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Trachoma in Viet Nam: results of 11 surveillance surveys conducted with the Global Trachoma Mapping Project

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ABSTRACT

Purpose: Following interventions against trachoma in Viet Nam, impact surveys conducted in 2003–2011 suggested that trachoma was no longer a public health problem. In 2014, we undertook surveillance surveys to estimate prevalence of trachomatous inflammation—follicular (TF) and trichiasis.

Methods: A population-based prevalence survey was undertaken in 11 evaluation units (EUs) encompassing 24 districts, using Global Trachoma Mapping Project methods. A two-stage cluster sampling design was used in each EU, whereby 20 clusters and 60 children per cluster were sampled. Consenting eligible participants (children aged 1–9 years and adults aged ≥ 50 years) were examined for trachoma.

Results: A total of 9391 households were surveyed, and 20,185 participants (98.8% of those enumerated) were examined for trachoma. EU-level TF prevalence in 1–9-year-olds ranged from 0% to 1.6%. In one cluster (in Hà Giang Province), the percentage of children with TF was 10.3%. The overall pattern of cluster-level percentages of children with TF, however, was consistent with an exponential distribution, which would be consistent with trachoma disappearing. Among people aged ≥ 50 years, prevalence of trichiasis by EU ranged from 0% to 0.75%; these estimates are equivalent to 0–0.13% in all ages. The prevalence of trichiasis unknown to the health system among people aged ≥ 50 years, by EU, ranged from 0% to 0.17%, which is equivalent to 0–0.03% in all ages.

Conclusion: Findings suggest that trachoma is no longer a public health problem in any of the 11 EUs surveyed. However, given the high proportion of children with TF in one cluster in Hà Giang Province, further investigations will be undertaken.

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Introduction

Trachoma is a neglected tropical disease that causes blindness.¹ In 2016, it was estimated that worldwide, 200 million people were at risk, and 3.2 million people needed surgery to avoid trachomatous blindness, in 42 countries.² According to criteria set by the World Health Organization (WHO), trachoma is a public health problem where the prevalence of trachomatous inflammation—follicular (TF) is $\geq 5\%$ in 1–9-year-olds, and/or the prevalence of trachomatous trichiasis unknown to the health system is $\geq 0.2\%$ in ≥ 15 -year-

olds (approximately equivalent to $\geq 0.1\%$ in the all-ages population).³ Global political commitment for elimination of trachoma as a public health problem was made manifest by a 1998 World Health Assembly resolution; the target date for achievement of this goal is December 2020.^{4,5}

Viet Nam has been fighting trachoma for more than 60 years. In 1950, the Ophthalmologic Institute of Hanoi (which later became the Viet Nam National Institute of Ophthalmology (VNIO)) estimated that more than 70% of the population on

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*See Appendix.

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the outskirts of Hanoi suffered from active trachoma at some time during their lives.⁶ In 1951, more than 200,000 people in North Viet Nam were treated for trachoma by mobile teams.⁶ Following sustained trachoma control efforts by the government, the national prevalence had declined to 7% in 1995.⁷ With the 1996 launch of the WHO Alliance for the Global Elimination of Trachoma by 2020 (GET2020), the government of Viet Nam and its partners started implementing the “SAFE strategy” against trachoma, i.e. surgery for trichiasis, antibiotics to clear infection with the causative organism (*Chlamydia trachomatis*), and facial cleanliness and environmental improvement to reduce transmission.⁸ In 2000–2001, 67 district-based surveys were undertaken in 27 suspected-endemic provinces to identify local needs for SAFE. After deployment of SAFE interventions, impact surveys were undertaken at four time points: 2003, 2004, 2005, and 2009–2011. These surveys suggested that trachoma was no longer a public health problem, according to WHO criteria. However, WHO’s standard operating procedures for validation of elimination as a public health problem⁹ had not yet been released. In 2014, given the need to complete a second round of surveys to establish that recrudescence of active trachoma had not occurred¹⁰, we undertook a series of pre-validation trachoma surveillance surveys in Viet Nam, aiming to estimate the prevalence of trachomatous inflammation—follicular (TF) in children aged 1–9 years and the prevalence of

trichiasis unknown to the health system in adults, in previously trachoma-endemic districts.

