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Evaluation of three years of the SAFE strategy (Surgery, Antibiotics, Facial cleanliness and Environmental improvement) for trachoma control in five districts of Ethiopia hyperendemic for trachoma

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Summary Trachoma surveys were conducted at baseline in five districts of Amhara National Regional State, Ethiopia (7478 participants in 1096 households) and at 3-year evaluation (5762 participants in 1117 households). Uptake of SAFE was assessed with programme monitoring data and interviews, and children (1—6 years) were swabbed for detection of ocular *Chlamydia*. At evaluation, 23 933 people had received trichiasis surgery; 93% of participants reported taking azithromycin at least once; 67% of household respondents (range 46—93) reported participation in trachoma health education; and household latrine coverage increased from 2% to 34%. In children aged 1—9 years percentage decline, by district, for outcomes was: 32% (95% CI 19—48) to 88% (95% CI 83—91) for trachomatous inflammation-follicular (TF); 87% (95% CI 83—91) to 99% (95% CI 97—100) for trachomatous inflammation-intense (TI); and 31% increase (95% CI −42 to −19) to 89% decrease (95% CI 85—93) for unclean face; and in adults percentage decline in trichiasis was 45% (95% CI −13 to 78) to 92% (95% CI 78—96). Overall prevalence of swabs positive for ocular *Chlamydia* was 3.1%. Although there were substantial

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reductions in outcomes in children and adults, the presence of ocular *Chlamydia* and TF in children suggests ongoing transmission. Continued implementation of SAFE is warranted.

1. Introduction

Trachoma is caused by *Chlamydia trachomatis* and is the leading infectious cause of preventable blindness globally. The WHO estimates that trachoma accounts for 2.9% of blindness globally.[1] Since 1997, the WHO has advocated for the SAFE strategy (Surgery, Antibiotics, Facial hygiene and Environmental improvement) for trachoma control.[2] The overall objective of the SAFE strategy is elimination of blinding trachoma, which entails suppression of infection and preventing blinding complications.[3] The WHO recommends implementation of the full SAFE strategy for at least 3 years in districts where prevalence of trachomatous inflammation-follicular (TF) in children aged 1—9 years exceeds 10% and prevalence of trachomatous trichiasis (TT) in adults aged ≥15 years exceeds 1%. Prevalence surveys should then be undertaken after 3 years to evaluate programme activities, refine programme targets and to determine when mass distribution of antibiotics should be stopped.[4,5]

Evaluations of trachoma control programmes are essential to enhance the evidence base for the global advocacy of the SAFE strategy. However, few national trachoma control programmes are routinely conducting evaluations of SAFE. Kuper et al. conducted an evaluation of the SAFE strategy in eight countries highlighting contextual factors affecting implementation of SAFE; however, this study did not assess programme impact.[6] A 3-year evaluation of SAFE in southern Sudan showed declines in active trachoma and unclean faces that were consistent with the levels of programme uptake.[7] A recent 2-year evaluation of SAFE in Gwembe District of southern Zambia showed dramatic declines in active trachoma; however, this study did not quantify the extent of the SAFE interventions.[8]

Blinding trachoma is a serious public health problem in Ethiopia with the Amhara National Regional State being disproportionately affected, bearing an estimated minimum of 45% of the national trichiasis burden and with approximately 1 in 20 of all adults suffering from trichiasis.[9] Trachoma control in Amhara started in 2001 with baseline surveys in four pilot *woredas* (districts).[10] Following licensing of azithromycin and successful piloting of mass treatment with azithromycin, the programme was expanded to cover an additional 15 *woredas* in 2003[11] and eventually the entire Amhara National Regional State in 2007.[12] We aimed to evaluate 3 years of the SAFE strategy by assessing the following: uptake of SAFE interventions; prevalence of active trachoma signs, unclean face and ocular chlamydial infection in children; and trachomatous trichiasis in adults.

2. Methods

2.1. The study sites and survey design

The study was conducted in five trachoma-hyperendemic districts of Amhara National Regional State of Ethiopia (Dera, Ebinat, Estie, Enebsie Sarmedir and Huleteju Enese). These districts were selected on the basis of pragmatic criteria of sound baseline surveys and completion of at least 3 years of implementation of the full SAFE strategy by the end of 2007. They were thus eligible for 3-year evaluations according to WHO standards.[5] The sequence of baseline and evaluation surveys is shown in Figure 1. Baseline surveys were designed to estimate 50% prevalence of active trachoma in children aged 1—9 years within a precision of 10% given a 5% level of significance, 95% CI and a design effect of 5. The evaluation survey was designed to estimate change in prevalence of TF in children aged 1—9 years of at least 20% (from approximately 50% at baseline to 30% at follow-up) given a 5% level of significance, 95% CI, 90% power and a design effect of 5. For both surveys, multi-stage cluster random sampling was used. At baseline, clusters were defined as villages (*kebeles*) and randomly selected in the first stage using a list of *kebeles* in each district with probability proportional to population size. In stage two at baseline, households were selected by the random walk method.[13]

