Institution: University of Brighton		
Unit of Assessment: C14 Geography and Environmental Studies		
Title of case study: Protecting human health from infectious diseases in low-resource settings		
Period when the underpinning research was undertaken: 2011 – 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
James Ebdon	Principal Lecturer (2012 – 14), Reader (2014 – 20), Professor of Environmental Microbiology (2020 – to date)	2004 – to date
Diogo Gomes Da Silva	Research Fellow	2015 – to date
Huw Taylor	Professor of Microbial Ecology (2011 – 17)	1993 – 2017 *deceased
Period when the claimed impact occurred: 2014 – 2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

University of Brighton (UoB) research has made life-saving advances in the fight against excreta-borne disease. It has reduced human health risk from diseases including cholera, Ebola, typhoid and childhood diarrhoea in regions of Africa, Asia and South America. Research has strengthened WHO and UNICEF sanitation guidance that has been deployed by Médecins Sans Frontières (MSF) in Mozambique to protect 446 staff and 4,330 patients at cholera treatment centres. Low-cost bacteriophage-based tools have helped the National Institute of Cholera and Enteric Diseases to prioritise effective public health interventions in urban slum districts in India (home to >100,000 people) and the Kenyan Medical Research Institute to protect 1,170 rural inhabitants.

2. Underpinning research

Infectious diseases caused by pathogens associated with poor water, sanitation and hygiene, such as *Vibrio cholerae* (cholera) and *Salmonella typhi* (typhoid), are responsible for 95,000 and 178,000 global deaths/year respectively. Understanding how these and other agents of disease such as *Ebolavirus* (11,315 deaths from 2013 – 16) are spread in low-income settings is critical for the prevention of onward transmission and for identifying the most effective control measures. Working with NGOs and humanitarian funders, UoB scientists have developed low-cost excreta management interventions and bacteriophage-based tracking tools to detect contamination sources, disrupt pathogen transmission and protect human health from a variety of infectious diseases.

2.1 Safer excreta management

When cholera or Ebola outbreaks occur in a low-income country, the rapid construction and successful operation of cholera treatment centres (CTC) and Ebola treatment centres (ETC) by NGOs can reduce mortality rates significantly. However, such emergency field centres generate considerable quantities of human excreta that can be the source of further disease transmission amongst patients, health-workers and local populations. Approaches for safely handling, containing and treating infectious waste are vital to safeguard health and prevent infection.

To address this challenge, UoB researchers developed a low-cost hydrated lime-based treatment capable of raising the pH of excreta to very high levels (>14) to inactivate pathogens, before encapsulating them within a lime slurry where they no longer pose an infection risk. The method was deployed initially by MSF to treat 600,000 litres of cholera-laden wastewater from three CTCs in Haiti [reference 3.1]. It has been optimised further with MSF and USAID funding in studies that compared the effect of excreta consistency (organic content), lime and chlorine dosing, mixing and contact time on treatment performance [3.2, 3.3]. UoB researchers conducted these optimisation studies in full-scale OXFAM® buckets using commercially available, locally sourced lime and chlorine solutions. The results provided the first validation of how the novel lime-based methods were performing in a real-world context and bridged the historical disconnect between lab-based observations and treatment performance reported from

the field during humanitarian crises. The optimisation studies were significant as they maximised the removal of pathogens, ensuring that MSF and other NGOs could use the lime-based approach to protect human health in a cost-effective manner [3.3].

Unlike chlorine-based excreta treatment (formerly prescribed in 2004 MSF Guidelines [source 5.1a]), lime does not readily produce explosive gases or toxic by-products, is less prone to spills and is better suited to treating waste with a high organic content (eg faeces, vomitus) [3.1-3.3]. As such, the method devised at UoB offers a safer and more effective means of excreta management, especially in situations where underlying geology or proximity to the water table prevents burial of waste. The low-cost *in situ* treatment plants also eliminate the hazardous practice of transporting contagious materials by truck to uncontrolled disposal sites.

