The Limits of Medical Interventions for the Elimination of Preventable Blindness

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Abstract: Background: Health authorities are working toward the global elimination of trachoma by the year 2020 with actions focused on the World Health Organization SAFE strategy (surgery of trichiasis, antibiotics, face washing and environmental changes) with emphasis on hygienist approaches for education. Objectives: The present survey was performed to assess the sustainability of the SAFE strategy 3 years after trachoma was eliminated from 6 villages. Methods: In February 2013 a rapid trachoma assessment was conducted in 6 villages of Kolofata’s district, Extreme north Region, Cameroon, where trachoma was eliminated in 2010. A total of 300 children (1–10 years) from 6 villages were examined by trained staff. Results: The prevalence of active trachoma (children aged > 1 and < 10 years) in 2013 was 15% and in at least 25% was observed absence of face washing and flies in their eyes and nose. Income level, quality of roads, hygiene, and illiteracy were similar in all the villages; they did not change between 2010 and 2013 and could not be analyzed as independent risk factors. Discussion: The heterogeneity of methods described for clinical trials makes it inappropriate to conduct meta-analysis for the present and for other SAFE-related trials. The results obtained after implementation of the SAFE strategy (recurrence) reveal that the causes (infectious agents and dirtiness) and effects (illness) were not connected by illiterate people living under conditions of extreme poverty. So far, antibiotics, surgery and hygiene education are insufficient for the sustainability of trachoma elimination and highlight that hypothetic-deductive processes seem not operational after implementing the awareness campaigns. Trachoma recurrence detected in 2013 in sedentary populations of Kolofata receiving efficacious treatments against Chlamydia sp. suggest that the elimination goals will be delayed if strategies are limited to medical actions. Restricting efforts to repeated pharmacological and surgical interventions for people infected with susceptible bacteria could be understood as the hidden side of a passive attitude toward basic education actions. Key words: trachoma, neglected diseases, blindness, SAFE strategy, recurrences, hygiene education, face washing, basic education, illiteracy, Cameroon

INTRODUCTION

The World Health Organization (WHO) established in 2007 a strategic and technical advisory group for neglected tropical diseases (NTD) to handle matters relating to worldwide prevention and control. Global Partners include representatives from member states, United Nations agencies, the World Bank, philanthropic foundations, universities, pharmaceutical companies, and international non-governmental organizations (NGOs). The goal is to assure access to quality-assured medicines and to improve the implementation of treatment by health authorities [1, 2]. The list of NTD includes trachoma, a preventable infectious disease that, according to WHO estimates, causes millions of people to suffer from visual impairment. Health authorities are working toward the global elimination of trachoma by the year 2020 with actions focused on the SAFE strategy, i.e., surgery for trichiasis, antibiotics, face washing and environmental changes with emphasis on hygienist approaches for sanitation education [2–4].

The intracellular bacteria Chlamydia trachomatis (and Chlamydia species) trigger conjunctival inflammatory
processes leading to trachoma. The most common surrogate marker for trachoma detects viable and non-infectious bacteria, amplifying its genomic or plasmid DNA by means of the polymerase chain reaction (PCR) [5–7].

The simplified grading scheme for assessment of active trachoma in communities devised by the WHO allows the rapid assessment of the disease progression occurring over years of infection and reinfection. The early signs of trachoma are detected by evertting the upper eyelid and examining with a 2.5 loupe.

The follicular stage (TF) is characterized by five or more white or yellow follicles of 0.5–2.0 mm on the upper tarsal conjunctiva. Trachomatous inflammation (TI) may be seen as inflammation worsens, with papillary hypertrophy and inflammatory thickening of the upper tarsal conjunctival tissues obscuring more than half the deep tarsal vessels. Trachomatous scarring (TS) begins as small stellate scarring in tarsal conjunctiva that with time coalesce to form dense fibrotic tissues that distort the normal lid architecture. This is followed by trachomatous trichiasis (TT) with at least one ingrown eyelash touching the globe. TT, which results from chronic or multiple infections with Chlamydia in the tarsal conjunctiva, may lead to irreversible impairment of visual function by blurring part of the pupil margin of the cornea (CO) as a result of micro-trauma inflicted by the eyelashes or by secondary bacterial infections [7–9].

