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Does fragmented implementation of the SAFE strategy (surgery, antibiotics, face washing, environmental improvements) reduce the prevalence of active trachoma infections among children aged 0-9 years?

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INTRODUCTION

- Trachoma is the leading cause of infectious blindness and affects more than 80 million people worldwide.
- An estimated 2.2 million develop visual impairment as a result of the disease, of whom 1.2 million continue to develop irreversible blindness.⁴

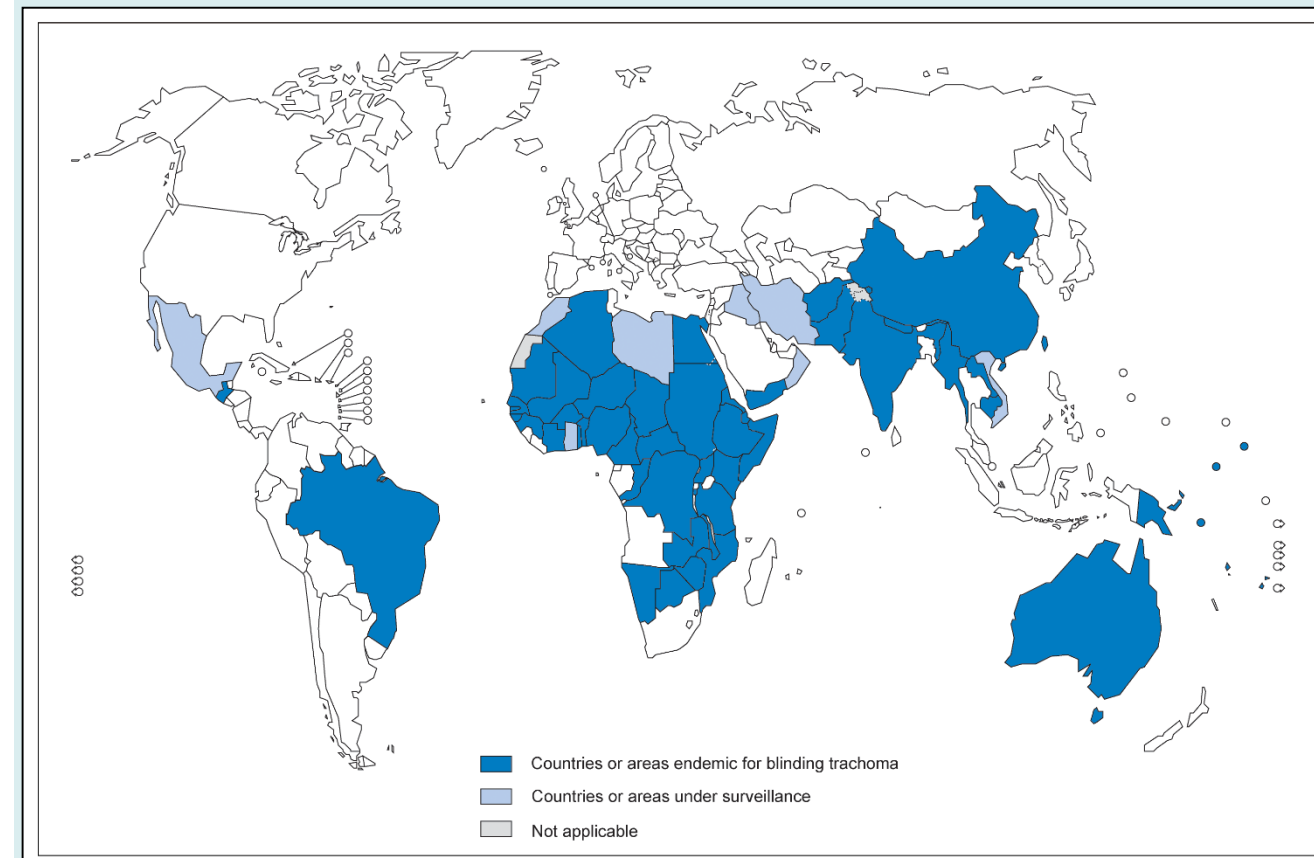


Fig 1. Worldwide distribution of active trachoma. Trachoma is endemic in 51 countries and is often seen in situations of poverty or unsanitary living conditions. Figure adapted from the World Health Organization (who.int).