Methods

We implemented population-based prevalence surveys (PBPSs) using the systems and methods of the WHO-recommended Global Trachoma Mapping Project (GTMP), including version 2 of the training system,^{11,12} with five exceptions: (1) graders were certified to participate in fieldwork if they passed a slide-based test, rather than an inter-grader agreement exercise using live subjects; (2) we did not collect data on access to water and sanitation; (3) examination was limited to 1–9-year-olds and ≥50-year-olds, unlike other GTMP projects where all consenting individuals aged ≥1 year living in sampled households were examined; (4) a fixed number of children (rather than a fixed number of households) was recruited in each sampled cluster; and (5) for individuals diagnosed with trichiasis, we asked questions about previous management of trichiasis through surgery or epilation.

Individual-level demographic and examination data were entered into the GTMP-LINKS application on Android smartphones, transmitted to the Cloud, then processed, and reviewed by VNIO (the agency designated by the Ministry of Health for oversight of ophthalmic issues in Viet Nam), as described elsewhere.¹² Our principal outcome measures were the evaluation unit (EU)-level TF prevalence in 1–9-year-

Table 1. Characteristics of survey population by evaluation unit, Global Trachoma Mapping Project, Viet Nam, 2014.

Province	Districts in evaluation unit	Population (2009) ¹³	Evaluation Unit	Justification for survey
Vinh Phuc	Vinh Tuong	189,000	1	Both districts had baseline prevalence of TF >10% in 2001 and both had interventions
	Me Linh	192,000	2	
	Yen Lac	145,000		
	Binh Xuyen	108,000		
Ha Tinh	Lap Thach	118,000	3	Both districts >10% in 2001 baseline and both had intervention
	Can Loc	128,000		
	Nghi Xuan	98,000		
Hoa Binh	Kim Boi	114,000	4	Both districts >10% in 2001 baseline and both had intervention
	Yen Thuy	60,000		
Hung Yen	Van Lam	113,000	5	District >10% in 2001 baseline and had intervention
Yen Bai	Van Chan	144,000	6	Both districts >10% in 2001 baseline and both had intervention
	Yen Bai town	91,000		
	Luc Yen	102,000	7	Baseline >10% but no intervention
	Van Yen	27,000		
Vinh Long	Tam Binh	154,000	8	Baseline 9.5% and 10.1% but no intervention
	Vung Liem	159,000		
Hà Giang	Bac Quang	45,000	9	2005 MoH survey of communes between 7.0–17.2%; intervention in 2 districts
	Yen Minh	78,000		
	Bac Me	47,000		
Ninh Thuan	Ninh Hai	89,000	10	Baseline survey 5.3–5.8% in southern Viet Nam (intervention in one)
	Ninh Phuoc	135,000		
Binh Thuan	Ham Tan	69,000	11	Baseline surveys 7.8–7.9%, no intervention
	Tuy Phong	140,000		
	Bac Binh	117,000		

olds, and the EU-level prevalence of trichiasis unknown to the health system in ≥ 50 -year-olds.

We surveyed 11 EUs (covering 24 districts) selected in consultation with programme partners. The full list of EUs and the rationale for conducting a survey in each one form Table 1.

Sample size calculations

We powered each survey to estimate the EU-level TF prevalence in 1–9-year-olds, using an expected prevalence of 10%, and aiming to have 95% confidence of estimating that prevalence with absolute precision of $\pm 3\%$. Our design effect, based on previous surveys, was 2.65, which resulted in a sample size estimate of 1019 children.¹² We additionally wished to estimate trichiasis prevalence in adults, but our sample size was calculated only using parameters relating to TF in children.

Sample selection

Selection of clusters

We used two-stage cluster sampling, categorizing villages (*thon*) as our first-stage clusters. A list of *thon* in each EU was obtained from the district authorities. We systematically selected 20 *thon* with probability proportional to population size, using a computer-generated random starting point.

