OPEN ACCESS

Can we eradicate trachoma? A survey of stakeholders

Catherine E Oldenburg ,[1,2] Solomon Aragie,[3] Abdou Amza,[4,5] Anthony W Solomon ,[6] Jessica Brogdon,[7] Benjamin F Arnold,[1,7] Jeremy D Keenan ,[1,2,7] Thomas M Lietman[1,2,7]

► Supplemental material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bjophthalmol-2020-315815).

[1]Department of Ophthalmology, University of California, San Francisco, California, USA
[2]Department of Epidemiology and Biostatistics, University of California, San Francisco, California, USA
[3]The Carter Center, Addis Ababa, Ethiopia
[4]Faculté Des Sciences De La Santé, Université Abdou Moumouni De Niamey, Niamey, Niger
[5]Programme National De Santé Oculaire, Niamey, Niger
[6]Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland
[7]F.I. Proctor Foundation, University of California, San Francisco, California, USA

Correspondence to
Catherine Oldenburg, 513 Parnassus Ave, Box 0412, San Francisco, CA 94143, USA; catherine.oldenburg@ucsf.edu

Received 3 January 2020
Revised 25 July 2020
Accepted 27 July 2020
Published Online First 27 August 2020

To cite: Oldenburg CE, Aragie S, Amza A, *et al*. *Br J Ophthalmol* 2021;**105**:1059–1062.

ABSTRACT

Background/Aims Although tremendous progress towards the 2020 goal of global elimination of trachoma as a public health problem has been made, it will not be achieved. Future targets are now being considered. One option is changing the goal to *eradication*. We surveyed trachoma experts to assess beliefs related to trachoma eradication and determine perceived obstacles to achieving it.

Methods We conducted a survey at the beginning of a trachoma eradication session at the 2019 Coalition for Operational Research on Neglected Tropical Diseases meeting in National Harbor, Maryland, USA. We asked respondents what the most important goal of azithromycin mass drug administration was for trachoma (control, elimination of infection or eradication) and if and when they believed trachoma eradication would occur. We then asked what the biggest obstacles were to global eradication.

Results Fifty-six surveys were returned (95%). Most (91%) participants reported that the most important goal of azithromycin mass drug administration was control or elimination of infection, and 24% of participants reported that global eradication was not possible. Of the 76% who reported a year by which they believed trachoma could be eradicated, most fell between 2040 and 2050. Commonly cited barriers to global eradication included lack of surveillance tools to confirm eradication or monitor for infection recrudescence (32%) and lack of resources (23%).

Conclusions Development of alternative indicators for trachoma surveillance and continued investment in trachoma programmes, particularly focused support in the most heavily affected populations, might increase enthusiasm for the feasibility of eradication.

INTRODUCTION

The WHO's current goal for the global trachoma programme is elimination as a public health problem by 2020.[1 2] The definition of elimination as a public health problem for trachoma is (1) reduction in prevalent of trachomatous inflammation—follicular (TF) in 1–9-year-olds to <5% in each formerly endemic evaluation unit (a rough equivalent of a health district); (2) reduction in prevalent of trachomatous trichiasis unknown to the health system in ≥15-year-olds to <0.2% in each formerly endemic evaluation unit; and (3) a system to identify and manage incident cases of TT. It is estimated that >150 *Chlamydia trachomatis* infections in a single eye are required to cause the conjunctival scarring-induced trichiasis that can lead to trachomatous blindness,[3] and that experiencing this number of infections would be an uncommon occurrence when the prevalent of TF is <5%. The previous restriction of our ambition for active trachoma to this target (TF prevalent <5%) therefore has some theoretical foundation, although specific targets were based on expert consensus.