The stated goal is to reduce blinding trachoma at the district level to less than 5% of active form among children (TF, TF/TI) aged one to nine years. In adults above 15 years of age, the goal is to maintain trichiasis recurrence below 10 percent and to reduce the prevalence of TT to less than 1 case per 1,000 in the population [5, 7, 8].

In endemic areas the elimination programs are based on the clinical assessment of pathognomonic signs and by surrogate markers [1, 2, 5]. The predictors for the elimination of trachoma use non-linear, stochastic, susceptible-positive PCR-susceptible epidemiological models. The authors demonstrated mathematically that reintroduced Chlamydia DNA may not repopulate the community, or may proceed so slowly that the surveillance might be ineffective. These approaches exhibit positive feedback, in which the putative infection marker returns slowly after mass treatment, drafting figures of age and time-dependent patterns in endemic settings that rely heavily on assumptions which may not hold up in practice [8, 10, 11].

We conducted a clinical survey three years after trachoma was eliminated from the district of Kolofata to assess the sustainability of the SAFE strategy in six villages where children with absence of face washing were reported. This work is aimed to identify the determinants in trachoma recurrence that once addressed, could contribute to the global efforts for the elimination of Chlamydia-triggered blindness [12, 13].

METHODS

Study population

In 2008, 2009 and 2010 the SAFE strategy was implemented according to WHO guidelines in all the villages of the rural district of Kolofata in the local languages (circa 120,000 inhabitants in the Sahelian area of the Far North Region of Cameroon). Mass antibiotic coverage was > 95% and free of charge TT surgery was offered to the population [2, 15–17].

In 2010 active trachoma was < 5%. During the 2012 poliomyelitis vaccination campaign the vaccinators reported numerous children presenting with absence of face washing in six villages where trachoma has been eliminated two years earlier. In compliance with the Declaration of Helsinki and the European Guidelines for Good Clinical Procedures, a clinical survey was conducted during the first week of February 2013 in six villages (population ranging between 1,450 and 1,900 sedentary inhabitants/village). The protocol was approved by the authors’ institutional review board and by the Ministry of Public Health, Cameroon. Informed consent was obtained from each participant and confirmed by individual fingerprints. The parent/guardian provided consent on behalf of children. The consent of each participant was validated by the signature or fingerprint of the village chief and by the local health worker. The target-population was 50 children over one year and less than 10 years of age who had lived in the village for at least one year prior to the study date in randomly selected households. When a family had left the community more than six months before the visit and the house remained empty, that household was replaced by the household nearest to it.

Children included in the study were examined by a senior nurse who everted the upper eyelid and examined the conjunctiva with a 2.5 magnifying glass and a flashlight held by an assistant, who also recorded the data. The examiner changed gloves after the examination of each patient. Before examining the next person, the examiner ensured that the assistant had filled out the study sheet in accordance with study protocol guidelines. Training sessions lasting four days ensured the standardization of procedures, and examiners who achieved at least 80% agreement proceeded to the field evaluation. Clinical signs associated with trachoma were evaluated in the training sessions (trachomatous follicles, TF; intense trachomatous inflammation, TI; entropion trichiasis, TT, trachomatous scarring, TS, and corneal opacities, CO). The conjunctiva was examined in 300 children.
using a 2.5 magnifying glass according to the grading card supplied by the Prevention of Blindness and Deafness Department of the WHO [1, 13, 14].

Environmental risk factors for trachoma

The present survey was conducted during the first week of February 2013 during the dry season, when the outside temperature oscillated between 24 +/− 2°C in the early morning and 34 +/− 4°C at noon [18].