Selection of households and participants

In selected *thon*, we used compact segment sampling to choose one segment (*xom*) at random. Within that *xom*, a household was visited if at least one child aged 1–9 years, or at least one adult aged ≥ 50 years, lived there (i.e., had slept there for the past month). If individuals in relevant age ranges were away from home but were expected to be available later the same day, an attempt was made to revisit the household. Once 60 children had been enrolled, the cluster was considered complete. If 60 children could not be enrolled in a single *xom*, the next-nearest *xom* was also visited.

Trachoma grading

Graders participating in the surveys had obtained a kappa for diagnosing TF of ≥ 0.9 in an inter-grader agreement test based on 50 conjunctival photographs of children with and without active trachoma.¹¹ Examination was undertaken according to the criteria set out in the WHO simplified trachoma grading scheme.¹³ Graders used binocular loupes with 2.5 \times magnification, and the sun (or if necessary, a torch) for illumination. When trichiasis was diagnosed in

an eye, the subject was asked if health workers had previously recommended surgery or epilation for that eye.

Data analysis

We conducted analyses in R (R Foundation for Statistical Computing, Vienna, Austria) and Structured Query Language. Cluster (*xom*)-level data on TF in 1–9-year-olds were adjusted for the age of those examined, using 1-year age bands and the data from the most recent Viet Nam census as the reference dataset.¹⁴ Similarly, cluster-level data on trichiasis were adjusted for the age and gender of those examined, using 5-year age bands and the most recent census data.¹² The EU-level prevalence of each sign was calculated as the mean of the adjusted cluster-level proportions. We calculated confidence intervals by bootstrapping, with replacement, over 10,000 replications. Prevalence estimates for trichiasis in those aged ≥ 50 years were used to calculate estimates for the all-ages population by multiplying the prevalence in ≥ 50 -year-olds by 0.173: the proportion of the national population aged ≥ 50 years, based on the 2009 national census.¹⁴

Although we powered our surveys to estimate TF prevalence at EU level, our compact segment sampling approach (involving examination of 60 consenting 1–9-year-olds in a block of adjacent households in one or two *xom*) means that the proportion of children with TF in a cluster estimates the true prevalence for that group of households. To visualize the distribution of TF by cluster across the entire surveyed area, the means of the northings and eastings for all households within a cluster (obtained by GPS) were calculated to provide a single set of coordinates; results were plotted using QGIS (<http://www.qgis.org/en/site/>). Using Mathematica 11.1 (Wolfram Research, Champaign, IL, USA), we fit the cluster-level TF prevalence data to a zero-inflated negative binomial, parametrized so the mean of the distribution scaled with the sample size in that community.

Ethical considerations

Ethical approval was granted by the ethics committees of the London School of Hygiene & Tropical Medicine, London, UK (reference 6319) and the Biomedical Ethics Board of National Institute of Ophthalmology, Hanoi, Viet Nam. We obtained informed verbal consent for examination from each participant or (for children) from their parent or guardian. Individuals with conjunctivitis, whether meeting the definition of active trachoma or not, were provided with two tubes of 1% tetracycline eye ointment; individuals with trichiasis were referred to a local surgeon.

Table 2. Characteristics of survey population by evaluation unit, Global Trachoma Mapping Project, Viet Nam, 2014.