During the evaluation a three-stage sampling plan was used. Six *kebeles* were randomly selected in each district with probability proportional to population size at the first stage. Clusters were then defined as state teams or development teams (the smallest administrative unit in Ethiopia comprising 50 households on average). In the second stage,

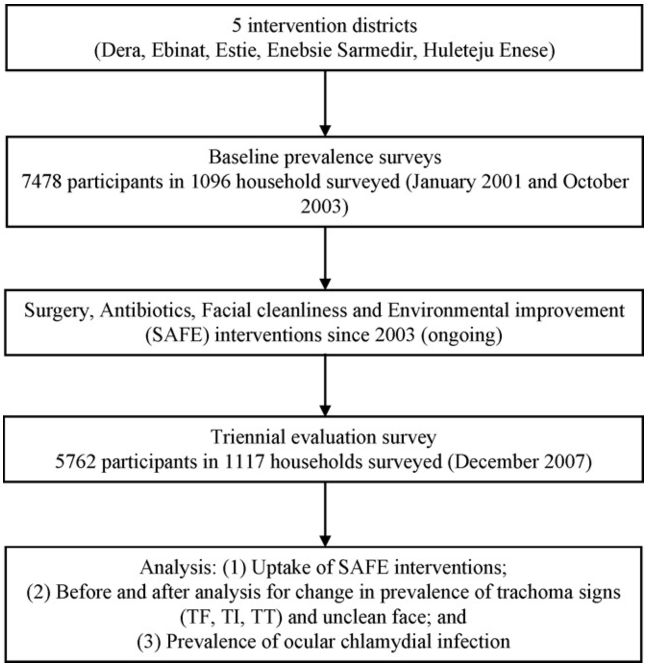

Figure 1 Survey design for evaluating the SAFE strategy for trachoma control in Ethiopia. TF: trachomatous inflammation-follicular; TI: trachomatous inflammation-intense; TT: trachomatous trichiasis.

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three clusters were randomly selected in each *kebele* by drawing folded pieces of paper with names of state teams from a hat. Finally, a sketch map was used to segment selected state teams into groups of five households and two segments randomly selected from each cluster by drawing folded pieces of paper with segment numbers from a hat.[14]

2.2. Interventions

Implementation of the full SAFE strategy was started in 2003. All interventions were conducted in accordance with standards advocated by the WHO, and included trichiasis surgery, mass distribution of azithromycin, trachoma health education, promotion of facial hygiene and promotion of pit latrines. Monitoring of programme activities was conducted and reported on a monthly basis.

2.3. Measurement of SAFE interventions

Programme monitoring data, interviews and observations were used to measure coverage and uptake of SAFE interventions. Heads of sampled households were interviewed, and all persons enumerated were questioned about treatment with azithromycin. Caregivers responded on behalf of children and household heads on behalf of those absent from the household.

2.3.1. Surgery

The number of persons who received trichiasis surgery was derived from monthly reports by trichiasis surgeons, compiled from trichiasis surgery registers.

2.3.2. Antibiotics

The population antibiotic coverage was the proportion of the eligible population treated with azithromycin derived by dividing the number of people treated with azithromycin at each distribution round with the population eligible to receive azithromycin (98% of total population). Individual antibiotic uptake was the proportion of survey participants taking azithromycin derived by inspection of household azithromycin registers, or as a self-report by participants where azithromycin registers were not available.

2.3.3. Facial cleanliness and health education

Frequency of washing faces of children was reported by caregivers on how frequently the faces of children were washed per day. Household health education coverage was derived from reports by household heads of ever participating in trachoma health education at home or elsewhere.

2.3.4. Environmental improvement

Household pit latrines constructed and the number of new pit latrines constructed was derived from monthly reports by community health extension workers on the number of households that had completed construction of latrines.

Households' pit latrine coverage was defined as the proportion of surveyed households with pit latrines. Numbers of households with a round-trip to collect water taking 30 min or less were derived from reports by persons responsible for water.