In infectious diseases, *control* typically refers to reduction in incidence or prevalent to an acceptable level via specific public health intervention.[4] For control of an infectious disease to be maintained, ongoing public health intervention is required. Alternative goals for an infectious disease include *elimination*, defined as reduction in incidence of infection to zero in a defined geographic region, and *eradication*, defined as permanent reduction to zero worldwide.[4] Though it includes the word 'elimination', strictly speaking, 'elimination of trachoma as a public health problem' is a control goal. For trachoma, in some settings, control may not be sustainable in the absence of continued intervention, due to the potential for resurgence from even low levels of transmission.[5–8] In other settings, trachoma is disappearing and may continue to disappear even in the absence of ongoing intervention, leading to the hypothesis that some districts achieving control may have actually eliminated the pathogen.[9–14] Since the prevalent of inflammation tends to lag behind that of infection, districts that still have low levels of TF may have no transmission of ocular *C. trachomatis*.

Although once endemic, endogenous transmission of ocular *C. trachomatis* has not been observed in the United States or Europe for decades.[15] More recently, mass drug administration of azithromycin has been shown to dramatically reduce the prevalent of ocular *C. trachomatis* infection in endemic populations.[16–18] Local elimination of ocular chlamydial infection, and ultimately worldwide eradication of the organism, may therefore, at least hypothetically, be a reasonable goal.[19]

The neglected tropical diseases community is currently setting goals for 2021–2030. To better understand current attitudes regarding the feasibility of eradication trachoma, which would represent a first step towards considering a change in focus from control to eradication, we conducted a survey of trachoma experts and other stakeholders.

MATERIALS AND METHODS

This survey was conducted at the beginning of a breakout session discussing the possibility of trachoma eradication during the Coalition for Operational Research on Neglected Tropical

Diseases annual meeting, held in November 2019 in National Harbor, Maryland. The survey was administered prior to the start of the session. Participants had each specifically registered for the session and had had prior access to its agenda and were thus aware of the session topic. However, they had not seen the material to be presented, been sensitised to the planned discussion points, or been forewarned of this survey. The survey form was distributed prior to the session opening and completed anonymously by each willing session participant. The anonymous survey was reviewed and deemed exempt by the Institutional Review Board at the University of California, San Francisco. Based on composition of meeting attendees during prior years, we anticipated that participants would represent a range of expertise, from academic expertise in neglected tropical diseases generally and trachoma specifically to programmatic and policy expertise in trachoma control. We considered all attendees to be experts in some aspect of neglected tropical disease or trachoma, and we asked participants to report whether their work focused on research, programmes and/or policy.

Questions were adapted from those in a previous survey assessing the feasibility of elimination and eradication of a variety of neglected tropical diseases, including trachoma, using mass drug administration.[20] The 11 questions were tailored to focus on trachoma eradication (Supplemental Material). Participants were asked to think specifically about ocular *C. trachomatis* infection rather than TF (or other signs of active trachoma, such as trachomatous inflammation—intense, TI) when responding. Definitions of control, elimination, and eradication were based on those as defined by Dowdle (1999) which include both the definition and whether ongoing intervention is required once the infection reaches a particular defined state.[4] These definitions were printed at the top of the survey instrument and projected from a PowerPoint slide on a wall of the meeting room. The operational definition of global eradication used in the survey instrument was 'permanent reduction of infection to zero worldwide, not requiring any further intervention'. Local elimination was defined as 'reduction of infection to zero in a defined geographical area, requiring continued measures to prevent re-establishment of infection'. Control was defined as 'reduction of infection to an acceptable level, requiring continued intervention'. Participants were asked what they conceived the most important goal of azithromycin mass drug administration to be (control, elimination, eradication), when they thought global eradication would occur (or if they thought eradication was not possible), and what they believed were the biggest obstacles to global eradication.

Data were analysed descriptively using Stata version 15.1 (StataCorp, College Station, Texas, USA).

RESULTS

Of 59 surveys distributed, 56 (95%) were returned. Respondents included individuals working in research (34%), trachoma programme implementation (46%) or both (16%); 8% were involved in policymaking (respondents could select more than one work area and thus percentages do not total 100%). The majority (94%) of respondents reported that they undertook trachoma-related work in sub-Saharan Africa. Participants also undertook trachoma-related work in East/Southeast Asia (32%), North Africa/Middle East (21%), South Asia (19%), South America (17%) and Australia (11%). Approximately, half (56%) had a doctoral degree (MD and/or PhD or equivalent).