2.2 Improved low-cost contaminant tracking

In 2012, Dr James Ebdon and Professor Huw Taylor published key evidence that *bacteriophages* (viruses) capable of infecting certain strains of bacteria (eg *Bacteroides* GB124) are restricted to the human gut in populations across the globe [3.4, 3.5] and hence indicate pathways of human faecal contamination in the environment. Detection and cultivation of these human-specific phages is low-cost, and unlike other Microbial Source Tracking (MST) approaches, does not rely upon complex expertise or equipment to detect the DNA or RNA of the organisms. The method is suitable for deployment in parts of the world where poor water quality and infectious disease have the greatest impact on health and where monitoring is most urgently needed.

Ebdon has enhanced this MST approach and its ability to detect phages, allowing scientists at the National Institute of Cholera and Enteric Diseases (NICED), India, to identify human faecal contamination of unwashed raw produce, street food, latrine surfaces and floodwaters. To apply the research and analyse outcomes, monitoring was carried out at 12 households in 2 urban slum districts (including typhoid positive dwellings). This allowed risk of exposure to be established and appropriate interventions to be identified [3.7]. Dr Diogo Gomes Da Silva and Ebdon have also used phages present in the faeces of cattle, goats, and poultry to improve monitoring of household drinking water in rural Kenya [3.6]. Stored household water was shown to be susceptible to cross-contamination by animal faeces (known to contain diarrhoeal pathogens eg *Salmonella*, *Campylobacter*, *Cryptosporidium*, *Giardia*) during an MRC-funded initiative (2017 – 19) involving 1,170 inhabitants of Siaya County. Findings were relayed to 234 participating households and stakeholders by partners the Kenyan Medical Research Institute (KEMRI) to identify the most appropriate interventions to take forward (eg fencing-off drinking troughs, household water treatment) to prevent life-threatening diarrhoeal diseases.

3. References to the research

[3.1] Sozzi, E., Fabre, K., Fesselet, J. F., Ebdon, J. E., Taylor, H. D., (2015). Minimizing the risk of disease transmission in emergency settings: novel in situ physico-chemical disinfection of pathogen-laden hospital wastewaters. *PLOS Neglected Tropical Diseases* 9(6), 1-20. https://doi.org/10.1371/journal.pntd.0003776. [Quality validation: peer-reviewed publication in international infectious diseases journal].

[3.2] Gomes Da Silva, D., Dias, E., Ebdon, J. E., Taylor, H. D., (2018). Assessment of recommended approaches for containment and safe handling of human excreta in emergency settings. *PLOS ONE* 13(7), 1-20 https://doi.org/10.1371/journal.pone.0201344. [Quality validation: peer-reviewed publication in international multi-disciplinary journal].

[3.3] Gomes Da Silva, D., Ives, K., Fesselet, J., Ebdon, J. E., Taylor, H. D., (2019). Assessment of recommendation for the containment and disinfection of human excreta in cholera treatment centers. *Water* 11(2), 188 https://doi.org/10.3390/w11020188. [Quality validation: peer-reviewed publication in international water science journal].

[3.4] Ebdon, J. E., Sellwood, J., Shore, J., Taylor, H. D., (2012). Phages of *Bacteroides* (GB-124): A novel tool for viral waterborne disease control? *Environmental Science & Technology* 46(2), 1163-1169 https://pubs.acs.org/doi/10.1021/es202874p. [Quality validation: peer-reviewed publication in international multi-disciplinary environmental sciences journal].

[3.5] Ogilvie, L., Bowler, L., Dedi, C., Diston, D., Cheek, E., Taylor, H. D., Ebdon, J. E., Jones, B. (2018). Resolution of habitat-associated ecogenomic signatures in bacteriophage genomes and application to microbial source tracking. *The ISME Journal* 12, 942-958. https://www.nature.com/articles/s41396-017-0015-7. [Quality validation: peer-reviewed publication in international microbial ecology journal].