2.4. Trachoma examination

Examination for trachoma signs was conducted by independent integrated eye-care workers (IECW) using the WHO simplified grading system.[15] The IECW were recruited from a non-evaluation district and had not participated in implementation of SAFE in the evaluation districts. Fifteen potential examiners underwent refresher training in using the simplified grading system by a senior examiner experienced in trachoma grading. A reliability study was then conducted using a set of 70 standardized photographs. Examiners had to achieve at least 80% inter-observer agreement in identifying trachoma signs compared to the senior examiner to participate in the survey. Seven trainees did not achieve the minimum inter-observer agreement of 80%. Of the eight trainees with inter-observer agreement of 80% and above, the best five were selected to be examiners. Our five examiners had good inter-observer agreement ranging from 87% ($\kappa = 0.73$) to 89% ($\kappa = 0.77$). The rest of the 10 trainees were assigned roles as interviewer (five) and examiner-assistants (five) following further training.

2.5. Outcome indicators

All persons living within each selected household who gave verbal consent were examined for trachoma signs using a torch and a ×2.5 magnifying binocular loupe. Participants were assigned a dichotomous outcome for each trachoma signs based on the worst-affected eye. Our outcome indicators included: active trachoma signs, TT, unclean face and ocular chlamydial infection.

Prior to screening for signs of trachoma, faces of children aged 1—9 years were briefly inspected for cleanliness and defined as not clean if nasal or/and ocular discharge were present. To evaluate signs of active trachoma, the primary outcome indicator was prevalence of TF in children aged 1—9 years; trachomatous inflammation-intense (TI) was a secondary outcome.

Eligible participants aged $\geq$15 years were examined for TT as defined by the presence of at least one eyelash touching the eyeball or evidence of epilation.

2.6. Ocular *Chlamydia* testing

Ocular swabs for chlamydial DNA were collected in a subsample of 900 (180 per district) children aged 1—6 years. Only one eligible child was sampled per household and in households where more than one child was eligible for ocular swabbing, one child was randomly selected by picking folded pieces of paper with names of all eligible children from a hat. A total of 10 children were swabbed in each cluster and if this sample was not reached in a cluster, sampling of additional households continued until 10 eligible children were swabbed. Negative control swabs, to test for DNA contamination, were collected from a randomly selected 10% sample of eligible children (one control per cluster). Using

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a new pair of gloves for each patient, the examiner everted the upper lid and assessed the clinical grades using the WHO simplified grading system. The examiner firmly swabbed the tarsal conjunctiva of the right eye, using a sterile Dacron polyester-tipped swab, in a horizontal motion three times rotating the swab with each motion. The negative control swab was passed within 2.5 cm from the conjunctiva without touching. The swab shaft was snapped by the examiner to fit the swab into the transport tube held by an assistant. The examiner and the assistant cleaned their hands with alcohol swabs after each examination. Samples and controls were immediately placed at 4 °C in the field, and transferred to −20 °C within 6 h, and kept at −20 °C until transported at 4 °C to the University of California, San Francisco, where they were frozen at −80 °C. Laboratory testing was conducted in a masked manner. The samples from the same state team were pooled into groups of five.[16] Amplicor PCR (Roche Diagnostics, Branchburg, NJ, USA) was used for the detection of chlamydial DNA according to the manufacturer's instructions.

2.7. Statistical analysis

Data were double entered by different entry clerks and compared for consistency using EpiInfo version 3.3.2 (CDC, Atlanta, GA, USA). Statistical analysis was conducted using Stata 9.2 (Stata Corp., College Station, TX, USA). Contingency table analysis was used to examine demographic characteristics. Differences in means and proportions were compared using the two sample t-test and χ^2 test, respectively. Point estimates and confidence intervals were derived using the SURVEY (SVY) routine in Stata which controlled for clustering and allowed for adjustments for the sampling design as well as weighting for sampling probability.[17] To estimate trichiasis burden for each district, baseline survey TT prevalence was modelled for sex-specific 10-year age groups using logistic regression and applied to the 10-year age group population estimates for males and females. Adjusting for differences in age, sex and household size, a before-and-after analysis was conducted comparing prevalence of our outcomes at baseline and evaluation surveys to generate change in prevalence of signs of TF, TI, TT and unclean face. The percentage decline in prevalence of outcome indicators was derived by standardizing the change in prevalence with the baseline prevalence. The 95% CIs of the change and percentage decline in prevalence were calculated using bootstrap methods.[18] The prevalence of ocular chlamydial infection in each district was obtained by maximum likelihood estimation.[19] The number of positive individual samples most likely to have resulted in the observed pooled PCR results was used to calculate the prevalence point estimate for that district (Mathematica 5.0; Wolfram Research Inc., Champaign, IL, USA).

2.8. Ethical considerations

Informed consent was sought from each individual and parents of children aged 10 years and younger in accordance with the tenets of the declaration of Helsinki. Individuals with signs of active trachoma (TF and/or TI) were offered treatment with 1% tetracycline eye ointment. TT patients were referred to the health centre where free eyelid surgery was available. Personal identifiers were removed from the data set before analyses were undertaken.