Province	Districts in evaluation unit	Number of households surveyed	Children aged 1–9 years			Adults aged ≥50 years		
			Number enumerated	Proportion examined (%)	Proportion male (%)	Number enumerated	Proportion examined (%)	Proportion male (%)
Vinh Phuc	Yen Lac, Me Linh	595	1,206	97.4	52.8	758	99.5	41.8
Vinh Phuc	Vinh Tuong, Binh Xuyen, Lap Thach	573	1,211	99.8	51.5	748	100.0	44.1
Ha Tinh	Can Loc, Nghi Xuan	846	1,212	98.2	52.6	482	98.8	37.1
Hoa Binh	Kim Boi, Yen Thuy	910	1,193	99.3	53.6	317	100.0	35.3
Hung Yen	Van Lam	905	1,218	98.3	54.2	1,192	99.3	41.9
Yen Bai	Van Chan, Yen Bai town	890	1,199	98.3	50.0	472	99.8	39.0
Yen Bai	Luc Yen, Van Yen	867	1,208	99.7	53.6	417	98.1	42.0
Vinh Long	Tam Binh, Vung Liem	1,342	1,214	98.9	48.6	1,609	99.9	42.3
Ha Giang	Bac Quang, Yen Minh, Bac Me	725	1,142	96.6	49.9	290	99.3	49.3
Ninh Thuan	Ninh Hai, Ninh Phuoc	1,011	1,208	97.9	49.5	882	95.8	42.0
Binh Thuan	Ham Tan, Tuy Phong, Bac Binh	727	1,203	99.9	51.5	58	100.0	29.8
Total		9,391	13,214	98.6	51.6	7,225	99.1	41.6

Results

Fieldwork was undertaken from May to August, 2014. In 9391 households, survey teams examined a total of 20,185 residents (98.8% of those enumerated), composed of 13,028 1–9-year-olds and 7,157 ≥ 50-year-olds. Table 2 summarizes the characteristics of the population sampled by EU. Overall, 52% of 1–9-year-olds examined and 42% of ≥50-year-olds examined were male. The mean ages of those examined were 4.8 years (standard deviation 2.6) for the 1–9-year-old group, and 63.4 years (10.4) for the ≥50-year-old group.

Prevalence of trachoma

The prevalence of TF in 1–9-year-olds was <5% in all 11 EUs and ranged from 0% to 1.6% (Table 3, Figure 1). Among people aged ≥50 years, prevalence of any trichiasis by EU ranged from 0% to 0.75%; these estimates are equivalent to prevalences of any trichiasis in all ages of 0–0.13%. Of 136 people identified as having trichiasis, 125 (92%) were known to the health system, meaning that management for eyes with trichiasis had previously been (1) offered but refused; (2) accepted and a surgical date set; or (3) received, but disease had subsequently recurred. Accounting for

Table 3. Prevalence of trachoma by evaluation unit, Global Trachoma Mapping Project, Viet Nam, 2014.

Province	Districts in Evaluation Unit	Prevalence of TF in children aged 1–9 years: % (95% CI) ¹	Trichiasis cases unknown to health system			
			All trichiasis cases		Prevalence in adults ≥50 years: % (95% CI) ²	
			Prevalence in adults ≥50 years: % (95% CI) ²	Prevalence in all ages: % ³	Prevalence in adults ≥50 years: % (95% CI) ²	Prevalence in all ages: % ³
Vinh Phuc	Yen Lac, Me Linh	0	0.75 (0.41–1.15)	0.13	0.17 (0–0.39)	0.03
Vinh Phuc	Vinh Tuong, Binh Xuyen, Lap Thach	0.2 (0–0.5)	0.72 (0.49–1.02)	0.13	0.01 (0–0.04)	0.00
Ha Tinh	Can Loc, Nghi Xuan	0.0 (0–0.1)	0.08 (0–0.21)	0.01	0	0.00
Hoa Binh	Kim Boi, Yen Thuy	0	0.17 (0–0.41)	0.03	0	0.00
Hung Yen	Van Lam	0	0.35 (0.14–0.58)	0.06	0.05 (0–0.12)	0.01
Yen Bai	Van Chan, Yen Bai town	0.1 (0–0.4)	0.22 (0.06–0.37)	0.04	0	0.00
Yen Bai	Luc Yen, Van Yen	0.2 (0–0.7)	0.04 (0–0.10)	0.01	0	0.00
Vinh Long	Tam Binh, Vung Liem	0	0	0.00	0	0.00
Ha Giang	Bac Quang, Yen Minh, Bac Me	1.5 (0.5–2.9)	0.30 (0.05–0.57)	0.05	0	0.00
Ninh Thuan	Ninh Hai, Ninh Phuoc	0.1 (0–0.4)	0.45 (0.22 – 0.79)	0.08	0	0.00
Binh Thuan	Ham Tan, Tuy Phong, Bac Binh	0.2 (0–0.5)	0.23 (0.06–0.50)	0.04	0	0.00

CI, confidence interval.