[3.6] Gomes Da Silva, D., Ebdon, J. E., Okotto-Okotto, J., Ade, F., Mito, O., Wanza, P., Kwoba, E., Mwangi, T., Yu, W., Wright, J., (2020). A longitudinal study of the association between domestic contact with livestock and contamination of household point-of-use stored drinking water in rural Siaya County (Kenya). *International Journal of Hygiene & Environmental Health* 230, article 113602 https://doi.org/10.1016/j.ijheh.2020.113602. [Quality validation: peer-reviewed publication in international water and sanitation journal].

Key research grants

[3.7] James Ebdon [PI], 2017 – 2019, '*Typhoid mapping and prediction in India - SaniPath Typhoid*'. Bill & Melinda Gates Foundation, Total funding GBP2,669,951 (USD3,298,528) UoB allocation: GBP165,086 (USD311,299).

[3.8] Diogo Gomes Da Silva [PI], 2017 – 2019, '*Drinking water under a 'one health' lens*'. Medical Research Council (MRC), Global Challenges Research Fund. [MR/P024920/1], Total funding GBP603,320 UoB allocation: GBP240,260.

[3.9] Huw Taylor [PI], 2017 – 2018, '*Applied research into the disinfection of human excreta in emergency settings using highly concentrated chlorine solutions'* (ARDHEES) Médecins Sans Frontières' (MSF), Total funding and UoB allocation GBP40,128.

[3.10] Huw Taylor [PI], 2015 – 2016, '*Applied research on disinfection of hands, surfaces & wastewater disinfection to prevent ongoing transmission of Ebola*' USAID, Total funding GBP447,824 (USD558,514), UoB allocation: GBP83,374 (USD135,804).

[3.11] James Ebdon, Huw Taylor, 2014 – 2015, *'Source tracking in India - SaniPath'* Bill & Melinda Gates Foundation, Total funding GBP2,392,209 (USD2,983,496) UoB allocation: GBP29,583.

4. Details of the impact

The research breakthroughs at UoB have helped protect some of the most vulnerable human populations globally, by supporting a 'multiple barrier approach' to disease control, particularly in low-resource and emergency settings. By collaborating with NGOs, policymakers and communities, UoB research has protected human health through evidence-led interventions into global-health policy (WHO/UNICEF) and on-site treatment practice to reduce risk to families, communities and those working to support the most vulnerable to virus and infection.

4.1 Protocols for the safe handling and disposal of human excreta

UoB scientists were mobilised initially to help MSF with the humanitarian response in Haiti following the 2010 earthquake and cholera outbreak, via the development and application of low-cost lime-based methods to protect communities located downstream of three CTCs from infection. Following subsequent USAID funding, the intervention extended to encompass the containment of *Ebolavirus* in response to the 2013 – 2016 outbreak. This work revealed critical knowledge gaps relating to the water, sanitation and hygiene (WASH) activities of international NGOs. In particular, the absence of information on the survival of the *Ebolavirus* within human excreta prompted the WHO/UNICEF to invite an international panel of experts (including Taylor for his microbial ecology expertise) to review critically existing WASH practices.

In October 2014, with direct input from Taylor, the WHO/UNICEF panel revised their guidance due to concerns about the potential dangers of using excreta chlorination protocols prescribed in 2004 MSF Guidelines [5.1a]. The revised guidance now recommends the lime-based procedures developed at the UoB to counter these concerns. WHO/UNICEF WASH guidelines on Ebola virus disease also now include protocols for managing excreta from ETC patients to accelerate '*the inactivation of the Ebola Virus using lime*' [5.2]; these guidelines are recommended by WHO/UNICEF as best operating practice for all international NGOs working in Ebola-affected areas of West Africa (including UNICEF, OXFAM, Save the Children and MSF).

Subsequent collaboration with Tufts University (2015 – 16), during which the UoB team compared the efficacy of emerging lime and existing chlorine approaches, resulted in further improvements in treatment efficacy (by refining the dosage, including a mixing step for lime and identifying the optimum duration of contact). UoB research is also referenced in the WHO's 2018 *Guidelines on sanitation and health* to demonstrate the suitability of phage and lime-based approaches for detecting and preventing faecal contamination in emergency settings [5.3].