Availability of latrines and water and their use and maintenance

When latrines or pumps were reported to be available, they were inspected to verify that they were functioning. In villages where there were no working latrines or water pumps, the response was completed as “No” for all subjects.

Animals wandering close to dwellings

The local health workers visited the dwellings and their surroundings to determine whether cows, sheep or goats were wandering free.

Multivariate analysis was performed to estimate the potential association of trachoma with housing conditions, illiteracy, accessibility and income level. Confidence intervals for the point prevalence estimates were generated using the estimator of variance to adjust for the clustering effects of trachoma at the household level (EPIINFO software) [18, 19]. In addition, a comprehensive scrutiny of trachoma reports from the Cochrane Library 2013, MEDLINE (January 1953 to August 2013), EMBASE (January 1980 to August 2013) and ClinicalTrials.gov (www.clinicaltrials.gov, 2013) was conducted. There were no language or date restrictions. The electronic databases were searched in November 2013 and contributions from epistemological approaches were included and discussed.

RESULTS

After implementation of the SAFE strategy in 2007 the prevalence of active forms of trachoma (TF + TI) dropped in this district from 31.5% (95% CI 26.4–37.5) to 3.1% in 2010 [16, 17]. More than 200 free of charge TT-surgeries were performed during this period. Between 2010 and 2013, the use and maintenance of latrines, the presence of herds close to dwellings and the water supply did not significantly differ among the six villages and could not be analyzed for their direct impact on the recurrence of trachoma.

The income levels, quality of roads, access to latrines/potable water and illiteracy were similar in all the villages of the district in 2010 and 2013 and could not be analyzed as time dependent risk factors [19].

Trachoma prevalence in the six villages (children aged > 1 and < 10) in January 2010 was < 5% and in 2013 15%, where at least 25% presented with absence of face washing and flies in their eyes and nose. In the six villages the difference in age and sex of examined children with and without signs of trachoma was not statistically significant (Table 1). Moreover, no statistically significant differences were found among sex and ages for active trachoma rates in and between the different villages.

During the 2013 clinical survey, 15% of examined children showed signs of active trachoma in the six villages (the prevalence of trachoma after implementing the SAFE strategy in 2010 was < 5%). No difference in TF or TI was observed for boys and girls aged 4 or less. The prevalence of TF was significantly higher for children under 5.

DISCUSSION

The implementation of the WHO strategy in 2008 effectively eliminated trachoma in 2010 [17] but did not protect against recurrence in at least six villages in the district of Kolofata. The same pattern of trachoma recurrence can be extracted from most other surveys in which repeated antibiotics were administered. Nevertheless, the heterogeneity of methods described for the different clinical trials makes it inappropriate to conduct meta-analysis for the present and for other SAFE-related trials and necessary to discuss the impact of different interventions qualitatively.

Trachoma trichiasis surgery (TTS) and recurrence of active trachoma

For TTS (S component of the SAFE strategy) WHO recommends bilamellar tarsal rotation (BLTR) or lid rotation to revert the in-turning eyelashes and thus alleviate pain