- Trachoma is caused by *C. trachomatis* and results from direct contact with secretions of the eyes, nose, and throat, fomite contact, or transfer through an arthropod vector (flies).⁵



Fig 2. Infection by *C. trachomatis* causing active trachoma. Repeated bacterial infection leads to scarring of the conjunctiva of the upper eyelid, which eventually leads to inversion of the eyelids (entropion). Eyelid inversion causes the eyelashes to touch the cornea and conjunctiva (trichiasis). Persistent abrasion of the cornea increases an individual's susceptibility to

secondary infections. Without preventive surgical treatment, trachoma-induced corneal irritation leads to irreversible blindness. Figure adapted from the Fred Hollows Foundation (hollows.org.au).

- The World Health Organization (WHO) has endorsed the SAFE strategy to eliminate blindness due to trachoma by 2020 and estimates that trachoma can be eliminated if all components of the SAFE strategy are implemented for at least 5 years.^{1,5}
- However, the four components of the SAFE strategy are infrequently implemented as a cohesive public health intervention due to: limited funding, lack of resources, geography, among other barriers to implementation.
- We propose that the implementation of the individual SAFE components is not sufficient to achieve a sustainable prevalence rate and therefore eliminate trachoma blindness.



Fig 3. The four components of the SAFE strategy to eliminate blindness. Elimination of blindness is achieved when the prevalence of active trachoma infections at the district level falls below 5% among children aged one to nine years.¹ Figure adapted from the International Trachoma Initiative (trachoma.org).

METHODS & PICO QUESTION

- A literature review was performed using PubMed to search for studies that evaluated the effectiveness of at least one component of the SAFE strategy in reducing trachoma-induced blindness.
- The search term [*trachoma*] was used in combination with the following modifying terms:
 - [SAFE] [antibiotics]
 - [hygiene] [face washing]
 - [blindness] [environmental improvements]
- Results were limited to studies published in English, available in full text, publication dates within the last 5 years, and studies with human species.
- Of 224 references meeting our search criteria, 6 references were further reviewed to ensure that the data addressed our research question:
 - Population:** Children aged 0-9 years with active trachoma
 - Intervention:** Implementation of all 4 components of the SAFE strategy
 - Comparison:** Implementation of any component(s) of the SAFE strategy
 - Outcomes:** Trachoma prevalence (*secondary: trachoma recurrence, blindness*)

Main search term	Modifying terms	Reference hits
Trachoma	+ SAFE	24
	+ Hygiene	58
	+ Blindness	55
	+ Antibiotics	62
	+ Face washing	5
	+ Environmental improvements	20
	Total	224

Table 1. Search terms used for the literature review.

RESULTS

- High rates of trachoma recurrence were found within years in every study that did not implement all four components of the SAFE strategy.^{2,6}
- Surgery implemented alone was shown to significantly improve visual acuity.³
- Azithromycin implemented alone was found to have a relative risk reduction of 20%. This observed benefit is negatively impacted due to sources of reinfection, such as individuals in the community who do not participate in the mass treatments and spread of infection to neighboring regions.^{2,3}
- Causality between face washing alone and reduction in the prevalence of trachoma infection is not established. However, implementation of water, sanitation, and hygiene interventions were strongly associated with reduced prevalence of active trachoma.^{1,4,6}
- Environmental improvement implemented alone showed inconsistent and varied results.³
- Individual SAFE components do not have consistent implementation protocols which leads to inconsistencies in data and unreliable recommendations.^{2,3}
- Implementation of all components of the SAFE strategy showed the greatest decrease in prevalence of trachoma infections and appear to have the greatest chance for long-term rates of non-significant recurrences of disease.^{3,6}

