UK Biobank Newcastle Participant Event Subtitles

M.E: So, to introduce myself, I'm Mark Effingham, I'm the Deputy Chief Exec based at our coordinating centre in Manchester, in Stockport, which is where we hold all of the biological samples and where our laboratories are based, and I'll be chairing the session this afternoon.

B.L: I'm Ben, I'm an epidemiologist and public health physician at Oxford. And I lead the epidemiologist group and our role really is to help the chief scientist at UK Biobank think about how we might enhance the study and analyses that might kind of help the study run more smoothly. So I'm gonna talk about the value of UK Biobank imaging data to population health research, but I'm going to start by describing the study design. I know that some of you will be familiar with that already, but some of the other data that we've collected. Because as you'll see the value of the imaging data, some of the value of the imaging data is that it's linked to all this other data that we've got in the resource. So as you're aware, UK Biobank is a scientific study that's following the health of half a million participants to understand how much genetic, physiological, lifestyle and all those environmental factors interact to cause disease. And it really is unique both in the kind of scale, so that's the number of people involved, the depth of information we have on their lifestyle, their health, but also the events that occur during the follow up and the length of that follow up. Now we've got over kind of 10 years.

So before UK Biobank, studies used to be either very small and collect lots of information or they were very large and had a very small amount of information in each participant. So UK Biobank really was a pioneer combining that kind of scale and depth. So we have a research database that's been kind of continually updated and enhanced and it's accessible to researchers all over the world who are using it to make scientific discoveries on a wide range of diseases for disease. Participants were recruited between 2006 - 2010 there was just under 60,000 from the northeast. 35,000 from Scotland. They were aged 40 to 69 in recruitment. They were all registered with the NHS and living within 25 miles of one of the 22 assessment centres. So over 9 million invites were sent and half a million participants attended. So those of you who are participants will recognise something like this in the assessment centre there's a touch screen questionnaire that had some very detailed questions, that was followed by a verbal interview, some physical measures including blood pressure, heart rate, height and weight. Spirometry, so that's lung function test you may have remembered kind of blowing into a tube. And then some participants there were some additional tests that were performed, and in all participants there was a sample collection of blood, urine and saliva. And the long term storage of those and those samples really required an industrial process. So both to kind of collect and then how they were then frozen and how were they then divided it into over 15 million aliquots and small samples. And they were taking to long term storage in facilities like this and because of the challenge of retrieving samples for particular analyses, it requires a robot working 24 hours a day.

So this is who's in UK Biobank. The average age is just over 50, half were, just over half were female, most were white ethnicity, but they were good numbers of people from non-white backgrounds and they tend to be more affluent than the UK population as a whole. But again, a good range from various socio-economic groups. And those participants have followed up. So we link the data from participants to mortality data. To cancer data that dates back to the 1970s, hospitalisations that dates back to the 1990s, and then half the participants who got some primary care data, provided dates and diagnosis from a GP. Following the pandemic, there's also a linkage to tests, to identify those as kind of PCR tests. The tests to identify when people had COVID. So following the baseline

questionnaire, there was a few areas, where we'd really like to get more information. But in order to do that participants would have to attend their assessments for days on end.

So we have these kind of set of enhancements, and maybe many of you would have filled these out, these are kind of web-based questionnaires for the 300,000 that provided their e-mail address, we sent these out relatively regularly as you can see dating back to 2011. On diet, occupational history, digestive health, chronic pain. And then we've got a few coming up. So we've got one on mental health and wellbeing, another on neuro developments, and then one on sleep. So watch out for those. So you would have reported some self-reported physical activity at baseline, but it's really important to get some objective measure of that. 100,000 participants wore a wrist based accelerometer and that connected physical activity over a seven day period and then 2,500 people repeated that four times over the course of the year to see how physical activity might vary by season. There's also been method over the last few years to turn all those samples I mentioned into data so that researchers can then access it There's biochemical measures, there's telomere lengths, which are these sort of bits in the chromosomes that we believe are associated with aging. Metabolomic data, that's the kind of cholesterol and triglycerides in the blood. Proteomics, that's the proteins that are circulating in your blood, and then some genetic information. And it's no exaggeration really to say that genetic data, but all this data has started to transform medical science. And some of that is now getting into clinical practice.

