

Institution: London School of Hygiene & Tropical Medicine		
Unit of Assessment: 1		
Title of case study: Eliminating trachoma via azithromycin		
Period when the underpinning research was undertaken: 2000-2000		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): David Mabey Anthony Solomon Robin Bailey Emma Harding-Esch Allen Foster Hannah Kuper Matthew Burton & associated research groups	Role(s) (e.g. job title): Professor PhD; Clinical Lecturer; Clinical Senior Lecturer Professor Assistant Professor; Associate Professor Professor Associate Professor; Professor Clinical Associate Professor; Clinical Professor	Period(s) employed: 21/10/86-current 1/1/99-9/4/14 29/05/94-current 12/9/05-31/1/12; 20/11/17-current 1/1/99-current 1/5/02-current 1/5/07-current
Period when the claimed impact occurred: 2013-2020		
Is this case study continued from a case study submitted in 2014? No		
1. Summary of the impact (indicative maximum 100 words)		
<p>LSHTM-led research found that mass treatment with a single oral dose of the antibiotic azithromycin can eliminate trachoma, a significant cause of blindness, from affected communities. As a result, the manufacturer agreed to donate azithromycin for trachoma control. More than 900 million doses of azithromycin have been donated, 397 million of which were given since 2013. The World Health Organization (WHO) estimates that the number of people at risk of trachoma was reduced by 91% between 2002 and 2020. Since 2013, 10 countries (from Africa, the Americas, Asia and the Middle East) eliminated trachoma as a public health problem with WHO validation, and a further four reported meeting elimination targets.</p>		
2. Underpinning research (indicative maximum 500 words)		
<p>Trachoma, an eye disease caused by <i>Chlamydia trachomatis</i>, is the leading infectious cause of blindness worldwide. It afflicts the world's poorest people, particularly in Africa, with disastrous consequences for affected individuals and communities, frequently compounding health problems and poverty. Prevention of blindness from trachoma is a major public health priority internationally. Multidisciplinary research at LSHTM within the Trachoma Research Group focused on clinical trials to improve the management and treatment of trachoma, the immunopathogenesis of the disease process, its socioeconomic impact, and the benefits of antibiotic treatment for other diseases.</p>		
Pre-REF background		
<p>Previous work by Mabey and Bailey at LSHTM in 1993 showed that a single oral dose of azithromycin was as effective at treating trachoma as applying ointment to both eyes twice a day for 6 weeks. This led to Pfizer agreeing to donate azithromycin for trachoma control and elimination in 1998.</p>		
Research from 2000 onwards		
<p>Solomon (LSHTM between 1999 and 2014, now WHO, leading trachoma elimination programme) and colleagues built on Bailey and Mabey's research and eliminated ocular <i>Chlamydia trachomatis</i> infection from a trachoma endemic village in Tanzania with a single round of mass treatment in 2000, with no infections in the village 5 years later (3.1). Burton found a similar effect in The Gambia from a single dose in 2004, but also identified how people moving across borders led to the infection being reintroduced following mass treatment (3.2). The Trachoma Research Group, and Gambian partners led by the national trachoma programme manager Ansumana Sillah, subsequently eliminated ocular <i>C. trachomatis</i> infection from two regions in The Gambia (3.3).</p>		

In 2002, researchers at LSHTM were funded by the International Trachoma Initiative (ITI) to evaluate and monitor trachoma control programmes in 8 countries. This resulted in a systematic review in 2013 of the evidence underlying the WHO-endorsed Surgery, Antibiotics, Facial Cleanliness and Environmental improvement (SAFE) strategy for trachoma control. The review found strong support for the efficacy of surgery and antibiotics, and weaker evidence for the effect of health education and environmental improvement.

Funded by the Bill & Melinda Gates Foundation, trachoma researchers at LSHTM set up the Partnership for the Rapid Elimination of Trachoma in 2008, in collaboration with colleagues at Johns Hopkins University and the University of California. The Partnership implemented a randomised, 2x2 factorial design trial in The Gambia, Tanzania and Niger to compare the impact and cost-effectiveness of different strategies for the administration of azithromycin. The trials demonstrated that in communities where there was low prevalence of trachoma, it was more cost-effective to use a test for *C. trachomatis* infection to decide when to stop mass drug administration than to follow WHO recommendations, which were based on clinical signs (3.4).

