomized controlled trial (Edwards, Cumberland et al. 2006) with staged interventions, beginning in Guarage, Oromia, and South Welo districts of Ethiopia between 2002 and 2003. A total of 1722 participants, 3- 9 years of age, in 37 communities were randomized into three intervention groups and one control group. Five communities were used in the control group and 32 received combined intervention activities to serve as the intervention group. Because 33 children with TI did not have follicles, the final analysis was based on a total of 1689 children.

Vietnam: Khandekar 2006 was a community-based health intervention study, whereby an intervention community was compared to a nonintervention community, conducted in two communities, My Thon (MT) and Xom Ngoia (XN), in the Gia Binh district of

Vietnam. In March of 2002, children aged less than15 years old in each community were assessed for inclusion in the study. Participants were chosen by random selection method with the help of Microsoft XL software. The total number of children assessed in the analysis of the study was 911.

Australia: Lansingh 2010 was a prospective, case-control, community based case study lasting 12 months from 2000 to 2001, including two hyper-endemic Aboriginal Australian communities. Both communities assessed children <15 years of age and were matched at baseline with regards to population age, gender, trachoma disease markers, as well as desert climate and environment. Community 1 had 86 participants and Community 2 had 91. After 3 months of intervention the total amount of children under 15 years of age re-assessed was 107, after 6 months the total increased to 111 and after 12 months the total was165.

4.3 Interventions

Including types, setting, duration

In Cumberland 2008, populations of all villages received radio broadcasts as a hygiene education intervention. In the intervention communities, all received antibiotics and one group received additional health information in the form of information education and communication materials (IEC). Themost comprehensive intervention communities included (in addition to MDA and IEC) drama and video. Though all intervention communities received MDA, approximately half of the intervention communities received azithromycin 2-5 months prior to the survey and most had received more than one dose. The interventions were on-going for three years.

In Khandekar 2006, the community of Xom Ngoia (XN) implemented the S and A components of the SAFE strategy. In My Thon (MT) the full SAFE strategy was implemented. The additional components of the full SAFE strategy included the provision of clean water and sanitary latrines as well as health behavior education. The specific interventions included:

- 281 double-vault and three septic tank latrines
- 241 bathrooms
- 273 dug wells
- 252 water tanks, tube wells, hand pumps
- 202 water filters
- 97 meetings
- 2 marches
- 2 performances
- 5 billboards of trachoma-control message
- 384 repetitions of message through village loud speaker

The post-intervention follow up occurred in 2005, three years after the interventions began.

In Lansingh 2010, health and facial cleanliness promotion and azithromycin were distributed to all members of both communities. Community 1 received an additional E component intervention through housing and environmental improvements. The specific improvements included:

- Road sealing- replacement of poorly built or maintained houses with appropriately designed houses
- Biweekly trash collection

- Repair or heating/cooling systems
- Upgrades in sewage and water lines
- Installation of rainwater tanks
- House yard fences bordering roads
- Planting of trees, grass, and native plants in areas where wind and dust were prevalent
- Earthworks and diversions to create micro-catchments and water ponding
- Installation of drinking-water fountains in the school and health clinic

4.4 Outcomes measures

Including diagnosis of trachoma, WASH interventions

In Cumberland 2008, outcome measures recorded in the study included prevalence of active trachoma, TF only, at baseline and then again post-intervention. The clinical diagnosis of active trachoma was graded using the WHO simplified grading system. Signs were recorded as being present if they were seen in either or both eyes. Additionally, eye swabs of all children were taken to detect the presence of Polymerase Chain Reaction (PCR) in ocular secretions *C. trachomatis* deoxyribonucleic acid (DNA).

Secondary outcomes measured knowledge and behavior related to trachoma control. These were measured through observations and questionnaires. Observations were made by field workers of household facilities, cleanliness and presence of flies in and around the houses. Questionnaires were delivered by a locally recruited interviewer to an adult care-giver in the home. Questions included demographic details of both, respondents and household, they were specific to care of livestock, knowledge of health-related issues, practical arrangements for sanitation which was supported by observations of field workers of beaten paths to the latrines and human faeces in the pit.

