

WORLD HEALTH ORGANIZATION
STRATEGIC AND TECHNICAL ADVISORY GROUP
FOR NEGLECTED TROPICAL DISEASES
WORKING GROUP ON MONITORING AND EVALUATION

DESIGN AND VALIDATION
OF A TRACHOMATOUS TRICHIASIS-ONLY SURVEY



World Health
Organization

Design and validation of a trachomatous trichiasis-only survey

Strategic and Technical Advisory Group for Neglected Tropical Diseases

Working Group on Monitoring and Evaluation



WHO/HTM/NTD/PCT/2017.08

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Abbreviations

| | |
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| TF | trachomatous inflammation—follicular |
| TT | trachomatous trichiasis |
| TS | trachomatous scarring |
| WHO | World Health Organization |

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1. Background

1.1 The Fifty-first World Health Assembly adopted resolution WHA51.11 in 1998, which targets the global elimination of trachoma as a public health problem by 2020 (1). The strategy recommended to achieve that goal is encapsulated by the acronym “SAFE”, which represents: Surgery for individuals with trachomatous trichiasis (TT; the late blinding stage of trachoma); and Antibiotics, Facial cleanliness and Environmental improvement (2). The A, F and E interventions are delivered to entire districts in which active (inflammatory) trachoma is common in order to treat ocular infection with *Chlamydia trachomatis*, the causative organism of trachoma, and sustainably reduce its transmission.

1.2 At a series of global scientific meetings on trachoma (3–6), elimination thresholds for trachoma were defined as a prevalence of the active trachoma sign “trachomatous inflammation—follicular” (TF) (7) of < 5% in children aged 1–9 years, and a prevalence of TT (7) unknown to the health system of < 0.2% in adults aged ≥ 15 years (8). The prevalence of these signs should be measured at district level, where districts are “the administrative unit for health care management”, which “for purposes of clarification, consists of a population unit between 100 000–250 000 persons” (5).

1.3 The World Health Organization (WHO) endorses the use of population-based prevalence surveys for estimating the prevalence of trachoma (9). In general, the prevalence of TF in children aged 1–9 years and the prevalence of TT in adults aged ≥ 15 years are measured at the same time in any district being surveyed. This was the approach of the Global Trachoma Mapping Project (10), which undertook baseline surveys in > 1500 districts worldwide in order to provide the data required to start interventions where needed (11).

1.4 The survey design recommended by WHO is a two-stage cluster random sample survey, which uses probability proportional to size sampling to select 20–30 villages (9), and random, systematic or quasi-random sampling to select 25–30 households in each of those villages (10). In most surveys, everyone aged ≥ 1 year living in selected households is examined.

1.5 Usually, surveys are powered to estimate the prevalence of TF in 1–9-year-olds (9,10). TF is most common in young children, whereas TT becomes increasingly common with increasing age (12–15); it is also, in the population as a whole, a much less common sign than TF. Because of this, and because the number of adults aged ≥ 15 years resident in a group of selected households is often not much more than the number of 1–9-year-olds resident in those households, the number of adults examined in a survey is generally not sufficient for estimating TT prevalence with good precision. These surveys simply accept poor precision in estimating TT (6,9,10).

1.6 Because TT is the blinding stage of trachoma, appropriate clinical management of TT (16–18) is the priority of trachoma elimination programmes. Obtaining precise data on TT prevalence helps programmes to plan surgical services, monitor progress and assess whether the trichiasis component of trachoma elimination has been successfully achieved.

1.7 There are four scenarios in which a TT-only survey may be warranted.

- 1) If at baseline survey, the estimated prevalence of TF in 1–9-year-olds is < 5% and of TT in adults is ≥ 0.2%, an impact survey to again measure the TF prevalence is not indicated; after interventions, a TT-only survey to re-estimate the TT prevalence is indicated.
- 2) If at surveillance survey, the estimated prevalence of TF in 1–9-year-olds is < 5% and of TT in adults is ≥ 0.2%, further surveys to again measure the TF prevalence are not indicated; after interventions, a TT-only survey to re-estimate the TT prevalence is indicated.

- 3) If a survey at any stage of the programme estimated the prevalence of TT with a questionable methodological approach, the programme may wish to conduct a TT-only survey.
- 4) If at baseline survey, the estimated prevalence of TF in 1–9-year-olds is $\geq 30\%$ and of TT in adults is $\geq 0.2\%$, at least 5 years of A, F and E interventions are recommended before an impact survey to again measure the TF prevalence. During this time, the programme may wish to undertake a TT-only survey to assess progress in addressing the TT backlog, facilitating adjustments in delivery of S interventions, if needed.

1.8 The work described in this report was commissioned by WHO to guide recommendations for optimizing the design of a TT-only survey. Doing that work provided an opportunity to also evaluate the precision of TT prevalence estimates in general.

2. Simulations with existing data

2.1 Simulations were undertaken to better understand two of the key parameters that influence the design of a TT-only survey: the age distribution of TT, and the extent to which observations of the presence or absence of TT correlate within clusters, expressed as the design effect.

2.2 Health ministries from Benin, Malawi and Nigeria kindly provided datasets from 491 surveys undertaken between 2012 and 2016 with the support of the Global Trachoma Mapping Project (10,19–26). Each of these surveys employed the population-based prevalence survey methodology (10) outlined in paragraphs 1.3–1.5 above. All surveys were conducted prior to the addition of data collection on the presence or absence of trichomatous scarring (TS) of the conjunctiva (7) in eyes with trichiasis (6) within the Global Trachoma Mapping Project’s training and fieldwork systems (27,28): these datasets therefore include data on all trichiasis, irrespective of the presence or absence of TS, and it is not possible to make presumptions as to the etiology of the cases. Included datasets represented a diversity of epidemiological situations for trichiasis (Table 1).

