TRANSCRIPT

EPISODE 1: Research in Global Health Emergencies

Hosted by: Rebecca Richards

Guest: Dr. Nayha Sethi

Transcripts may have been edited for clarity.

Rebecca: Hello and welcome to the first full episode of our new Global Health Justice podcast: “Just Emergencies”!

I’m Rebecca Richards and for the first episode, I sat down with Dr. Nayha Sethi to talk about Research during Global Health Emergencies and some of the ethical and justice issues that can come along with it.

So let’s get into it!

[Intro Music]

This is "Just Emergencies"**,** the podcast where we show that global health emergencies are anything but just. In each episode we explore an issue, question, or event that makes us think about global health emergencies, humanitarian crises, and how to best respond to them.

Without further ado, let’s get into the episode!

Rebecca: So I’m here today with the fantastic Dr. Nayha Sethi who is a Chancellor’s fellow here at the University of Edinburgh’s Usher Institute of Population Health Sciences and Informatics, and she’s also a Deputy Director of the Law School’s interdisciplinary Mason Institute. She’s done a lot of work around health research regulation and she actually co-authored a background paper for the Nuffield Council on bioethics on the very topic of research during Global Health Emergencies. So she really knows what she's talking about, and here's what she had to say.

Rebecca: *Hi Nayha, thanks so much for being the first guest on 'Just Emergencies' and for helping me kick off the podcast.*

Dr. Sethi: You're very welcome. It's a pleasure to be here. Thanks for asking me to take part.

Rebecca: *Of course.*

In that Nuffield background paper, you mention that global health emergencies might mean different things in different institutions or to different researchers. So what are we talking about here? What does 'Global Health Emergencies' mean in the context of your research?

Dr. Sethi: So that's a good question. I think it might be helpful to talk about quite a narrow definition. Thinking from a kind of global governance perspective. So the World Health Organisation (WHO) - which is a key international actor in the context of global health emergencies - has a very specific definition; it doesn't refer necessarily to global health emergencies, but it refers to 'Public Health Emergencies of International Concern'. And so, the WHO will declare a Public Health Emergency of International Concern, which will trigger a whole set of interventions.

Under the international health regulations, Public Health Emergencies of International Concern is defined as an extraordinary event which is determined a) to constitute a public health risk to other states through the international spread of disease, and b) to potentially require a co-ordinated international response.

So this definition implies a situation that is serious, unusual, or unexpected, and carries implications for public health that are beyond the affected state's national border. And that might require immediate international action.

But the problem with this definition - or any specific definition - of a global health emergency is that it’s going to raise really important question for research. For example, we need to think about what it is that might make a public health issue an emergency. What might make it a global health emergency? There are broader questions around who determines what counts as a public health emergency. Is it just up to the Director General of the World Health Organisation? In fact, the Director

General during the West African Ebola Outbreak was actually criticised for delaying her declaration of public health emergency.

We also need to think about what the implications will be for emergencies that don't trigger the WHO public health emergency declaration. For example, AMR - Antimicrobial Resistance - isn't necessarily declared as a public health emergency, but it absolutely is an emerging, very very pressing global crisis in terms of global health.

We also need to think about other emergencies. For example, natural disasters like tsunamis and earthquakes, thinking about climate change and environmental impact, also thinking about war and terrorism. I think it's important that whenever we're talking about global health emergencies to remember that we need to think about a broader conceptualisation than merely the spread of infectious disease.

Rebecca: *So you're interested in research during global health emergencies. So what does that research look like? What are we trying to learn when we're doing research in global health emergencies?*

Dr. Sethi: So, research during global health emergencies really involves a very diverse spectrum of research activities. Some of the research might be dedicated towards understanding how infectious diseases emerge and develop. For example, if we're talking about any kind of infectious disease, we might want to understand what contributes to the development of the disease. How does it spread? How might we prevent it? What are effective policies for containment?

Research might also be targeted towards developing therapies in order to treat individuals. For example, during the West African Ebola Outbreak from 2013 to 2016, there were no effective treatments for patients. So a lot of research activities focussed on developing treatments to contain that virus.

On the other hand, as well as having research that involves highly invasive procedures like testing experimental interventions, we also have minimally invasive types of research, like observational studies, rather than intervention.