In Khandekar 2006, both eyes of all family members were examined using the WHO trachoma grading scale, if trachoma was reported in either eye the person was considered to be suffering from active trachoma, TF/TI.

Secondary outcomes were assessed through close-ended questionnaires, included measuring the knowledge, attitude and practice (KAP) regarding trachoma among mothers in both villages. Questions related to attitude and practice had five grades, from fully agree to entirely disagree, and questions related to knowledge included: common symptoms of trachoma, blinding complications of trachoma, methods of prevention, of water sources for drinking and face washing and the advantages of a sanitary latrine. Evaluation of water and sanitation status was done by a water engineer who quantitatively and qualitatively recorded the status of the water, latrine and other sanitation facilities in and around the house.

In Lansingh 2010, baseline measures of trachoma prevalence, facial cleanliness, and nasal discharge were measured. Assessments of trachoma and facial cleanliness were made at 3, 6, 12 months post intervention. Clinical assessment of trachoma was conducted by a single examiner using the WHO simplified grading system. Active trachoma was defined as the presence of TF or TI.

Secondary measures were taken by Aboriginal Health Workers (AHW) trained to assist with examinations, promote health education when participants visited clinics for any

reason, and conduct the health education campaign at the home level. An active health education campaign with emphasis on facial cleanliness was instituted in schools, primarily facilitated by teachers and personnel from the Nganampa Health Council.

Absolute facial cleanliness was defined as the absence of eye and nasal discharge. Partial facial cleanliness was defined as having either eye or nasal discharge, but not both. A dirty face" had eye and nasal discharge; the quality of discharge was also recorded as clear, abundant, or mucopurulent. Health Living Practices (HLP) were measured by survey at baseline and approximately 8 months post-intervention, to be considered passing eight of the nine must be met. These practices included:

- Washing people
- Washing clothes and bedding
- Removing waste safely
- Improving nutrition
- Reducing crowding
- Reduction negative contact between people and animals, vermin or insects
- Reducing the negative impact of dust
- Controlling temperature of the lining environment and
- Reducing trauma around the house and living environment
- Surveys were conducted house by house to assess each

4.5 Effects of intervention

Due to the heterogeneity of study design conducting a meta-analysis was not considered appropriate and a narrative summary of the results are presented.

Primary Outcome: Prevalence of Active Trachoma

In Cumberland 2008, the overall prevalence (standard deviation: SD) of active trachoma in the 37 communities was 71.4% in 2002 and 35.6 % in 2005, illustrating around a 50% reduction prevalence. The cluster summarized prevalence (SD) of active trachoma estimated in the control communities was 60.7% in 2002, 55.1% in 2003 and 54.5% in 2005. The reduction in the intervention community was found statistically significant but the reduction in the control communities, only receiving radio as an intervention, was not statistically significant (P=0.692).

In communities receiving azithromycin and video educational interventions, a reduction in the odds of active trachoma did not occur. However, after adjustment for age, results suggested an almost 70% reduction in odds of active trachoma in children living in communities that received antibiotic treatment and IEC health education materials and those in communities who additionally received the video health messages.

Table 3: Summary of odds of trachoma after intervention in Cumberland 2008

Intervention	Age	Odds Ratio	95% CI	Significance
antibiotic treatment IEC health education video health	All	0.93	0.42-2.07	P=.0860
antibiotic treatment IEC health education	Children	0.35	0.13-089	P=0.027
antibiotic treatment IEC health education video health	Children	0.31	0.11-.089	P=0.029

In Khandekar 2006 study, the village with the added value of the F and E components experienced a decrease in the prevalence of trachoma from 13.8% at baseline to 2.3% post-intervention, a prevalence difference of 11.53%. Prevalence of active trachoma

dropped as well in XN (SA only) from 10.2% to 5.54%, an absolute difference of 4.7%. The additional decline in children <15 years of age was calculated by subtracting the absolute decline of each village resulting in 6.8% due to the added benefit of F and E components in MT (SAFE).