The group at LSHTM led the largest infectious disease mapping project ever undertaken, between 2012 and 2016. The Global Trachoma Mapping Project (GTMP), in collaboration with Sightsavers, mapped the global prevalence of trachoma. More than 550 teams of trained surveyors, including ophthalmic nurses, carried out visits and examined approximately 2.6 million people for trachoma in 1,546 districts in 34 countries. The project, led by Solomon as Chief Scientist and Mabey, aimed to gather information on the scale of trachoma as a public health problem and to determine priority areas for intervention and evaluation (3.5). The project was funded by the UK government and managed by Sightsavers, and was a partnership of more than 53 organisations, including LSHTM, 30 ministries of health, the International Trachoma Initiative, WHO, and over 20 eye health NGOs. The team collected all data electronically, using Android smartphones. Tropical Data, led by Harding-Esch, has continued the work of the GTMP since 2016. This service supported surveys in over 1,419 evaluation units across 39 countries, representing over 90% of all data reported during that period to the WHO Alliance for the Global Elimination of Trachoma by 2020 (GET2020) database.

Azithromycin can also be used to treat a number of other bacterial infections, including ear infections, strep throat, pneumonia, and intestinal infections. Given its experience with azithromycin, LSHTM was awarded funding by the Gates Foundation to study the impact of twice-yearly mass treatment on all-cause mortality in children aged under 5 years in Niger, Tanzania and Malawi in 2018. Mass treatment with azithromycin led to a 13% reduction in under 5 mortality overall, and a 25% reduction in mortality of infants aged 1 to 6 months (3.6).

3. References to the research (indicative maximum of six references)

3.1 Solomon AW, Holland MJ, Alexander NDE, Massae PA, Aguirre A, Natividad-Sancho A, Molina S, Safari S, Shao JF, Courtright P, Peeling RW, West SK, Bailey RL, Foster A and Mabey DCW. 2004. Mass treatment with single-dose azithromycin for trachoma. *New England Journal of Medicine*, 351(19): 1962–1971, doi:[10.1056/NEJMoa040979](https://doi.org/10.1056/NEJMoa040979).

3.2 Burton MJ, Holland MJ, Makalo P, Aryee EAN, Alexander NDE, Sillah A, Faal H, West SK, Foster A, Johnson GJ, Mabey DCW and Bailey RL. 2005. Re-emergence of Chlamydia trachomatis infection after mass antibiotic treatment of a trachoma-endemic Gambian community: a longitudinal study. *Lancet*. 365(9467): 1321–1328, doi:[10.1016/S0140-6736\(05\)61029-X](https://doi.org/10.1016/S0140-6736(05)61029-X).

3.3 Harding-Esch EM, Edwards T, Sillah A, Sarr I, Roberts CH, Snell P, Aryee E, Molina S, Holland MJ, Mabey DCW and Bailey RL. 2009. Active trachoma and ocular Chlamydia trachomatis infection in two Gambian regions: on course for elimination by 2020? *PLoS Neglected Tropical Diseases*, 3(12): e573, doi:[10.1371/journal.pntd.0000573](https://doi.org/10.1371/journal.pntd.0000573).

3.4 Ray KJ, Lietman TM, Porco TC, Keenan JD, Bailey RL, Solomon AW, Burton MJ, Harding-Esch E, Holland MJ, Mabey D. 2009. When can antibiotic treatments for trachoma be

discontinued? Graduating communities in three African countries. *PLoS Neglected Tropical Diseases*. 16;3(6):e458. doi: [10.1371/journal.pntd.0000458](https://doi.org/10.1371/journal.pntd.0000458).

3.5 Solomon AW, Puvluck AL, Courtright P, Abore A, Adamu L, Alemayehu W, Alemu M, **Alexander NDE**, Kello AB, Bero B, **Brooker SJ**, Chu BK, Dejene M, Emerson P, Flueckiger EM, Gadisa S, Gass K, Gebre T, Habtumu Z, Harvey E, Haslam D, King J, Le Mesurier R, Lewallen S, Lietman TM, MacArthur C, Mariotti SP, Massey A, Mathieu E, Mekasha A, Millar T, Mpyet C, Munoz BE, Ngondi J, Ogden S, Pearce J, Sarah V, Sisay A, Smith JL, Taylor HR, Thomson J, West SK, Willis R, Bush S, Haddad D, **Foster A**. 2015. The Global Trachoma Mapping Project: Methodology of a 34-Country Population-Based Study. *Ophthalmic Epidemiology*. 22(3):214-25. doi: [10.3109/09286586.2015.1037401](https://doi.org/10.3109/09286586.2015.1037401).

