Centre for Personalised Medicine podcast

Series 2, Episode 7

Why research regulation falls short in genomic medicine

SPEAKERS

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Rachel Horton
Welcome to the Centre for Personalised Medicine podcast, where we explore the promises and pitfalls of personalised medicine, and ask questions about the ethical and societal challenges it creates. I'm Rachel Horton, and I'm here with Gabby Samuel. In today's episode, we're looking at neoliberalism- how in our society, we tend to focus a lot on risk and try to control it through regulation, but this doesn't always work well in ensuring ethical practice, particularly in relation to genetics. We're joined by Dr Kate Lyle, Senior Research Fellow at the Clinical Ethics, Law and Society group at Oxford, who recently published a great article in the Journal of Medical Ethics exploring this issue.

Kate, please, could we start by talking about how you got interested in this area?

Kate Lyle
Yeah, I'm a sociologist, and my research background is in health and healthcare technologies. I'm particularly interested in the implementation of new technologies and how they change practice, and what we need to do to incorporate those in practice. So I'm currently looking at genomic medicine, and looking at how we can help prepare patients and professionals for the changes that this will bring in practice, and particularly focusing on the social and ethical challenges that it raises.

So we're focusing on this concept of ethical preparedness. So really trying to look at what can we do to give people the skills and support that they need to anticipate and navigate the ethical challenges that genomic medicine will raise for them, when they arise, and be able to and feel like they can approach… they know how to approach them, whatever those challenges might be. So part of this is about looking at how ethics is approached through the regulatory systems around research and healthcare practice. And we find that, unfortunately, sometimes they sit in contrast to an ethical preparedness approach.

Rachel Horton
And can you tell us a bit more about that?

Kate Lyle
Yeah, so the research ethics systems in the UK are very compliance-focused. So we've got lots of policies that are intended to tell researchers what is and isn't allowed- what they are allowed to do and what they aren't allowed to do in quite a restricted way. So this compliance-focused approach to research ethics has its roots in broader neoliberal

approaches to governance.

Rachel Horton
Could you tell us a bit more about neoliberal approaches? And what they mean?

Kate Lyle
Yeah, so neoliberalism is a political and economic ideology, that essentially centres everything around the individual and their rights and responsibilities to make their own choices and manage their own risks. So there's a big focus on quantifying risk, the idea being that if all risks associated with certain activities and certain behaviours can be quantified and made clear to people, then they are free to make their own judgments about what levels of risk are acceptable to them, and what they're prepared to take on. And then importantly, they are they can, then they're held responsible for their own choices that they make, and whatever might come of those choices.

Gabrielle Samuel
So, could you just tell us how that ideology about risk links to healthcare research, to make that connection?

Kate Lyle
Yeah, so in that context, that neoliberal context, research and healthcare research is seen as a risk. So we all need to be made aware of all the potential risks of participating in the research, and then we can make an informed decision about whether those risks are acceptable to us, and if this is something that we want to be part of.

And this idea of healthcare research being risky activity has been reinforced by a series of very high profile scandals that I'm sure you will remember. So such as there was the unauthorised retention of organs at Alder Hey hospital, and then also the case of Harold Shipman, the GP that murdered hundreds of patients. These sort of high profile scandals have provided more impetus for the government to intervene to try and regulate and minimise risks around healthcare practice and research.

And the way this has been done, it's been through the development of regulatory policies that tell people what to do. And then institutions that have been set up to ensure that people are complying with those regulations. And because as we've already said, individual rights and autonomy are so central to neoliberal approaches, there's been this really concentrated attention on the concept of consent in research.

Rachel Horton
So what's sort of the issue with that? In terms of what's, what's the problem with this major focus on consent?