The decline of active trachoma in XN (SA) was considered to be due to the impact of the S and A components. When the impact of the F and E strategy under the circumstances of this study was controlled for, a decline of 59.2% in active trachoma was attributed to the additional activities of the F and E components of the SAFE strategy in MT. (6.83/11.53 * 100= 59.2 %)

In Lansingh 2010, a reduction in prevalence of trachoma was observed three months after antibiotic administration. At that time, the active trachoma prevalence reduced from 47.7% to 21.2% in community 1(AFE) and from 49.6% to 24.2% in community 2 (AF). By 12 months it rose to 30% in community 2 (AF) but remained stable at community 1 (AFE).

The reduction in trachoma prevalence between pre-intervention and 12 month post-intervention was significant for both communities.

X^2=9.1 community 1 P=.003

X^2=8.1community 2 P= .005

However there was no significant difference in the trachoma prevalence between the two communities at any examination.

Bellow is table 4, Trachoma Prevalence Overview, a synopsis of the results in change of trachoma prevalence found in the included articles.

Table 4: Reported reduction of trachoma prevalence

Reference	Length of Study	Baseline trachoma prevalence		Post-intervention	Percent reduction	Added Value
Cumberland 2008	3 years	Control	60.7%	54.5%	10%	
		Overall:	71.4%	35.6%	50%	
Khandekar 2006	3 years	Control	10.2%	5.54%	46.1%	59.2%
		Intervention	13.8%	2.3%	83%	
Lansingh 2010	1 year	Control	49.6%	30.0%		
		Intervention	47.7%	21.2%		

Secondary outcome:

CHANGES IN KNOWLEDGE ATTITUDE AND PRACTICE

In Cumberland 2008, there was no evidence of a difference in awareness of trachoma and trichiasis across intervention arms, however community summarized awareness was greater than 80% in all. Since the previous surveys in 2002 and 2003, more householders were reported to know at least one trachoma prevention method as compared to not knowing any in communities receiving printed and video health education.

In Khandekar 2006, the levels of KAP among the mothers of both villages at baseline and at the end of two years were compared. An improvement in knowledge of the subcomponents of trachoma prevention among the mothers in MT (SAFE) was greater than among the mothers in XN (SA). However, the attitude and practice of trachoma control continued to be at the same level among the mothers of both villages.

Lansingh 2010 did not measure KAP as a secondary outcome for trachoma knowledge; instead the study looked specifically at facial cleanliness in regards to a measure of the added benefit of the 'E' intervention. Post intervention follow –up at12 months showed a greater percentage of clean faces and less prevalence of nasal discharge in community 2, the non-'E' intervention community. This was due to the fact that both communities received interventions in hygiene education which would affect this outcome.

Facial cleanliness: Clean faces

- Baseline:
    - community 1: 30%
    - community 2 23%
- Follow up (12 month):
    - community 1 57%
    - community 2 85% ($x^2 = 6.5$, $p=0.01$)

4.6 Quality of the evidence

Establishing a reliable study design is crucial in providing quality evidence, yet it is always a challenge. To minimize risk of bias, a study has to establish appropriate sample size, randomize participants, control for confounders, and select controls to match cases (Khandekar, Ton et al. 2006). In this review, the study with the most comprehensive description of these elements was Khandekar 2006. In Cumberland 2008 and Lansingh 2010 it was unclear if risk of selection/sampling and confounding bias was accounted for or if it was simply omitted in the reporting stage. In regards to this review, the analysis was conducted with information provided only from the respective articles.