And then some research might involve the use of very large amounts of electronic data. For example, for public health surveillance. Trying to map emerging trends and trying to develop contingency plans so that we can have earlier detection of health emergencies.

Some research can also be very high tech. For example, with the Zika virus we had some research looking at vector control and development of GM [genetically modified] mosquitoes. But equally, there was some research dedicated to focussing on infrastructure and how we could improve the water supply.

So it's quite a broad range of research activities.

Rebecca: *So is there anything that makes research during global health emergencies different from public health research or medical research during, let's call them 'normal times', when there's not a crisis going on?*

Dr. Sethi: Yes, I think there are some really important points of differentiation.

So traditionally, the purpose of research is really about the production of generalisable knowledge. In contrast, treatment or practice is typically focused on diagnosis on therapy in order to benefit the individual patient. So the global health emergency setting quite radically challenges this treatment/research distinction.

You can see how the lines between these activities might be blurred when we have, on one hand, the imperative to learn as much as possible as quickly as possible, and on the other hand, the imperative to treat individuals that are affected in these disaster situations. So the distinctions between the patient receiving the treatment and the participation involved in the research can somewhat disappear.

This can be problematic in many ways. For example, in terms of understanding whether we might need ethical approval for our activities. Whether we need to follow some kind of research protocol. Thinking about what kind of consent we might need to obtain from individuals. What levels of risk might be acceptable to ask them to expose themselves to.

I also think that conducting research in the emergency setting can implicate numerous different actors and organisations that are going to be operating at different levels that can be quite different to locally based research in a lab. For example, global health emergency research is going to include involving local communities, but different local communities perhaps from different countries and across different borders. Thinking about different participants, patients, governments, non-governmental organisations, humanitarian response workers, pharmaceutical companies, collaborative networks, international organisations like the World Health Organisation, different public-private-partnerships. And each of these actors are going to be bringing in their own priorities and potentially their own conflicting values as well.

I think another layer of complexity that we need to be aware of in the health emergency setting is the limited resources that can be available during these times. Rapid response can be quite critical and research might not be taking place in the nice, shiny labs that it might occur in in non-emergency settings.

There's also going to be issues around timeliness for obtaining ethics reviews of research protocols. There's going to be challenges around study design as well. Questions around whether Randomised Control Trials (RCTs) are the most appropriate models for conducting research during health emergencies. We need to ask: is it ethical to offer placebos to participants when there are no pre-existing treatments and when access to an investigational drug is the only potential option that an individual might have to get better?

There have been some debates recently around whether we should nonetheless stick to the gold standard randomised control trial model. I think some would argue that the RCT model is the best way for us to get scientifically variable, robust evidence. But others have suggested that we really need to be thinking about adaptive trial designs.

So adaptive trials basically do what they say on the tin. They're adapted during a study according to interim results about how effective or ineffective a given intervention is. So rather than having a fixed, pre-determined research protocol like we would have with a RCT, adaptive trial designs can allow for some flexibility. So advocates of adaptive trial designs suggest that more patients ultimately will receive some kind of

treatment because study arms will be dropped if we can see from an interim analysis that another arm is better.

So those are some of the ways - not all - in which the emergency setting might raise different kind of questions around how we approach our research.

Rebecca: *Right. And so you mentioned there that randomised control trials are usually sort of seen as the 'Gold Standard' because they get that scientific validity. And then you also mentioned that often research in global health emergencies isn't being conducted in labs or with those sort of perfect conditions that we might think. So what does that mean for the applicability of the things we find out in one setting to other settings?*

Dr. Sethi: So I think that relates to a really important question about priority setting and about social value in research. So thinking about whether or not the research questions that we're asking actually apply to the communities in which we're conducting the research. And that's a really important question for researchers to actually reflect upon before they embark upon any research: What is it that we're trying to find out? Why are we trying to find it out? Is it actually going to benefit the communities where we're conducting the research? Are they going to have access to any therapeutics or investigational drugs that might actually subsequently emerge from the research?

