I think we've got to probably move straight on, because Tommy Johansson, our next speaker, who is the chief executive of AMRA, needs to catch a plane in very short order. To prevent him from being trapped in London for another night, let's move right on. I want to emphasise how important AMRA has been as a collaborator in delivering outcomes from this resource. Tommy.

Thank you, Paul. AMRA is a Swedish company, and we have developed a technology to automatically do segmentation and the quantification of different fat compartments in the body and, also, to quantify muscle volumes, so to describe your body composition. We have applied that technology on the first 6000 participants in the UK Biobank and I will present the results, but what we can see that the fat distribution in the body tells a lot about your disease risk. Let's see that. Here overweight and obesity is defined by BMI today, and BMI is calculated by taking your weight, divided by height square, and I have included my own numbers, so you can see that I'm borderline normal, under 25. If you are above 25 up to 30, you're overweight, and above 30, you're obese. You can also use waist circumference to describe risk and you can see, if you're a male above 94 centimetres you are at higher risk. I will come back to these numbers. If we look at the prevalence of obesity among adults in the US, it's quite scary, as it has gone from ten per cent in the 60s to 37 per cent today, and it's predicted to increase a lot.

If we instead look at the number of people with the overweight, we see in the top, US. That's 75 per cent, or three out of four people are overweight or obese, but we can also see that England is not far behind at 70 per cent, and we see the same trend around the world, really. In the UK Biobank, AMRAs technology is used to collect MRI images in six minutes, and we are investing heavily to do quantification of the liver fat percentage, visceral fat volumes, the abdominal subcutaneous fat, which you see in blue. Also, the lean thigh muscle volume and the muscle fat infiltration. To better understand the fat distribution in the body, we have developed this star concept. We call it the BCP, Body Composition Profile, where we look at the fat distribution. We are quantifying visceral fat, since other studies have shown that it's very well connected to insulin resistance, a good predictor of cardiovascular events. We look at liver fats, which also is connected to insulin resistance. It's a debated predictor of cardiovascular events, but also believed to be well connected to liver disease, NASH and other diseases.

We look at muscle fat infiltration, which has proven to be connected to sarcopenia, and muscle degeneration. It's also a predictor of cardiovascular events and has proven to be a predictor of high mortality. We look at the total abdominal fat, divided by height squared, so it's a sort of BMI, but fat tissue specific. We look at the lean muscle tissue volume, which is connected to sarcopenia and cachexia, and loss of muscle is also a predictor in most end-stage diseases. Finally, we look at fat ratio, the relation between the fat and muscle, so it's sort of a fitness level. The star in the middle, that's really the healthy ideal profile, and it has proven that people that look like this are metabolic disease free. We'll come back to that. I will present results

from a study that was published in obesity in May by Linge et al, and here we have selected seven identical men from the UK Biobank, all of them with BMI 27, and with the same waist circumference of 91. They're extremely identical, but you can see that the amount of visceral fat goes from 2.4 litres to 9.3 litres.

I'll see if I have a pointer. All the same BMI, and the same waist circumference, and if you look at their profiles, can also seen that it looks very different. In the bottom we see the visceral fat increasing. On the top right corner, we have the liver fat and to the left, the muscle fat. That's the most interesting numbers. What we tried to understand, what does it mean if you have this profile with only the standard visceral fat, or if you had this one with extended visceral fat and liver fat, but okay with muscle fat. To do this, we can use number seven here as an example. For all the 6021 people we have done the BCP, and done all the measurements, and we have also compared these subjects with their disease history. We have been focusing on the history of coronary heart disease, type 2 diabetes, and advanced metabolic disease free, so approximately 30 per cent of the 6000 seems to be metabolic disease free. Then, we use a multivariable statistic modelling to calculate the probability that the person with this profile already has type 2 diabetes, and a coronary heart disease history, or is metabolic disease free.