Selection Bias:

Of the three studies reviewed, one study, Lansingh 2010, did not mention randomizing participants. Cumberland 2008 stated that the participants and communities were randomly chosen. Delays with distribution prevented the study to stick to the original randomization schedule and local NGO's were responsible for distribution of interventions on their own schedule. The details of the original design were reported in the 2003 study published in 2006. Khandekar 2006 also stated random selection. The researchers also tried to minimize systematic error by having an appropriate sized population of all ages. In contrast, the Lansingh 2010 study did mention that the effect size (which at the time had not been tested for the E component) was beyond the detectable level since the number of children surveyed in both communities was relative low.

Comparability

In Cumberland 2008, the communities used in the study were randomly selected from different zones within the trachoma control program areas. There was however no additional information offered about the comparability of these villages. In Khandekar 2006 and Lansingh 2010 the studied villages were chosen specifically because of comparable characteristics. In Khandekar 2008, the villages had almost similar population profiles and sanitation status, only the water sources differed. In order to prevent cross-contamination between groups, study villages were in separate communities with five other villages between them and markets and educational centers

were also different. In Lansingh 2010, the two communities were matched in general at baseline with regard to population age, gender, trachoma disease markers, as well as desert climate and environment, although mobility was much higher at communit1.

Compliance

Azithromycin Coverage:

During Mass Drug Administration (MDA) 100% of the community is targeted for treatment as a means of preventive chemotherapy. As in most public health initiatives coverage results above 80% are considered reliable in achieving intervention outcomes. In Cumberland 2008, 92% coverage of azithromycin distribution took place. Lansingh 2010, only achieved an antibiotic coverage of 73 and 55% in communities 1 and 2 respectively, and Khandekar 2006 did not specify coverage rates on MDA that took place.

Compliance of Water and Sanitation

Compliance of the 'F' and 'E' components were measured by frequency of face washing, latrine use, and other sanitation interventions:

In Cumberland 2008, additional householders, in intervention villages, reported family members used pit latrines for defecation. As well, 60-70% of all householders in each arms of the study reported good rubbish disposal practices. In intervention communities there was a 15% decrease of community summarized prevalence of animal faeces in the immediate proximity to the house.

In Khandekar 2006, access to a sanitary latrine and use by all members of the family (including children) improved in both villages in two years but it was better in MF (SAFE) than in XN (SA). Additionally, fly density was significantly lower in MT (SAFE) than in XN (SA) at the end of two years.

X^2=270, df= 2 P= 0.00001

Water facilities improved in both villages after two years of intervention. However, in XN (SA) the quality of water and cleanliness around the water source remained unsatisfactory in about one-third of the houses.

In Lansingh 2010, baseline prevalence of an absolutely clean face at community 1 was 30% and 23% at community 2 while that of a dirty face was 64% and 58% respectively (difference not significant). No nasal discharge occurred post-intervention in children less than 10 years was 30% at community 1compared to 12% in community 2.

X^2=5.7 P=0.02

Community 1 showed positive post-intervention NHC survey results with substantial gains in washing clothes/bedding and removing waste safely following the intervening; however few houses reached the required score in most categories.

Confounders

In order to minimize misrepresentation of the overall effects of the added value of the WASH components, the studies controlled for confounding variables known to affect prevalence of trachoma. In Khandekar 2006, the following variables were considered important confounders so information to determine their influence on the study was

collected and controlled for: age, gender, educational level, occupation, level of poverty and access to mass media. While active trachoma rates were projected for the study population, the rates by age and gender were adjusted to compensate for the differential representation of subgroups. The effects of these confounders were found to be minimal in this study. In both Khandekar 2006 and Lansingh 2010, climate was mentioned were considered a possible confounder. It was observed that trachoma prevalence was higher during certain seasons. For this reason both studies planned prevalence assessments at similar times and in similar conditions.

Though Lansingh 2010 accounted for climate other confounders were not controlled for. The level of dust and flies were not assessed in community 2, and the houses were not surveyed before or after the intervention. By not controlling for these confounders there was no valid information of the number of houses that might have passed the various HLP categories in community 2, and whether the A/F interventions there made any difference. Cumberland made no mention of controlling for confounders in the 2008 study design.