<table>
<thead>
<tr>
<th>Examined (N)</th>
<th>Age (years)</th>
<th>Sex N (%)</th>
<th>Active trachoma</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>TF N (%)</td>
<td>TF TI N (%)</td>
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<tr>
<td>Boys: 80 (27%)</td>
<td>1–4</td>
<td>13 (4.3%)</td>
<td>2 (0.7%)</td>
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<tr>
<td>Girls: 86 (28%)</td>
<td>11 (3.6%)</td>
<td>3 (1.0%)</td>
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<tr>
<td>55%</td>
<td>24 (8.0%)</td>
<td>5 (1.7%)</td>
<td></td>
</tr>
<tr>
<td>Boys: 69 (23%)</td>
<td>5 (1.7%)</td>
<td>1 (0.3%)</td>
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</tr>
<tr>
<td>Girls: 65 (22%)</td>
<td>8 (2.7%)</td>
<td>2 (0.7%)</td>
<td></td>
</tr>
<tr>
<td>45%</td>
<td>13 (4.4%)</td>
<td>3 (1%)</td>
<td></td>
</tr>
<tr>
<td>Total 300</td>
<td></td>
<td>37 (12.3%)</td>
<td>8 (2.7%)</td>
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<td></td>
<td>45 (15%)</td>
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Table 1. Distribution by age and sex of active trachoma in children from six villages during the 2013 survey (*: from 300 examined)
and improve the quality of life [9, 20, 21]. So far, in patients with less severe forms of TT in Ethiopia, there was no evidence that TTS results in better visual outcomes than epilation [22–24]. Earlier studies had shown either no improvement or deterioration of visual acuity after TTS [22]. Later, it was reported that the BLTR procedure significantly improved visual acuity [25]. Moreover, a report from Oman [26] indicates that the rate of blindness decreased significantly in people who underwent lid surgery. TT recurrence after surgery shows rates ranging between 7.4% at one year to 62% at three years [25–27]. In this survey, TT recurrence was 10%. This finding does not support the suggestion that TTS on adult eye-lids have a direct effect on trachoma recurrence in previously cured children (cure meaning the absence of objective signs evoking active trachoma) or on the transmissibility of Chlamydia sp. to healthy people.

**The trachoma paradox of antibiotics (A)**

NTDs management purports that mass treatment distribution is the mainstay of trachoma treatment and that community-targeted repeated exposure to antibiotics is the key to program success [2, 4, 7, 8, 28]. However, antibiotics may partially reduce the risk and prevalence of positive PCR at levels estimated at 20% (relative risk-reduction). In fact, randomized trials with oral macrolides compared to controls revealed that it was extremely difficult to assess the real scope of their effects [10, 29].

For an initial trachoma level of 50%, annual treatment lasting for more than seven years was reported to achieve prevalence of < 5% in 71 communities in Tanzania [30]. For initial prevalence rates of 10–20%, it was suggested that three or less rounds of antibiotic treatment reduce the prevalence rates to expected thresholds [31, 32]. Elimination strategies based on PCR (Chlamydia-plasmid) simulation models predicted that targeting treatment to households had the potential to be as effective as and significantly more cost-effective than mass treatment [10, 33]. Studies were conducted on risk factors assessment by means of random-intercept logistic regression models for households with at least one child who did not participate in two mass distributions of antibiotics compared to households where all children participated in both. The results predicted that at-risk households should be targeted by social mobilization programs in the communities [32, 34].

At least three annual treatments should be administered at > 80% coverage in communities with a > 10% prevalence of TF in children 1–9 years of age, and mathematical speculations also suggested that where the prevalence of active trachoma is 50% or more and coverage is > 75%, seven years (or probably more) of annual repeated mass antibiotic treatment will be necessary to approach levels of positive PCR rates < 5% [35–39]. Moreover, it was recommended that the households in highly prevalent villages already treated with multiple rounds of azithromycin should be receiving antibiotics for yet undetermined periods [10–13].

Generally speaking, it is accepted that all communities may need at least three rounds of antibiotics (entire geographic area) with impact surveys regardless of whether or not the villages had initial low prevalence rates [2, 7, 36, 37]. However, the global data-analysis of 29 randomized clinical trials (14 trials with 3,587 participants and 15 trials with 8,678 participants) failed to establish the real kinetic impact of antibiotics on clinical active trachoma and positive PCR. These studies reported firstly, that the quality of the evidence for the A component of SAFE is low, and secondly, as previously indicated, that the heterogeneity and the lack of summary statistics are not consistent enough to be pooled for meta-analysis [28, 35–38]. So far, WHO experts recommend repeated annual high coverage with active antibiotics achieve a prevalence of < 5% based on the initial rates of clinical signs evoking active trachoma or on the rates of positive PCR [30, 39].