3.6 Keenan JD, **Bailey RL**, West SK, Arzika AM, Hart J, Weaver J, Kalua K, Mrango Z, Ray KJ, Cook C, Lebas E, O'Brien KS, Emerson PM, Porco TC, Lietman TM; MORDOR Study Group. 2018. Azithromycin to Reduce Childhood Mortality in Sub-Saharan Africa. *New England Journal of Medicine*. 6;378(17):1583-1592. doi: [10.1056/NEJMoa1715474](https://doi.org/10.1056/NEJMoa1715474).

We believe this body of research meets the 'at least 2*' definition given its reach, significance and rigour.

4. Details of the impact (indicative maximum 750 words)

LSHTM research into the impact of azithromycin, and the global mapping of trachoma, was life-changing for millions of people in trachoma-affected communities. It also accelerated progress towards global elimination of trachoma. Although the December 2020 target for Global Elimination of Trachoma as a public health problem 2020 (GET2020) was not met and the target has been reset to 2030, considerable steps towards elimination have been achieved, underpinned by LSHTM-generated evidence and data.

The LSHTM team presented annually (both before and after 2013) at the WHO-hosted meeting of partners in the WHO Alliance for GET2020 to ensure research findings were translated into policy and practice, nationally and internationally (5.1). This annual meeting was routinely attended by national trachoma control programme managers from all currently or formerly endemic countries, and by the major NGOs involved in control of trachoma.

Treatment and elimination

Through the vast reach of the Global Trachoma Mapping Project (GTMP) and Tropical Data, and underpinned by LSHTM research demonstrating efficacy, optimal administration, and cost-effectiveness, Pfizer has shipped approximately 397 million azithromycin doses to national trachoma control programmes since 2013 (5.2). Year on year, these programmes scaled up considerably, with LSHTM expertise continuously involved via leadership (Solomon, Bailey, Foster), technical support for resource provision, and advocacy.

According to WHO estimates, 95.2 million people were given antibiotics for treatment of trachoma in 2019 alone (5.3), demonstrating the sustained impact of the research. WHO also estimates that the number of people at risk of trachoma has gone down from 1.5 billion in 2002 to 137 million in 2020, a reduction of 91%, and the number of people requiring surgery for trachomatous trichiasis has been reduced from 7.6 million in 2002 to 2 million in 2020, a drop of 74% (5.4).

Since 2013 and as of July 2020, 12 countries reported achieving the GET2020 elimination goals: Cambodia, China, Ghana, The Gambia, Islamic Republic of Iran, Iraq, Lao People's Democratic Republic, Mexico, Morocco, Myanmar, Nepal, and Togo. 8 of these (Cambodia, China, Islamic Republic of Iran, Lao People's Democratic Republic, Ghana, Mexico, Morocco, and Nepal) have been validated by WHO as having eliminated trachoma as a public health problem (5.4).

A guide for programme managers on trachoma control, published jointly in 2006 by WHO, LSHTM and the International Trachoma Initiative and co-authored by Solomon, Kuper, Mabey and Foster,

was downloaded over 7,000 times between 2016 and 2020 (5.5), demonstrating the guide is still useful at a local level over a decade later.

After findings demonstrated that twice-yearly treatment of azithromycin could significantly reduce under-5 mortality, the WHO issued recommendations in 2020 suggesting mass treatment of children aged 1 to 11 months with azithromycin should be considered in sub-Saharan African settings where under 5 mortality was more than 80 per 1000. These recommendations were underpinned by LSHTM's evidence and several LSHTM staff served as experts to the consultation in March 2018 (5.6).

In 2014, Mabey was appointed as a Commander of the British Empire for services to health development in Africa and Asia. In 2019, he received the Prince Mahidol Award in the field of Public Health for his work on trachoma in Africa (5.7).

Allocation of resources

Information produced by the GTMP helped to guide implementation of azithromycin and surgical treatment. The GTMP mapped areas where no data previously existed, due to remoteness, insecurity, or competing public health priorities. As a result, it revealed that interventions would be required to eliminate trachoma for 100 million people living in areas previously categorised as 'suspected endemic'. Up to 1,100 local surveyors and analysts were trained to carry out disease mapping, and open access disease maps were made available via the online 'Trachoma Atlas'. These findings doubled the population known to need action against trachoma, resulting in a global at-risk population of 200 million people, and completed the global baseline trachoma map.

For example, on the basis of GTMP data, approximately 38% of the total population at risk were found to live in Ethiopia, which had one of the highest trachoma prevalence rates in the world. Ethiopia's Federal Minister for Health announced the 'Fast Track Initiative' in 2014 to clear the estimated backlog of more than 700,000 who needed trichiasis surgery. The country trained over 1,000 Integrated Eye Care Workers to perform surgery and 17,000 health extension workers to identify and refer trichiasis cases, and set up 50 mobile surgical teams. Ethiopia implemented this initiative nationwide and committed USD1.7million of government money. In 2016 it achieved 84% coverage of endemic districts with surgery and antibiotics (5.8).