Masking

Khandekar 2006 was the only study to specifically mention masking as a way to minimize observer's bias. Though the study was unable to mask the field staff that assessed the status of the water and sanitation, the results in the houses of MT (SAFE) and XN (SA) were coded and given to an external evaluator.

Applicability

Factors affecting generalizability of methods were different for each study and a summary of methodological elements are presented in Table 5. Cumberland 2008 found additional value to health education yet acknowledged that educational campaigns are time consuming and produce variable results. Additionally, the community mass media intervention used does not present an effective method of ensuring sustainable prevention in hyperendemic rural populations which may have limited access to mass media including radios. Control for sampling bias was considered in the study design, even though it was reported in a previous article. The Lansingh 2010 study however lacked complete applicability of evidence due to the previously mentioned absence of a reliable and valid study design. The methods used in Khandekar 2006, including leveraging local organizations with skills of social marketing and community commitment could be promoted in other rural areas of developing countries as a form of trachoma control.

Table 5: Methodological evaluation of the quality of included studies

Quality of Evidence	Cumberland 2008	Khandekar 2006	Lansingh 2010
Selection Bias: Random Sampling Sample Size	 Yes N/A	 Yes Yes	 Yes No
Comparability	No	Yes	Yes
Compliance: 'A' Coverage (over 80%)	Yes	N/A	No

'F' &'E'	Yes	Yes	Yes
Confounders: Descriptive variables	No	Yes	No
Climate	No	Yes	Yes
Masking	No	Yes	No
Applicability	Yes	Yes	No
TOTAL YES:	4	8	4

Chapter V

DISCUSSION AND CONCLUSION

5.1 Primary outcome

Trachoma prevalence

All articles included in the review observed a decrease in prevalence of trachoma over the entire length of study. Although the decrease occurred at different rates, the decline in trachoma was apparent in all villages, both control and intervention for all three studies reviewed in the control communities. Where no additional interventions took place, the decrease was due to the natural improvements in socioeconomic status (Kuper, Solomon et al. 2003). Even without intervention, change in village demographics and employment brought additional income resulting in access to water and sanitation facilities as well as increased access to mass media through additional purchasing of radio and TV.

In Cumberland 2008 and Khandekar 2006, the decrease in trachoma prevalence was significant not only between the pre and post interventions but between the intervention and non-intervention communities. This suggests that adding water, sanitation, and hygiene education interventions to the ongoing mass antibiotic distribution had a significant impact on reducing the prevalence of trachoma. In contrast however, Lansingh 2010 found a significant decline between pre and post intervention but not between villages. The study was unable to determine if the 'E' environmental component added significant value to the SAFE strategy between the two villages studied. There are many reasons for the variability in results between the three studies including quality of study design and coverage rates of antibiotic.

In Cumberland 2008, the decline in prevalence was attributed to treatment of azithromycin; however, the other components studied as well reported added value to the decline of trachoma prevalence, around a 50% decrease from baseline to post-intervention follow up. The study suggested that health education and community based programs appeared to have additional positive results on the 'AFE' components of SAFE, but percentage prevalence decrease as a result of the AFE components was not separately calculated. Khandekar 2006, did calculate the added benefit and found providing the 'F' and 'E' components in addition to the 'S' and 'A' contributed to a nearly 60% decline in active trachoma prevalence. These components were additionally responsible for the decline of more than one-third of the active trachoma prevalence in children, confirming the association of water and sanitation improvement with the decline of active trachoma.

In the Lansingh 2010 case study, the 'A' and 'F' components of the SAFE strategy interventions significantly reduced the prevalence of trachoma in both communities 1 and 2. Though both communities achieved significant reductions in trachoma prevalence between pre-intervention and 12 month post-intervention assessments, there was no evidence that the specific environmental changes implemented in community 1 had any additional impact to the improvement of facial cleanliness and antibiotic distribution. The reason for the lack of significant change was due to the small sample size, low antibiotic coverage, and problems with the overall study design.