In 2017, UoB's optimised lime-based protocols were adopted as part of revised Standard Operating Procedures (SOP) for MSF's CTC facilities [5.1]. In 2018, MSF treated 63,722 people for cholera in 16 outbreaks affecting 6 countries (Cameroon, DR Congo, Haiti, Niger, Nigeria, South Sudan) using UoB protocols for excreta management. This figure rose further in 2019 as MSF responded to outbreaks in Yemen and Mozambique in the wake of cyclones Idai and Kenneth; in Beira (Mozambique), MSF had 446 staff assisting with WASH activities at three purpose-built CTCs treating 4,330 patients [5.4]. UoB researchers continue to work closely with 'on-the-ground' MSF staff on refinements to the SOP and through the provision of real-time advice on the safe handling of cholera-laden waste. In March 2020, MSF released a revised SOP (Comprehensive Method) for use at all its on-site treatment Centres [5.1b].

4.2 Improved approaches for the surveillance of potential disease transmission routes

In 2017, UoB scientists were sub-contracted by Emory University to provide MST expertise to a Gates Foundation-funded collaboration with NICED, India. The initiative aimed to protect slum-dwellers from typhoid fever (an important cause of avoidable morbidity and mortality) in Kolkata's slums, home to over 1.5 million people. The UoB contribution to the SaniPath typhoid project has, for the first time, made it possible for NICED staff to separate the human faecal pollution pathways (along which *S. typhi* and/or *Paratyphi A* travels) from the pervasive 'background noise' of non-human faecal contamination in such settings [5.5].

The new capability within the SaniPath Exposure Assessment Tool (not available before 2017) allows users, including staff at NICED, to gain valuable understanding of the relative importance of human faecal contamination pathways and to identify high risk practices and situations [5.5, 5.6]. Our ability to pin-point human faecal transmission within domestic and environmental settings is providing local communities in three districts of Kolkata (home to >100,000 people) with the knowledge necessary to avoid hazardous activities such as eating unwashed raw produce or the use of unhygienic food preparation areas. UoB findings have demonstrated to NICED and the SaniPath international scientific advisory committee why previous WASH interventions targeting alternative transmission routes (eg drinking water supplies) were not accompanied by declines in typhoid incidence [5.5, 5.6].

Phage-based monitoring has been utilised by KEMRI to improve the protection of 1,170 inhabitants (234 households) in rural Kenya, where 29% of households rely on unprotected surface waters for drinking water supply and where childhood diarrhoea from livestock affects 20% of children under five. UoB methods in Kenya work by quantifying faecal contamination arising from animal sources and the risk of encountering 'zoonotic' pathogens. Regional water quality testing capacity has been strengthened by the training of 16 laboratory researchers, academics, and technicians from institutions across the region in rapid, low-cost, phage-based approaches in 2019. The MRC-funded project has facilitated more effective management of rural water supplies in Kenya by indicating which interventions stakeholders and householders need to invest in and builds on other laboratory training events staged by UoB researchers in Brazil (44 participants, 2015) and India (22 participants, 2017) [5.7].

In April 2015, the US Environmental Protection Agency (EPA) conducted a high-level review [5.8] into alternative water quality indicators, as evidence emerged that bacterial indicators (used for the last 100 years) do not adequately indicate risk from viral pathogens, a leading cause of recreational waterborne illness [5.9]. This review and the subsequent EPA Experts Workshop [5.9] held in March 2016 used evidence from 9 UoB publications on phage-based recreational water quality indicators, eg their removal by wastewater treatment, relationship with viral pathogens (*norovirus*, *Adenovirus*) and their densities in faecally-impacted waters from the US, EU and UK. As such, UoB research has made it possible for the EPA to develop criteria for

water quality that reflect accurately the 'latest scientific knowledge' (as required in the US Clean Water Act) and effectively protect the health of 331 million US citizens.