So the NHS is already piloting the use of genetic studies to improve the prediction of heart disease, and that's happening in the Northeast. And a lot of that work's been informed by the data in UK Biobank. So there's a repeat assessment that happens straight after the baseline survey, and that was on 20,000 participants to assess how those baseline measures might vary over the short term. And then this multimodal imaging study for a target of 100,000 people, that's ongoing at the moment. We've got MRI of the brain, heart and abdomen. And we'll hear some results from each of those studies from colleagues later. There's a full body DEXA scan. That's a kind of photocopier like machine here. That's a carotid ultrasound where we use ultrasound scan to image the large vessels in the neck and ECG that identifies your heart rhythm. And in addition to that, there's repeat imaging of the whole of that, of the whole of those scans. And that's extremely valuable. The feeling is that changes in lots of those measures might be more informative than the single measures alone and also allows us to say, well, what happens before and after the disease. This is the world's largest, alone, this is the world's largest multimodal imaging study.

So as mentioned the imaging really allows us to look at the kind of structure and function of disease. So rather than rely on the health events when people go to hospital or they get diagnosed by the GP we'll be able to see signs of disease in the body before they occur. And that means we've got new risk factors for disease. So things that might mean that you're more or less likely to get particular diseases and a better understanding of the disease pathways. And then amongst those who have had a particular disease, how that disease might have changed the structure and function of the body and that better understands the complications and then how to prevent those complications.

So I've just dug out some of the latest, latest research just to give you a flavour of some of the work that's going on. So we have a study down here. It's looking at liver fat, they've characterized liver fats, they're kind of how do you measure it in the study and that's useful for other researchers. They then don't have to do all that work of trying to measure liver fat, they can rely on this study. We've got a study here looking at heart structure and function cardiac outcomes, so that's work that just wasn't possible at this scale before. A study here looking at alcohol consumption and the structure and function of the brain. The impacts of cardiac and mental health on brain aging. Better understanding of the relationship between air pollution and cardiac disease. And then a study here

looking at muscle composition and all-cause mortality. You might have seen some reports like this in the news before. Where you've got two people. And they're both the same age, both the same sex, have the same BMI and percent body fat. So, you would have thought they would have had the same amount of the same amount of body fat. But in actual fact, this individual has very much more internal body fat than this individual. And UK Biobank's allowing us to understand what's the relevance of that? Does that matter? This is some of the work I've been involved in the last few years. See an image like this from a DEXA scan So that's that human photocopier that I mentioned earlier and rather than just look at BMI or total body fat and its relationship with particular risk factors or cardiovascular outcomes and we've got, we've got blood pressure here. And we can actually look at what's the independent effects of having more fat around your tummy, more fat around your hips, and more fat inside. And what we've found in these preliminary results is that it's the fat around your kind of internal abdominal organs that seems to matter for blood pressure. As we've found no relationship between blood pressure and the fat that's stored just under the tissue around the abdomen or hips.

This is a study that I think I mentioned previously so this a colleague of mine who's interested in the relationship between alcohol and dementia. And she's using the MRI scans to better understand that cause pathway. So what aspects of the brain are affected. And she's found that even, unfortunately, relatively low quantities of alcohol intake over the week, so 7-14 units seems to be associated with a reduced amount of grey matter and that's believed to be relevant for cognition function. The last bit of research I wanted to highlight was the, COVID imaging study that we did following the pandemic. So we knew that we had participants who were scanned before the pandemic. We knew that some participants in our cohort had COVID and also knew that some people hadn't had COVID yet. Could we invite those people back to compare those who had COVID to those who hadn't had COVID taking into account the other factors that might affect changes in their brains and to their brain. And what did we find. So we found that particular parts of the brain seem to be affected more than others. And in particular this left parahippocampal gyrus which is related to sense of smell so we know that COVID especially when it started had an effect on some people's sense of smell so that really makes sense. And also the reduction in total brain volume. Now the clinical relevance of that is still unknown. We don't know where to the extent to which that will recover, but it just illustrates the value really in inviting people back to that second, that repeat imaging study. And this is an example of COVID that's been looked into the study of diseases.