Most participants reported that the most important goal of azithromycin mass drug administration for trachoma was control (N=22, 41%) or local elimination (N=27, 50%), and 9% (N=5) reported that the most important goal was global eradication. When asked when global eradication would occur, 76% (N=42) of all respondents reported an estimated year (figure 1). The remaining 24% (N=13) reported that global eradication was not possible. Of those who indicated that global eradication was possible, 14% reported that it would occur before 2030, 40% by 2040, 21% by 2050, while 24% reported that it would take until 2060 or later.

The most frequently cited barriers to global eradication were a lack of appropriate surveillance tools to confirm interruption of transmission or monitor for subsequent re-emergence (32%) and lack of resources (23%). Other identified barriers included politics and war/insecurity (19%), antimicrobial resistance (15%), lack of community awareness/involvement (13%) and ineffective interventions (9%).

DISCUSSION

Most trachoma stakeholders surveyed did not believe that eradication of ocular *C. trachomatis* was the principal goal of azithromycin mass drug administration. However, approximately three-quarters of participants indicated, at least implicitly, that they believed that global eradication is feasible by providing a date by which they thought it could be achieved. These findings are not necessarily contradictory. The current goal of mass drug administration for trachoma is elimination as a public health problem, a control goal, and the fact that most respondents felt this was the primary goal of the current programme is in line with global policy.[21] Participants who believed that eradication was a possibility generally thought that it could happen between 2040 and 2050. Although eradication by 2030 is likely unrealistic, global elimination as a public health problem by 2030 (a change from the current 2020 goal) and global eradication by 2050 might be targets around which consensus could be built. Reduction in ocular *C. trachomatis* transmission to zero should be followed, after a delay, by a reduction to zero in the incidence of trachomatous trichiasis.

Although global elimination of trachoma as a public health problem will not be achieved by December 2020, trachoma programmes have made tremendous progress.[22] In many districts, the prevalent of trachoma is declining rapidly, in some areas even in the absence of active intervention.[9 23 24] The number of people living in districts worldwide in which the TF prevalent was ≥5% declined by 91% between 2002 and 2019.[25] That global

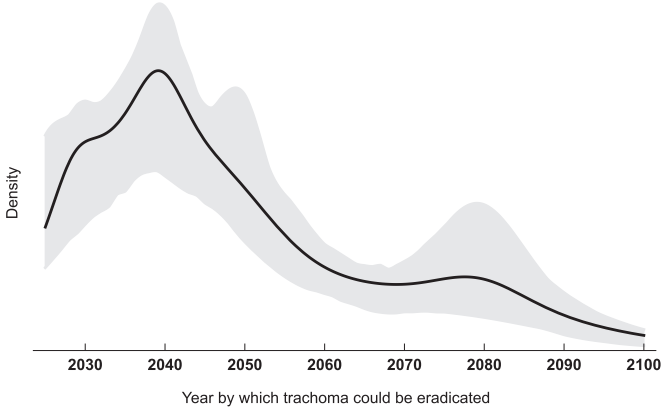

Figure 1 Density plot of estimates for year of achievement of trachoma eradication. Grey shaded area indicates 95% CI.

elimination as a public health problem will not be achieved by 2020 should not be taken as evidence that elimination as a public health problem or eradication are impossible—to the contrary, the current epidemiological evidence suggests that the targets set for elimination as a public health problem will be reached in all but a handful of districts in the next decade.[26] Refocusing efforts in remaining high-prevalent districts by intensifying interventions (which might include, eg, more frequent antibiotic distribution) could facilitate elimination and eventually global eradication.[27]

