NUFFIELD COUNCIL ON BIOETHICS

Research and innovation in global health emergencies: ethical challenges

This note draws on contributions to a [workshop](#) hosted by the Nuffield Council on Bioethics in December 2016, and on the background paper commissioned for that workshop. Both the [background paper](#) and the [meeting note](#) are available on the Council's website.

Overview

- Research and innovation constitute a key part of the response to a global health emergency, both for the potential they offer for delivering improved healthcare and humanitarian assistance at the time, and because of the need for systematic learning from experience to improve emergency response in the future.

- As the recent Ebola and Zika epidemics have illustrated, however, conducting research in the context of global health emergencies can raise ethical issues that may complicate the challenges already facing those responsible for emergency response.

- From the perspectives both of those affected by the emergency and of front-line workers, 'research' activities cannot be fully separated out from other activities that form part of emergency response, including humanitarian initiatives, care services and public health measures. Yet these different areas of practice often have different approaches to ethics.

- Emergency response involves many different organisations and individuals, and effective collaboration is a particular challenge: for example in priority-setting, flexible use of funding streams, logistics, and coordination of services. These challenges are exacerbated when existing healthcare structures are inadequate and overstretched.

- Developing trust between all parties, and ensuring that the (diverse) voices of local populations are heard, is crucial in order to ensure that research is genuinely focused on the needs of those directly affected by the emergency. However, creating such trust is rarely straightforward.

- Further work is required to develop an ethical approach that recognises the complex relationships between research and other essential services in a global health emergency, and to develop a code of conduct to facilitate collaboration and co-operation in research between all external stakeholders, including funders, researchers, and those concerned with immediate humanitarian response.

'Research' as an intrinsic element of emergency response

What are the challenges?

- Ethical guidance distinguishes sharply between 'research' (understood as the endeavour to generate knowledge for future benefit) and 'treatment' (concerned with individual benefit now). However, research interventions may at the same time have a therapeutic effect: for example where experimental treatments prove more efficacious than existing alternatives. Research activities may also be identical to public health activities: for example in the collection of data on levels of infection.

- Frontline staff working within these fields of research, care (encompassing both medical treatment and wider humanitarian assistance), and public health often operate with different regulatory and ethical norms and practices. Those providing direct healthcare and humanitarian assistance to people affected by global health emergencies are often well placed to conduct research but may be unfamiliar with the requirements of research ethics guidance and processes. Researchers and public health practitioners have different rules with respect to consent for using patient information that can prevent effective data-sharing.

- Ethical scrutiny of research (for example review of research proposals by research ethics committees) tends to focus more on the minimisation of risk to participants, than on the scope for any direct benefit. Yet people often take part in research for the benefits they perceive to be associated with it: whether these are access to particular medical treatments, or other associated benefits.

- Research is often regarded as secondary to activities concerned with public health and care for individuals. However, it could be argued that there is an ethical imperative to collect information systematically in order to improve emergency response in the future.

What is needed?

- Analysis to map where specific activities within research, care and public health interventions coincide in global health emergencies, and hence where tensions may arise: for example when providing an experimental treatment; when seeking consent; and when collecting or using data.

- Empirical research on how these apparently distinct activities are perceived in practice by those directly affected.

- Development of a holistic ethical approach for evidence-based care and social action in the context of global health emergencies, building on existing work in this field, and corresponding with pre-existing regulatory regimes.[i]

Collaboration and engagement

What are the challenges?

- The multiplicity of actors involved in emergency response, and the shortness of time to act, exacerbate many existing and well-documented ethical challenges in research in low-income countries. Frontline workers come from diverse professional backgrounds, with different expectations and priorities, sometimes using the same language to mean different things (for example 'vulnerability' or 'community engagement').

- Funders (governmental, charitable and commercial) are similarly diverse. Sources of funding may be linked with very specific aims, limiting scope both for research to be an intrinsic part of emergency response, and for effective collaborative working. Specific funding approaches may also have unintended consequences for the provision of existing local services. Funders' expectations, realised through performance management requirements, can exercise considerable influence on the ground.

- Ensuring that the populations affected have a strong voice in shaping emergency response, and recognising the potential for diverse voices within those populations, is critical but difficult, especially where there is an existing lack of trust in governments or others in positions of

authority. Building trusting and trustworthy relationships may be particularly difficult where there is a military component to the response, and/or where containment measures are contemplated.

- Responsibilities towards frontline staff, whether engaged in research, care or public health, are ethically complex: can a differential response, in which frontline staff (whether expatriate or local) receive priority access to care, be justified? Can differential treatment between expatriate and local staff be justified?
- There is a tension between the importance of ensuring that local practitioners are involved and influential in research, and the need to avoid diverting staff away from other essential services, including health care and humanitarian assistance.

What is needed?