The fact of the matter is that macrolides are antibiotics with excellent bioavailability and a potent antibacterial effect on intracellular microorganisms. Nevertheless, as reported in the present survey and other studies, trachoma re-emerges in treated communities [28, 34, 40]. Moreover, there are no data demonstrating that macrolides (azithromycin) distributed to trachomatosus populations reduce the susceptibility of Chlamydia to these antibiotics.

The macrolide pharmacodynamics or pharmacokinetic profiles and the antimicrobial spectra of action do not justify repeated treatments for infections triggered by antibiotic-susceptible bacteria. Presently and according to this, the conjunction of scientific evidence drafts a *sui generis* paradox: first of all, macrolides kill *Chlamydia in vitro* in a few hours; secondly, they dramatically reduce the rates of positive *Chlamydia* culture and positive PCR; and thirdly, the conjunctival signs of active trachoma are eliminated after treatment (*circa* four weeks). In short, there is no medical evidence to justify repeated antibiotic treatments for infections caused by sensitive germs, and these findings suggest that repeated exposure to antibiotics for the elimination of sensitive *Chlamydia* should be related *stricto-senso* to determinants other than medical science.

**Facial cleanliness (F), environmental improvement (E) and trachoma recurrence**

The promotion of sanitation and facial cleanliness has been cited as the key to trachoma elimination because it promises to limit the exchange of infected secretions. Although a dirty face has been blamed as the pathway by
which trachoma spreads in children with ocular and nasal discharge [41], there is still no standard regarding what constitutes a clean face [42].

Changing children’s face-washing habits was tested in an endemic area in Tanzania following non-formal adult education techniques at the neighborhood level. This intervention increased clean face levels from 9% to nearly 35% over the course of a year, showing that the vast majority of the population had not integrated the knowledge of F and E components [43]. Moreover, the ocular and nasal discharge in Sudan [44], and flies on a face and absence of face washing in Nigeria and Mali [45–47] were reported as independent risk factors for active trachoma.

The significant effect of face washing combined with topical tetracycline in reducing TF/TI compared to topical tetracycline alone did not support the beneficial effect of face washing alone [47, 48], while the presence of flies on a face and the use of soap were independently associated with active trachoma in Ethiopia. It should be noted that children from illiterate households were five times more likely to have trachoma. Moreover, despite high antibiotic coverage in rural Ethiopian communities, trachoma prevalence remained at levels > 35% after one or two educational interventions for improvement of hygiene and face washing [49, 50].

Studies on the advantage of latrines in trachoma endemic districts in Amhara, Ethiopia showed that heads of households adopting latrines were 1.9 times more likely to have a higher education level than their non-adopting neighbors [51].

Antibiotics associated with F and E components (washing faces of children three or more times daily and using a pit latrine in the household) showed an independent but inconclusive effect on active trachoma [52, 53]. In Tanzania, latrine use decreased the risk of trachoma (no difference in risk between those sharing and those who have their own latrine). In Sudan, but not in Ethiopia, the access to a latrine also decreased trachoma [54–56]. Only one out of three studies showed that health education for improvement of hygiene produced tangible results. Similarly on the global level, sanitation provision did not significantly reduce trachoma prevalence in two out of three surveys [55, 56].

Although results are inconclusive for the effectiveness of F + E in eliminating trachoma (and avoiding recurrence), the environmental interventions are crucial to the overall health of the community [7, 13, 55, 57]. Nevertheless, scientific evidence linking a lower incidence of trachoma and F and E is even less clear than that for surgery (S) and antibiotics (A).

