Institution: Imperial College London

Unit of Assessment: 01 Clinical Medicine

Title of case study: Improving the response to Ebola outbreaks

Period when the underpinning research was undertaken: 2013-2020

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:
Anne Cori	Lecturer in Statistical Infectious Disease Epidemiology	2013 - present
Christl Donnelly	Professor of Statistical Epidemiology	2000 - present
Neil Ferguson	Professor of Mathematical Biology	2000 - present
Tini Garske	Senior Lecturer in Infectious Disease Analysis	2006 - present
Ilaria Dorigatti	Lecturer/Sir Henry Dale Fellow	2011 - present

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)

The emergence and transmission of Ebola virus in West Africa in 2014 necessitated a rapid global response to contain its spread. Imperial researchers undertook epidemiological analyses and modelling to understand its transmission, severity and intervention impact. Imperial estimates informed the World Health Organisation's (WHO) declaration of the epidemic as a public health emergency resulting in rapid funding for the response whilst real-time estimates and short-term projections of incidence and bed capacity were provided to UK government and WHO. These were used to improve situational awareness, monitor progress in epidemic control and adjust interventions and logistical planning.

2. Underpinning research (indicative maximum 500 words)

From 2014, following the declaration of an Ebola outbreak in West Africa, and building on experience in modelling emerging and re-emerging infections (including SARS and pandemic influenza), Imperial researchers developed an extensive research programme to improve the understanding of Ebola virus disease epidemiology and generate quantitative evidence to support efforts to control Ebola epidemics, in collaboration with WHO and Ministries of Health of the affected countries.

Before the 2013-16 West African epidemic, limited data were available to precisely characterise the natural history, transmissibility or severity of Ebola. Real-time analysis of data collected early in each outbreak since 2013 enabled estimates of key epidemiological characteristics (1, 2). This showed that the unusually large Ebola epidemics, in West Africa (2013-16) and in Democratic Republic of the Congo (DRC, 2018-2020), had similar characteristics to smaller outbreaks, (including those in 2017, 2018 and 2020 in DRC) with moderate transmissibility (reproduction number ≤2.0) but high mortality (case fatality ratio, CFR, approximately 70%).

A crucial contribution was projecting the potential scale of each epidemic at an early stage (1, 2). Regular updates allowed quantitative monitoring and evaluation of progress made in epidemic control (3), and provided situational awareness, via regular reports shared with WHO and key stakeholders, to support decision-making.

Although drivers of Ebola transmission, for example, unsafe funerals, were known before the West African epidemic, this knowledge was supported by little quantitative evidence. The Imperial research was the first to rigorously identify and quantify heterogeneities in Ebola transmissibility and severity. The research demonstrated that delayed hospitalisation and funeral exposures directly correlated with transmission intensity, and provided a quantification of this relationship, showing that isolating 70% of cases within four days of symptoms should be sufficient for control (4). Imperial researchers provided the first comprehensive study of clinical presentation, transmissibility and severity of paediatric Ebola (5) and designed a new method to identify healthcare facilities or regions with unusual CFRs.

Using mathematical modelling, Imperial researchers explored the potential impact of interventions, including using rapid diagnostic tests (6) or different vaccination strategies. Researchers from the Imperial team worked closely with WHO and countries in 2014-15, and building on this experience, the team deployed staff to WHO Headquarters (four researchers, cumulatively for 15 weeks in 2018-19) and to the field (two researchers, cumulatively for 24 weeks in 2017-2019) in later outbreaks to assist daily data management and analysis. Such integration of researchers into the WHO epidemiology teams was critical in ensuring the research addressed policy makers' priority needs.

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

(1) WHO Ebola Response Team* (2014). Ebola Virus Disease in West Africa - The First 9 Months of the Epidemic and Forward Projections. *New England Journal of Medicine*, 371 (16): 1481-95. DOI. *Christl Donnelly is corresponding author.

(2) Ebola Outbreak Epidemiology Team* (2018). Outbreak of Ebola virus disease in the Democratic Republic of the Congo, April-May, 2018: an epidemiological study. *Lancet*, 392 (10143): 213-221. DOI. *Imperial authors include I Dorigatti, CA Donnelly, A Cori, T Garske, NM Ferguson, and KAM Gaythorpe.

(3) WHO Ebola Response Team* (2015). West African Ebola Epidemics after One Year – Slowing but Not Yet under Control. *New England Journal of Medicine;* 372 (6): 584-87. DOI. * Christl Donnelly and Neil Ferguson are corresponding authors.

(4) International Ebola Response Team, Agua-Agum, J., Ariyarajah, A., Aylward, B., Bawo, L., Bilivogui, P., Blake, I.M., Brennan, R.J., Cawthorne, A., Cleary, E., Clement, P., Conteh, R., Cori, A., Dafae, F., Dahl, B., Dangou, J-M., Diallo, B., Donnelly, C.A., Dorigatti, I., Dye, C., Eckmanns, T., Fallah, T., Ferguson, N.M. et al. (2016). Exposure Patterns Driving Ebola Transmission in West Africa: A Retrospective Observational Study. *PLoS Med*, 13 (11): 584-87. DOI.