3. Results

3.1. Characteristics of survey households and participants

Table 1 summarizes the characteristics of survey households and participants. A total of 7478 participants in 1096 households were surveyed at baseline, and 5762 participants in 1117 households were surveyed at the triennial evaluation. There was no difference in the overall mean household size between the baseline (5.1 people; SD = 1.9) and evaluation surveys (5.2 people; SD = 1.9). However, the mean household size was significantly different at evaluation survey compared to the baseline in Estie (4.7 vs. 5.4; $P < 0.001$), Enebsie Sarmedir (5.6 vs. 4.4; $P < 0.001$) and Huleteju Enese (5.5 vs. 4.2; $P < 0.001$). The overall mean age of the survey participants was 21.8 years (SD = 18.5) and 19.8 years (SD = 19.8) at baseline and evaluation surveys, respectively ($P < 0.001$). Overall, there were more male participants in the evaluation than in the baseline survey (50% vs. 48%; $P = 0.022$). Households' characteristics in the baseline vs. evaluation survey were: households with round-trip to collect water 30 min or less (65% vs. 81%); household pit latrine coverage (2% vs. 34%); households using improved water sources (20% vs. 35%).

3.2. Uptake of SAFE interventions

The uptake of SAFE interventions is summarized in Table 2. A total of 1117 household heads were interviewed and data on antibiotics uptake obtained from 5478 (95%) participants. Based on monthly reports, a total of 23 993 people had received trichiasis surgery between 2003 and 2007. Azithromycin distribution reports revealed that population coverage with azithromycin ranged from 30% (pilot distribution round one in Estie) to 92% (distribution round three in Enebsie Sarmedir). Overall, the population coverage increased at each subsequent distribution round in all districts with coverage during the last reported distribution round being 80% or more in four districts (Ebinat, Estie, Enebsie Sarmedir and Huleteju Enese). The overall individual antibiotic uptake was: at least one treatment (93%); at least two treatments (90%); and three or more treatments (57%). The proportion of people reporting taking three or more treatments was higher in Ebinat and Estie since four distribution rounds had taken place compared to the other districts with only three distribution rounds. Overall, 67% of household respondents reported participation in health education; however, health education coverage was significantly lower in Estie ($P < 0.001$), Enebsie Sarmedir ($P < 0.001$) and Huleteju Enese ($P = 0.006$) than the mean of all five districts. The overall proportion of households with caregivers of children reporting washing children's faces one or more times per day was 89%. The total number of new pit latrines constructed between 2003 and 2007 was 176 867 with over 40% of latrines having been constructed in Huleteju Enese alone. Overall, there was a 31% increase (range 8—56%) in

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Table 1 Characteristics of study households and participants

District (*woreda*)	Baseline survey					Evaluation survey				
	Dera	Ebinat	Estie	Enebsie Sarmedir	Huleteju Enese	Dera	Ebinat	Estie	Enebsie Sarmedir	Huleteju Enese
Estimated population	248 652	234 650	335 450	142 705	261 744	250 048	234 650	335 450	161 052	312 687
Survey date	Jan 2001	Jan 2001	Jan 2001	Oct 2003	Oct 2003	Dec 2007	Dec 2007	Dec 2007	Dec 2007	Dec 2007
No. households surveyed	280	238	359	60	159	221	223	232	233	207
Household size [mean (SD)]	5.0 (1.8)	5.6 (1.8)	5.4 (1.9)	4.4 (2.0)	4.2 (1.6)	5.1 (1.8)	5.2 (1.9)	4.7 (1.6)	5.6 (2.0)	5.5 (1.8)
No. persons surveyed	1403	1343	1932	823	1977	1113	1129	1079	1301	1140
Age [mean (SD)] (years)	23.3 (19.3)	21.6 (18.3)	22.5 (19.8)	22.0 (18.5)	20.6 (16.7)	20.2 (17.5)	18.4 (16.4)	22.0 (19.0)	19.5 (16.5)	19.0 (15.5)
Males (%)	48%	52%	49%	49%	44%	50%	49%	48%	50%	50%
No. children aged 1—9 years	429	431	635	287	650	398	416	382	443	409
Age [mean (SD)] (years)	5.1 (2.4)	5.1 (2.3)	4.8 (2.4)	5.1 (2.5)	5.0 (2.3)	4.9 (2.5)	5.1 (2.5)	4.8 (2.4)	5.3 (2.5)	5.4 (2.4)
Males (%)	48%	52%	50%	51%	46%	51%	50%	46%	52%	48%
No. adults aged $\geq$15 years	736	688	1018	443	1043	516	457	548	415	380
Age [mean (SD)] (years)	36.3 (16.7)	35.4 (15.7)	36.8 (17.3)	35.2 (15.7)	33.0 (13.7)	33.7 (15.0)	33.5 (14.0)	36.4 (15.4)	35.2 (14.4)	32.7 (13.0)
Males (%)	47%	50%	47%	47%	43%	46%	44%	46%	37%	41%
Households with $\leq$30 min round-trip to collect water (%)	67%	54%	62%	88%	76%	85%	58%	94%	90%	86%
Households pit latrine coverage (%)	0%	0%	1%	5%	13%	40%	8%	26%	61%	56%
Households reporting using 'improved' water source (%)[a]	16%	27%	8%	52%	33%	23%	36%	48%	50%	12%