### Lack of sustainability of the trachoma elimination strategy

In accordance with the WHO recommendations, the trachoma control program in the Kolofata Health District called for one mass treatment per year for three years. The treatment consisted of one dose of azithromycin eye-drops 1.5% in both eyes in the morning and evening over three consecutive days. The first round of treatment began on 23 February 2008 and ended on 10 March 2008, and the second was undertaken between the 5th and 20th of January 2009. Trachoma recurrence observed in 2013 are urging medical practitioners to accept the limitations of hard science (epidemiology, ophthalmology and microbiology) and the probability of drawing wrong conclusions from the environment. In fact, active drugs, surgical procedures and education for improvement of hygiene have been shown to have only a limited capacity to eliminate trachoma in this and other surveys [7, 13, 20, 28]. Hence, the trachoma recurrence detected in 2013 in six villages of the district of Kolofata (sedentary population) treated with antibiotics reveals that the conclusions and assumptions implicit in statistical models may perform even if its assumptions are violated by the true reality from which the data were generated [10, 13, 14, 28, 55].

Considering that the recurrence do not support the long-term elimination strategy as it was conceived and implemented (trachomatous villages require repeated treatments to irreversibly eliminate *Chlamydia* and clinical signs), it is advisable to formally deconstruct the acronym SAFE and to integrate additional variables [58, 59].

Recurrent trachoma demonstrates that the villagers were unable to couple and integrate knowledge to their lifestyle during the awareness campaigns disseminating new F and E knowledge [57]. This reveals that improvement of hygiene cannot be expected just from pharmacological research, statistical predictors, brochures, publications, talks, awareness campaigns or websites [60, 61]. On this matter, a recent example from Mali showed the effect of community knowledge and healthy behavior on the elimination of blinding trachoma, where clear messages on the radio about trachoma had been heard by 60% of respondents. The majority of respondents knew the word trachoma and were able to repeat the prevention measures, although there was no significant difference in facial cleanliness when comparing children whose primary caregiver had or had not heard the messages [62].

The quality of nutrition, sanitation and especially of massive basic education in the 20th century was the determining [57, 58, 60], but the present resource allocation exclusively focuses on antibiotics, TT-surgery, awareness campaigns limited (only) to improvement of hygiene, so-
phisticated mathematical predictors, elegant epidemiological cartography, microorganism detection procedures and discussions regarding shape, size, color and number of local inflammatory reactions. The International Coalition for Trachoma Control (ICTC) advocates the WHO-endorsed SAFE strategy with a range of partners, including the London School of Hygiene & Tropical Medicine, the International Trachoma Initiative at The Task Force for Global Health, Atlanta, GA and The Carter Center, Atlanta, GA. The WHO advocates raising funds for medical interventions (epidemiology research, mass distribution of azithromycin, trichiasis surgery, and education for improving sanitation). The United States Agency for International Development announced significant efforts for drugs, and a portion of the U.S. global health partnership allocated funds for medical interventions (covering mapping, drug managers training and drug delivery) [1–4]. Moreover, the International Trachoma Initiative, Helen Keller International and the Carter Center, in partnership with the Lions Clubs International Foundation and the Hilton Foundation, the International Trachoma Initiative, and several organizations and ministries of health, have dedicated significant efforts to the SAFE strategy [2–4, 63–65]. However, repeated antibiotic treatments administered to people who never exposed to pathogenic agents and dirtiness) and effects (illness, conjunctivitis, blindness) were not necessarily connected in people treated with active antibiotics on susceptible bacteria.

Considering that at least 30% of girls and more than 25% of boys in trachomatous regions miss out on schooling [66], the interventions for trachoma elimination in areas with illiterate people living in conditions of extreme poverty must avoid a status of broad passive acceptance (SAFE should not be a dogma) [60]. At this point, the recurrence of trachoma and the lack of long term efficacy of medical-based interventions raise several questions:

a- The conflicting and inconclusive results reported for the A, F and E components indicate that the causes (infectious agents and dirtiness) and effects (illness, conjunctivitis, blindness) were not necessarily connected in people treated with active antibiotics on susceptible bacteria.