Table 1. Summary of survey data used in simulations

| Country ([State], where applicable) | Number of surveys | Range of trichiasis prevalences in adults aged ≥ 15 years (%) |
|-------------------------------------|-------------------|--|
| Benin | 27 | 0.1–1.9 |
| Malawi | 24 | 0.0–0.6 |
| Nigeria [Bauchi] | 20 | 0.1–3.3 |
| Nigeria [Benue] | 23 | 0.0–0.4 |
| Nigeria [FCT] | 6 | 0.0–0.3 |
| Nigeria [Gombe] | 11 | 0.5–3.9 |
| Nigeria [Jigawa] | 4 | 1.9–3.1 |
| Nigeria [Kaduna] | 23 | 0.0–0.8 |
| Nigeria [Kano] | 44 | 0.0–2.9 |
| Nigeria [Katsina] | 34 | 0.0–3.6 |
| Nigeria [Kebbi] | 2 | 0.4–1.8 |
| Nigeria [Kogi] | 4 | 0.0–0.0 |
| Nigeria [Kwara] | 8 | 0.0–0.2 |
| Nigeria [Niger] | 25 | 0.0–0.4 |
| Nigeria [Sokoto] | 3 | 0.3–1.0 |
| Nigeria [Taraba] | 13 | 0.0–0.8 |

2.3 Using the `sqldf` package in R (29), trichiasis prevalences by age and gender were calculated using the same approach as that used by the Global Trachoma Mapping Project (10). Raw data were grouped by cluster, then age and gender. For each cluster, the number of individuals examined and the number observed to have trichiasis were determined for each age and gender group; then the proportion of individuals with trichiasis in that group was weighted by the proportion of residents expected to have that age and gender (with underlying population data derived from www.worldpop.org, using the zonal statistics tool in ArcGIS 10.3 (30)). The sum of weighted proportions within a cluster produced the age- and gender-adjusted cluster-level proportion for adults aged ≥ 15 years. The mean of the cluster-level proportions was calculated to determine the adjusted survey-level prevalences summarized in Table 1 and which are presented in more detail elsewhere (19–26). The mean of the age-specific trichiasis proportions across all clusters was calculated to explore the age distribution of trichiasis in each survey, and the mean of the age-specific survey-level prevalences was calculated to generate age-specific prevalence curves for each country (Fig. 1).

2.4 These data indicate that trichiasis is first apparent in these populations at an age of about 30–40 years, and increases with increasing age thereafter, but that there is at least moderate heterogeneity between settings.

Fig. 1. Age-specific prevalences of trichiasis by survey (evaluation unit, EU) and country (Benin, Malawi and Nigeria), Global Trachoma Mapping Project, 2012–2016

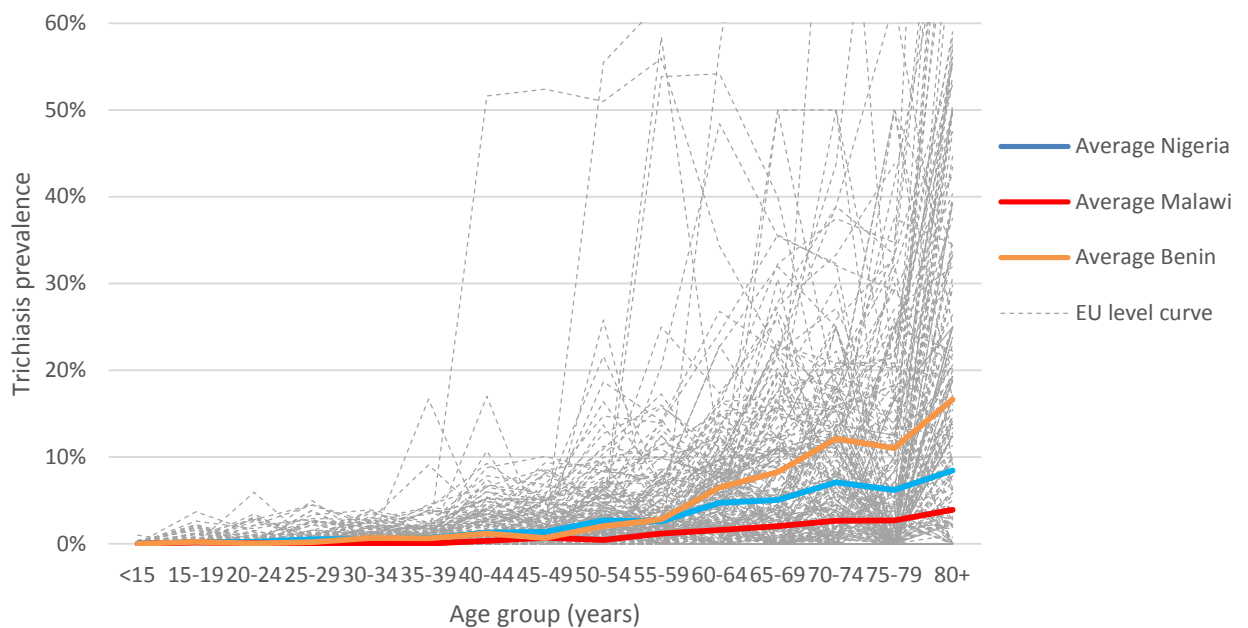


Table 2. Proportion of trichiasis cases within different age groups, by country (Benin, Malawi and Nigeria), Global Trachoma Mapping Project, 2012–2016

| Country | Proportion (%) of all trichiasis cases in subjects, by age | | |
|---------|--|------------|------------|
| | ≥ 15 years | ≥ 30 years | ≥ 40 years |
| Malawi | 100 | 92 | 89 |
| Benin | 99 | 95 | 85 |
| Nigeria | 97 | 92 | 83 |

Between countries, the proportion of all trichiasis cases in those aged ≥ 40 years varies more than the proportion of all trichiasis cases in those aged ≥ 15 years (Table 2).

2.5 The design effect (for observations of trichiasis in ≥ 15-year-olds) arising from the cluster-sampled design was calculated for each survey as $design\ effect = 1 + m\alpha^2\mu$, where m is cluster size, α is standard deviation over the mean and μ is the mean prevalence. The design effects ranged from 1.1 to 5.1, with the value of 5.1 being an outlier placed a considerable interval above the rest of values observed. Because the vast majority of design effects were contained within a narrow numerical range (Table 3), it was considered that using a universal design effect for TT-only surveys would be appropriate. Ordered from smallest to largest, the 75th centile of design effects was 1.47.

Table 3. Distribution of design effects for trichiasis (Benin, Malawi and Nigeria), Global Trachoma Mapping Project, 2012–2016

| Design effect | Cumulative percentage |
|---------------|-----------------------|
| 1.0 | 23.8% |
| 1.0–1.5 | 76.2% |
| 1.0–2.0 | 91.7% |
| 1.0–2.5 | 97.7% |
| 1.0–3.0 | 98.6% |
| 1.0–3.5 | 99.1% |
| 1.0–4.0 | 99.5% |
| 1.0–4.5 | 99.5% |
| 1.0–5.1 | 100.0% |

2.6 To investigate what might be required of a TT-only survey powered to estimate TT prevalence in different age ranges, the following assumptions were made:

1. Interventions reduce the prevalence of TT uniformly across the whole population.
2. The ≥ 40 years age group constitutes 34% of the population aged ≥ 15 years.
3. The ≥ 40 years age group includes 85% of TT cases in the population aged ≥ 15 years.
4. A design effect of 1.47 should be used.