Most recently, in response to the COVID-19 pandemic, WHO/UNICEF have produced interim guidance entitled *Water, sanitation, hygiene and waste management for the COVID-19 virus* to aid global efforts to control the disease. UoB's phage and lime-based research are used in this guidance, which highlights that '*chlorine is ineffective for disinfecting media containing large amounts of solid and dissolved organic matter*' and that '*where there is no off-site treatment, in-situ treatment can be done using lime*'). This early policy development to contain, control and remove a virulent new virus from human waste serves to demonstrate the flexibility of solutions developed at UoB to protect human health in low-resource settings [5.10].

5. Sources to corroborate the impact

[5.1a] *MSF Cholera Guidelines*: 2nd Edition (2004), Médecins Sans Frontières, pp1-158. https://www.humanitarianresponse.info/en/operations/iraq/document/msf-cholera-guidelines-2004 [Accessed: 29 January 2021]

[5.1b] Revised *MSF Standard Operating Procedure (March 2020). On-site CTC wastewater treatment with lime*. WatSan Unit, Public Health Department, MSF-Operational Centre Amsterdam, with a covering note explaining the inclusion of our lime-based approach.

[5.2] WHO/UNICEF (2014) *Ebola Virus Disease: Key questions and answers concerning water, sanitation and hygiene*. WHO/EVD/WSH/14 (pp.2 & 3 first paragraph describe how lime treatment can be used to accelerate the inactivation of the Ebola virus). https://www.who.int/csr/resources/publications/ebola/water-sanitation-hygiene/en/ [Accessed 29 January 2021]

[5.3] WHO (2018) *Guidelines on sanitation and health*. Geneva: World Health Organization (Chapter 6 Excreta-related pathogens, pp.114, 121 & 124 describes UoB phage research). https://www.who.int/water_sanitation_health/publications/guidelines-on-sanitation-and-health/en/ [Accessed 29 January 2021]

[5.4] Testimonial from the WatSan Unit Coordinator, Public Health Department, MSF-OCA/Artsen Zonder Grenzen - confirms how UoB research into the 'Assessment of Recommended Approaches for Containment and Safe Handling of Human Excreta in Emergency Settings' is informing the implementation of lime-based SOPS in Mozambique.

[5.5] Testimonial from Emory University, Atlanta (PI on Gates-funded SaniPath Typhoid project) that confirms the outcomes of the Sanipath project on communities in Kolkata.

[5.6] Bill & Melinda Gates Foundation. Typhoid elimination https://www.gatesfoundation.org/What-We-Do/Global-Health/Enteric-and-Diarrheal-Diseases [Accessed 29 January 2021]

[5.7] Testimonial from Kenyan Medical Research Institute confirming how the results of the MRC project are being used to identify acceptable interventions in Siaya County and beyond.

[5.8] US Environmental Protection Agency, Office of Water (2015) *Review of Coliphages as Possible Indicators of Fecal Contamination for Ambient Water Quality.* Washington DC, USA (EPA 820-R-15-098 2015). Seven UoB papers (Ebdon et al. 2007, 2012; Nnane et al. 2011; Payan et al. 2005; Purnell et al. 2011, 2015; Vijayavel et al. 2010) were used as evidence in this high-level review (pp.4, 5, 66, 86, 98-100, 107).

[5.9] US Environmental Protection Agency (2017) *Proceedings from a Coliphage Experts Workshop'* July 2017 (EPA 822-R-17-003 2017). This features two UoB phage studies (Blanch et al. 2004, 2006) and a further Environmental Protection Agency paper on the successful use of GB-124 in the US (McMinn et al. 2014) pp. B-35, B-46 and B-50).

[5.10] WHO/UNICEF (23 April 2020) *Water, sanitation, hygiene, and waste management for the COVID-19 virus. Interim guidance*. WHO/2019-nCoV/IPC_WASH/2020.2 (Sections 3 & 4, p.3) https://apps.who.int/iris/handle/10665/331499 [Accessed 29 January 2021]