That, we have done for all people, and if we look back to the seven with the same BMI and waist circumference, we see a very different risk profile. All the data are very identical, but not on the inside. They have different fat distribution. If we drill into that a little bit more, you can see that the first one is almost like the star shape. A high association to being metabolic disease free, low risk for coronary heart disease and diabetes. While this one with elevated visceral fat, has much higher risk for coronary heart disease. If we continue, if you have even more visceral fat, the risk increases a lot. If you add on liver fat with high visceral fat, you get much higher risk for diabetes. Finally, number seven here, is the comorbidity type, with too much of everything. As you can see, it's a very low chance that this person is disease free, and maybe a six times higher risk for diabetes, only depending on fat distribution. Fat distribution matters. To summarise our findings, we see that a low amount of visceral fat and muscle fat is very much associated to being metabolic disease free.

A high amount of visceral fat and muscle fat is connected to both high associations to coronary heart disease and type 2 diabetes. When we looked at liver fat we got a different message. A high amount of liver fat, together with a high amount of visceral fat increases your diabetes risk, but if you have a high amount of visceral fat and a low amount of liver fat, the coronary heart disease [unclear word 0:08:43.4] or risk increases, which is a bit strange. We don't see any significance with liver fat connected to being healthy. We also have tried to do the same, just using sex, age, lifestyle and BMI, and using single measurements, and we can't find the same associations, so it has proven to be very valuable to understand the fat distribution in the body, and [?has given us 0:09:12.5] in the fat distribution, seems to increase the risk quite a lot for different diseases. So far, we have only been able to look at the historic disease data. With the increased number of participants, we can drill down into more rare diseases, compare different ethnic groups, look into sociodemographics, but what we are really looking forward to is to get the outcomes from the health care

records, because then we can start to really look at disease prediction, to see whether we can predict disease.

As an example, our vision is really that today you almost need to get the heart attack, then you get treated, but if we could find the three per cent with the highest risk to get the heart attack, we maybe can start to treat them before they get the disease, which will help the individual and the society, of course, a lot. Finally, I would like to thank our collaborators, the Linköping University team, University of Westminster, of course, the staff and participants of the UK Biobank, and Pfizer, which also have helped to fund this study. Thank you very much.

Maybe two minutes, you stay.

Okay.

As Tommy has to rush off and I know that there will be a lot of interest in his presentation, let's just take two or three minutes, if there are one or two questions from the audience. Does anyone have a question for Tommy before he rushes off? Andrew's coming in with a microphone. One down from Ewan.

M1: As well as these values, can we get at the raw data, eventually, as well, of that six-minute MRI scan?

Yes, so we have already reported back the individual measurements of these five different measurements, so they are available for this first 6000. Yes.

M1: Sorry, what about the raw data? What about the MRI scan, itself?

It's not reported back, today. Of course, the images are available and we report back the numbers. Yes.

Another question. Yes, the images are available through Biobank, as with the other images. Yes. Is there another question?

M2: Yes, Tommy, so the liver fat association with CHD being lower, you said, was unusual. I suspect it's probably because once you have CHD, there's an obesity paradox. You tend to be losing weight, so I suspect that's partly the explanation. What we need is serial data to try and unpick some of these things, as well.

Yes. I'm not a scientist. I can't answer the details, but I know we also have been looking at the statins, which could be also an effect, but we can't see any connection to that.

M2: No, there's plenty of published data that liver function levels, so marks of liver fat, decline once you get to a certain age, and with chronic disease they start to go down again. I suspect that's part of the explanation.

Okay, thank you.

Maybe one more question, and then we'll have to stop. If there are other questions, perhaps they could be directed to Jimmy Bell after the end of these sessions.

M3: Hi, there. Thanks for a good talk. What can you say about why fat is distributed so differently in different people?

I'm not really the right person, but what we can see, in the inner all the time, that you can never see on the outside, or use BMI, or waist circumference to understand how fat is distributed. The seven examples we saw here are not unusual. We can really pick any seven people in the UK Biobank and it's a very different picture of fat distribution in the body.

Okay. Let's give Tommy another round of applause, thank you.

Thank you. I need to rush home to celebrate Midsummer, which is the biggest event in Sweden. Thank you.

I can tell it's going to be a late night.

[END OF TRANSCRIPT]