

Impact case study (REF3b)

<p>Institution: London School of Hygiene & Tropical Medicine (LSHTM)</p>
<p>Unit of Assessment: UoA2 – Public Health, Health Services & Primary Care</p>
<p>Title of case study: Supporting decision-making on the introduction of <i>Haemophilus influenzae</i> type b (Hib) vaccine in low- and middle-income countries</p>
<p>1. Summary of the impact Research at LSHTM has been central to the introduction of the Hib vaccine in developing countries. School staff were involved in the 1990s Gambia Hib vaccine trial, which demonstrated the impact of Hib vaccine on pneumonia. Through their work on the subsequent Hib Initiative, their research was instrumental in speeding up evidence-based decision-making for Hib vaccine introduction in a number of countries, mainly in Asia and Africa. The project has been an outstanding success, with Hib vaccine now introduced into 71 of the 73 countries eligible for GAVI Alliance support.</p> <p>2. Underpinning research In 2008 Hib was the third biggest cause of vaccine-preventable deaths in children under 5 years. Hib vaccine, first licensed in the US in 1990, was introduced into routine vaccination schedules in most high-income countries within a few years, leading to the elimination of invasive Hib disease in those countries. However, the use of Hib vaccine in developing countries remained low due to high cost and uncertain disease burden.</p> <p>A team at LSHTM has focused a substantial programme of research on supporting decision-making for Hib vaccine introduction. Between 1993 and 1996, a large trial in The Gambia demonstrated the efficacy of the vaccine for the prevention of Hib invasive disease and pneumonia in Africa for the first time.^{3.1} LSHTM staff members at that time (Peter Smith, Professor of Tropical Epidemiology, at LSHTM since 1979, and Shabbar Jaffar, now Professor of Epidemiology, at LSHTM since 1996, then Lecturer) were involved in the design, oversight and analysis of the trial, which was led by Professors Kim Mulholland and Sir Brian Greenwood, both of whom later joined LSHTM (in 2005 and 1996, respectively). However, by 2000, only one sub-Saharan African country (The Gambia) had introduced Hib vaccine.</p> <p>The GAVI Alliance, a private-public global health partnership, was set up in 2000 to increase access to immunisation in poor countries. Initially, it offered Hib vaccine free of charge to eligible countries for five years. However, by early 2005, only 14 countries had made use of this offer due to lack of awareness and concerns about financial sustainability. In response, the GAVI Alliance invited proposals for a project aiming to accelerate the use of evidence-informed decision-making about Hib vaccine. In late 2005, Kim Mulholland (by then Professor of Child Health and Vaccinology at LSHTM) secured the US\$37m project in partnership with Johns Hopkins University, with WHO and US Centers for Disease Control (CDC) as collaborators.</p> <p>Within the Hib Initiative consortium, LSHTM was responsible for epidemiological studies (lead, Kim Mulholland; also Karen Edmond, LSHTM 2002-12, initially Research Fellow), health economics (lead, Ulla Griffiths, LSHTM Lecturer since 2006) and mathematical modelling (Andrew Clark, LSHTM Research Fellow since 2002). The group developed epidemiological methods for determining the effectiveness of Hib vaccine.^{3.2} It contributed to estimating the global burden of Hib disease,^{3.3.3.4} showing that Hib caused 371,000 deaths in children under 5 each year, and that the substantial disease burden caused by Hib is almost entirely vaccine-preventable.^{3.3} The group also showed that Hib conjugate vaccine is cost saving or highly cost effective in low- and middle-income countries.^{3.5} In addition, starting in 2007, a number of country-specific studies were undertaken in Mozambique, Ethiopia, Pakistan, Bangladesh, Vietnam, Belarus and Uzbekistan, all with a view to aiding decision-making on introducing the vaccine.^{3.6} The project supported countries through the various stages of decision-making and vaccine introduction. The Hib Initiative Project will wind up at the end of 2013.</p>