¹Adjusted for age, in one-year bands.

²Adjusted for gender and age, in five-year bands.

³The all-ages (population level) estimate was derived by multiplying the prevalence in ≥50-year-olds by 0.173: the proportion of the 2009 national population aged ≥50 years.

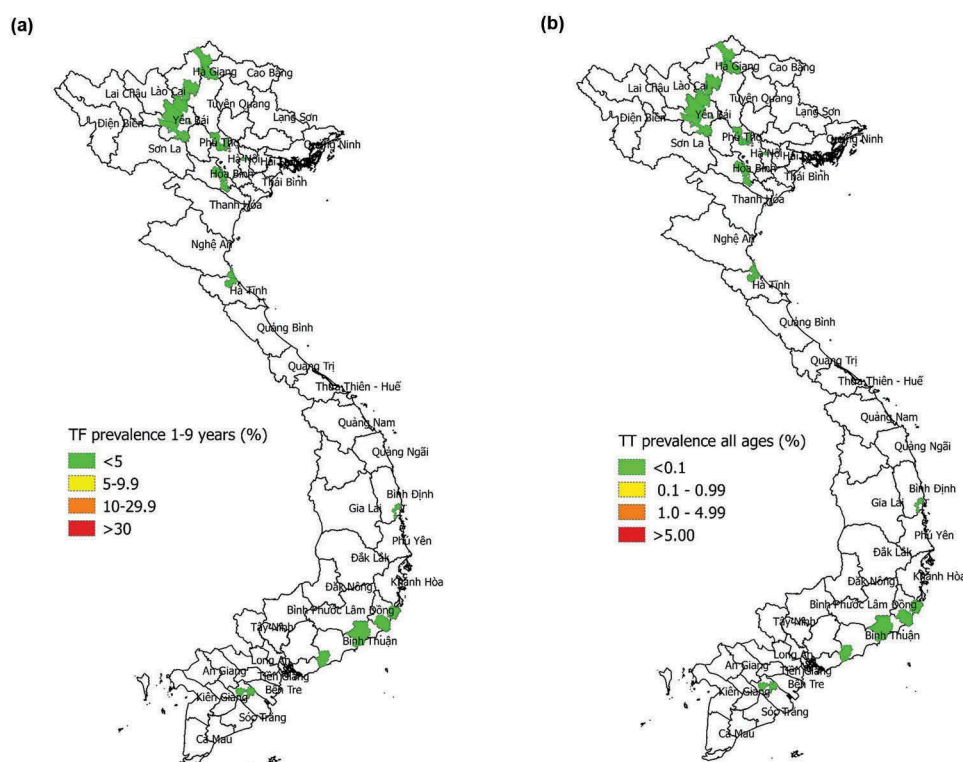


Figure 1. Prevalence of (a) trichomatous inflammation—follicular (TF) in children aged 1–9 years and (b) trichiasis unknown to the health system in all ages, Global Trachoma Mapping Project, Viet Nam, 2014.

previous management of trichiasis, the prevalence of trichiasis unknown to the health system among people aged ≥ 50 years, by EU, ranged from 0% to 0.17%, which was equivalent to 0–0.03% in all ages (Table 3, Figure 1).

Distribution of trichiasis by age, gender

The age- and gender-specific distribution of trichiasis (in all EUs pooled together) is shown in Figure 2. The age/gender-specific prevalence of trichiasis known to the health system increased with age; however, there were no statistically significant differences among males compared to females (Figure 2(a)). There were very few cases of trichiasis unknown to the health system (Figure 2(b)).

