[MALE SPEAKER]
[Other comments:]

Okay, we're going to move rapidly on, so hopefully two ten-minute talks gentlemen, so we have time for questions. So just, come up. Peter Wurtz has done a lot of work on NMR and he works at Nightingale. So Peter tell us about metabolomics and your particular vision.

Yes, thanks Navid. It's a great pleasure to be here today and to tell about some of the most exciting scientific projects that I've ever been part of that we're now announcing today. So the talk will outline some of the aspects of how detailed metabolic profiling can really help to enrich the UK Biobank data resource. So many of us work to realise the promise of personalised medicine, but a key challenge for that is that in order to understand all this data for the individual levels, you first need to measure them at large-scale studies such as UK Biobank. I think today we've seen talks about genetics and how this is now starting to become true by measuring these panels at a very large biobank scale. Then we start to better understand the role of this data for the individual. So UK Biobank has really raised the bar for the genomic data and the healthcare records in integration, but one key aspect that has been missing is really this detailed metabolic profiling or molecular profiling from broad samples.

If you have such detailed metabolic profiling, you can really better understand and use also the other layers of data available in large-scale biobanks such as the genomic data or the clinical phenotyping, imaging, questionnaire data indices end-points. So you really add value to the biobank by also having molecular profiling at a very large scale. Well, until recently, there have been technical limitations to make this happen at the scale of studies like the UK Biobank, but this is now changing. So we are proud to announce that Nightingale and UK Biobank together will engage on this new initiative to measure all half a million blood samples really with the goal to enhance biomedical research and also with a view towards taking this to clinical applications. So this project will be conducted over a duration of 30 months from the initial commencement of the blood analysis expected at the beginning of next year.

So, how are we going to enrich the UK Biobank resource with this detailed metabolic profiling? So Nightingale has developed this NMR metabolomics technology, which, from a single blood sample, a single experimental run, captures the comprehensive metabolic profile of both lipid measures and small molecules circulating in the bloodstream. So if we look in detail at these molecular biomarkers that will be provided to the UK Biobank resource, these cover measures of cholesterol and triglyceride metabolism, both existing measures used in clinical practice and much more fine grain measures of lipid metabolism, fatty acid concentrations like Omega 3, reflecting dietary intake, other fatty acids reflecting also adiposity, ketones, glycolysis-related metabolites, markers of inflammation. Also, for instance, amino acids for which many of these have been shown to predict the risk of future type 2 diabetes, heart disease and even neurological diseases later in life.

One particular fine grain profiling will be on lipoprotein lipid metabolism where we capture

lipoprotein subclasses carrying the cholesterol, triglycerides and phospholipids in the blood circulation, obtaining much more fine grain information than the routine lipid panel provides. So all together, there are 225 metabolic measures that will be provided by this assay. So why are we so excited about this? Well, Nightingale is specialising in this comprehensive metabolic profiling using NMR metabolomics and we've conducted quite a number of studies in much smaller cohorts with around half a million samples or so measured from biobanks and trials. Many scientific applications are already showcasing added value to biobanks and trial studies, but now going to the scale of UK Biobank, we expect that this is now changing the game and really enhancing the possibilities to do better biomedical research and also uncover novel clinical applications.

So really the scientific opportunities of how to use this data in connection with all the other risk data available in UK Biobank is just endless. So it ranges from biomarker discovery, a better understanding of disease mechanisms on a molecular level, molecular readout of various lifestyle effects like diet and physical activity, all the way towards health tracking and realising the goal of precision medicine. I'm just going to highlight three examples here. So one example is combining this detailed metabolic profiling with the vast resource of genetic data available in the UK Biobank, where we get for many of the genes, a more comprehensible molecular readout of what these genes are doing on a molecular level as seen in the blood concentrations of biomarkers in all these individuals. So we can then better understand how genetic basis is regulating metabolism, but we can also use the genetic data converted around and use that to better understand what the role is of these biomarkers and are they potentially causal for future disease onset.

A particularly exciting application of this is to look at what the detailed metabolic profiles are for the genetic variance that mimics the effects of known and novel drug targets. So this gives the opportunity before the drug targets are tested in humans, to see what the detailed metabolic readout is with these, potentially uncovering a better molecular understanding of what the effects of the drugs are and even in some cases could highlight potential side effects. If this application, together with genetic data is further combined with profiling of a randomised clinical trial, one can even start to separate the on and off target effects of these different medications. There are some recent applications for both statins and PCSK9 inhibitors where we showcase how this detailed metabolic data provides a better understanding of the molecular mechanisms of these lipid-lowering drugs.

Another exciting application is the biomarker discovery, which now can be taken to a whole different level with the scale of UK Biobank. Some results are shown here for a small-scale study where we had around 10,000 individuals looking at metabolic profiling and the future risk of heart disease and stroke, where we uncovered novel biomarkers, predictive of future heart disease risk as strongly predictive or even stronger than LDL cholesterol. We see examples where if you subdivide the individuals into young and old individuals, you can start to uncover the patient groups for which these novel biomarkers are relevant to, with the goal of really enhancing eventually clinical decision-making based on this biomarker data. So you can better improve the prediction of future disease risk so you can target prevention to the right individuals, but in addition, you can

also better track the health state over time, so the molecular effects of both lifestyle and pharmacological interventions.

So we are pretty excited about this initiative and there have been many studies with cohorts done already that have highlighted the potential of metabolic profiling to better predict future disease risk and realise some of the promise of personalised medicine. There really have been technical limitations to go to the scale of studies like UK Biobank, but it is clear there is a call from both the research and clinical community that can advance these detailed molecular profiling technologies to the scale, to the throughput and low cost and standardisation required for clinical use. We believe that this initiative together with UK Biobank is giving us a major leap towards realising that goal. So we look forward to working together with the biomedical research community really to unleash the promise of this detailed metabolic profiling on an unprecedented scale. Thank you.

[Applause]

[END OF TRANSCRIPT]