The likely barriers to global eradication of ocular *C. trachomatis* identified by participants are worth thinking through. First among these was inadequate surveillance systems. Because of a lack of validated tools to measure ocular *C. trachomatis* transmission intensity, programmes currently undertake surveillance by conducting serial population-based surveys in which prevalent of the clinical sign TF is the primary outcome measure.[28] Confirming eradication would potentially require far more intense surveillance with identification of individual cases of infection, as was done in the smallpox eradication programme.[29] Alternatively, smarter approaches may now be possible: serological markers of *C. trachomatis* exposure hold promise,[30 31] for example, but have not yet been used to monitor trachoma systematically and at scale. One shortcoming is that currently available serological tests cannot distinguish between exposure to genital and ocular *C. trachomatis* biovars, although this is less of an issue among children, who are considered the target population for serological surveillance for trachoma. Development of a test that could discriminate between these strains would represent a major advance. Second, a lack of financial resources to support an eradication goal was cited. Current district-level surveys cost a median of $8298 (IQR: $6532–$10 111, 2017 USD).[32] Surveys to support confirmation of eradication could be much more resource-intensive, since the required sample sizes would be likely to be considerably greater. This would hinder both implementation of interventions to interrupt transmission and subsequent ongoing surveillance to detect potential resurgence. Eradication would undoubtedly be more resource-intensive than control. Whether an eradication goal would be perceived as being too lofty and thus demotivating or a more sustainable solution that would galvanise the public health community is a question that can only be answered through wider discussion. Third, politics and insecurity are undoubtedly problematic. Political engagement and programmatic work have commenced, however, in some very challenging environments, including areas experiencing political instability and humanitarian crises; we are hopeful that this will continue. Fourth, taking measures to avoid worsening antimicrobial resistance is a global priority.[33] Evidence generated alongside azithromycin mass drug administration for trachoma to date has generally shown that mass azithromycin distribution selects for macrolide resistance, but that prevalent of resistant strains returns to baseline levels once antibiotic selection pressure is removed.[34] However, we agree that vigilance will be needed, regardless of the programmatic goal. Fifth, inadequate community engagement could threaten eradication, for example, if communities are suspicious of trachoma programme activities as has been observed in some communities in polio vaccination campaigns.[35]

Is deliberate identification and treatment of every last infection required for global eradication? In the United States and Europe, where trachoma was once endemic, there has been no evidence of endogenous transmission for decades.[36] Despite the absence of systematic surveillance, infection has disappeared. Ocular chlamydia transmission occurs slowly and once brought to a low level, re-establishment of infection may be difficult.[37] Instead, it is possible that it will disappear in the absence of specific intervention.[38] Demonstrating the possibility of this phenomenon at district-level (or larger) scale would be helpful to inform future policy debate. If identification and treatment of all infections were not required for trachoma eradication, costs associated with declaring eradication would be significantly lower.

This study had several limitations. It was conducted in a single session of a single operational research meeting and was unlikely to be representative of all trachoma experts, perhaps particularly excluding those not involved in operational research. The COR-NTD meeting involves diverse expertise ranging from academic scientists to trachoma programme managers. While individuals with different expertise may have different understandings of and experience with definitions used for infectious disease control, elimination, and eradication, responses to this survey also reflect those of individuals on the ground implementing trachoma programmes. The location of the meeting may also have led to under-representation of experts who are nationals of countries where trachoma is endemic, as securing a visa can be an obstacle to conference attendance,[39] and flights and accommodation can be prohibitively expensive. Although we asked participants where the bulk of their trachoma work was conducted, we did not ask about where they were based. Trachoma programmes typically refer to 'elimination as a public health problem' as the end-goal for trachoma control, which refers to disease- and service-related targets, not true elimination of infection. Participants who are used to seeing 'elimination' used to refer to trachoma control may have confused the definitions used in this survey. We did not verify if participants were using the definitions of eradication printed on the survey itself and projected on the meeting room wall. However, the primary goal of the survey was to understand perceptions related to eradication of infection, not elimination. Finally, the survey was administered during a session on trachoma eradication. Attendees presumably had some enthusiasm for the topic, with 'trachoma eradication' naysayers potentially staying away.

Although most trachoma experts surveyed here did not report that global eradication was the rationale for azithromycin mass drug administration, most reported a date by which they believed trachoma would be globally eradicated. Continued investment in trachoma control efforts, coupled with identification of new ways to assess transmission and development of more effective interventions, could strengthen support for adopting a formal eradication goal.

Twitter Anthony W. Solomon @anthonywsolomon and Catherine E. Oldenburg @CatieOldenburg.