Distribution of TF at cluster level

Of the 220 clusters surveyed, the proportion of 1–9-year-olds with TF was 0% in 200 clusters; 1.6 to 3.5% in 19 clusters, and 10.3% in one cluster in Yên Minh district of Hà Giang Province (Figure 3). Using maximum likelihood estimation, we calculated a shape parameter for the negative binomial distribution of 0.17 (95% CI 0.07–388, bootstrap percentile, $n = 999$),

the very wide confidence intervals commensurate with the fact that only 20 clusters contained cases of TF.

Discussion

This series of pre-validation trachoma surveillance surveys showed that all 11 of the formerly endemic EUs studied now have TF prevalence estimates below the 5% elimination threshold. While in two of 11 EUs, our data suggest that the prevalence of trichiasis in all ages was $> 0.1\%$ in 2014, most people with trichiasis appear to be “known to the health system”. The prevalence of trichiasis unknown to the health system in all ages was below the elimination threshold in each EU.

These surveys were epidemiologically robust. Whereas previous trachoma surveys in Viet Nam used the assurance sampling trachoma rapid assessment (ASTRA) methodology,¹⁵ we used PBPS methods recommended by WHO.¹² Unlike ASTRA, PBPS provide point prevalence estimates for TF and trichiasis,¹⁶ which are needed to determine if elimination thresholds have been reached.⁹ A second point of difference was the fact that individuals with trichiasis were asked about previous management recommendations from health workers: the first GTMP-supported survey in which this was

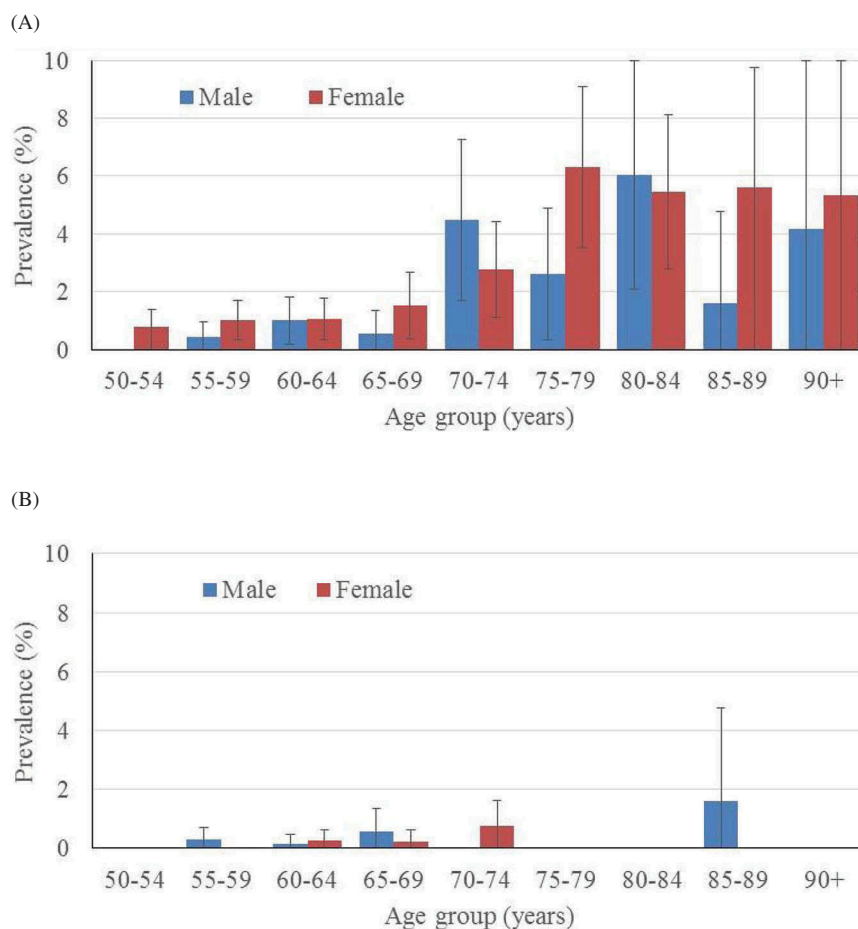


Figure 2. Age- and gender-specific prevalence of trichiasis (A) known, and (B) unknown to the health system in those aged ≥ 50 years; data from all evaluation units combined, Global Trachoma Mapping Project, Viet Nam, 2014.