[a] Improved water source = capped spring, protected hand-dug well, tube well, borehole, cart with small tank, or piped water.

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Table 2 Uptake of Surgery, Antibiotics, Facial cleanliness and Environmental improvement (SAFE) interventions, 2003—2007

SAFE interventions			Dera	Ebinat	Estie	Enebsie Sarmedir	Huleteju Enese
Surgery	Persons received trichiasis surgery[a]		3052	3684	6520	2753	7984
Antibiotics	Population antibiotic coverage[a]	2003		44%			
		2004		82%	30%	81%	88%
		2005	67%	81%	78%	82%	92%
		2006	72%	80%	76%	92%	90%
		2007	75%		85%		
	Individual antibiotic uptake	≥1 time	92%	91%	93%	92%	95%
		≥2 times	87%	92%	89%	88%	93%
		≥3 times	54%	68%	58%	52%	51%
Facial cleanliness	Household health education coverage		96%	90%	45%	43%	57%
	Frequency of washing faces of children ≥1 time per day		91%	87%	90%	76%	95%
Environmental improvement	Household pit latrines constructed[a]		15 901	16 330	28 153	44 662	71 821
	Increase in household pit latrine coverage		40%	8%	25%	56%	44%
	Increase in households with round-trip to collect water ≤30 min		19%	4%	32%	1%	10%

[a] From programme monthly monitoring data.

the proportion of households with latrines at the evaluation survey compared to the baseline. The overall proportion of households reporting round trip to collect water ≤30 min increased by 16% (range by district 1—32%).

3.3. Change in prevalence of active trachoma signs and unclean face in children aged 1—9 years

The prevalence change and percentage decline of the outcome indicators are shown in Table 3. All of the declines in TF, TI and unclean face were statistically significant. However, unclean face increased in Estie [percentage increase = 31% (95% CI −42 to −19)].

3.4. Change in prevalence of TT in adults

Figure 2 summarizes the estimated TT backlog, number of TT surgeries and prevalence of TT in adults aged ≥15 years by district. The prevalence of TT declined in all districts (Table 3) but the declines in TT in Ebinat and Estie were not statistically significant. The dramatic decline in prevalence of TT in Huleteju Enese was consistent with the number of TT surgeries conducted (Figure 2).

3.5. Prevalence of ocular chlamydia infection

Table 4 shows the prevalence of ocular chlamydial infection and prevalence of active trachoma signs in children aged 1—6 years. Overall prevalence of *C. trachomatis* infection was 3.1% (95% CI 2.1—4.5) and ranged from 1.1% in Dera to 4.4% in Ebinat and Enebsie Sarmedir. The mean combined prevalence of *C. trachomatis* infection in two districts (Dera and Estie) where the last mass distribution of azithromycin was in 2007 was 1.4% (95% CI 0.5—3.2), which was significantly lower than in the combined three districts (Ebinat, Enebsie Sarmedir and Huleteju Enese) where the last distribution was in 2006: 4.3% (95% CI 2.7—6.3); $P = 0.01$. All 90 control swabs tested negative for *C. trachomatis* DNA. There was no difference in the prevalence of active trachoma signs in all children eligible for testing for ocular chlamydia compared to the sub-sample tested (Table 4).

We estimated the number of children age 1—9 years likely to have ocular *Chlamydia* based on our findings. With an overall prevalence of infection in children aged 1—6 years of 3.1% and assuming that 60% of infection load was in children aged 1—6 years, we estimated a prevalence of infection of 2.0% in children aged 7—9 years. An overall estimated prevalence of infection in children aged 1—9 years of 2.7% was then derived, equivalent to an infection rate of 27 per 1000 children aged 1—9 years.

