

Great, thank you. I realise that [laughs] everybody is leaving, it must be my effect, that's okay! So, my day job is keeping the good ship EBI sailing the seas and giving the data, such as the UK Biobank, back to you all, but I run a small but perfectly formed research group as well and we have got into studying this wonderful wild organism called humans and this wonderful capture of them by UK Biobank looking at their basic biology. I'm interested in everything in this wonderful organism and that includes eyes, and a year-and-a-half ago I met the wonderful Eye Consortium in Moorfields and I've become part of it.

So, I'm going to just - I can probably skip all of this, we know all of this, but at the end of major round, as Rory mentioned, the Eye Consortium went to Rory and said, 'We reckon we can get, if you give us ten minutes of time, we can do more things than you can imagine with eyes.' These two people, [?P Lang 0:01:10.5] and Pearse persuaded, raised enough money to run this programme.

So, this is a quick crash course on the eye, it is a living tissue that you can image directly at the cellular level, near cellular level through the lens, it's quite remarkable. What many ophthalmologists are particularly interested in is these retinal layers which actually process light and so the major technique that we are using or looking at is this thing called optical coherence tomography. This is going into the eye, so the bottom is the bottom of the retina and that was the fovea or the place where you do most of your vision, passing through there. The lines, by the way, are blood vessels going through the eye.

So, we have these datasets to use as potential phenotypes and there's been hundreds of years almost of understanding the structure of this tissue and much of it is around these retinal layers which is shown schematically on the right and then just one, the very top layer, showing there on the left-hand side. So, ophthalmologists think of this as a series of thicknesses of these retinal layers across the eye. Eyes also don't only have a sort of thickness in a z-dimension, they also have a space, the OCT scan is centred on that place of highest vision and there are a couple of standard ways of sort of splitting up the eye, and the way that we are tending to use it is this right-hand bullseye scheme which splits the eye into nine different sections looking straight on from this. The device to measure OCT is Topcon, it comes with software that will automatically segment these thicknesses and also produce this bullseye. So, over time, all the OCT scans have been processed through the Topcon. We still are waiting for the last 20,000 sets of scans to be processed to give us these figures, these measurements.

Now one interesting thing about UK Biobank from my perspective is its scale. It's great for genetics, but it's great for something else, which Daniel mentioned as well, is you can be really harsh on the QC. So, we have been ruthless on the QC of these images at first and this is probably quite excessive, but we decided to completely discard anything that looked even the slightest bit off when we did this to give us a super clean dataset of 42,000-odd cases. Just to convince you that that makes sense, this is a very simple PCA plot of one of the layers, just showing the first two principal components before QC and the data scientists amongst you will notice there is some disturbing structure in that PCA plot. This is after the QC, we don't use these PCs to

do the QC and that is a much, much happier first two principal components. We have just, in the last couple of weeks, run our first initial GWASs here. I have learnt not to look at the loci until we're really happy with all of our statistics, so please no one ask me what the loci are. I officially do not know until we have decided that everything is clean because, as all of us know, as soon as you open the box you get too excited and then you keep tracking that one locus down and trying to recover it. So, I think this goes to good community practice, do not reveal your loci until the end, but as you can see, that is a very good looking Manhattan plot with ridiculous p-values and the LD regression score is good on this.

These derived variables don't have to just be used for genetics, here are some very classic things that you might associate some of these variables to. We're just looking here at the first principal components across what ends up being a 93-dimensional space against, here, height, weight, age, sex and one of the optical measures, refractive error. You can see we get sort of obvious correlations and we'd like to extend this to many of the other variables in the UK Biobank. Those principal components themselves are interesting, going back to the bullseye, this is a picture of the principal components of one layer across the bullseye and you can see the first principal component is a general thickness across the entire space, but the other principal components really do look like different subparts of the eye. For the data scientists about this, I think principal components is the first technique you should use. I'm actually not a big fan of it because it enforces orthogonality of all the components past the first one, so I prefer something a little more relaxed, but this shows a lot of promise.

We don't want to stop there and we already have played around with and we'd like to develop further more detailed ways of thinking about the eye. In this case about putting more subset segmentations around this eye framework and this has worked to place a kind of hexagonal grid across the eye rather than that, a nine-way bullseye from the software.

So, just to say, we have joined this happy crew of the UK Biobank Eye and Vision Consortium. They do many more things than OCT and I have had a crash course in eyes just to get to this point and most of this work was done by Hannah Currant who's a student who I hope hasn't left yet, and many, many thanks to Praveen, Anthony, Pearse and Zaynah from Moorfields who supported this, so thank you [applause].

[END OF TRANSCRIPT]