So lastly I was just going to talk about who's using the resource So we've gone from a resource that about 5 years ago used about half by researchers in the UK to a resource that's now predominately global in scope There's now over 30,000 researchers around the world working on the data And they've produced as of last year over 4,500 scientific papers And those papers are appearing in major scientific journals, they really are having impact on a wide range of research fields. This is my last side and it was just to make the point that this is the world's largest multi-model imaging study, but a lot of its value I hope I've made clear comes from the fact we've got all these other measures in UK Biobank. So you're not only restricted to looking at relationships within the study itself and you can look at, you know, imaging cognition, imaging and lifestyle, imaging and the environment. And it's that combination of depth of information, the duration of follow-up and the size of our cohort, that's really enabling cutting edge discoveries in science. Thanks. And a big thank you to you. I think that's the last point I want to make. I mean, this is really dependent on you. Volunteering and giving your time and you continue to give your time and I hope I've made it clear really how valuable that is. Thank you very much.

S.P: It's a great pleasure to talk to you today. And again before I forget it later, thank you very much for being part of UK Biobank. And I hope that after today's session you will seriously consider to also contribute to the imaging part of it, because it clearly I think is an absolutely wonderful resource and we can learn lots of things.

So I'd just like to give you a little glimpse and before I start, I would just like to say that I'm very selfish and selective today. I'm only presenting work from our group rather than from the, how many 30,000, 30,000 researchers around the world that use this resource. So I can't show you everything, so I'm just going to be selfish. I've split the talk into two parts. 1st I will talk to you about how we can use artificial intelligence to basically unlock the massive potential of these heart MRI scans that we acquire in 100,000 people in UK Biobank, because I'm sure I can convince you, showing you some of the images that it's impossible to do that manually. And then I will show you a few examples of how we then use this unlocked data to learn something about cardiovascular health.

So if you do decide to come to this visit, it's a 3 to 4 hour visit, but the MRI of the heart takes 20 minutes. And unlike when you are maybe a patient and you get seen by me in a hospital and you get a cardiac MRI scan, we don't put a needle in. We don't give you any medication to stress the heart. We don't give you a contrast agent. So this is not quite like a clinical scan, but we get a lot of information just by putting you in the scanner asking you to hold your breath. A few times and acquiring the range of images that just images the heart in different orientations and uses what we call different sequences to get slightly different information on the heart and the big arteries in your body. So you can see there that we basically acquire information or we can acquire images that can provide us information on your heart shape, your heart size and the pumping function of your heart. But what I'm really excited about and that's quite unique to MRI as opposed to maybe some other imaging techniques such as ultrasound or CT, we can actually characterize the heart muscle tissue in itself. We could measure fibrosis and scar tissue in the heart muscle. And then we can also measure flow across the valves like your aortic valve and we can look at the size and the function of this big vessel in your body, the aorta.

Now, UK Biobank does an amazing job. This is the largest study, as you've heard, acquiring MRI scans of the heart in the world, and that comes with challenges. First of all, you need to acquire 100,000 participant scans with high quality. But then the work really starts for people like me. How do you then unlock the data? How do you analyze the data? How do you make sure that the image quality is good enough and that the data that we derive is reliable and robust? And how do you do that in 100,000 people and manually you can't do it. Just to give you an example, we analyze parts of the heart as experts and that took 8 experts seven months to analyze the cardiac chambers, the hard size and the pumping function. We now can do that in seconds using computers, and I'll show you a little bit how we do that, but basically the challenges are the automated quality control of the images and the analysis. We do, but also the actual analysis and drawing contours through your heart. That gives us then the numbers that are important.

So here we are, very grateful that the British Heart Foundation gave us a fairly small amount of money, but I think very well invested into this research that funded experts in two universities, one at Queen Mary University of London, the other one in Oxford, to basically look through 1500 images of each participant to identify the 54 images that contained the structures we wanted to analyse, draw circles around the pre chambers of the heart and the main chambers of the heart to get the sort of numbers that inform pumping function size of the heart. But you can imagine that this is impossible to do in 100,000. So 1500 images times 100,000 you're looking at 150 million images. Look through to draw 50-54 million contours. That's impossible, so we need to find automated ways and an expert can do this, and an expert does a lot of things in the background, but you can break

that down and I'll show that you can train computers using artificial intelligence to do it similarly well to an expert. And the first task is image segmentation. So you can see here again the range of images from those 1500 images of one single participant here. And you can see maybe that the heart is imaged in different orientations, some have colours, some not. They give you different information on the heart. And the first step when you want to analyze is of those 1500 images to identify the ones you want to look at with the right orientation or that give you information on pumping function. And I'm sure you've all been online. You've filled in online forms. And then the computer asks you, can I just check that you're not a robot? And you take yes. And then you've got a few images and you say, can you please identify the tractors in these images? And then you click on a few images and then the computer knows that you're not a robot. Now what you've done there is you've done some image classification, you've identified the images with the tractor in it, and at the same time you've helped Google develop automated Image classification systems that in the future will identify tractors.