4. Discussion

Routine evaluations of the SAFE strategy for trachoma control are essential for monitoring progress towards ultimate intervention goals as well as refining programme targets. Our evaluations in five trachoma-hyperendemic districts of Amhara revealed reductions in prevalence of TF, TI, TT and unclean face following 3 years of trachoma control interventions. Implementation of SAFE resulted in a dramatic decline in TI and considerable decline in TF in all five districts. In one district with intensive trichiasis surgery efforts, the prevalence of TT in adults declined by over

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Table 3 Baseline and triennial evaluation prevalence of active trachoma signs and unclean face in children aged 1–9 years, and trachomatous trichiasis in adults aged ≥15 years

Outcome indicator	District	Prevalence [% (95% CI)][a]			
		Baseline survey	Evaluation survey	Change in prevalence	Percentage decline in prevalence
Trachomatous inflammation-follicular (TF) in children aged 1–9 years	Dera	49 (45 to 56)	15 (10 to 20)	−35 (−43 to −28)	71 (59 to 80)
	Ebinat	79 (75 to 82)	54 (48 to 61)	−25 (−33 to −16)	32 (21 to 41)
	Estie	68 (64 to 70)	46 (36 to 53)	−21 (−33 to −12)	32 (19 to 48)
	Enebsie Sarmedir	90 (86 to 92)	11 (8 to 15)	−79 (−83 to −72)	88 (83 to 91)
	Huleteju Enese	73 (70 to 78)	36 (29 to 43)	−37 (−46 to −30)	51 (42 to 60)
Trachomatous inflammation-intense (TI) in children aged 1–9 years	Dera	63 (60 to 68)	2 (1 to 3)	−62 (−65 to −58)	97 (94 to 99)
	Ebinat	88 (85 to 91)	12 (8 to 15)	−77 (−81 to −71)	87 (83 to 91)
	Estie	80 (76 to 83)	2 (1 to 4)	−78 (−81 to −74)	97 (95 to 99)
	Enebsie Sarmedir	60 (54 to 66)	1 (0.1 to 2)	−59 (−65 to −53)	99 (97 to 100)
	Huleteju Enese	58 (54 to 62)	3 (1 to 6)	−55 (−60 to −50)	94 (90 to 97)
Trachomatous trichiasis (TT) in adults aged ≥15 years	Dera	4.5 (3.2 to 5.9)	0.8 (0.3 to 1.6)	−3.7 (−5.3 to −2.2)	82 (63 to 94)
	Ebinat	5.4 (3.9 to 7.1)	3.0 (1.7 to 4.7)	−2.4 (−4.6 to −0.1)	44 (2 to 70)
	Estie	3.2 (2.3 to 4.3)	1.8 (0.8 to 3.3)	−1.4 (−2.9 to −0.04)	45 (−13 to 78)
	Enebsie Sarmedir	4.4 (2.8 to 6.3)	2.2 (1.0 to 3.9)	−2.1 (−4.4 to −0.1)	49 (−3 to 78)
	Huleteju Enese	2.0 (1.3 to 2.7)	0.1 (0.09 to 0.4)	−1.7 (−2.6 to −1.0)	92 (78 to 96)
Unclean face in children aged 1–9 years	Dera	70 (65 to 76)	24 (17 to 30)	−46 (−53 to −38)	66 (56 to 74)
	Ebinat	68 (63 to 73)	25 (18 to 30)	−44 (−51 to −37)	64 (56 to74)
	Estie	67 (63 to 70)	87 (82 to 92)	21 (13 to 27)	−31 (−42 to −19)
	Enebsie Sarmedir	97 (95 to 99)	63 (57 to 70)	−34 (−40 to −27)	35 (28 to 41)
	Huleteju Enese	81 (78 to 85)	8 (6 to 12)	−73 (−77 to −67)	89 (85 to 93)

[a] Prevalence estimates weighted for sampling design and adjusted for age, sex and household size.

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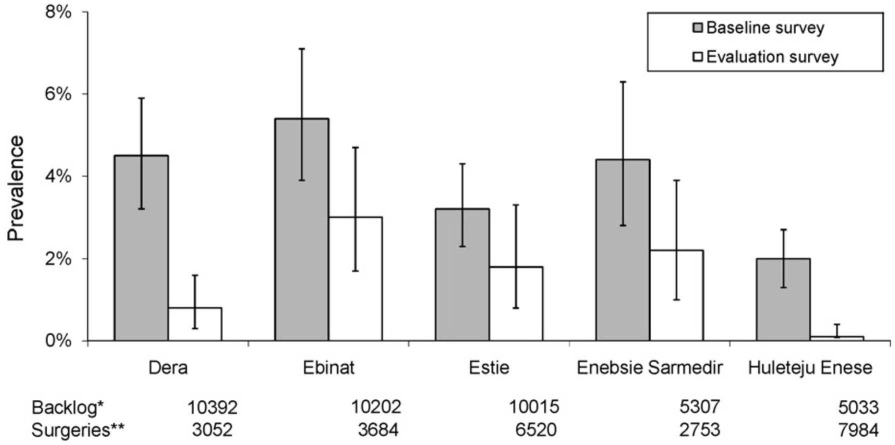

Figure 2 Estimated trachomatous trichiasis (TT) backlog, number of TT surgeries and prevalence of TT in adults aged ≥15 years. * Estimated from baseline prevalence of TT; ** No. of TT surgeries reported 2003—2007.