(5) WHO Ebola Response Team, Agua-Agum, J., Ariyarajah, A., Blake, I.M., Cori, A., Dorigatti, I., Dye, C., Eckmanns, T., Ferguson, N.M., Fowler, R.A., Fraser, C., Garske, T., et al (2015). Ebola virus disease among children in West Africa. *New England Journal of Medicine*, 372 (13): 1274-77. DOI.

(6) Nouvellet, P., Garske, T., Mills, H.L., Nedjati-Gilani, G., Hinsley, W., Blake, I.M., Van Kerkhove, M.D., Cori, A., Dorigatti, I., Jombart, T., Riley, S., Fraser, C., Donnelly, C.A., Ferguson, N.M. (2015). The role of rapid diagnostics in managing Ebola epidemics. *Nature*, 528 (7580): S109-S116. DOI.

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

As the WHO Collaborating Centre for Infectious Disease modelling, the Imperial team provided real-time analyses (and direct support via deployed personnel) to WHO and governments during the 2013-16 West African Ebola epidemic and three subsequent epidemics in DRC. In 2014-15, a key aspect was direct support for the UK Government via

the Scientific Advisory Group for Emergencies (SAGE) and the then Departments for International Development (DFID) and Health (DH) [**A, B**]. Much of the work made use of confidential data shared by the affected countries, and so was only summarised in confidential reports and presentations shared with WHO, countries and key other stakeholders throughout each epidemic. UK modelling is referred to, though not explicitly described, in UK SAGE minutes [**A, B**]. Additional letters of support are therefore provided to confirm the impact.

West African Ebola epidemic

The initial assessment of the epidemic in research reference (1) (co-authored with WHO) directly informed the WHO declaration of the epidemic as a Public Health Emergency of International Concern (PHEIC); [**C**] states "*this study provides the evidence needed for an urgent wakeup call requiring intensive scaling up of control measures"* and this is confirmed in supporting letter from Bruce Aylward, then the WHO lead for the response [**D**]: "*These estimates informed … WHO to declare the epidemic a Public Health Emergency of International Concern in 2014*".

It additionally prompted a rapid scale-up of funding for the international response ("*Importantly, the technical credibility of these early forecasts added further urgency to the response and informed the strategic and operational planning of WHO and the broader national and international response"* [**D**]).

[redacted]

The team's estimates of the case fatality ratio and how it varied with age, sex, and location (references 1, 3) *"were instrumental in shaping the understanding of the risk of death by programme managers, donors, politicians, and others, and adjusting the response priorities accordingly*" [**D**].

The team shared transmission estimates and short-term incidence projections with WHO and other stakeholders (including UK government [**A, B**]) every one to two weeks. These reports improved situational awareness, the monitoring of progress in epidemic control and consequent adjustments to interventions and associated logistical planning [**D-F**].

Projections made as the epidemic declined were used to plan progressive withdrawal of international staff and equipment and the dismantling of Ebola Treatment Units (ETUs) and mobile laboratories [**D, F**].

The team generated reasonable worst-case scenario projections for the UK government and projected bed capacity requirements [**A**]. Investigations into the drivers of transmissibility (reference 4) were used to establish which interventions would be most effective. Safe burials were highlighted in modelling presented to UK SAGE: "*Modelling: the risk of transmission at burials was highlighted as a continued area of concern"* [**A**] and "*The need to focus on transmission that occurs in the few days before death, in addition to transmission during burials, was highlighted"* [**B**]. The need for earlier hospitalisation was also noted in [**A**] as an output from the modelling.

Incubation period distribution estimates (research reference 1) were used by WHO to support the recommendation to follow up contacts of Ebola cases for 21 days [**D**]. Estimates of the

typical duration of hospital stays were used by WHO for logistical planning of bed capacity and food requirements for ETUs [**D**, **G**, cites reference 1].

Ebola epidemics in DRC (2017-)
Following promising trial results demonstrating safety and high efficacy of the rVSV Ebola vaccine, the Imperial team used mathematical modelling to quantify the potential impact of different vaccination strategies on Ebola epidemics. This evidence was presented at WHO/SAGE working groups and used by WHO to inform policy recommendations regarding Ebola vaccination [**H, I**]; compassionate use of vaccination was added to the traditional Ebola intervention toolkit in 2018 [**H**].

During each Ebola epidemic since West Africa, the team has continued to provide regular situation reports to WHO, DFID and other partners, including real-time quantification of severity and transmissibility, short term projection of case incidence, bed capacity needed, number of vaccine doses required, as well as measures of the risk of spatial spread. These analyses have been critical in assisting decision-making during these outbreaks and contributed to the evidence WHO used to declare the 2018-19 Ebola epidemic a PHEIC [**D**].

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

[**A**] UK SAGE committee meeting minutes 29th October 2014 (Archived here)

[**B**] UK SAGE committee meeting minutes 8th December 2014 (Archived here)

[**C**] WHO Press Release 22nd September 2014 (Archived here).

[**D**] Supporting Letter from Dr Bruce Aylward, Special Representative of the Director-General for the Ebola Response, WHO.

[redacted]

[redacted]

[**G**] Nutritional care of children and adults with Ebola virus disease in treatment centres: Interim guideline. WHO 2014. Archived here.

[**H**] WHO SAGE Vaccine Committee Meeting April 2017. Ebola vaccine background document. Archived here.

[**I**] WHO SAGE Vaccine Committee Meeting October 2018. Ebola vaccine background document. Archived here.