So we've done the same with these images. We've told the computer essentially what image orientation you've got, what types of images you acquiring, and the AI tool that we've developed can now reliably pull out the images with a particular bit of information so that we can then analyze them. So that's the first step that an expert does, and we can now do this automatically. The second step, I'm not showing you on the slide, is quality control of the images. So you need to make sure that the image quality is good enough for us even to start drawing some contours, segmentations to analyse. If half of your heart wasn't there, say because we haven't covered the entire heart, then you shouldn't really analyze it because the results will be unreliable. Now you can again train an artificial intelligence algorithm to do that automatically and it does it really well. So even before we start doing any analysis, we can actually run through this algorithm. And that tells you these images may be not of sufficient quality. And then the third step is drawing these contours that I've shown you that it takes lots of experts months to analyse and 5000 we can now apply that really well and you get these automatic contours.

But then the next step is how do you know that the computer, we know the computer does it really well on average. But in an individual patient, sometimes it's wrong. And how do we know whether it's correct or not? And you can actually, again, you can train artificial intelligence to do that quite well. We've worked with the team at Imperial College with computer scientists to try and develop a system that's able to predict the automated segmentation quality. And you can see there that the classification method that our colleagues developed was really, really reliable over 95% certainty identifying high quality and low quality image contours in the 4800 studies that we as experts judge how good the quality is. So we now have a tool that not only checks the quality, it pulls out the correct images to start with image classification, it checks the quality of images, then it segments them and then it checks and sort of grades its own homework, how well it's done, the segmentation. And that gives us then the data, all the numbers that we want to use in research studies. And all of this information is fed back into UK Biobank and made available to researchers around the world.

So here is another example with sort of an end to end pipeline as we call it. Starting from image segmentation quality control, then the contouring and then the check that the segmentation worked for biomarker that when we developed the sequences of this MRI program, we weren't even thinking about that this is something we might be interested in, but we can actually measure the fat around your heart. And that is again done with artificial intelligence with all of these steps involved. And I would like to show you now a few examples of how you then use this data. And I'd like to start with this example of the fat measurements around the heart. Why is that potentially of interest? So if you will all be familiar with conditions like diabetes, hypertension or high blood pressure and high

cholesterol. So what you can see is in participants that have higher. Fat around the heart that you are more likely to have diabetes, high blood pressure or high cholesterol. So what we see here is that what we intuitively thought that this is a risk factor maybe for diabetes, for hypertension, that this seems to be the case now. The next step, what we are looking forward to doing soon is to see whether this fat around the heart also can help us predict who might be developing diabetes. So this is in people who have diabetes they've got more fat around the heart, but in the future we believe that this is a good marker to maybe help predict to us at a higher risk of developing diabetes, high blood pressure and high cholesterol. And this is something looking into predicting a new onset of disease that we've done with another marker using the heart MRI scans called T1 or schmolli sequence.

Our Oxford colleagues have developed again an analysis pipeline similar to what I've explained, pulling out the correct images, doing the quality control, segmenting, doing quality control again and extracting the data. We then looked at whether these T1 values that are usually a bit higher if you've got something not quite right with your heart. So if you're developing fibrosis or scarring in your heart muscle, these T1 values will go up and what we see here on the right hand side is that with higher values of T1, so a more unusual abnormal heart, that the risk of developing cardiovascular diseases is higher, the risk of developing atrial fibrillation, the most common heart rhythm problem, is higher, and the risk of developing heart failure. So a pumping failure, pumping reduction of the pumping function of your heart is becoming more likely and also we can predict the risk of dying of any cause, dying of heart disease, as you can see here. So it's a very powerful marker, probably informed by a lot of risk factors like high blood pressure, aging, high cholesterol, smoking and through this then leads to higher risk of dying and developing these cardiovascular diseases.