done. These questions were added in order to help the country determine whether EUs had reached elimination thresholds for trichiasis, which are couched in terms of the prevalence of trichiasis “unknown to the health system” – that is, the prevalence of trichiasis, counting only those individuals with the condition who have not previously been offered an operation or epilation for it.¹⁷ Following successful implementation of the questions in Viet Nam, their use was adopted throughout the GTMP.

There were some weaknesses in our work in Viet Nam that should be acknowledged. Although we took our methodological template from previous WHO guidance¹⁸ and worked within the framework of the GTMP,¹² we did not examine individuals aged 10–49 years, in order to try to save time for our fieldworkers, who went house-to-house to recruit survey subjects in steeply mountainous terrain. The relatively small numbers of ≥ 50 -year-olds examined in each EU resulted in relatively wide confidence intervals around the trichiasis prevalence estimates

(Table 3). The lack of examination of adults aged < 50 years potentially limits the comparison of our findings to elimination targets, since in many trachoma-endemic settings, trichiasis can be seen in people less than 50 years old. We have assumed that the prevalence of trichiasis in people aged < 50 years was negligible. To a certain extent, this assumption is supported by the age distribution of trichiasis cases that the teams identified in the field (Figure 2), which underpinned our transformation of the trichiasis prevalence estimates in ≥ 50 -year-olds to all-ages estimates. Our assessment of the trichiasis situation is further limited by the fact that we did not record the presence or absence of scars in the tarsal conjunctivae of eyes noted to have trichiasis, because the recommendation to do so was released after our surveys were complete.¹⁹ However, this point may be moot for Viet Nam, because the data at hand, allowing for the limitations noted above, suggest that elimination threshold prevalences for trichiasis have been reached.

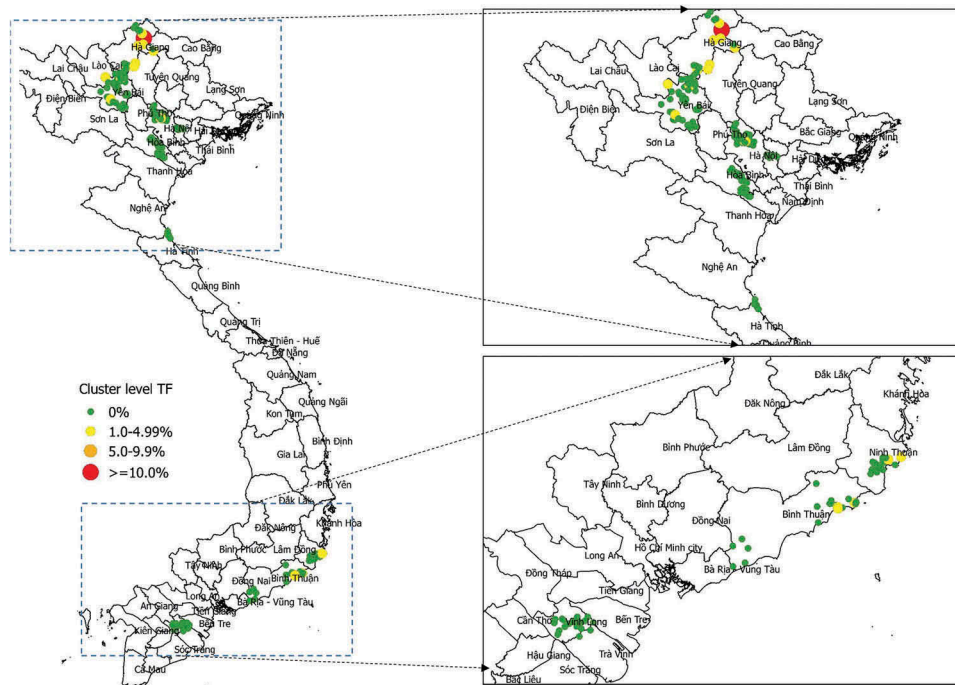


Figure 3. Geographic distribution of cluster-level prevalence of TF in children aged 1–9 years, Global Trachoma Mapping Project, Viet Nam, 2014.