With these assumptions, a prevalence of 0.2% in those aged ≥ 15 years would correspond to a prevalence of 0.5% in the ≥ 40 years age group $\left(\frac{0.002 \times 0.85}{0.34}\right)$.

To estimate an expected prevalence of 0.5% with an absolute precision of ± 0.25%, the sample size would be as follows:

$$n = design\ effect \times \left(\frac{z^2 \times p(1-p)}{e^2}\right) = 1.47 \times \left(\frac{1.96^2 \times 0.005(1-0.005)}{0.0025^2}\right)$$

where z = the standard normal deviate corresponding to 95% confidence intervals, p = the expected prevalence, and e = the desired absolute precision, expressed as half the width of the desired confidence interval.

This gives a sample size of **4496 adults aged ≥ 40 years**.

The sample size decreases as the age group sampled widens (Table 4) because the variance increases as the expected proportion increases towards 50%, then declines again beyond 50%. If the required absolute precision is held constant, therefore, a larger sample size is needed the closer the expected prevalence is to 50%, to allow the signal to be discerned beyond the noise.

Table 4. Alternative sample size calculations for different age groups and precisions, design effect = 1.47

| Age group sampled | Expected prevalence (%) | Absolute precision | | | |
|-------------------|-------------------------|--------------------|--------------|--------------|--------------|
| | | $\pm 0.15\%$ | $\pm 0.20\%$ | $\pm 0.25\%$ | $\pm 0.50\%$ |
| ≥ 15 years | 0.2 | 5010 | 2818 | 1803 | 451 |
| ≥ 40 years | 0.5 | 12487 | 7024 | 4496 | 1124 |

2.7 In the 491 Global Trachoma Mapping Project survey datasets from Benin, Malawi and Nigeria, there was a mean of 3.0 (survey-level range in means 1.4–6.1) people aged ≥ 15 years per selected household; a mean of 2.3 (1.2–4.6) people aged ≥ 30 years per selected household; and a mean of 1.5 (1.0–2.2) people aged ≥ 40 years per selected household. If 30 households are sampled per cluster (as was often done within the Global Trachoma Mapping Project), then 32 clusters would be needed to include 2818 residents aged ≥ 15 years, ignoring non-response.

3. Conjunctival scarring, and lower lid trichiasis

3.1 The Second Global Scientific Meeting on Trachomatous Trichiasis (Cape Town, November 2015) (6) discussed the criteria for diagnosing TT in prevalence surveys. The meeting proposed that the definition of TT be changed to require trichiasis (or evidence of recent epilation of in-turned eyelashes) AND EITHER (i) the presence of TS in the same eye, OR (ii) the inability of the grader to evert the eyelid to examine the conjunctiva. (Assuming the grader is competent and experienced, inability to evert the eyelid is generally due to a lack of eyelashes – often due to epilation – and/or a heavily scarred, stiff eyelid.) This proposal was not fully accepted. Instead, the meeting recommended that collection of data on TS should continue, and the question be revisited at a later date.

3.2 The meeting recommended also that data on both upper and lower lid trichiasis should be collected in trachoma prevalence surveys (6).

4. Draft design

4.1 The draft design for a TT-only survey is a population-based prevalence survey designed to estimate, with absolute precision of $\pm 0.20\%$, an expected TT prevalence of 0.2% in adults aged ≥ 15 years, using a design effect of 1.47. As shown in Table 4, an estimated 2818 adults aged ≥ 15 years should be examined.

4.2 An alternative approach, as currently used by at least one national trachoma elimination programme, would be to structure the survey to include only adults aged ≥ 40 years. The validation exercise was designed to test both potential approaches.

5. Validating the draft design: precision

5.1 To test the validity of the proposed design and to compare the relative costs of different approaches with the precision attained, four field-based district-level surveys were implemented in 2016. Four districts (Am-Timan, Chad; Budaka, Uganda; Monduli, United Republic of Tanzania; and Touboro, Cameroon) were surveyed. The four districts (Fig. 2) were at different stages of progress towards trachoma elimination. The characteristics of the four districts are summarized in Table 5.

Table 5. Characteristics of four districts involved in the trachomatous trichiasis (TT)-only survey validation exercise, 2016

| District | Population | Proportion of ≥ 15-year-olds aged ≥ 40 years (%) | Baseline TT prevalence estimate in those aged ≥ 15 years (%) [year of survey] | Baseline TF prevalence estimate in those aged 1–9 years (%) [year of survey; year MDA commenced] | Next TF prevalence estimate due (year) | Rationale for conducting a TT-only survey ¹ |
|--------------------------------------|------------|--|---|--|--|--|
| Am-Timan, Chad | 233 447 | 30 | 6.2 [2002] | 26.9 [2002, 2014] | 2017 | (3) ² |
| Budaka, Uganda | 192 853 | 28 | 3.1 [2012] | 2.2 [2012, not indicated] | Not indicated | (1) |
| Monduli, United Republic of Tanzania | 174 482 | 34 | 5.5 [2004] | 57.6 [2004, 2015] | 2018 | (4) |
| Touboro, Cameroon | 287 087 | 35 | 0.5 [2011] | 3.0 [2011, not indicated] | Not indicated | (1) |

MDA, mass drug administration; TF, trachomatous inflammation—follicular

¹ Rationales have been coded here using the same designations as in paragraph 1.7 of this report, namely: (1) if at baseline survey, the estimated prevalence of TF in children is < 5% and of TT in adults is ≥ 0.2%, an impact survey to again measure the TF prevalence is not indicated; after interventions, a TT-only survey to re-estimate the TT prevalence is indicated; (3) if a survey at any stage of the programme estimated the prevalence of TT with a questionable methodological approach, the programme may wish to conduct a TT-only survey; (4) if at baseline survey, the estimated prevalence of TF in children is ≥ 30% and of TT in adults is ≥ 0.2%, at least 5 years of A, F and E interventions are recommended before an impact survey to again measure the TF prevalence. During this time, the programme may wish to undertake a TT-only survey to assess progress in addressing the TT backlog, facilitating adjustments in delivery of S interventions, if needed.