Now we can also use machine learning or if you like artificial intelligence to do something with the images that a clinician can't see. So I've talked about segmentation and making the analysis easier, but as a clinician, when I look at these heart MRI scans, I can see fairly coarse things like the wall thickness and certain areas of the heart. Or I can see maybe some scars in the heart or where somebody had a heart attack. But what I can't really do is to appreciate the at the smallest unit of the image, the pixel, whether there are patterns in these pixels that I just can't see with the naked eye, and this is what a technique called radiomics does and it's a quite a complicated technique, but it extracts about 400 variables from these images on the texture 1st order. So some mathematical numbers that come out and something about the shape of your heart. If you're then using all of this information to try and see whether it predicts, for example, again atrial fibrillation or heart failure, you can see that it provides added information to just. And looking at the predictive risk from high blood pressure, age and all those other risk factors we know for heart disease. So it has more information on telling you whether in the future you might develop atrial fibrillation or heart failure then just the risk factors alone. And also we know that these measures with heart MRI, like the wall thickness, are determined not only by factors like high blood pressure smoking. They're also determined in your genes, your DNA and what you can do. Because UK Biobank has the information on the DNA and the genetics in all of you, we can see which parts of the gene are contributing to these measures of wall thickness, for example, which we know is linked to outcomes.

So why is this information? Because we can learn from these studies. And pharmaceutical companies, for example, are very interested in knowing which genes are involved in, say, wall thickening, because they might be able to produce better medications to reduce the blood pressure. That also takes away the effects on the heart. That puts you at a higher risk of developing heart attacks or strokes. So there's a huge amount of information in the UK Biobank that can be used in a clever way and that brings me to the end, but I'm here later for questions also. I hope you've

realized that I'm really enthusiastic about UK Biobank as a researcher having been involved for about 15 years now. I think the scale of UK Biobank and this heart MRI scans is just astonishing and really a unique research opportunity that allows you to develop artificial intelligence tools for image classification, segmentation and quality control. You can derive new markers from these hard MRI scans and develop them and validate them. That might be useful in the future. You can learn new things about how disease might lead to adverse outcomes through studies of, for example fibrosis using these T1 marker that I've mentioned. Also we can learn about the genetic architecture of the CMR phenotypes like wall thickness or the size of the heart. What I really like is working in a multidisciplinary team. So as a cardiologist, as a clinician I have wonderful opportunities to collaborate with researchers around the world in computer science and physics. Engineering, artificial intelligence mathematicians, so it's really wonderful. And also what I really like is whilst I have progressed over the last 15 years in my career with UK Biobank as sort of my main research platform if you like.

I've seen a lot of junior doctors, medical students, junior doctors become really excited about research and sort of they are now independent researchers themselves. So I think that's absolutely wonderful to see and I think UK Biobank benefits patients for prevention, diagnosis and better prediction and then treatment and management of patients. And I would like to thank you again for being part of UK Biobank. Please do consider to participate in the imaging visit. There's a lot of other people that you can see. They're funders, collaborators, colleagues that deserve a mention. But thank you for your attention.

O.L: So, let's see... So I'm Olof Dahlqvist Leinhard and I'm Chief Scientist for AMRA Medical, that's a biological company in Sweden. We have been collaborating with and doing research on UK Biobank data and imaging study. And what we are looking at is the fat and muscle imaging data in UK Biobank. And what I'm going to talk about today is the importance of having a good balance inside the body because it's correlated with a lot of diseases. So, the protocol we are working with is 6 minutes on average per series of images just of the cardiovascular imaging programme. Here we can see the fat image from the scan and the water image from the scan. Using this image we will measure a small area so 2-3mm where it's fat tissue and where it's water I want to schedule automatically the scans of the different compartments in the image, which is subcutaneous fat... visceral fat, that Ben was talking about, the dangerous belly fat. By imaging the liver you can see how much fat is in your liver. Then we can look at the muscle tissues and if there's different tolerances in different muscle groups within the thigh region and how much fat is within our muscles.

As I mentioned first I'm going to talk about fat distribution in different muscle composition. So now we see 6 different males, all with approximately the same BMI, the same size as I am. As you can see looking at the images they are very different. Down here we see a lot of visceral composition. Looking up here it's less. Looking at the muscles we can appreciate that some muscles are better than others. They're bigger with less fat. So, looking at these numbers we can see the concentration of fats in the liver. But in a sense we can see the volume of visceral fat, volume of subcutaneous fat... muscle volume in the thighs and the fat distribution. We quickly realise that what is weird is that in all these person that look the same, we realise what's normal, what's high, what's low from inside. It's a complex thing. The subjects gave us something to develop - graphs or statistics. Here you have a functional diagram. Visceral fat, liver fat and muscle fat. The build up of fat suggests more round in shape. Then you can see more values in the fat. This one that is star shaped but it tells us different things about body composition. And then we find all different types of shapes in the participants. So here you have a standard shape but also of importance we have one with elevated visceral fat, and

elevated liver fat and here we have low liver fat but elevated visceral fat. A lot different variations, this is.