We also sought to trim fieldwork time by not collecting household-level data on access to water and sanitation, which was routinely integrated within trachoma surveys in other GTMP sub-projects.^{20–26} Due to a paucity of cases of active trachoma, our graders did not undertake live subject inter-grader agreement exercises to qualify for survey deployment, but were instead assessed using a standard set of 50 conjunctival photographs. During the GTMP, Lao PDR²⁷ and Cambodia²⁸ circumvented a similar lack of local cases by sending trainee graders to Ethiopia for field training and certification, but this was not possible for Viet Nam. It is possible that this lack of live-subject testing makes our data less accurate. Finally, in most EUs, males were relatively under-represented in the sample of ≥ 50 -year-olds examined (Table 2). This is a source of potential bias that would tend to lead to overestimation of trichiasis prevalence (because trichiasis occurs more frequently in women than in men)²⁹; age- and gender-based standardization will have partially, but not completely, compensated. In all other respects, the usual quality assurance and quality control measures of the GTMP³⁰ were deployed, and within the limitations we have identified, we are confident of the strength of the data we present here.³¹

Notwithstanding the wide confidence intervals for the distribution shape parameter, the cluster-level distribution of TF cases was consistent with a geometric distribution. We expect to see this pattern when an

infectious disease is disappearing^{32,33}; it was not consistent with a Poisson distribution. Occasional higher prevalence communities are expected with a geometric distribution. These do not necessarily represent persistent outliers. Selecting a community in the tail of the geometric distribution with a high prevalence is a predictable event. These outliers do not necessarily have more transmission potential in the future, and may regress towards the mean on future visits. While a single cluster in Hà Giang Province had more than one in 10 children with TF, it may not necessarily be a focus of disease of public health significance. Nonetheless, further investigations will be undertaken in Hà Giang.

In the last few decades, Viet Nam has made huge progress against trachoma. Momentum was accelerated following national adoption of the SAFE strategy in the late 1990s. From 2000 to 2008, 83,830 surgeries for trichiasis were performed, more than 2.1 million azithromycin (Zithromax®, Pfizer, New York, NY) treatments were distributed to people in 850 endemic communes of 21 northern and central coastal provinces.³⁴ The F and E components of SAFE were also implemented. Evaluations completed in 2004 and 2005 concluded that (1) health promotion activities were excellent and implementation of water and sanitation improvement activities were underway³⁵ and (2) that F & E had significantly contributed to reductions in the prevalence of active trachoma.³⁶ National-level estimates for 2015 suggested

that 91% of households had access to drinking water within a 30 minute round-trip, while 81% of households had access to improved sanitation.³⁷

The data presented here suggest that Viet Nam is on track to meet GET2020 targets, and we recommend that the country now starts populating a dossier on trachoma's elimination as a public health problem.⁹ This dossier could serve as a valuable information repository whilst further work is undertaken to investigate (and, if necessary, manage) trachoma in Hà Giang and its surrounds. Members of the WHO Alliance for GET2020 are ready and willing to support.

Conflict of interest

None of the following authors have any proprietary interests or conflicts of interest related to this submission: Nguyen Xuan Hiep, Jeremiah M. Ngondi, Vu Tuan Anh, Tran Minh Dat, Cung Hong Son, Tran Van An, Nguyen Chi Dung, Nguyen Duy Thang, Brian K. Chu, Rebecca Willis, Ana Bakhtiari, Alexandre L. Pavluck, James Johnson, Joshua Sidwell, Molly Brady, Rob Henry, Aryc Mosher, Travis C. Porco, Thomas M. Lietman, Lisa Rotondo, Susan Lewallen, Paul Courtright, Anthony W. Solomon.

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