5.3 Secondary outcome

Knowledge, Practice, Attitude (KPA)

Changing deep-rooted cultural behaviors is difficult; however if effective it creates a collective and sustainable awareness. In Cumberland 2008, the percentage of householders surveyed who knew about trachoma was 45%; of those only 20% knew about trachoma risk factors and treatment options. Previously, the emphasis for prevention and treatment methods for trachoma focused on traditional beliefs and practices. It was reported that in 2003 and 2005, a shift occurred away from traditional beliefs to a better understanding of trachoma and the SAFE strategy as a preventative method and cure. Even with these changes, the knowledge and good practices surveyed remained around 40% on average since baseline and percentages of reported correct treatment methods remained low in all districts surveyed post intervention.

In the Khandekar 2006 study, a notable improvement in the KAP of mothers after two years was demonstrated. The reason for the improvement was due to the leveraging of organizations within the village in addition to passive advocacy through mass media. The model included using women's associations and involving school teachers to educate the community. Lansingh 2010, did not measure KAP as an outcome of the added benefit of the 'E' component.

Facial Cleanliness and nasal discharge:

In Lansingh 2010, contrary to the assumed outcome, community 2 which received on the 'A' and 'F' components of SAFE performed better than community 1, which had the additional 'E' component, in regards to facial cleanliness and nasal discharge. These

secondary outcomes however were not easily correlated to the small difference in prevalence of trachoma.

5.4 Authors Conclusions

Implication for practice

In order to eliminate blinding trachoma as a public health problem, recurrence of the active form of the disease must be interrupted before repeated scarring leads to trichiasis. The antibiotic component of the SAFE strategy is a quick fix to the immediate problem. The 'F' and 'E' components are the more sustainable interventions, yet little research has been done on the actual amount of added value the individual 'A''F'&'E' components have to one another. After thorough review of the articles, articles were found which documented the 'F' and 'E' components provide significant value to the overall decrease of prevalence of active. However, the limited results of the search suggest more research can better elucidate the ability of the "F" and "E" components to reduce trachoma prevalence and ultimately impact blinding.

Recommendations for research

Because several impact studies are taking place to leverage for donation of Pfizer donated Zithromax® by ITI, researchers can continue to study the impact of the added value of the 'A''F'&'E' components by establishing more rigorous study designs at baseline. This would include making sure to have a randomized selection process, applying specific interventions, and controlling for confounding variable. Additionally, with the information already provided a review of the overall impact of the SAFE strategy would be beneficial in advocating for more collaborative efforts between sectors.

Table 6: Summary of included studies and health measures

PAPER	INTERVENTION	COUNTRY and POPULATION	STUDY QUALITY	HEALTH OUTCOME	AGE GROUP	MEASURE	STATISTICAL TEST
Cumberland 2008	Control: only radio MDA and radio MDA, radio and information education and communication materials (IEC) MDA, IEC, and community video and drama	Ethiopia 1689	Good	Trachoma	3-9 years	Change in Prevalence	OR 0.35 radio, MDA, IEC CI 0.13-0.89 P Value: 0.027 OR 0.31 radio, MDA, IEC, and video CI 0.022-.89 P Value: 0.029
Khandekar 2006	Water Supply Sanitation Supply	Vietnam 911	Great	Trachoma	< 15	Change in Prevalence	
Lansingh 2010	Environmental Enhancements Water Supply	Australia 111	Poor	Trachoma	< 15	Change in Prevalence	X^2=9.1 community 1 P Value:0.003 X^2=8.1 community 2 P Value:0.005 OR 0.99 CI 0.93-1.05

Perhaps these summaries of studies are better placed in an appendix.