Kate Lyle
Of course, consent is absolutely important in research and risks need to be communicated to potential participants, so they can make those informed decisions. But the problem comes when the focus of ethics is so much on consent, that it overshadows other important ethical factors that also need to be considered. So there are criticisms that consent has

come to be seen as an ethical panacea, and is often the only frame of reference that's used to consider whether specific research activities are ethical or not. So really, what I'm saying is, while consent is really important, and we absolutely shouldn't be doing research without consent, at the same time, it shouldn't be seen as a proxy for ethical research.

Gabrielle Samuel
That sounds really interesting, Kate, and it's something that's come up in my research as well. I was just wondering if you could give us an example to illustrate what you mean?

Kate Lyle
Yeah, so there's a really good example that we wrote about in the paper. Where this focus on consent has gotten in the way of, or potentially got in the way of really good research. So a few years ago, a team of researchers were trying to set up a trial that was looking at rapid genetic testing to guide antibiotic use. So this was a really great study that had potential to make a clear difference to care.

So the background to this is that there are particular antibiotics called aminoglycosides that are frequently used to treat sick babies but they also have the potential to cause hearing loss in a small portion of the population that have a particular genetic variant. So it's about one in 500 people have this genetic variant. So ideally, you'd want to test for that variant first. And then you can give an alternative treatment, if you find that they have the variant that will mean that they go deaf.

So genetic testing for this variant is frequently done in non-emergency settings. So, it's really common with children that have cystic fibrosis, so we know that they're going to, they're likely to need quite a lot of antibiotic throughout their life. So they are frequently tested for this variant. And then, if they have the variant, then they can be given a different line of treatment. That's equally effective. Because the issue with aminoglycosides is they are recommended as the first line of treatment not because they're more effective, but because they don't readily contribute towards antibiotic resistance as some other antibiotics do. So there are other equally effective treatments available.

So testing for this variant is traditionally done through the NHS laboratory, and it takes about three or four days to come back. So this is fine in a secondary care or primary care setting. But in an emergency setting, that's not going to be any good when we need to act straightaway on the results.

So the research team saw a clear need here for a rapid point-of-care test that could be used in a neonatal intensive care unit to test babies when they come in to see if they have this variant. And then could be given an appropriate course of antibiotics. And they calculated that this could prevent approximately 180 cases of irreversible deafness each year, which is quite a significant impact. So they worked with an industry partner, they developed the point-of-care test that could deliver the results in less than 30 minutes. And that was approved for use by the regulatory body. And then they applied for research ethics approval to run a study to see if it was possible to implement this technology within current practice within the neonatal intensive care unit.

Rachel Horton
That sounds like a really great idea on the face of it, what were the challenges in making that actually happen?

Kate Lyle
Well, the real challenge that they had in getting this through the ethics system was focused around consent. Obviously the shorter timeframe for the delivery of the results was the main selling feature of the test, but that shorter timeframe also meant that there was less time for seeking consent from participants to use the test. And this raised a problem in terms of the regulations.

So generally with genetic tests, the consent process can take quite a long time. And it's important to give patients time to weigh up the pros and cons of the test and decide whether they want to have it. Whether they want to go through with testing, especially as often the result of that test won't actually affect their treatment options. But the difference here is that there is clear action that can be taken on the basis of a positive or a negative result. But that action needs to be implemented very quickly.

So the researchers decided that they would seek consent for the clinical use of the test, and participation in the research separately. So essentially, when a baby was admitted to the neonatal unit, the parents would be told “we're going to do a range of tests on your child, one of which will involve looking at if they've got a genetic predisposition to deafness if we give them a certain antibiotic”. So that was sort of consent to use the test. And then at a later point, the parents will be asked whether they would consent for their child's data to be used in the clinical trial. And at this point, if they said, “No, we don't want to be part of that trial”, then their data wouldn't be included. So a two stage approach to consent.

The individual ethics committee that looked at the study, after some deliberation, decided they were quite happy with this approach. But then their decision to approve it was revoked at a higher level on the basis that the trial might be in breach of the Human Tissue Act because of this approach to consent.