Reference	Study design	Study strengths	Study weaknesses	Statistical significance	Findings
Goldschmidt et al., 2014	Ecologic	<ul style="list-style-type: none"> Evaluates individual risk factors associated with disease Provides prevalence data of trachoma infections after implementation of the SAFE strategy 	<ul style="list-style-type: none"> Does not establish causality between SAFE strategy implementation and reduction in active trachoma infections 	N/A Prevalence: Baseline: 31.5% 3 years: 3.1% 6 years: 15%	<ul style="list-style-type: none"> Short-term SAFE strategy implementation resulted in an unsustained reduction in active trachoma prevalence Social determinants (e.g. income level, literacy, social infrastructure) were suspected to have a role in active trachoma recurrence
Stocks et al., 2014	Meta-analysis	<ul style="list-style-type: none"> Strong evidence between hygiene factors and active trachoma infection Minimal publication bias 	<ul style="list-style-type: none"> Poorly defined criteria for face washing and environmental control Measures of association were not always evident in all review papers 	"F" - OR 0.42, 95% CI 0.32-0.52 "E" - OR 0.85, 95% CI 0.23-0.61	<ul style="list-style-type: none"> "F" and "E" components of the SAFE strategy Sanitation and facial cleanliness was associated with reduced odds of active trachoma
Harding-Esch et al., 2013	RCT	<ul style="list-style-type: none"> Comprehensively compares across regions covering a large population of children Addresses social determinants of health Establishes quality control measures in laboratory assessment and field grading of trachomas 	<ul style="list-style-type: none"> Does not control for re-infection from neighboring countries or districts or whether this can lead to re-establishment of trachoma in a district which had previously eliminated trachoma Does not assess long-term outcomes 	"A" - RR 1.17, 95% CI 0.65-1.53	<ul style="list-style-type: none"> Multiple Mass Drug Administrations (MDA) may not be superior to single MDA round "A" component of the SAFE strategy should be refined to ensure appropriate use of resources while maintaining prevalence below the elimination rate
Lavett et al., 2013	Meta-analysis	<ul style="list-style-type: none"> Large, 15-year data set examining prevalence, infection, clinical findings, and efficacy of SAFE protocols. 	<ul style="list-style-type: none"> Conflict of interest was found in one of the studies (employee of the International Association for Prevention of Blindness) 	N/A Prevalence: Baseline: 9.7% 5 years: 0%	<ul style="list-style-type: none"> Scale up is needed of SAFE components to reach 2020 goal
Travers et al., 2013	Systemic-review	<ul style="list-style-type: none"> Each article identified Trachoma by using the WHO grading scale and/or diagnostic swab testing for ocular Chlamydia infection. 	<ul style="list-style-type: none"> One of the studies used did not mention randomizing participants 	"F" & "E" - OR 0.31, 95% CI 0.11-0.89	<ul style="list-style-type: none"> "F" and "E" components of the SAFE strategy provided significant value to overall decrease of prevalence of active trachoma

Table 2. Literature review. References were further scrutinized for internal & external validity (i.e. study strengths, study weakness, statistical significance, findings).

CONCLUSION & DISCUSSION

- Trachoma treatments have largely been ineffective in the past due to high rates of surgical failure, non-adherence to antibiotics, and ineffective sanitary educational campaigns.²⁻⁶
- The prevalence of primary and re-infection have been shown to be decreased when surgery/antibiotics are combined with face washing and environmental interventions (i.e. implementation of all components of the SAFE strategy).^{2,3}
- The SAFE strategy has shown potential to eliminate trachoma if implemented concurrently and for a minimum of five years.⁵
- A continued effort must be made after this time to decrease the chance of re-infection through continued "F" and "E" protocols. However, these protocols alone will not decrease the prevalence of trachoma infections but may benefit the community as a whole in areas such as sanitation, infrastructure, and reduced morbidities and mortality rates.^{1,4,6}

RECOMMENDATIONS

- Integrate all components of the SAFE strategy with a standardized protocol**
 - Cohesive implementation of the SAFE strategy for a minimum of 5 years has shown promise in eliminating trachoma-induced blindness worldwide.
 - A continued effort to pursue concurrent implementation of all four components of the SAFE strategy can achieve the long-term goals of the WHO to eliminate infectious blindness.
 - Implementation of the SAFE strategy in its entirety should be conducted with standardized protocols (i.e. clear definitions and benchmarks of each of the components should be developed and used in each SAFE strategy program).
- Provide robust and culturally sensitive education to improve "F" and "E"**
 - A more robust educational component be implemented to educate the public about the disease and ways to prevent its spread.
 - This may be difficult due to the diversity of regions (e.g. clean water access) in which trachoma is endemic, but the value of improving prevention education would be worth the effort.
- Address social determinants that increase the risk of contracting trachoma**
 - Trachoma is most prevalent among impoverished and marginalized populations. This subset of individuals is also more likely to be illiterate.
 - A lack of basic education impedes SAFE strategy implementation, particularly in implementing the "F" and "E" components.
 - In order to benefit from the goals of hygiene education, communities must instill their citizens with the skills to assimilate and integrate educational campaigns.
- Ramp up all four components of the SAFE strategy**
 - The 2020 goal of elimination of trachoma-induced blindness cannot be achieved at the current levels of SAFE strategy implementation.
 - If this goal is reached there is an enormous backlog of adults who will need surgery to cure their active trachoma damage.



Fig 4. Large-scale implementation of the SAFE strategy. Organizations such as the Queen Elizabeth Diamond Jubilee Trust Trachoma Initiative have plans to implement large-scale SAFE strategy programs in several endemic countries beginning in 2015. Figure adapted from the International Trachoma Initiative (trachoma.org).

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