90%. Results of *C. trachomatis* detection by PCR techniques showed low prevalence of *C. trachomatis* DNA overall, but with a three-fold difference in prevalence between districts that had received treatment in the previous 9 months and those untreated for over a year (3.1% overall, 1.4% in recently treated, 4.3% in districts not treated for over a year). This suggests that transmission was continuing with a rapid resurgence of infection in districts where the last mass distribution of azithromycin had taken place more than a year before the evaluation. All five districts are still above the WHO threshold for implementing mass intervention with Antibiotics, Facial cleanliness, Environmental improvements (A,F,E): prevalence of TF ≥10% in children aged 1—9 years. Thus continued intervention with the SAFE strategy is warranted. It is likely that 3-year evaluations of SAFE in trachoma-hyperendemic settings are too early to demonstrate declines in TF to below 10%; therefore, 5-year SAFE implementation and evaluations plans should be considered in these settings. The notion of a 5-year implementation and evaluation plan is supported by findings of recent mathematical models on elimination of trachoma simulated using data from a trachoma-hyperendemic area of Ethiopia (Gurage Zone).[20] Consistent with a recent WHO recommendation, the argument that blinding trachoma can be eliminated by 3 years of SAFE is not supported by our data.[21]

Laboratory testing for ocular *C. trachomatis* has been suggested for evaluation of SAFE, especially for targeting mass antibiotic distribution and deciding when infection has been eliminated.[22,23] However, trachoma control programmes do not routinely include laboratory diagnosis of trachoma in prevalence surveys because of logistical limitations and the prohibitive cost of processing the currently recommended NAAT tests for *C. trachomatis*.[24] To date, this state of the art technique has largely been used in research settings. In addition, there is neither an internationally recognized reference laboratory facility for ocular chlamydial testing nor recommended threshold levels for ocular *Chlamydia* infection — both of which limit our ability to interpret findings from PCR studies. Despite these challenges, we undertook intensive planning and well-coordinated collection of ocular swabs for *C. trachomatis* testing by PCR in a sub-sample of 900 children aged 1—6 years. Based on the results of *C. trachomatis* detection, we estimate that prevalence of infection to be approximately 2.7% in children aged 1—9 years. This would mean that out of every thousand children aged 1—9 years, 27 would have ocular *C. trachomatis* while 973 would not. Consequently, the majority of the children would not benefit if they were treated with antibiotics immediately. However, as mentioned above, we believe our results indicate a rapid

Table 4 Prevalence of ocular *Chlamydia trachomatis* infection and active trachoma signs in children aged 1—6 years

District	Date of last azithromycin mass distribution	Ocular *C. trachomatis* infection		Prevalence of active trachoma signs [% (95% CI)]	
		No. tested[a]	Prevalence [% (95% CI)]	All children eligible for CT testing ($n = 1448$)	Sub-sample of children tested ($n = 895$)[a]
Dera	May 2007	180	1.1 (0.1—4.0)	24.9 (13.0—42.3)	27.3 (14.5—45.4)
Ebinat	May 2006	180	4.4 (1.9—8.6)	67.6 (58.5—75.6)	70.5 (59.2—79.8)
Estie	March 2007	180	1.7 (0.3—4.8)	55.2 (46.3—63.8)	55.3 (45.0—65.2)
Enebsie Sarmedir	December 2006	180	4.4 (1.9—8.6)	15.6 (10.3—22.9)	16.7 (10.0—26.6)
Huleteju Enese	December 2006	180	3.9 (1.6—7.8)	48.2 (40.8—55.6)	48.3 (40.5—56.1)
Total		900	3.1 (2.1—4.5)	47.0 (42.5—51.6)	48.0 (43.0—53.2)

[a] Five children tested for *C. trachomatis* but not examined for trachoma signs.

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resurgence of infection in districts where antibiotics distribution had not taken place for more than a year. Therefore, despite 97.3% of children not having evidence of ocular *C. trachomatis*, our results do not make a case for stopping treatment since this would mean potentially losing the gains from the past 3 years of intervention to resurgence of disease.