Gabrielle Samuel
So, why would it be in breach of the Human Tissue Act? Why did they think that?

Kate Lyle
So yeah, so this is quite interesting. So the Human Tissue Act, regulates health care, research and practice. And the point of it is to ensure appropriate use of human tissue and this came off, particularly… this regulation particularly came off the back of the scandal that we talked about earlier, where organs were being retained without permission in a hospital. So yeah, so this act was set up to make sure that everybody knew what they should and shouldn't be doing with human tissue. And the Act specifically mentions DNA material in there and says that DNA analysis should never be done without qualifying consent. And the ethics body felt that the researchers approach to consent didn't meet this standard of qualifying consent.

So there was a lot of back and forth between different organisations and legal advice was

sought. And then eventually, they came to the decision that they could approve the trial design, on the basis that administering the test represented a *clinical* decision, rather than a research question. And so then when it came to be seen as a clinical decision, then that was governed by a *different* part of the Human Tissue Act. That says that if it's being used for medical diagnosis, or treatment, then DNA *can* be analysed without explicit consent.

Gabrielle Samuel
This sounds really confusing, like, I can imagine, as a practitioner, how would you know, like, the rules for research, and the regulations for clinical practice?

Kate Lyle
Yeah, it does feel like a minefield. And I think what I find really interesting about it is that so they *did* finally approve the study with the original consent process in place, so they didn't change anything around it. It was just, it was focused on the semantics around it, of how we classify certain activities. The researchers didn't have to change anything, everybody had to change their mindset about what that activity represented. So even though the trial was approved, in the end, this was a real problem for the researchers, it significantly delayed the start of their trial. And at one point, they thought they weren't ever going to be able to do the trial at all. And that fundamentally challenged the whole concept of genetic point-of-care testing.

Rachel Horton
It's interesting how, like oblivious in a way the regulations were to the context that like, here you need is a quick result. And that was the whole point of the test and there was nothing that could account for that and a sort of like, another way needed to be found within that same regulation to make it happen, rather than being able to look at the idea at face value and say, this makes sense. Can we make it happen?

Kate Lyle
Yeah, yeah, exactly. And I think now, this is such a great example of how the focus on consent can really sort of blinker you to what are the real ethical issues at stake. And I think here, the ethics body were really focused on: what is permissible, permissible within the remit of the regulations, and even within the wording of the regulations, rather than what is ethical in the context of that specific situation? And think the important things in that specific situation was that the point-of-care test had already been approved. So we knew that it worked for detecting that variant, testing for that variant is recommended in other settings, in secondary care settings. And so this was *just* about saying, can we detect this variant *quickly* to act on it quickly in an emergency situation? So from that perspective, I think you could argue that it would be unethical to *not* trial that innovation, considering it could make such a difference to practice and to improve care for those children.

Gabrielle Samuel
I think that's quite interesting, because I… often when I'm looking at ethical research, you don't hear that counter is, is it unethical *not* to do the research. That's not often considered, right? It's always about risks. And, yeah, so I just think that's quite an interesting reflection, because all of my work around big data kind of hits that same issue with consent? So when I spoke to research ethics committee members, they focus on this need for consent to

approve research, even when it's so difficult to get consent. And I'm just wondering, after you've done all this research, what's the way forward? Like, what can we do?

Kate Lyle
I think that we would argue that the way forward is ethical preparedness. And I think one of my, one of the other problems with this focus on consent and this compliance approach, so not only does it potentially exclude consideration of the other ethical issues that are really… the ethical issues that are really, really at stake and potentially prevent really good research. It also sends the message that ethics is not for researchers to think about, it's for institutions to think about, it's for… there's *separate* bodies that will decide for you if something is ethical, so it's not your job. So you just… you just write your protocol, and then somebody else will tell you if that's ethical or not. I think that's a really dangerous message to give because it is essentially absolving researchers of having any sort of responsibility for ensuring ethical practice.