² Baseline survey conducted at region-level.

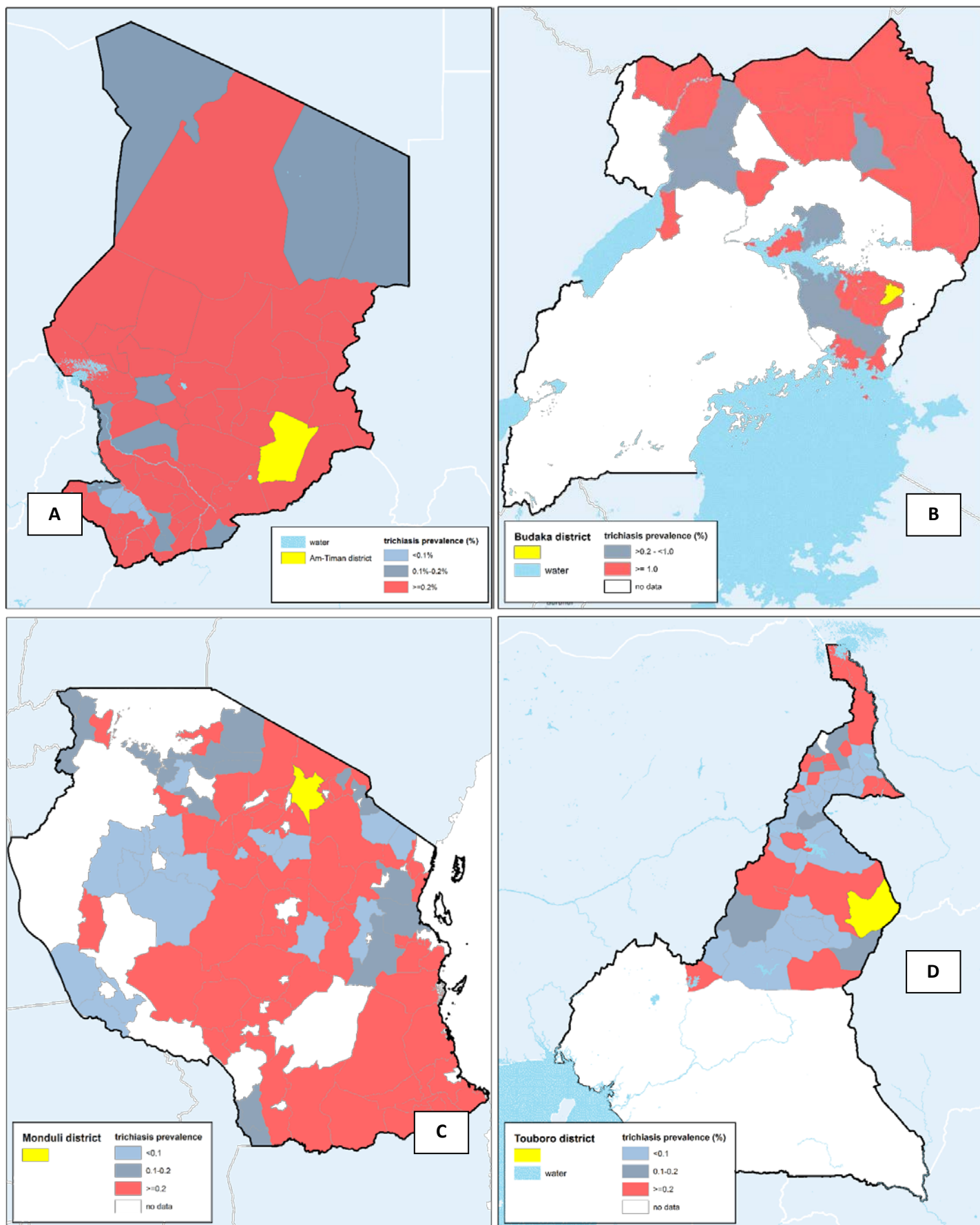
5.2 Protocols were approved by the Cameroon Ministry of Public Health (18 July 2016); the Chad Ministry of Health (002/PR/PM/MESRS/SG/CNBT/2014); the Uganda Ministry of Health (HS 2012); the National Institute for Medical Research, United Republic of Tanzania (NIMR/HQ/R.8a/Vol.IX/2085); and the Research Ethics Committee of the London School of Hygiene & Tropical Medicine (10360).

5.3 To maximize survey quality, a standardized system for training field teams was devised by a panel of experts. The training schedule and training materials were based on those developed by the Global Trachoma Mapping Project (27). Training included an objective structured clinical examination (OSCE) for graders, to provide a standardized method for assessing graders' readiness to contribute to field work. Field work began immediately following the three-day training.

5.4 Oversampling was undertaken in each survey in order to generate data for subsequent simulations: 60 clusters were sampled per district. In all 60 clusters in Monduli, and in half (30) of the clusters in Am-Timan, Budaka and Touboro, all consenting individuals aged ≥ 1 year living in selected households were included. In the other 30 clusters of Am-Timan, Budaka and Touboro, consenting individuals aged ≥ 40 years living in the selected households were included.

Participating individuals were examined by a certified grader using binocular $\times 2.5$ magnifying loupes and a torch. Eyes that were observed to have trichiasis were further assessed for the presence or absence of TS, with TT defined as the presence of trichiasis, plus either the presence of TS or an inability to evert the eyelid in the same eye.

Fig 2. Location of districts surveyed in the trichomatous trichiasis-only survey validation exercise, 2016, and most recent trichiasis prevalence data in surrounding districts (31,32)
 A, Am-Timan; B, Budaka; C, Monduli; D, Touboro



Monduli deployed 12 graders who each recorded their own data. The survey teams in Am-Timan, Budaka and Touboro were each composed of one grader plus one designated recorder; a total of four graders and four recorders in Am-Timan; six graders and six recorders in Budaka; and five graders and five recorders in Touboro.

Data were entered into LINKS (33), the Android-phone-based data collection app used in 29 countries for the Global Trachoma Mapping Project, and an additional six countries for surveys of other neglected tropical diseases. Best practices for data management were used, including the use of external (objective) data managers, regular calculation of descriptive statistics and generation of point maps showing cluster locations to compare with district shapefiles. Data were stored on a secure server which was backed up hourly. Raw and cleaned datasets, the data cleaning log, and age- and gender-adjusted prevalence estimates were reviewed and approved by the relevant health ministry.