So in the first publication just to start off the pilot stage we looked at 6,000 participants and then we looked at the diseased they had at the time of coming to an imaging assessment. And we found the visceral fat, and yes this confirmed that this is linked to cardiovascular disease and type 2 diabetes. And we also saw that subcutaneous fat is not to be associated with type 2 diabetes. So it's this internal fat that's important. But what was more unexpected. Even the visceral fat have differences. In participants that had high visceral fat and high liver fat had higher risk of diabetes but those that had high visceral fat and low liver fat still had higher risk of cardiac disease So we published our paper with 22,000 participants. So we can see something happening, they either have high or low visceral fat. And then there's the factor of liver fat which has the highest factor and can be high or low. So the options are low-low or low-high and here we can see the results.

So over three years, exactly the same participants And then they have been fractioned Some participants had both high visceral and liver fat And the red line shows high visceral fat the blue, the second line is high liver fat. And we can start to see that, yes, high visceral fat is connected to incidents of cardiovascular disease. What was also really interesting to see is the high visceral fat in combination with low liver fat was absolutely the highest incase of disease risk. It was the opposite for diabetes the blue group was the highest, almost 3 times higher. And as an example of how we found these results The ------- but when we took the findings and found that also the Dallas Heart Study had tested that ------ Do we see the same thing? Yes. The patterns are the same That's interesting to see is this is a study of 2,000 and we've been doing this for over 12 years and use the strength and the power of UK Biobank to make these more generic findings. Some so we come back to how important is muscle health So, the way I see we build muscle and here we have sizeable muscles and they are nice, muscle tissue, no fibrosis or fat in the muscle tissue and as we get older, we get metabolic diseases or severe disease or inactive or have nerve issues in the muscles. We scanned for muscle tissue loss an increase in muscle fat and those that had loss in muscle function And often this happens at the same time. So first, the muscles get smaller ---------- So looking at the muscle a big part of the problem is the size of it how tall you are, and how much fat you carry. So the first thing we did was develop and find a good way of measuring how the muscle and how much muscle should you have and then see how lean is that muscle. This allows us to take the cartoons here and make them into measures. This is normal muscle composition, only low muscle volume or only high muscle fat... or small muscles and high fat. I'm looking at in this one is high level of fat And ---------- they had normal muscle composition ---------- And what's interesting is how many had muscle disease That's ---------- We're looking at the first muscle composition and found that we have almost four times higher prevalence of cardiovascular disease among the 14% of our sample and it is 23 times higher in high muscle fat ---------- ---------- ---------- ---------- ---------- many others have used the same approach but I am looking at so many more 1,000s I followed them and looked at different features ---------- 10.5% higher ---------- ---------- Result. that in normal muscle composition after 6 years at the longest time we see that 2% have died. While in the survivors those with low muscle composition. So it's actually 3.7X higher risk of dying if you have adverse muscle composition. It's really fascinating results. It was actually almost stronger than looking at individuals than previously thought.

So to summarise so I've been talking about uneven fat distribution, first of all visceral fat is deadly to cardiovascular disease. We saw that unbalanced or uneven fat distribution Muscle fat infiltration and low muscle volume leads to poor function and high mortality Or ---------- And finally, just a few more words... I'm a researcher at AMRA Medical. We've see that this resource, the UK Biobank

really helps us identify more individualized risk factors for disease output and in a very large sample size and we can link these biomarkers to important outcomes... mortality, hospitalisation and so on ---------- the longitudinal imaging project ---------- ---------- less muscle fat distribution and less visceral fat ---------- ---------- ---------- muscles or visceral fat. Thanks to this study you have really good impact and results to research. I'd like to start by thank you, all the participants for enabling such high levels of research. Thank you. Thanks. Thank you.