Rebecca: *So as this is a 'justice' podcast, obviously we have to ask the question: What sort of ethical issues can arise during research in global health emergencies? What are the kind of things we need to pay attention to? What's at stake, ethically speaking, here?*

Dr. Sethi: I think I've already touched upon this idea of justice thinking from a kind of fairness and inequality perspective, and thinking from an access and benefit-sharing perspective, and a social value perspective.

There are some other issues that I think are really important. We need to be thinking about consent here. So there are different types of consent: for example, explicit, implied, informed, broad, blanket, dynamic [consent].... the list goes on. We need to think about what kind of consent is going to be appropriate or inappropriate in a given context.

So as I mentioned previously, the lines between research and treatment/response are blurred in the global health emergency setting. So we need to kind of ask: what are we asking individuals to consent to? Is there a risk of therapeutic misconception where even though researchers might have explained that a RCT is taking place - that the purpose of this study is to generate generalizable knowledge and that there's a chance that an individual participant might just receive a placebo -, the individual might still think that they're undergoing treatment and that they will nonetheless access an investigational drug?

We need to ask whether participations are going to have unrealistic hopes around experimental therapeutics and perhaps not weigh up the potential risks of participation. Some other important questions we might want to ask around consent include: What are you seeking consent for? When do you seek consent? When is consent necessary or sufficient? Who do you seek consent from, if not the patient? For example, what if patients are unconscious? What if they're minors? What if there are different power dynamics or there's undue influence going on?

So those are some issues around consent.

I think we also need to think about trust and trustworthiness. So there may be some historical memories of exploitation and different dynamics - particularly if we're thinking of researchers coming in from wealthier nations to poorer nations. There might be issues around exploitation. We need to think about colonialism, for example. Thinking about the different power dynamics and relationships between researchers and local communities. Context-sensitivity is incredibly important here: understanding what the needs are. What the pinch-points might be for local communities?

Remembering that potentially these participants may be quite vulnerable. We shouldn't assume that individuals are vulnerable, but we need to be aware that obviously there are various conceptualisations of vulnerability as well. But it's worthwhile considering whether patients and participations in a global health emergency setting might be subject to heightened vulnerability. Thinking about the fact that they're going through particular hardships, for example, having been displaced from their homes, being ill, having lost loved ones. The health emergencies actually might be taking place during times of war, during times of mass

migration. So we need to think very broadly about what else is going on at the moment in time in which we're trying to conduct this research.

I mentioned a little bit about benefit-sharing. I think it's important to think about not just about whether or not research findings are shared with those communities, but also thinking about access to the drugs that might have been developed. Access to any profits, for example: if commercial companies are involved, if pharmaceutical companies are involved and they're developing drugs, are these drugs that the host communities can actually afford to access? These are massive questions around justice as well.

Rebecca: *Are there any other sort of examples of when things went wrong in global health emergency research? And if there are, have we learnt anything from it? Or what have we learnt? What are the lessons to take forward there?*

Dr. Sethi: Yeah, I mean there's quite a few. We're human beings and we're constantly getting things wrong and we're constantly trying to learn from our mistakes.

I think definitely there are some examples of where we could have done better. So, for example, the MERS virus and H5N1 also known as avian or bird flu raised important questions around ownership of virus samples and who stands to benefit from any vaccines or therapeutics that are developed by virtue of those samples.

Indonesia refused to share its H5N1 virus samples with the World Health Organisation in recognition and out of protest of the fact that low-income countries traditionally struggled to access the very expensive vaccines that have resulted from sharing such samples. So often these samples will be sent to WHO approved labs in wealthier countries, who will then develop vaccines. So the poorer countries may not be able to access the vaccines, as I mentioned before. But there are also intellectual property (IP) issues here, where the wealthier labs might then have access to the IP for these drugs as well.

So in response, the WHO set up the Pandemic Influenza Preparedness Framework to facilitate more equitable virus sharing, so strengthening

the sharing of viruses and low income countries' access to any resulting vaccines. But there's still a lot of room for improvement, there.

Another example that comes to mind is again the West African Ebola Outbreak from 2013 to 2016. So as I mentioned before, the World Health Organisation received criticism in the delay experienced in actually triggering Public Health Emergency. Aside from that, there were also issues around the timeliness of obtaining ethical approval. As I mentioned, there were also debates around trial design and whether or not randomised control trials were ever appropriate, or whether adaptive trial designs needed to be considered.