5.5 All analyses were conducted using R (29,34-38). Prevalences were calculated using the methodologies established by the Global Trachoma Mapping Project (10), as described in section 2.3. This involved calculating the age- and gender-adjusted cluster-level proportions of people with trichiasis, then taking the mean of the adjusted cluster-level proportions as the district-level prevalence. For the purposes of this validation exercise, age- and gender-adjustment was undertaken to calculate adjusted district-level prevalences for both ≥ 15 -year-olds and ≥ 40 -year-olds. To calculate confidence intervals, bootstrapping (39) was performed with replacement over 10 000 replications, first by resampling 60 clusters (to determine the 95% confidence intervals of the “true” prevalence), and by resampling 30 clusters; in each bootstrapping set, the 2.5th and 97.5th centiles of the ordered means so obtained were used as the lower and upper bounds, respectively, of the confidence interval.

5.6 Numbers of households enrolled, people examined, and prevalences and design effects for different age groups, are summarized for each district in Table 7. Frequency distributions of prevalence estimates for ≥ 15 -year-olds and ≥ 40 -year-olds, derived by bootstrapping, are shown for illustrative purposes in Fig. 3.

5.7 Prevalence estimates produced with data from either 30 or 60 clusters were similar, as shown for ≥ 40 -year-olds in Table 6.

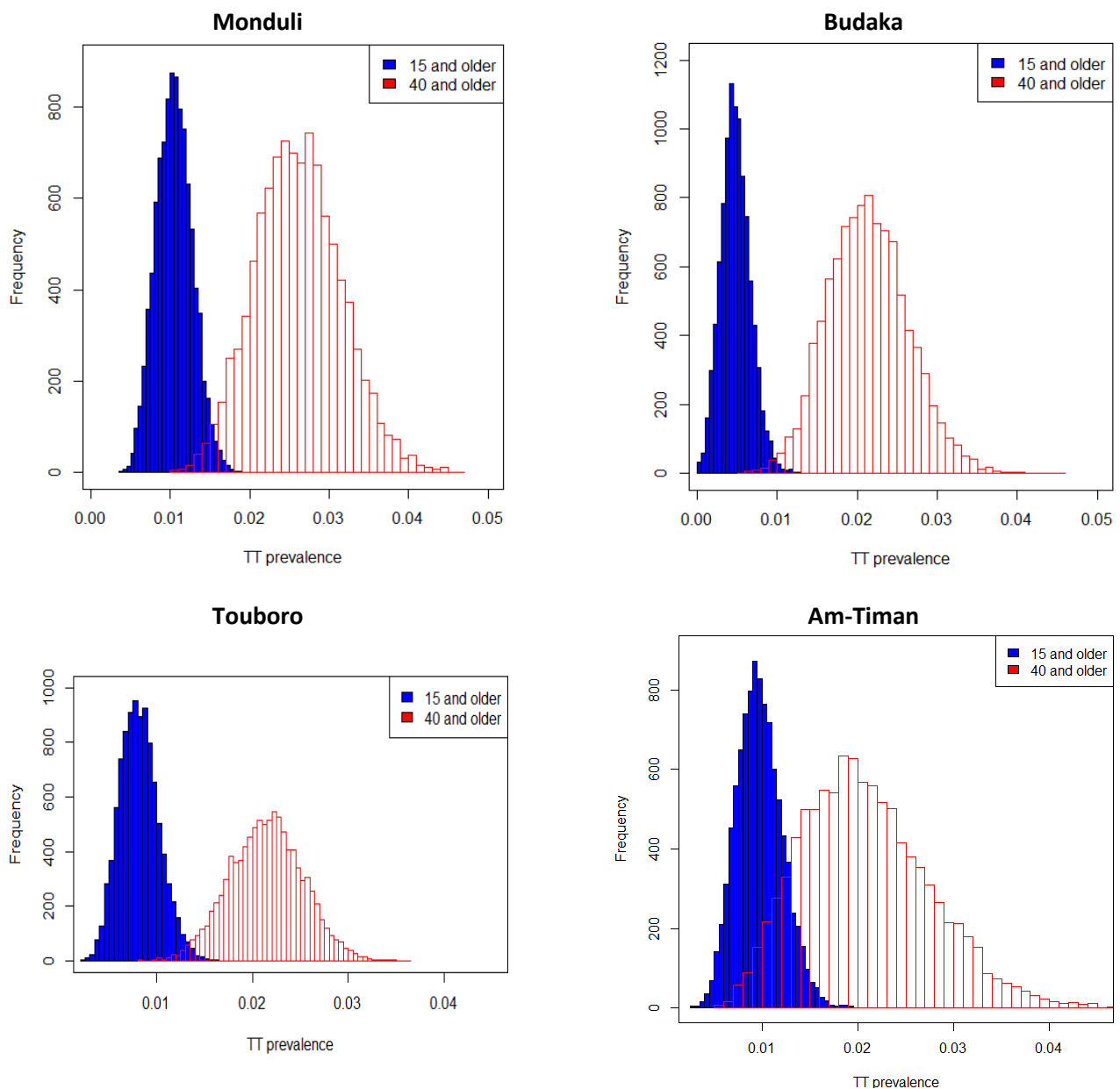
Table 6. Trachomatous trichiasis prevalence estimates in ≥ 40 -year-olds, with 95% confidence interval (CI) bounds, determined by bootstrapping with (a) samples of 60 clusters, versus (b) samples of 30 clusters, with replacement, in each bootstrap sample, over 10 000 replications

| District | 60 clusters | | | 30 clusters | | |
|----------|-------------------------|---------------------------|---------------------------|-------------------------|---------------------------|---------------------------|
| | Prevalence estimate (%) | Lower bound of 95% CI (%) | Upper bound of 95% CI (%) | Prevalence estimate (%) | Lower bound of 95% CI (%) | Upper bound of 95% CI (%) |
| Am-Timan | 2.3 | 1.9 | 3.9 | 2.3 | 1.5 | 4.4 |
| Budaka | 2.4 | 1.7 | 3.1 | 2.4 | 1.5 | 3.4 |
| Monduli | 3.0 | 2.1 | 4.1 | 3.0 | 1.8 | 4.6 |
| Touboro | 2.0 | 1.4 | 2.6 | 2.0 | 1.3 | 3.0 |