Contributors CO, TML: study design, acquisition of data, interpretation of data, drafting article. SA, AWS, JB, BFA, JDK: study design, acquisition of data, interpretation of data, critical revision of article. AA: study design, interpretation of data, critical revision of article.

Funding CO was supported by a Research to Prevent Blindness Career Development Award (no award number).

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iDs
Catherine E Oldenburg http://orcid.org/0000-0002-0763-399X
Anthony W Solomon http://orcid.org/0000-0001-7101-6649
Jeremy D Keenan http://orcid.org/0000-0002-7118-1457

REFERENCES

1 World Health Organization. *Future approaches to trachoma control: report of a global scientific meeting, Geneva, 17–20 June 1996*. Geneva, 1997.
2 World Health Organization. *Accelerating work to overcome the global impact of neglected tropical diseases: a roadmap for intervention (WHO/HTM/NTD/2012.1)*. Geneva, 2012.
3 Gambhir M, Basáñez M-G, Burton MJ, *et al.* The development of an age-structured model for trachoma transmission dynamics, pathogenesis and control. *PLoS Negl Trop Dis* 2009;3:e462–8.
4 Dowdle WR. The principles of disease elimination and eradication. *MMWR Recomm Rep* 1999;48:23–7.
5 Lakew T, House J, Hong KC, *et al.* Reduction and return of infectious trachoma in severely affected communities in Ethiopia. *PLoS Negl Trop Dis* 2009;3:e376–7.
6 Keenan JD, Tadesse Z, Gebresillasie S, *et al.* Mass azithromycin distribution for hyperendemic trachoma following a cluster-randomized trial: a continuation study of randomly re-assigned subclusters (TANA II). *PLoS Med* 2018;15:e1002633.
7 Nash SD, Stewart AEP, Zerihun M, *et al.* Ocular chlamydia trachomatis infection under the surgery, antibiotics, facial cleanliness, and environmental improvement strategy in Amhara, Ethiopia, 2011–2015. *Clin Infect Dis* 2018;10:e0005080–7.
8 Stewart A, Zerihun M, Gessese D, *et al.* Progress to eliminate trachoma as a public health problem in Amhara National Regional State, Ethiopia: results of 152 population-based surveys. *Am J Trop Med Hyg* 2019;101:1286–95.
9 Pant P, Bhatta R, Chaudhary J, *et al.* Control of trachoma from Achham district, Nepal: a cross-sectional study from the Nepal National trachoma program. *PLoS Negl Trop Dis* 2016;10:e0004462.
10 Jha H, Chaduary JSP, Bhatta R, *et al.* Disappearance of trachoma from Western Nepal. *Clin Infect Dis* 2002;35:765–8.
11 West SK, Zambrano AI, Sharma S, *et al.* Surveillance surveys for reemergent trachoma in formerly endemic districts in Nepal from 2 to 10 years after mass drug administration cessation. *JAMA Ophthalmol* 2017;135:1141–6.
12 Senyonjo LG, Debrah O, Martin DL, *et al.* Serological and PCR-based markers of ocular chlamydia trachomatis transmission in northern Ghana after elimination of trachoma as a public health problem. *PLoS Negl Trop Dis* 2018;12:1–16.
13 Biebesheimer JB, House J, Hong KC, *et al.* Complete local elimination of infectious trachoma from severely affected communities after six biannual mass azithromycin distributions. *Ophthalmology* 2009;116:2047–50.
14 Baral K, Osaki S, Shreshta B, *et al.* Reliability of clinical diagnosis in identifying infectious trachoma in a low-prevalence area of Nepal. *Bull World Health Organ* 1999;77:461–6.
15 Thygeson P. Epidemiologic observations on trachoma in the United States. *Invest Ophthalmol Vis Sci* 1963;2:482–9.
16 Solomon AW, Holland MJ, Alexander NDE, *et al.* Mass treatment with single-dose azithromycin for trachoma. *N Engl J Med* 2004;351:1962–71.