S.G: Thanks and good afternoon, everybody. So, yeah, after the talks and our researchers earlier, I thought I'd give a little bit of an update on the visit itself and what you might expect if you choose to come along for an imaging visit But before that a very quick update on where we are with the imaging so far. So. The imaging enhancements it is MRI of the brain, the heart, of the abdomen, a DEXA image which looks at bone density and a carotid ultrasound image just at the side of your neck, and we also do a 12 lead ECG to measure your heart rhythm whilst you're laying in the centre. And we also offer a cardiac monitor where you can wear and take away for a couple of weeks and then post back to us that monitors your heart rate over that period and picks up arrhythmias and things that might not occur frequently. And also we squeeze in a repeat some of the baseline measures that you would have already done at the first visit that you had.

And so that's the main baseline imaging enhancement we've also now got funding for this repeat of imaging and where we hope to have 60,000 of the 100,000 come back and do it all again a couple years after their initial visit. In terms of the timeline, so you will have all attended your first visit sometime between 2006 and 2010. So quite a long time ago now. The imaging enhancement study really started back in late 2012 when the funding was agreed and we fairly quickly went around and procured the scanners and found the sites to host our pilots, and that study began in April 2014 in Stockport. That study ran for about 2 years, we scanned about 7000 participants as part of that pilot and I think it was mentioned before about how UK Biobank imaging is world leading, the world's largest study. Well actually we were the world's largest study just through the pilots alone. So the similar studies at the time were four or 5000 participants. We got 7000 just in our pilot. So that was confirmed successful in 2016 and that enabled the funding to release to our other sites and Newcastle site here opened in April 2017 as our second site that we've been running for about five years now here. We opened up our third site in Reading in 2018, so the year after and we have a fourth site in Bristol that opened in February 2020. Now you might remember. February 2020 was quite an interesting time to decide to open a new centre and that closed in March 2020 and we actually gave it over to the NHS and the NHS used the site for about a year to scan patients and that was amazing to be able to do that. All of the other sites, including the one here in Newcastle, we actually did a COVID study.

So we invited participants who'd already had imaging back for another repeat imaging scan and then the research that was described earlier to compare participants who had had COVID, and participants who hadn't had COVID was able to be done. So it was great that we were able to keep the sites open and operational during that time and actually do some research that wouldn't have been possible elsewhere. We're up to today now, baseline imaging has started again at all of our sites and we just have the full cohort repeats funding confirmed. And that's going to start here in Newcastle in the next few months. In terms of location, obviously we are in Newcastle but this site actually covers quite a large area, so we will be inviting participants not only from Newcastle but from Sunderland and Middlesbrough down into North Yorkshire, as far as Leeds, anybody who now lives in Cumbria and Carlisle way. They'll be traveling over the Pennines to come here for a visit. Participants in Edinburgh, who first came to Edinburgh will be invited to come to Newcastle. And

participants from Glasgow. A significant number of people have made that journey all the way from Glasgow and Edinburgh, up from Leeds to come to Newcastle site. And we fully reimburse any travel expenses you might have, whether you've driven or caught the train, if you catch the train then we'll put on taxi service for you to get from the train station to our site as well. So we're trying to make it easy possible for you to be able to join us.

The site itself, is quite close to the centre of Newcastle Just to the east and so you can find the laser. This is the Tyne Bridge and here, so we're about a mile to the east of the centre and there's lots of buses that go down Walker Rd and there's parking on site. So you actually come down Walker Rd and then turn down into an industrial estate and a lot of participants question whether they are in the right place or not because it is an industrial estate. At least this in fact our site. It's a warehouse and that was very specifically chosen because of the ease and speed that can convert it into an imaging centre that we did look at hospital locations originally. But actually there is a lot of complication that comes with siting something like this in a hospital environment. But once you come through our front door, it does look quite a lot like a hospital or a clinic we've got a shiny desk and lots of equipment in there and staff in full uniform. This is our MR control area. A large spacious area and then the doors through to the MR rooms.

This is one of our MR scanners, this is a Siemens. This is a 1.5 Tesla scanner. And we have a large Skyra scanner, that's 3 Tesla as well. This is the view that the radiographers have from the control room looking down to the bore, and hopefully you see it's quite a wide bore, it's quite a large aperture there that you slide into. It is, I will admit, a little disconcerting for some people, but it is amazing how many people come along to the visits and say they're effectively attending because they're worried that they might be claustrophobic in an MR scanner and they want to try this before they have to go in one for real and so, yeah, we are nice and welcoming and friendly and will try and get you on some scanners and the vast majority of people were able to do the scan without any problems. This is our DEXA scanner, again it's a large bed and the arm that moves over the top of you whilst you lie on your back, and again on your side and for a lateral view and your side. Yeah, once you're inside the warehouse, it doesn't look like a warehouse, it's a nice image and hopefully will be welcoming.