Table 7. Summary results of the trichomatous trichiasis (TT)-only survey validation exercise, 2016

| District (no. of clusters, house- holds) | Age group (years) | Persons examined | Persons with TT | Proportion of all TT cases in the district (%) | Crude age- group- specific TT prevalence (%) | Crude TT prevalence in ≥ 15- year-olds (%) | Age- and gender- adjusted TT prevalence in ≥ 15- year-olds (%) [95% CI] | Design effect for TT in ≥ 15- year-olds | Crude TT prevalence in ≥40- year-olds (%) | Age- and gender- adjusted TT prevalence in ≥40-year- olds (%) [95%CI] | Design effect for TT in ≥40- year-olds |
|--|-------------------------|---------------------|--------------------|--|--|--|--|--|---|---|---|
| Am-Timan (60, 1798) | < 15 | 1713 | 0 | 0.0 | 0.0 | 2.5 | 1.0 [0.5–1.5] | 1.2 | 3.6 | 2.0 [1.0–3.6] | 1.11 |
| | 15–39 | 722 | 3 | 10.7 | 0.4 | | | | | | |
| | ≥ 40 | 353 | 25 | 89.2 | 7.1 | | | | | | |
| Budaka (60, 1729) | < 15 | 2541 | 0 | 0.0 | 0.0 | 0.9 | 0.6 [0.3–0.8] | 1.2 | 3.2 | 2.5 [1.7–3.1] | 1.03 |
| | 15–39 | 1542 | 0 | 0.0 | 0.0 | | | | | | |
| | ≥ 40 | 1340 | 50 | 100.0 | 3.7 | | | | | | |
| Monduli (60, 1894) | < 15 | 2877 | 1 | 0.7 | 0.03 | 1.9 | 1.2 [0.9–1.7] | 3.5 | 4.4 | 3.0 [2.1–4.1] | 1.05 |
| | 15–39 | 1782 | 4 | 2.8 | 0.2 | | | | | | |
| | ≥ 40 | 3149 | 136 | 96.5 | 4.3 | | | | | | |
| Touboro (60, 1816) | < 15 | 1446 | 0 | 0.0 | 0.0 | 1.1 | 0.9 [0.5–1.2] | 1.3 | 2.4 | 2.0 [1.4–2.6] | 1.02 |
| | 15–39 | 1501 | 4 | 13.3 | 0.3 | | | | | | |
| | ≥ 40 | 1160 | 17 | 86.7 | 2.2 | | | | | | |

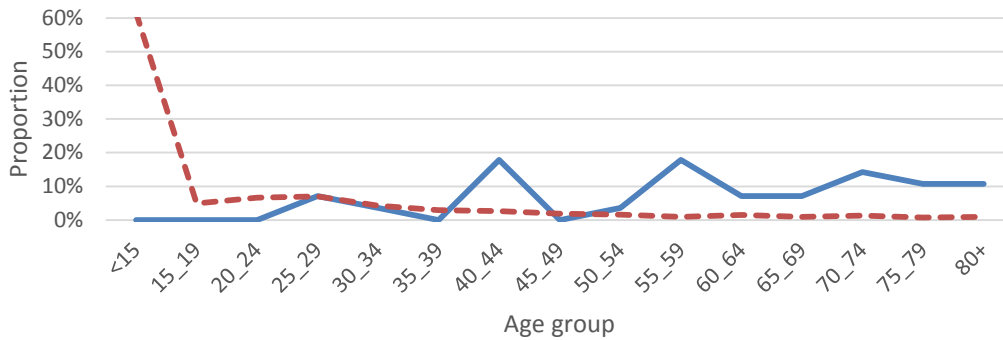
Fig. 3 Frequency distributions of trichomatous trichiasis (TT) prevalence estimates in ≥ 15 -year-olds and ≥ 40 -year-olds obtained by bootstrapping samples of 60 clusters, with replacement, from each district, over 10 000 replications



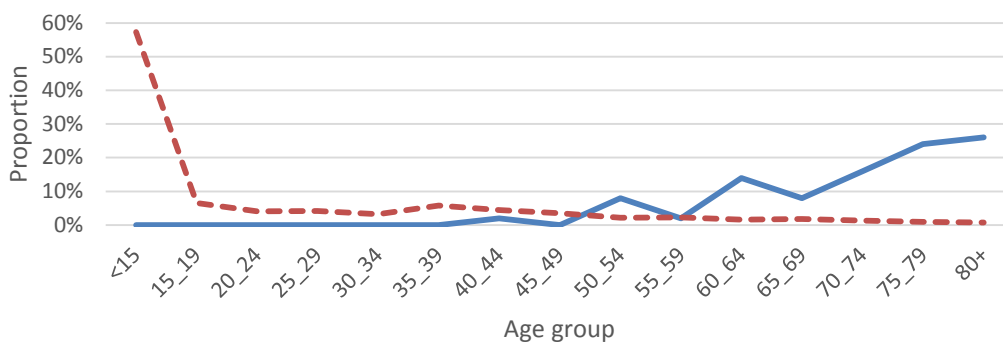
5.8 As expected, in each district, most TT cases found were in older individuals: $> 86\%$ of cases occurred in people aged ≥ 40 years. However, the ratio between the prevalence estimated in those aged ≥ 40 -years, and the prevalence estimated in those aged ≥ 15 -years ranged from 2.0 to 4.2 (Table 7). In addition, in Am-Timan and Touboro, the TT prevalence spiked unexpectedly in 40–44-year-olds (Fig. 4, panels (a) and (d)); this is likely to represent an age reporting bias in individuals with TT, which is a fundamental challenge introduced by age-specific recruitment.