These data could be used to argue for more frequent treatments (for example, twice a year for at least 3 years). Recent evidence based on mathematical modelling suggests that twice a year treatment with antibiotics would have to be done for approximately 5 years to achieve elimination of infection in 95% of the villages.[20] A trial comparing bi-annual and yearly antibiotic treatment strategies suggested that elimination of *C. trachomatis* infection was more rapid in villages that had received bi-annual treatment.[25] Nonetheless, there is still no evidence on what the long-term impact of annual or bi-annual mass antibiotic treatment will be once the treatments have stopped, since stopping antibiotic treatment results in a resurgence of infection.[19] At present, the number of years of antibiotic treatment required to sustain elimination of *C. trachomatis* infection is unknown. However, it is intuitively knowable that it is not feasible to continue treatment with antibiotics indefinitely and indeed such a strategy would not be sustainable.

Conversely, the same data obtained from the ocular swabs could be used to argue that a more rational use of the valuable antibiotic azithromycin would be to implement an intensive attack phase of annual mass treatment for 3 years to reduce infection, and subsequently reduce treatments to once every 2 years in a maintenance phase with a greater emphasis on the F and E components of SAFE to reduce transmission. This approach would allow for a larger total population to be covered with the full SAFE strategy using the same available quantity of donated antibiotics.

Consistent with other studies, our study found TI to be more sensitive to trachoma control intervention than TF.[26,27] However, TI is not currently recommended for decision making on the basis of potential for misdiagnosis. From our field experience, trachoma examiners have improved in their ability to diagnose TI especially since the original WHO set of trachoma slides[28] has been superseded by more robust computer-based images and random presentation of the images during training.[5] Given that, compared to TF, people with TI have higher infection rates,[29] more copies of *C. trachomatis* DNA[30,31] and that TI is associated with higher incidence of TS,[32] it is likely that incidence of TT (blinding trachoma) is correlated to the prevalence of TI. Therefore, despite the levels of TF (in the absence of TI) shown by our evaluation, it is likely that, with the dramatic decline in TI, there will be fewer incident cases of blinding trachoma in the future. TF has been shown to persist following antibiotic treatment.[33] Thus, exclusion of TI from the current WHO trachoma control programme evaluation protocol[5] probably fails to capture the true effect of the SAFE strategy.

Through prevalence surveys, age-specific prevalence of TT enables calculation of TT backlog thus allowing pragmatic planning for implementation of an eyelid surgery strategy geared towards clearing the TT backlog. Use of the random walk method for sampling households at baseline survey posed a potential limitation. Bias could have been introduced since the village guides may have been more likely to direct the survey teams to households where they knew there were persons with TT. Nonetheless, our evaluation suggests that with an intensive TT surgery programme, it is possible to achieve the surgical targets in a few years as exemplified by Huleteju Enese district.

Our study has a number of strengths. Firstly, we used independent and qualified examiners who had not participated in delivering interventions. Secondly, we examined all eligible household participants for trachoma signs thus enabling estimation of outcomes for both active trachoma signs and trichiasis. Our study is also unique in that we undertook sampling of ocular PCR swabs for *C. trachomatis* testing thus providing a measure of infection under programme conditions. The absence of *C. trachomatis* testing at baseline presents a potential limitation of our study. Our *C. trachomatis* infection results would have been made more informative by looking at the change in prevalence of *C. trachomatis* infection before and after interventions. Nonetheless, our evaluation prevalence of *C. trachomatis* infection is consistent with what has been documented in eight trachoma-hyperendemic villages in Gurage Zone of Ethiopia following two treatments with azithromycin.[19]

This large 3-year evaluation of SAFE in five trachoma-hyperendemic districts of the Amhara region of Ethiopia revealed substantial declines in active trachoma signs and TT following 3 years of SAFE interventions. Cross-sectional prevalence of *C. trachomatis* infection suggested ongoing transmission of ocular *C. trachomatis*. Based on these findings, continued intervention with the SAFE strategy is still warranted. We suggest that 5-year intervention and evaluation plans should be adopted for such trachoma-hyperendemic settings.

Authors' contributions: JN, TG, EBS, LA, TT, MZ, JK and PME designed the study; JN, TT, MZ and BA supervised and conducted field work; VC conducted laboratory testing of PCR swabs; JN and YE conducted data analysis; JN and PME drafted the manuscript which all authors revised and approved. JN is guarantor of the paper.

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Ethical approval: Amhara Regional Health Bureau, Bahir Dar, Ethiopia and Emory University Institutional Review Board, Atlanta, Georgia, USA (IRB # 079-2006).

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