3. References to the research

3.1 Mulholland, K, Hilton, S, Adegbola, R, Usen, S, Oparaugo, A, Omosigho, C, Weber, M, Palmer, A, Schneider, G, Jobe, K, Lahai, G, Jaffar, S, Secka, O, Lin, K, Ethevenaux, C and Greenwood, B (1997) Randomised trial of *Haemophilus influenzae* type-b tetanus protein conjugate vaccine for prevention of pneumonia and meningitis in Gambian infants, *Lancet*, 349(9060): 1191–1197, doi:10.1016/S0140-6736(96)09267-7. Citation count: 281

3.2 O'Loughlin, RE, Edmond, K, Mangtani, P, Cohen, AL, Shetty, S, Hajjeh, R and Mulholland, K (2010) Methodology and measurement of the effectiveness of *Haemophilus influenzae* type b vaccine: systematic review, *Vaccine*, 28(38): 6128–6136, doi:10.1016/j.vaccine.2010.06.107. Citation count: 9

3.3 Watt, JP, Wolfson, LJ, O'Brien, KL, Henkle, E, Deloria-Knoll, M, McCall, N, Lee, E, Levine, OS, Hajjeh, R, Mulholland, K and Cherian, T for the Hib and Pneumococcal Global Burden of Disease Study Team (2009) Burden of disease caused by *Haemophilus influenzae* type b in children younger than 5 years: global estimates, *Lancet*, 374(9693): 903–911, doi:10.1016/S0140-6736(09)61203-4. Citation count: 121

3.4 Edmond, K, Clark, A, Korczak, VS, Sanderson, C, Griffiths, UK and Rudan, I (2010) Global and regional risk of disabling sequelae from bacterial meningitis: a systematic review and meta-analysis, *Lancet Infectious Diseases*, 10(5): 317–328, doi:10.1016/S1473-3099(10)70048-7. Citation count: 57

3.5 Griffiths, UK, Clark, A and Hajjeh, R (2013) Cost-effectiveness of *Haemophilus influenzae* type b conjugate vaccine in low- and middle-income countries: regional analysis and assessment of major determinants, *Journal of Paediatrics*, 163(1) (Suppl.): S50–S59.e9, doi:10.1016/j.jpeds.2013.03.031. Citation count: 0

3.6 Griffiths, UK, Clark, A, Shimanovich, V, Glinskaya, I, Tursunova, D, Kim, L, Mosina, L, Hajjeh, R and Edmond, K (2011) Comparative economic evaluation of *Haemophilus influenzae* type b vaccination in Belarus and Uzbekistan, *PLoS One*, 6(6): e21472, doi:10.1371/journal.pone.0021472. Citation count: 2

4. Details of the impact

The research carried out by the LSHTM team as part of the Hib Initiative directly contributed to a large number of low- and middle-income countries deciding to introduce the vaccine, reducing their paediatric death and disease burden very significantly.

The research LSHTM did within the Hib Initiative allowed health ministries in developing countries to establish the disease burden of Hib and make evidence-based arguments in favour of introducing a suitable vaccine. The resulting figures show the very significant rise in Hib vaccine take-up. While in 2005, only 91 out of 193 WHO member states (47%) were using Hib vaccine, this number had risen to 163 out of 193 (84%) by 2010.^{5.1} The greatest increase occurred in GAVI-eligible countries, with an increase from 24 (33%) in 2007 to 71 (97%) out of 73 countries by June 2013. In India and Nigeria, Hib vaccine is used only regionally.

According to the 2013 WHO report on GAVI progress, 153m children were vaccinated with Hib through GAVI support during 2000–2012, which has prevented approximately 658,000 deaths.^{5.2} Deaths prevented in GAVI countries during the period 2008–2013 are estimated as 509,000.^{5.2} In 2011, the GAVI Alliance committed to vaccinating a further 224m children with Hib vaccine by 2015.

The example of Mozambique (which introduced the vaccine in 2009 following a country-specific study supported by the LSHTM team to aid decision-making) impressively illustrates the impact of Hib vaccine adoption on a country's death and disease burden in a rural high-HIV epidemic area. Among children under 1 and under 5, significant reductions occurred in rates of invasive Hib disease (91% and 85%, respectively) and very severe pneumonia (29% and 34%, respectively).^{5.3}

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Radiologically-confirmed pneumonia incidence fell by 33% in children under 2.