Fig. 4. Proportion of all people examined (dotted red lines) and proportion of individuals with trichomatous trichiasis (solid blue lines), by age group, in each district

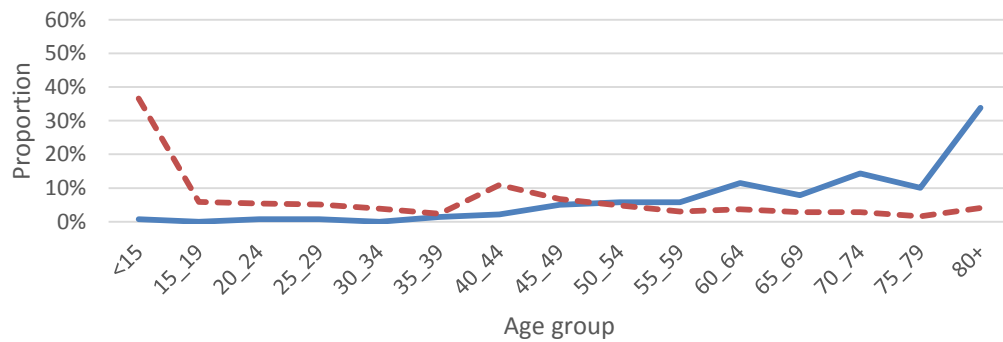
(a) Am-Timan



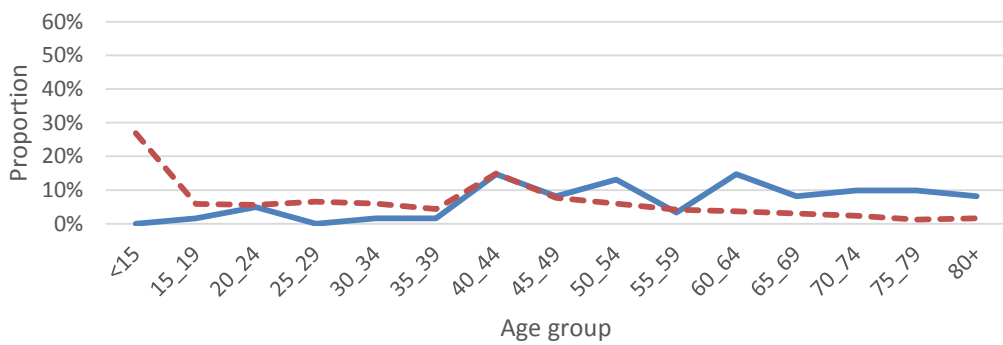
(b) Budaka



(c) Monduli



(d) Touboro



5.9 Although the target sample size of individuals aged ≥ 15 years is 2818, if 30 households are selected per cluster and the mean number of persons aged ≥ 15 years per household is 2.6 (Monduli District, Table 7), the survey would require 37 clusters.

To understand the precision associated with reducing the number of clusters, data from the Monduli District dataset (in which everyone aged ≥ 1 year was invited to be examined) were bootstrapped, with replacement, over 10 000 replications; first selecting 30 clusters, then 40 clusters, then 50 clusters in each resample. As expected, the standard deviation becomes smaller and the confidence intervals become tighter as more clusters are included.

Table 8. Estimated trachomatous trichiasis (TT) prevalence in ≥ 15 -year-olds, with 95% confidence intervals (CI) generated by bootstrapping, with replacement, 30, 40 or 50 clusters from the Monduli dataset, with 10 000 replications for each exercise

| Number of clusters in each resample | Estimated TT prevalence (%) | Standard deviation (%) | Lower bound of 95% CI (%) | Upper bound of 95% CI (%) |
|-------------------------------------|-----------------------------|------------------------|---------------------------|---------------------------|
| 30 | 1.23 | 0.30 | 0.69 | 1.86 |
| 40 | 1.23 | 0.26 | 0.77 | 1.77 |
| 50 | 1.22 | 0.23 | 0.80 | 1.76 |

6. Validating the draft design: cost

6.1 To be practicable, a methodology should allow surveys to be implemented at as low a cost as possible, while still providing information that is epidemiologically valid and therefore useful for programme planning. Prevalence estimates that are incorrect can lead to resources being misdirected to areas that do not need them (in the event of an overestimated prevalence) or withheld from populations that require them to preserve sight. Understood in this context, we can consider the trade-off between precision and cost as an issue addressable through a cost-effectiveness analysis. The purpose of the following exercise was to compare the cost and precision of examining only those aged ≥ 40 years with the cost and precision of examining all those aged ≥ 15 years. Time was used as a proxy for cost.

6.2 Data from Monduli and Budaka were explored. (In Monduli, all consenting individuals aged ≥ 1 year resident in selected households were included, in all 60 clusters; in Budaka, recruitment was as for Monduli in 30 clusters, while in the other 30 clusters, consenting individuals aged ≥ 40 years resident in selected households were included.) Time-stamps were recorded automatically by LINKS at every instance of data entry.

6.3 The time required to complete each component of the data collection process was calculated by determining mean times across all relevant observations. At cluster level, the time elapsed from arrival at the cluster (time point A) and arrival at the first household in that cluster (time point B) was calculated. At household level, the time elapsed from time point B and the start of the first clinical examination in the household (time point C₁) was calculated; as was the time elapsed between time point B and the end of the final (n^{th}) examination in the household (time point D_n). At individual level, the difference between the start (time point C_{1-n}) and end of each examination (time point D_{1-n}) was calculated. Finally, the time elapsed between D_n in the final household of a cluster and the time of arrival in the cluster (time point A) was calculated (Table 9).

Table 9. Mean times (with 95% confidence intervals [CI]) spent undertaking each survey activity in trachomatous trichiasis-only surveys, Monduli and Budaka districts, 2016

| Activity | | Time (h:mm:ss) [95%CI] | |
|--|---------------------|---------------------------|---------------------------|
| | | Monduli ¹ | Budaka ¹ |
| Preparing to begin data collection, per cluster | | 0:40:42 (0:33:15–0:48:10) | 0:06:54 (0:04:59–0:08:49) |
| Setting up and talking prior to first exam, per household | ≥ 1-year clusters | 0:03:38 (0:03:05–0:04:10) | 0:01:08 (0:01:02–0:01:14) |
| | ≥ 40-years clusters | [not applicable] | 0:02:18 (0:01:46–0:02:50) |
| Examining individuals, per individual | ≥ 1-year-olds | 0:01:27 (0:01:26–0:01:29) | 0:00:30 (0:00:29–0:00:30) |
| | ≥ 15-year-olds | 0:01:36 (0:01:34–0:01:38) | 0:00:33 (0:00:32–0:00:33) |
| | ≥ 40-year-olds | 0:01:43 (0:01:40–0:01:45) | 0:00:53 (0:00:52–0:00:54) |
| Total time at household, per household | ≥ 1-year clusters | 0:15:10 (0:13:31–0:16:49) | 0:04:58 (0:04:40–0:05:17) |
| | ≥ 40-years clusters | [not applicable] | 0:05:00 (0:04:15–0:05:46) |
| Total time between households, per cluster | | 0:29:31 | 3:10:15 |

¹In Monduli, teams were composed of two graders, each of whom recorded his or her own examination findings. In Budaka, a team was composed of one grader and one recorder.