Gabrielle Samuel
I find this a really interesting tension, between on the one hand, researchers needing to have some form of responsibility about… ethics is different, you know, bureaucratic ethics and everyday ethics, but needing to have that ethical reflection in everyday decision making, versus concerns that I've seen raised in the literature about if we give everything, all the responsibilities to researchers, they have a vested interest. So how… we need to ensure that those vested interests have some form of gate-keeper. See what I mean?

Kate Lyle
No, I completely agree with that. And I don't think, you know, the answer is not to go from one end of the scale to the other. We don't, and I would *never* advocate at not having regulation, I think regulation is really important, and we do need it. We *also* need researchers and healthcare practitioners that are able to take responsibility for ethical issues, and are able to *look* for ethical issues in their own practice, and then think about "how do I navigate those?"

And I think part of navigating those is not to say, it's not this individual individualistic approach of "oh well your responsibility, you're responsible for ensuring ethical practice", it needs to be… It's a community response, isn't it? As a research community, we all need to… everybody wants to do ethical research practice, and as a community, we need to find the best way to ensuring that. And regulation has a role. And researchers have a role. We just need to redress that balance a little bit, and make more space for us to have these discussions about how should we be navigating certain challenges in practice, so that it's not always just a "well let's just look up the regulation and see what that says", because we're never going to get all of the answers from regulation.

Gabrielle Samuel
And so we just correct me if I'm wrong. So what you're saying is that in terms of regulation, rather than having it as this kind of hierarchical system, where it's above you and tells you what you should do or should not do, but it should be much more kind of iterative, back-and-forward approach where you can have discussions with regulators about ethical issues.

Kate Lyle
Yeah, yeah, with regulators, but also with researchers as well. I think there's much more… we need to make much more space for that. So that regulation is something that we draw on, as part of a variety of resources that we would draw upon to work out "what is the most ethical thing to do in *specific* contexts". I think that's the key thing we need a more situated approach that takes in other considerations in specific settings, which regulation can't do. By its very nature, it has to be decontextualized and standardised and that is not always going to give us the right answers for specific situations.

Rachel Horton
If you had one message for people to take away from this podcast, what would it be?

Kate Lyle
I think my message would be for the research community as a whole. And by that, I mean individual researchers, as well as regulators and ethics committees, and funders and publishers of academic research. That we just all need to think about the role of consent, and how that's been positioned in relation to research ethics, and just really think about it. Consent is not the only ethical issue. We all need to question how we approach ethics, and particularly this role that we've given to consent. Consent is not the only thing and we all need to think about our own responsibilities in relation to ensuring ethics, ethical research practice.

Rachel Horton
Kate where can we go to find out more about your work?

Kate Lyle
You can read about that case study in the paper that I wrote in *The Journal of Medical Ethics*. It's called "Beyond regulatory approaches to ethics: making space for ethical preparedness in healthcare research". And on the website, you can also access a blog that I wrote to go alongside that paper, which is called "Is neoliberalism bad for our health?"

Rachel Horton
Thank you so much, Kate for making the time to talk to us today. It's been really great to talk more about your paper. And thank you for listening to this episode of the Centre for Personalised Medicine podcast. If you'd like to find out more about personalised medicine and its promises and challenges, please visit the Centre for Personalised Medicine website at cpm.well.ox.ac.uk.

Note
The test trialled in the Pharmacogenetics to Avoid Loss Of Hearing (PALOH) study discussed in this episode has gone on to be conditionally recommended by NICE for use within the NHS (https://www.manchester.ac.uk/discover/news/genetic-test-to-prevent-newborn-babies-going-deaf-recommended-by-nice/). The PALOH study has been celebrated as ground-breaking, winning the New Statesman Positive Impact in Healthcare Award 2022 (https://mft.nhs.uk/2022/12/14/national-recognition-for-manchester-led-research-that-could-save-the-hearing-of-hundreds-of-babies-each-year/).