Another pertinent example is Bangladesh, which also introduced the Hib vaccine in 2009, citing advocacy by the Hib Initiative as a catalyst for action for its adoption.^{5.4} The measure is expected to save 20,000 lives in Bangladesh per year.^{5.5}

A number of other countries specifically studied by the LSHTM team to aid decision-making also introduced the Hib vaccine within the impact assessment period. These included Pakistan (2008), Uzbekistan (2009) and Vietnam (2010). Work in India is ongoing as the country slowly moves towards full implementation, with implementation strongly recommended by local authorities.^{5.6}

Apart from their direct research input into the Hib Initiative, the LSHTM team also actively helped promote awareness and understanding of their findings among decision-makers at country and international organisation level. They actively sought to change country policy,^{5.7} with Griffiths presenting the findings at no fewer than nine high-level international gatherings between 2008 and 2012. These included, among others:

- a meeting involving the Indian Ministry of Health and WHO in 2008, which discussed proposed plans for estimating the cost-effectiveness of Hib vaccine in India
- a meeting with officials from the Belarus Ministry of Health in Minsk in 2009, where Griffiths again reported on cost-effectiveness
- a presentation at WHO in Geneva in 2012, where Griffiths highlighted that the vaccine has been shown to be cost-effective for all countries, and is likely to be cost-saving in Africa.^{5.8}

Since 2008, other team members have been engaged in similar advocacy work based on the research. Mulholland has spoken at 15 international meetings in major plenaries as well as at smaller regional and country meetings, and Edmond built a trusting relationship with decision-makers in Mongolia (2007–2010).

The GAVI Alliance calls the Hib Initiative a 'success story', stating that 'By pooling the knowledge and expertise of the Johns Hopkins Bloomberg School of Public Health, LSHTM, and the CDC, the Hib Initiative used a combination of collecting and disseminating existing data, research and advocacy to help countries build a case for adopting the Hib vaccine.'^{5.9} The Deputy Chief Executive Officer of the GAVI Alliance has affirmed that 'the success of the Hib Initiative program can be seen by the excellent uptake of Hib vaccine by GAVI eligible countries during the relatively short period of the project. LSHTM played a major role in this project, particularly in the areas of gathering, synthesizing and generating the epidemiology and economic evidence'.^{5.10}

5. Sources to corroborate the impact

5.1 International Vaccine Access Center (IVAC) (2013) *Vaccine Information Management System (VIMS) Report: Global Vaccine Introduction*. Baltimore, MD: Johns Hopkins Bloomberg School of Public Health, <http://www.jhsph.edu/research/centers-and-institutes/ivac/vims/IVAC-VIMS-Report-2013-03.pdf> (accessed 12 September 2013).

5.2 WHO (2012) WHO Report on GAVI Progress 2000-2011 & Projected Achievements 2012, rev. March 2013, [unpublished].

5.3 Sigaúque, B, Vubil, D, Sozinho, A, Quintó, L, Morais, L, Sacoor, C, Carvalho, MG, Verani, JR, Alonso, PL and Roca A (2013) *Haemophilus influenzae* type b disease among children in rural Mozambique: impact of vaccine introduction, *Journal of Pediatrics*, 163(1) (Suppl.): S19-S24, doi:10.1016/j.jpeds.2013.03.026.

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5.5 <http://www.icddrb.org/media-centre/news/2016-hib-vaccine-introduced-into-routine-immunization-in-bangladesh>.

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[http://www.who.int/immunization/sage/meetings/2012/november/9. Cost effectiveness of Hib vaccine review of literature Griffiths U 2012.pdf](http://www.who.int/immunization/sage/meetings/2012/november/9_Cost_effectiveness_of_Hib_vaccine_review_of_literature_Griffiths_U_2012.pdf)

5.9 Hib Initiative: a GAVI success story, <http://www.gavialliance.org/library/news/roi/2010/hib-initiative--a-gavi-success-story/>.

5.10 Deputy Chief Executive Officer, GAVI Alliance.