6.4 Examining individuals with TT took more time than examining individuals without TT (Table 10).

Table 10. Mean examination time (with 95% confidence intervals [CI]) for those with and without trachomatous trichiasis (TT) in TT-only surveys, Monduli and Budaka Districts, 2016

| TT status | Examination time (h:mm:ss) [95% CI] | |
|-------------------|-------------------------------------|---------------------------|
| | Monduli ¹ | Budaka ¹ |
| TT present | 0:03:35 (0:03:11–0:03:59) | 0:01:59 (0:01:47–0:02:11) |
| TT absent | 0:01:25 (0:01:23–0:01:28) | 0:00:34 (0:00:33–0:00:34) |

¹In Monduli, teams were composed of two graders, each of whom recorded his or her own examination findings. In Budaka, a team was composed of one grader and one recorder.

6.5 The mean total times required per cluster to examine people in different age categories are shown in Table 11. The data for Budaka are displayed separately for clusters in which all individuals aged ≥ 1 year were invited to participate and for those clusters in which only individuals aged ≥ 40 years were invited to participate.

Table 11. Number of persons examined per household, time required to examine and proportion of trichomatous trichiasis (TT) found in different age categories in TT-only surveys, Budaka and Monduli districts, 2016

| District, age range examined | Age (years) | Household count | Persons examined per household | Time per cluster | Proportion of TT cases found in that age group (%) |
|------------------------------|-------------|-----------------|--------------------------------|------------------|--|
| Monduli, ≥ 1-year-olds | ≥ 40 | 32 | 1.8 | 4:43:08 | 96.5 |
| | ≥ 15 | 32 | 2.6 | 5:25:19 | 99.3 |
| | ≥ 1 | 32 | 4.1 | 6:47:32 | 100.0 |
| Budaka, ≥ 1-year-olds | ≥ 40 | 31 | 1.7 | 4:40:22 | 100.0 |
| | ≥ 15 | 31 | 3.1 | 5:16:41 | 100.0 |
| | ≥ 1 | 31 | 5.8 | 6:30:58 | 100.0 |
| Budaka, ≥ 40-year-olds | ≥ 40 | 27 | 1.7 | 3:51:32 | 100.0 |

7. Discussion

The data presented here demonstrate that for a TT-only survey, there are several potential difficulties involved in limiting recruitment to those aged ≥ 40 years. First, there is variability in the proportion of all TT cases which are found in ≥ 40 -year-olds, and although this is also true for the proportion of all TT cases which are found in ≥ 15 -year-olds, the latter is less marked than the former. In other words, some precision is gained by including the 15–39-year-old population in the survey, because the (greater) uncertainty surrounding the proportion of TT found in those aged ≥ 40 years is removed. In any case, the elimination target is defined as a TT prevalence in those aged ≥ 15 years (8).

Second, examining only individuals aged ≥ 40 years provides an incentive for those aged slightly less than or slightly more than this threshold to misrepresent their age if they are either enthusiastic or reluctant, respectively, to be examined. Such incentives also apply to those aged almost 15 years, if this is the cut-off age for examination, but as the prevalence of TT is very low in the 10–20-year-olds age bracket, that will bias prevalence estimates far less.

Surveying 30 households in which only ≥ 40 -year-olds are examined takes less time than surveying 30 households in which all ≥ 15 -year-olds are examined. Using, for the sake of comparability, data from clusters in which everyone aged ≥ 1 year was examined, theoretically, the time saved by examining only ≥ 40 -year-olds (compared to examining all ≥ 15 -year-olds) would have been 42 minutes (Monduli) and 36 minutes (Budaka). However, the total time required to examine only ≥ 40 -year-olds in one 30-household cluster still approaches half a day's work for one team, even before taking into account the travel time to and from the cluster. Randomly selected clusters in a district-level survey are typically situated some distance from each other, and it is therefore unlikely that it would be possible for one team to consistently complete examination of two clusters of ≥ 40 -year-olds per day. The time saved by excluding 15–39-year-olds would probably not result in savings in direct survey costs. A considerable proportion of time spent per cluster is used in sensitizing village leaders and discussions at household level, which is not strongly related to the age group being examined.

8. Recommendations

8.1 TT-only surveys are not routine, and are recommended only for specific epidemiological contexts, particularly:

1. If at baseline survey, the estimated prevalence of TF in 1–9-year-olds is < 5% and of TT in adults is $\geq 0.2\%$, an impact survey to again measure the TF prevalence is not indicated; after interventions, a TT-only survey to re-estimate the TT prevalence is indicated.
2. If at surveillance survey, the estimated prevalence of TF in 1–9-year-olds is < 5% and of TT in adults is $\geq 0.2\%$, further surveys to again measure the TF prevalence are not indicated; after interventions, a TT-only survey to re-estimate the TT prevalence is indicated.
3. If a survey at any stage of the programme estimated the prevalence of TT with a questionable methodological approach, the programme may wish to conduct a TT-only survey.
4. If at baseline survey, the estimated prevalence of TF in 1–9-year-olds is $\geq 30\%$ and of TT in adults is $\geq 0.2\%$, at least 5 years of A, F and E interventions are recommended before an impact survey to again measure the TF prevalence. During this time, the programme may wish to undertake a TT-only survey to assess progress in tackling the TT backlog, facilitating adjustments in delivery of the S component as needed.

8.2 When undertaken, a TT-only survey should be implemented as a population-based prevalence survey designed to estimate the prevalence of TT in adults aged ≥ 15 years. The sample size is calculated to estimate, with 95% confidence, an expected TT prevalence of 0.2% with absolute precision of 0.2% and a design effect of 1.47, yielding 2818 as the target number of adults aged ≥ 15 years to be examined. This should be appropriately inflated to account for the expected non-response rate. The number of clusters, c , that would ideally be included is given by $c = (2818 \times [\text{non-response inflator}]) / (h \times a)$, where h is the number of households that can be examined by 1 team in 1 day, and a is the expected number of adults resident in each house, as determined by the most recent census or recent population-based trachoma survey experience. If c , determined by the above formula, is ≥ 30 , 30 clusters should be used.

8.3 When trichiasis is observed, the eye should be evaluated for the presence or absence of TS, as defined within the WHO simplified trachoma grading scheme (7), and the subject should be asked scripted questions to determine whether interventions to manage the trichiasis in that eye have previously been recommended by health care workers (6,27).

8.3 Prevalence calculations should incorporate adjustment for age and gender of those examined, using the methods published by the Global Trachoma Mapping Project (10).

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