- A code of conduct to facilitate collaboration and cooperation between all external stakeholders, with an emphasis on the role of local populations in shaping the agenda.
- Greater flexibility by funders to help reduce the dangers of working in the silos of research, care, public health measures, and capacity-building.
- Access for frontline staff to better knowledge of the disciplines of others working in the field, and of local needs and traditions (whether through training or other means).

Priority setting and who decides

What are the challenges?

- Once an emergency has been declared, it may be too late to initiate research that has a realistic chance of directly helping those affected. Anticipation is crucial, and the WHO has initiated a programme of work, including mapping gaps in knowledge, identifying 'priority pathogens' on which medical counter-measures are urgently needed, and developing an R&D roadmap to clarify regulatory and ethical pathways.[ii] The Coalition for Epidemic Preparedness Innovations (CEPI) was launched in January 2017 to take forward vaccine research in these priority areas.[iii] However, responding to the unexpected remains a challenge: for example, a priority list of pathogens would have been unlikely to have included the Zika virus.
- While valuable, the 'top-down' international approach is only one part of the picture: affected populations themselves have a central role in setting priorities in research in response to a specific emergency. There are further challenges in defining both the population concerned (likely to be multiple and shifting populations, with diverse and conflicting priorities), and other stakeholders.
- Developing sustainable capacity in lower income countries – in terms of both infrastructure and expertise across the various domains of research, care and public health – is essential in order to support countries in taking control both of preventive measures, and of emergency response in the future. Who is responsible for this? Traditional research ethics emphasises the ethical importance of the legacy left after research. However, can such responsibilities be placed on those engaged in short-term response / research, who may simply not have the resources to be part of a long-term programme of support?
- There is little consensus on what are the most appropriate criteria for priority setting in the context of a particular emergency, and who should decide. For example: should priority be given to approaches that are immediately available and hence easier to carry out logistically? Can higher risk approaches be justified if there is reason to believe that they might have higher impact?
- Current orthodoxy states that research should never compromise response: that response-related activities always take priority. Given the complex way in which research and other response activities intersect, can this stand?

What is needed?

- Further anticipatory work in advance of future emergencies, including bringing together evidence on best practice in methods of humanitarian response,[iv] and developing a framework to help support priority-setting decisions at local level.
- Development of a consensus among funders on responsibilities for capacity building, and how this can be supported on an ongoing basis.

How to conduct research: do the 'usual rules' apply?

What are the challenges?

- Traditional approaches to the development of experimental treatments, in particular the 'gold standard' of the randomised controlled trial (RCT), may be locally unacceptable in the face of epidemic disease with high mortality and no existing treatment. More work is required, outside the context of a specific emergency, in developing consensus on what forms of trial design can be ethically acceptable, and in exploring whether this may, or may not, vary, depending on the context in which the trial takes place.

- There is a lack of consensus on what constitutes an appropriate level of governance of research ethics in an emergency. It should not be a question of lowering standards, but of ensuring a proportionate approach: for example with respect to flexibility on the mechanics and timing of ethical review. One way of conceptualising a proportionate approach could be with reference to 'errors that matter': for example the potential for the research to cause physical harm to participants or loss of community trust; or risks to the quality of data that could undermine or negate the value of the research.

- While essential, ethical guidelines and review processes are not enough, and the way they are applied in practice in emergencies may at times hinder potentially valuable research. There is a need both for 'ethical confidence' in exercising discretion among practitioners on the ground that goes beyond simple compliance, and for accountability for decisions made, including decisions to deviate from established practice.

What is needed?

- Analysis to clarify what ethical challenges are unique to research in emergencies, rather than simply exacerbated by emergencies, and to make explicit the values that underpin ethical considerations for both.
- Further work to develop standard protocols and frameworks in advance, for example with respect to data-sharing, thus narrowing what needs to be the subject of development and review at the time of an emergency.
- Exploration of the scope for greater flexibility with respect to international requirements on trials, such as those set out in Good Clinical Practice.
- Development of more flexible approaches of ethical review, building on examples of existing good practice.
- Development of tools to support reflective practice on the part of practitioners, to help fill the gap between high level principles and codes, and the reality of unpredictable challenges on the round: for example through collaborative work to develop best practice guidance.

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i   For example, WHO (2016) Guidance for managing ethical issues in infectious disease outbreaks, available at: http://apps.who.int/iris/bitstream/10665/250580/1/9789241549837-eng.pdf.
ii WHO (2016) A research and development blueprint for action to prevent epidemics: plan of action, available at: http://www.who.int/blueprint/about/r_d_blueprint_plan_of_action.pdf?ua=1.
iii Coalition for Epidemic Preparedness Innovations (2017) Homepage, available at: http://cepi.net/.
iv For an overview of the challenges, see: The Lancet (2017) *Series: health in humanitarian crises*, available at: http://www.thelancet.com/series/health-in-humanitarian-crises.