But there are also really important questions around engagement with local communities. Which again speaks to context sensitivity and trust and trustworthiness. So in order to contain the spread of disease, it was very important at that time that dead bodies were contained and touching of dead bodies remained minimal. But burial practices were very very important to local communities that were affected. And there were some important lessons we needed to learn in terms of the need to engage with local communities in order to understand traditional practices, to understand that burial practices were very very important culturally.

So researchers actually ended up engaging with tribal elders. They were able to understand the importance of these rituals of burial practices. And then they were able to communicate with the elders and through the elders to local communities why they needed to contain the bodies as quickly as possible and why touching the bodies was risky in terms of spreading the disease. I think that's another example of where a lack of cultural sensitivity could have been avoided by some early engagement.

Rebecca: *And in one of your papers, I came across this term 'helicopter research'. And this brought to mind 'helicopter parenting', but I'm assuming it's not the quite the same thing. So could you maybe explain what helicopter research is and why it's an issue?*

Dr. Sethi: Sure. So ‘helicopter research’ is a term that's used to describe research that often involves a researcher or a research team from a wealthier country often flying - maybe not just not flying - to a developing or poorer country, a low income country, in order to carry out research.

So often the researchers might collect data, or samples, or both, in the host country and then they'll leave taking that data and those samples with them. And then they'll publish that research back in the developed and wealthier country.

So helicopter research is often connected and traced back to colonialism and practices of colonisers and researching indigenous peoples, their cultures and traditions, and essentially creating a monopoly on who gets access to use this information and to benefit from it. Often these would have been used in genetic samples in the context of trying to prove a superiority in terms of knowledge gathering.

Obviously this type of research is problematic for many reasons. For example, research might involve only minimal collaboration with local researchers and that can be quite instrumental, for example, in order to gain access to local participations or networks or just to help with wider logistical organisation. This can mean that in spite of the research being highly dependent upon the country in question - the host country -, there is a lack of benefit sharing, there's a lack of building any capacity for local researchers, or contributing to helping develop local infrastructure, for example, by providing training and access to the latest technologies that these host countries might not otherwise have access to.

Another big problem can be that researchers may have little knowledge or understanding of the communities they're conducting their research in. And that can preclude them from identifying different ethical issues that might arise with their research.

So I just mentioned the issue around burial practices during Ebola, but I'm also thinking about genetic research. For example, the Havasupai Tribe in the US, they consented to their blood samples being used to study increases that were going on in their community of rates of diabetes. But in fact the research was also conducted on inbreeding and alcoholism and trying to understand the origin of Havasupai Tribe. This directly went against the Tribe's own kind of traditional identity and their narrative origin story.

Another issue is that research findings might not necessarily be fed back to the communities that the research is being conducted in. And again, as I mention, often they don't stand to benefit from the therapies that result from the research. So in terms of questions of justice: again, deeply problematic.

But I do think it's important to note that not all internationally collaborative research is exploitative. Not all internationally collaborative research is helicopter research. If we're thinking about global health emergencies, international collaboration is paramount. Wealthier have the means of conducting research that lower income countries may not have. So you could argue that we have an ethical obligation, a moral imperative, to allocate resources to conducting important research that otherwise could not take place. I think what we need to think about is: What kind of research are we doing? Who stands to benefit? How are we doing that research? So it's not necessarily that international research collaborations are bad in and of themselves. It's thinking about all the different questions that I've tried to outline.

Rebecca: *Well thank you so much for taking the time and having a chat with me. It's been fascinating.*

Dr. Sethi: No problem. Thanks for having me.

[Outro music]

That's it for today – we hope you enjoyed the today's episode.

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If you have any questions, comments, or ideas for topics *you'd* like to hear about in future episodes, please emails us at ghe@ed.ac.uk. We're also on twitter as @GanguliMitra and @reb_richards.

Be sure to check out and explore our website “Justice in Global Health Emergencies and Humanitarian Crises” for more great content, just go to https://www.ghe.law.ed.ac.uk/.

Thanks for listening and see you again on the first Monday of the month for the next episode.

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