The visit itself as I said, has a number of stages, so we have the abdominal scanning and this sort of picture that we get from that. We also do the heart scans that Steffan mentioned and I just want really to show that we're not just talking about static structural images, we also collect functional images. So we show in this instance, you know how the heart is working, the heart pumping, and you're able then to visualize issues with valves or the muscles, the way the muscles are working. So the whole imaging visit really is on structural and functional imaging. And this is the output from one of our brains scans again is actually a functional scan So whilst you're in the brain scanner, you'll be asked to perform a task where there'll be a little button box and we'll show some images on the screen and ask to push either the left button or the right button depending on which side matches the image you're being shown and the scanner picks up blood flow whilst you're performing that task so you can see which areas of the brain are engaged in that task, so we can start to look for interesting associations with that data. This is a little faint, but this is a picture of a carotid artery from the ultrasound and this shows the thickness of the wall of the ultrasound and again that has various associations with the health conditions and cardiovascular, things like high blood pressure which can lead to a thickening of the arteries there. A really important measure.

And finally we have the DEXA which shows bone density, so you'll get a massive image of a skeleton you can get pictures of the hips and spine and look for things like osteoporosis from those images. So we collect all of these images as well as doing a repeat of those baseline The visit itself. You arrive

and you're welcomed, but then you'll be asked to the screening again. So when you phone up to make an appointments or are called for appointments and you'll go through a screening exercise where we will check that it's safe for you to take part and that you'll be able to do as much of the imaging as possible. You will be asked to repeat that in the centre just to check that nothing's changed also it's the radiographer's to keep you safe so they'll repeat that screening that's perfectly normal. You'll get changed and go into the MRI itself and the MRI, there's three stations. They last about 40 minutes, including getting you on and off the scanner. And the scanners can be noisy. I Will try. Excuse me. Through my phone to give you an example of this. See if I can get this to work. OK. You get the idea. It makes some very odd noises some bleeps, alarms, jackhammer, sounds like that. You're given earplugs to wear during the scan You'll lay in the scanner and you can hear all these things going on It's absolutely normal. Quite a lot of people express concern that they think somethings wrong, maybe the table is vibrating. It's perfectly normal. We just want you to be prepared for that eventuality. So you have around half an hour on the scanner, you get on and off. And then you do another scan that scans the heart and the abdominal imaging and then you have the DEXA and the carotid ultrasound and that lasts about the same time.

Once you've done all of that, you get changed again you provide your sample. And then you repeat those baseline measures, so you'll still need to do touchscreen questionnaires, physical measures that I'm sure you can remember from the original visit. And then you're free to go and that whole visit, it takes around 4 1/2 hours obviously depends on how quickly you're able to do some of the some baseline measures, it's around 4 1/2 hours. And the day is structured, it tries to make sure that the scanners are fully utilized the whole day. So we start at 8 o'clock in the morning, and 1st 3 participants come in, one will go to the brain scanner, one the cardiac scanner and into DEXA and ultrasound they will do that and then they swap. So you basically go around in circuits where those three participants will do all the three areas of imaging. And then you will get changed and come out and do baseline and as you're coming off the imaging scanners, there'll be another group of people ready to go on.

So you get these repeated, appointments throughout the day and the final participants leave around 8 o'clock in the evening so there are different appointment slots throughout the day. We are open seven days a week, 18 participants per day. Not quite 365 days a year, we close at Christmas. Yeah, we try and get as much use as we possibly can out of those scanners while we have them. So where we're at now, we have this target of 100,000 participants, we are nearly at 60,000 participants that and over 15,000 of those have come to our site in Newcastle. And we've done some great images for the Dementia platform UK and the COVID study as well. And we mentioned, but we're going to start what's known as full cohort repeat imaging this year and we're starting in Newcastle. So it's actually the baseline imaging, as we know it, the first imaging visit, is coming to an end. I think probably within about 6 months we'll have fully exhausted all of our first time appointments and we will be focusing then 100% on repeat imaging. This is hopefully a call that you will all want to come along for an imaging visit and hoping you'll make an appointment to come along in the next few months. Yeah, I hope you're willing and able to join us. Thank you.