Since February 2016, Tropical Data has supported more than 1500 surveys across 41 countries, examining 5 million people. In the Tropical Data consortium of scientific, technological and implementing partners which built on the methodologies developed and implemented by the GTMP, LSHTM provided scientific oversight (Harding-Esch as Chief Scientist), the International Trachoma Initiative provided the core data management service, RTI International managed the system technology, Sightsavers provided project management, documentation, budgeting and training packages, and the WHO set standards and protected country interests. The work of Tropical Data has allowed 109,511,552 treatments to be donated to support mass drug administration (MDA), confirmed that MDA could be stopped in 485 Evaluation Units (EUs), confirmed that MDA was not needed in 220 EUs, and helped countries confirm completion of pre-validation surveillance in 264 EUs (5.9).

5. Sources to corroborate the impact (indicative maximum of 10 references)

5.1 World Health Organization, Department of Control of Neglected Tropical Diseases. Report of the 18th meeting of the WHO Alliance for the Global Elimination of Trachoma by 2020. Addis Ababa, 28-29 April 2014.

World Health Organization, Department of Control of Neglected Tropical Diseases. Report of the 19th meeting of the WHO alliance for the Global Elimination of Trachoma by 2020. Hammamet, Tunisia, 27-29 April 2015.

- Lists participants from LSHTM: Bailey, Brooker, Burton, Last, Flueckiger, Mabey. (Flueckiger presentation)

World Health Organization Strategic and Technical Advisory Group on Neglected Tropical Diseases. Technical consultation on trachoma surveillance. Task Force for Global Health, 11–12

September 2014, Decatur (GA), USA (WHO/HTM/ NTD/2015.02). Geneva: World Health Organization; 2015.

- Lists participants from LSHTM: Alexander, Bailey, Burton, Flueckiger

5.2 Total doses of Zithromax shipped to trachoma elimination programmes 1999-2018, source Trachoma Elimination Programme. Accessed at:

https://www.trachomacoalition.org/sites/default/files/content/resources/files/zithromax_Final.pdf

5.3 World Health Organization. Trachoma key facts. Accessed at:

<https://www.who.int/news-room/fact-sheets/detail/trachoma#:~:text=Key%20facts,Blindness%20from%20trachoma%20is%20irreversible.>

5.4 World Health Organization Alliance for the Global Elimination of Trachoma by 2020, GET2020 database as of 17 April 2018. Overview epidemiology.

Accessed at:

https://www.trachomacoalition.org/sites/default/files/content/resources/files/GET2020_2018_Global_Final.pdf

- Shows elimination status of countries and countries validated as having eliminated trachoma

World Health Organization. Weekly epidemiological record. 24 July 2020. No 30, 2020, 95, 349-360. WHO Alliance for the Global Elimination of Trachoma by 2020: progress report 2019.

- Lists countries achieving elimination by July 2020 and progress towards trachoma elimination
- Details implementation of the SAFE strategy 2019

5.5 Solomon AW, et al. Trachoma control: a guide for programme managers. Geneva: World Health Organization; 2006.

- Download information accessed at https://apps.who.int/iris/handle/10665/43405?search-result=true&query=Trachoma+control%3A+a+guide+for+programme+managers&scope=&rpp=10&sort_by=score&order=desc
- Downloaded 7,563 times from 2016 to August 2020 (statistics available only from 2016)

5.6 WHO guideline on mass drug administration of azithromycin to children under five years of age to promote child survival. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.

- Reference 4, pg vii. Bailey, Kirkwood, Greenwood and Smith expert advisors

5.7 The Queen's Birthday Honours 2014: the Prime Minister's List.

- Professor David Mabey awarded CBE for services to International Health Development in Africa and Asia (pg 15)

Professor David Mabey wins Prince Mahidol Award announcement, accessed at: <http://www.princemahidolaward.org/people/professor-david-mabey/>

5.8 World Health Organization. Alliance for the Global Elimination of trachoma by 2020. Eliminating trachoma: accelerating towards 2020. 2016 roadmap, accessed at: <https://www.trachomacoalition.org/2016-roadmap/>

- Details of Ethiopia's progress in tackling trachoma under the Trachoma Mapping Project

5.9 tropicaldata.org

- FAQs at the bottom show roles of different organisations

Sightsavers, accessed at: <https://www.sightsavers.org/programmes/mhealth/tropical-data/>

Gives information on numbers treated and countries taking part