17 Chidambaram JD, Alemayehu W, Melese M, *et al.* Effect of a single mass antibiotic distribution on the prevalence of infectious trachoma. *JAMA* 2006;295:1142–6.
18 Solomon AW, Harding-Esch EM, Alexander NDE, *et al.* Two doses of azithromycin to eliminate trachoma in a tanzanian community. *N Engl J Med* 2008;358:1870–1.
19 Lietman TM, Oldenburg CE, Keenan JD. Trachoma: time to talk eradication. *Ophthalmology* 2019.
20 Keenan JD, Hotez PJ, Amza A, *et al.* Elimination and eradication of neglected tropical diseases with mass drug administrations: a survey of experts. *PLoS Negl Trop Dis* 2013;7:e2562.
21 World Health Assembly. *Global elimination of blinding trachoma*. Switzerland: Geneva, 1998.
22 Burki T. Trachoma: great gains, but elimination target missed. *Lancet Infect Dis* 2019;19:815.
23 Harding-esch EM, Edwards T, Sillah A, *et al.* Active trachoma and ocular chlamydia trachomatis infection in two gambian regions : on course for elimination by 2020? *PLoS Negl Trop Dis* 2009;3:e573.
24 Mpyet C, Goyol M, Ogoshi C. Personal and environmental risk factors for active trachoma in children in Yobe state, north-eastern Nigeria. *Trop Med Int Heal* 2010;15:168–72.
25 World Health Organization. WHO alliance for the global elimination of trachoma by 2020: progress report on elimination of trachoma, 2018. *Wkly Epidemiol Rec* 2019;29:317–28.
26 Cama A, Keenan JD, Dejene M, *et al.* Impact of the global trachoma mapping project. *Ophthalmic Epidemiol* 2018;25:1–2.
27 House JI, Ayele B, Porco TC, *et al.* Assessment of herd protection against trachoma due to repeated mass antibiotic distributions: a cluster-randomised trial. *Lancet* 2009;373:1111–18.
28 Nash SD, Stewart AEP, Astale T, *et al.* Trachoma prevalence remains below threshold in five districts after stopping mass drug administration: results of five surveillance surveys within a hyperendemic setting in Amhara, Ethiopia. *Trans R Soc Trop Med Hyg* 2018;112:538–45.
29 Henderson DA. Principles and lessons from the smallpox eradication programme. *Bull World Health Organ* 1988;65:535–46.
30 Pinsent A, Solomon AW, Bailey RL, *et al.* The utility of serology for elimination surveillance of trachoma. *Nat Commun* 2018;9:25–8.
31 Goodhew EB, Priest JW, Moss DM, *et al.* CT694 and pgp3 as serological tools for monitoring trachoma programs. *PLoS Negl Trop Dis* 2012;6:e1873–10.
32 Stelmach RD, Flueckiger RM, Shutt J, *et al.* The costs of monitoring trachoma elimination: impact, surveillance, and trachomatous trichiasis (TT)-only surveys. *PLoS Negl Trop Dis* 2019;13:e0007605.
33 Interagency Coordination Group on Antimicrobial Resistance. No time to wait: Securing the future from drug-resistant infections. Report to the secretary-general of the United Nations, April 2019. Geneva, 2019.
34 O'Brien K, Emerson P, Hooper PJ, *et al.* Antimicrobial resistance following mass azithromycin distribution for trachoma: a systematic review. *Lancet Infect Dis* 2018; S1437–3099:30444–4.
35 Usman S, Bologna L, Stamidis KV. The CORE Group partners project in North East Nigeria: community engagement strategies to combat skepticism and build trust for vaccine acceptance. *Am J Trop Med Hyg* 2019;101:68–73.
36 Allen SK, Semba RD, Trachoma T. "Menace" in the United States,1897–1960. *Surv Ophthalmol* 2002;47:500–9.
37 Lietman TM, Gebre T, Ayele B, *et al.* The epidemiological dynamics of infectious trachoma may facilitate elimination. *Epidemics* 2011;3:119–24.
38 Chidambaram JD, Lee DC, Porco TC, *et al.* Mass antibiotics for trachoma and the allee effect. *Lancet Infect Dis* 2005;5:194–6.
39 Hawkes N. British competitiveness at risk from visa system that rejects conference delegates, warn scientists. 2018;363:4779.