Cumberland, P., T. Edwards, et al. (2008). "The impact of community level treatment and preventative interventions on trachoma prevalence in rural Ethiopia." Int J Epidemiol

Methods	Type of trial: randomized control study
	Allocation: staged cluster intervention
	Unit of randomization: community staged cluster intervention
Participants Baseline	Country: Ethiopia
	Districts: • Gurage • Oromia • South Welo
	Communities: 40 originally The final survey included 5 control villages and 32 intervention
	Baseline Year: 2002
	Number (n): 1958
	Age: 3-9
	Clinical Grading: WHO
	Lab tests: Yes
	Inclusion criteria: Active trachoma: TF
	Prevalence: 71.4%
Interventions	Control: only radio
	MDA and radio
	MDA, radio and information education and communication materials (IEC)
	MDA, IEC, and community video and drama
Participants Post-intervention	Country: Ethiopia
	Districts: Gurage Oromia South Welo
	Communities: 40 (5 control and 32 intervention)
	Year: 2005
	Number (n): 1689
	Age:3-9
	Communities: 37 of the original 40 (3 were found
	Clinical Grading
	Lab tests
	Inclusion criteria: Active trachoma: TF
	Prevalence: 34.0%
Effect Measure	OR 0.35 radio, MDA, IEC
	CI 95%: 0.13-0.89
	P Value: 0.027
	OR 0.31 radio, MDA, IEC, and video
	CI 95%: 0.022-.89
	P Value: 0.029

Khandekar, R., T. K. Ton, et al. (2006). "Impact of face washing and environmental improvement on reduction of active trachoma in Vietnam-a public health intervention study." Ophthalmic Epidemiol

Methods	Type of trial: health intervention study
	Allocation: unmatched 1:1
	Unit of randomization: community
Participants Baseline	Country: Vietnam
	Districts: MT XN
	Communities: 2
	Year: 2002
	Number (n): MT: 447 XN:463
	Age: <15
	Clinical Grading: WHO
	Inclusion criteria: Active trachoma: TF/ TI
	Prevalence: MT: 13.8% XN:10.2%
Interventions	281 double-vault and three septic tank latrines
	241 bathrooms
	273 dug wells
	252 water tanks
	tube well
	hand pump
	97 meetings
	2 marches
	2 performances
	5 billboards
	384 times through village loud speaker
Participants Post-intervention	Country: Vietnam
	Districts: MT XN
	Communities: 2
	Year: 2005
	Number (n): MT: 482 XN:429
	Age:
	Age: <15
	Clinical Grading: WHO
	Inclusion criteria: Active trachoma: TF/TI
	Prevalence: MT: 2.3% XN:5.5%

Lansingh, V. C., B. N. Mukesh, et al. (2010). "Trachoma control in two Central Australian Aboriginal communities: a case study." Int Ophthalmol

Methods	Type of trial: prospective case study
	Allocation:
	Unit of randomization: community
Participants Baseline	Country: Australia
	Communities: 2
	Year: 1999 through August 2000
	Number (n): Community 1: 86 Community 2:91
	Age: < 15
	Clinical Grading: WHO
	Inclusion criteria: Active trachoma: TF/ TI
	Prevalence: Community 1: 48% Community 2: 50%
Interventions	• Road sealing- replacement of poorly built or maintained houses with appropriately designed houses
	• Biweekly trash collection
	• Repair or heating/cooling systems
	• Upgrades in sewage and water lines
	• Installation of rainwater tanks
	• House yard fences bordering roads
	• Planting of trees, grass, and native plants in areas where wind and dust were prevalent
	• Earthworks and diversions to create micro-catchments and water ponding
	• Installation of drinking-water fountains in the school and health clinic
Participants Post-intervention	Country: Australia
	Communities: 2
	Year: 2001
	Number (n): 3 month 6 month 12 month Community 1: 35 41 79 Community 2: 72 70 86
	Age:<15
	Communities: 2
	Clinical Grading:WHO
	Inclusion criteria: Active trachoma: TF/TI
	Prevalence: Community 1 Community 2 3 month: 21.2% 24.2% 6 month 12 month 30%
Effect Measure	X^2=9.1 community 1
	P Value: .003
	X^2=8.1community 2

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