F: Thank you very much Rory. It's a great pleasure to be here. I'm the new chair of the new Ethics Advisory Committee, so I just wanted to tell you a little bit about the changes that have been in ethics governance at UK Biobank. The Ethics Governance Council was established by the funders when UK Biobank began its recruitment back in 2006 and that very much acted as an independent guardian of the UK Biobank ethics and governance framework also set up around that time. It monitored and reported publicly on the conformity of the UK Biobank project to that framework. It was responsible to advise on the interests of research participants and the general public in relation to Biobank and it's quite a separate, rightly so, entity from UK Biobank. In 2018, the governance council itself recommended that its oversight role might now, having moved on in time be more effectively discharged by better integration within UK Biobank as an advisory committee of the UK Biobank Board and I was very honoured to be asked to be chair of that new committee.

So the remit of the Ethics Advisory Committee - my impression is to be a bit more hands on in providing ethical advice and ethical research. So we are asked to advice the UK Biobank Board on ethical issues that arise in the maintenance, development and use of the UK Biobank resource, including identifying, defining and examining relevant ethical issues. I'm going to give you an example of one of those in a minute, delivering key research in those areas providing advice, guidance and recommendations on those relevant ethical issues and reviewing and advising policies which have an ethical dimension that is relevant to UK Biobank. We are quite a small committee at the moment, looking for further members over this next year, but our expertise is quite broad already. We've got clinical bioethics, law, philosophy, epidemiology, molecular science and broadcasting experience. So we've got quite a wide range to look at some of these issues.

So, although as we've already heard and you've heard in previous conferences, UK Biobank is a very distinct entity with very clear policies on consent and feedback. I think it is worth just thinking about its position within the government provision for five million whole genomes. I see that as a set of overlapping activities. I'm not aiming to identify the boundaries of those, but what I do think is that those activities will gradually become more and more overlapping. So it is worth thinking about those ethical issues at those interfaces. If we think of UK Biobank as a largely research exercise, half a million people will form ultimately ten per cent of that vision so it is a significant component, then clinical practice, the 100,000 genome project and the new genome medicine service are both clinical practice, but also need to be a research enterprise and therefore overlapping. The proposed plans to offer whole genomes to health volunteers of course may have a commercial component to it but will end up in clinical practice and also be referred.

So there is overlap between these three different areas and I think that there is ongoing debate about the types of consent that each require and I think that's an important debate, but not easily solved. There is ongoing debate on the type of feedback for each but I think UK Biobank has been particularly prescient in not offering feedback. Diagnosis and prediction of course are often conflated and that's an important area and we're looking at healthy genomes or people who come with particular signs and symptoms. Genomics continues to attract a very deterministic discourse so that the interpretation of uncertainty can be very variable. I just want to give you a cautionary tale that's already come from UK Biobank data which I think sets up a
very good example for the Ethics Advisory Committee to think about when it's looking at these overlapping boundaries. So this is a composite example of cases that have come to my attention from around the country. So I've made it sound like one, but I know that there are quite a few of these already.

This is Jane who is aged 50 and she's given a direct to consumer ancestry test as a present. You can get them for £49 now, so not a very expensive present. She then sends off her raw data for secondary analysis for medical results. Again, that's increasingly common practice, I understand, and in that secondary analysis a BRCA1 mutation is found. Now she's got no family history of breast or ovarian cancer but she's concerned by that result because of the prevailing deterministic discourse I think around those types of results. So she would like a risk-reducing mastectomy and oophorectomy and she has a willing surgeon to perform those. However, when she is seen in the clinical service, NHS Sanger sequencing shows no BRCA1 mutation. Initially when these cases came up, we thought, well that's an artefact, it's just one to those things. But actually I think many of you in the audience will know this much more than most clinicians do, that snipper rays, which most of these ancestry tests of course use, are really bad at calling rare variants which is a BRCA1 variant. In fact, UK Biobank data has very nicely shown that about 85 to 95 per cent of rare variants called by direct to consumer tests are in fact wrong.

So I think a very good example of why feedback of this sort of information is actually a really bad idea. An extra screen for people like this may not be so damaging, but clearly risk-reducing surgery when it's not at all indicated could be hugely so. So I think there are two things that have become clear from UK Biobank data already and that's through comparing the snipper rays with sequencing data, that snipper rays are really bad at calling rare variants, so that's to do with the analytical validity. Your genetic code isn't necessarily a genetic code that you think it is, but also that the clinical validity may not be quite what people think it is in the sense that penetrance of pathogenic mutations in health populations seems to be much, much lower. Again, this is one of many papers I think that have highlighted this, that mutations that apparently seem very strong or penetrance of 85 per cent if ascertained through a disease population, if you look in the healthy population the penetrance might only be ten per cent. Clearly that has really important implications for feedback and then subsequent clinical management.

So I think both of those examples are really good examples of why we need to be very careful about feedback, especially when genomics are still continually presented as a very deterministic exercise and where I think UK Biobank has been very prescient in saying that there is no feedback of any of its results. It stays firmly in the research setting. So, what we would like the new Ethics Advisory Committee to be is an agile, responsive service for UK Biobank that's relevant for current and future activity of UK Biobank. But that also looks around UK Biobank and is relevant for other cohort activity, but also relevant for clinical practice and the commercial endeavour of looking at whole genomes as we go forward and as we realise that those activities increasingly overlap. Thank you very much.

[Applause]
[END OF TRANSCRIPT]