b- The "health education" knowledge has not been assimilated by people never attending educational institutions: human knowledge proceeds neither from the experience of objects nor solely from an innate programming performed in the subject. Knowledge concerns a process of equilibration, in which cognitive structures assimilate and accommodate new possibilities when the equilibrium is disturbed [67, 68]. The absence of face washing observed after the implementation of the SAFE strategy reveal that hypothetic-deductive processes of assimilation and integration did not operate (in children, mothers and future mothers never receiving the benefits of basic education). Accordingly, F and E cannot be assumed purely as conscious and natural human knowledge [69]; flies in the eyes and nose and massive body dirtiness reveal a lack of acquisitions generally integrated during basic education processes. The rationale that presupposes that illiterate people "should know" and associate concepts about risks to their health [69, 70] should be comprehensively revised because awareness campaigns seem to be inefficient for transmitting and fixing knowledge [70].

Improving trachoma interventions

F and E efficacy depends upon the capacity of populations to assimilate and accommodate [68] new situations (causes) in life, and only basic education (minimal reading, writing, calculations and understanding skills) assures the long-term efficacy of medical interventions [71], keeping in mind that there is an un-transmittable part, which is not where one believes it to be. The untransmittable part (“transcription”) does not yet exist in a form that can be welcomed or received and should be built by interactions between teacher and learner [72].

So far, the nations with the lowest levels of life threatening infectious diseases are those with the highest education standards [57, 58], and it can be hypothesized that a lack of formal commitment to basic education interferes with and truncates the blindness elimination goals. In fact, in the early 90s in Tanzania it was shown that women not attending basic education classes were at a greater risk for blinding complications from trachoma [73], and in four hospitals in Tunisia more than 20 years ago it was reported that basic education was significantly associated with trachoma and blindness [74]. Moreover, Morocco is the first country reporting compliance with trachoma elimination targets where the ratio of children of official school age who were enrolled versus the population of the corresponding school age was < 39% in the 70s and 95.7% in 2011 (for primary female enrollment, the rate was of 32% in the early 70s and 95% as of 2011) [75].

The Gambia is presently close to the elimination target for active trachoma. The rates of pupils enrolled in education in The Gambia was < 55% in 1991 for primary levels and > 80% in 2011, of which 66% completed the full course at the primary level. At the secondary level, the enrollment rate was 17% in 1991 and > 40% in 2011. Here, trachoma prevalence in the early 60s was 66% and fell to 2.4 in the late 90s. Among young people aged 10–19, it fell from 52.5% to 1.4%, and among those aged > 20 years from 36.7 to 0%. This dramatic decrease in active trachoma was associated with education improvements and was observed without the targeted medical interventions [76–78].
In Nepal, the national blindness survey reported that 0.84% of the population was blind in 1981 and the percentage was reduced to 0.34 in 2012. Approximately 6.0% of the population had trachoma in 1981 and only 0.4% in 2013. Up to the early 90s, less than 45% was literate. Nepal announced its determination to eliminate trachoma by 2014, reporting that literacy rates in the last decade reached levels of 85% (15–24 years) with 76% primary completion rate [79].

The National Sample Survey on Disabilities in China in 1987 included 125,000 people in Sichuan Province, where blinding trachoma was the second leading cause of the eight visual impairments (172,9 cases per 100,000). In the period 1990–2000, adult literacy rates increased dramatically in people aged 15 and over, and presently the enrollment rate among school-age children is > 90%. These educational efforts showed that trachoma was the eighth cause of visual impairment with 58 cases per 100,000 in 2006, all among individuals over 40 [80, 81]. The direct influence of schooling on trachoma prevalence rates was also reported from Bauru-São Paulo Brazil in 2006 [82] and from Nigeria in 2010 [83].

Finally, two or three out five illiterate people in the world are women, and more than 75% of them are in Sub-Saharan Africa and south west Asia. In Sub-Saharan rural areas, trachoma prevalence overlaps regional rates of illiteracy [4, 84, 85]. Nevertheless, as shown in Table 2, the key word “education” was rarely noted in the 4219 trachoma research reports and always associated with “health education”.

### Table 2. Trachoma scientific research

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