Chance, Risk & Health Measuring the Unmeasurable

## Michael Healy, Rothamsted, 1947-1965

And I knew very well my excitement as a student when I first saw one of these electrical machines doing division all by itself, you pressed the button, it whirred backwards and forwards and out came the answer. 'The Millionaire' computer was Fisher's own purchase when he was appointed here in 1919. He shocked the director by saying what I must have is a calculating machine; such a thing had never been heard of.

## Voice-over

At Rothamsted the search for certainty enabled British farmers to maximise their productivity and Fisher's methods were swiftly adopted worldwide. Fisher thought of himself not as a statistician, but as a scientist, and in 1929 he was elected a Fellow of the Royal Society in recognition of his achievements at Rothamsted.

## Stephen Senn, University College, London

He was someone who was fascinated by biology from a very early stage of his life but he also was a very good mathematician, and somehow he realised that he could apply his mathematical insight to biological problems, and this was something which really opened a whole new world for him.

## Voice-over

Rothamsted could more easily accommodate new world than a university might have done. It also gave him time and space to develop his own research into genetics. But he brought his obsession home with him.

# Joan Fisher Box

He started breeding mice at home, and the eye colours and coat colours grew more and more numerous, and the mice grew more and more numerous.

## Voice-over

After fourteen years at Rothamsted Fisher finally began an academic career in genetics, and the mice went with him. From a professorship at University College, London, he went on to teach at Cambridge.

# Joan Fisher Box

Yes, he led a double life from the beginning. It was both genetics and statistics, there was never any cessation.

## Voice-over

Anthony Edwards is a Fellow of Keyes, Fisher's college, and was his last undergraduate student.

# **Anthony Edwards**

I'd heard this name but I could see no reason why this famous statistician should be teaching genetics, and in any case I thought he must be a contemporary of Isaac Newton's, it hadn't occurred to me that this man might still be alive. I just turned up on spec, as it were, in the afternoon and when I went through the open door of the Department of Genetics to ask for the person whom I'd been told to go and see I thought he was the hall porter.

## Voice-over

His appearance held clues to the roots of his genius.

## **Anthony Edwards**

He was a short man, a wiry, tough man, bearded, pipe-smoker, he had very short sight and had always had very short sight, and one of the things I keep in my room in college was his last pair of spectacles, and I thought you might like to see how very, very small and how the glass is very thick at the edges for some, appropriate for somebody who was extremely short-sighted.

### Voice-over

His capacity to imagine, to visualise multiple dimensions of geometry gave him a unique perspective.

### **Anthony Edwards**

He had to depend very much on learning by ear and he did develop the most extraordinary ability to do complex mathematics and complex geometrical arguments in his head without writing things down.

### Voice-over

It enabled him to make intuitive new connections across areas of science which had been considered distinct. As a biologist and statistician Alan Grafen shares Fisher's range of interests.

## Alan Grafen

Fisher thought in pictures and he solved very complicated problems using pictures in his mind. It's possible to imagine that because he couldn't see very well out there in the world, he turned his eyes inward and saw very clearly in his mind, the formula came out of some deep recesses of his subconscious.

### Voice-over

Fisher went up to Cambridge in 1909. His extraordinary insight inspired even his earliest achievements.

## **Anthony Edwards**

When Fisher came up to Keyes as a scholar he will have been allocated a room, and as a scholar it will have been in one of the inner courts, and as it happens the room in question is next door to the staircase that I'm on now. With that splendid naivety which your twenty year old will have, he will have just set off on a course solving problems in a way which will have been entirely original to him, and although the method of maximum likelihood can be found in earlier works it is the development which started on that staircase in 1912 which led to his great 1922 on the mathematical foundations of theoretical statistics, from which the modern theory of estimation flows.

#### Voice-over

The concept of maximum likelihood is one of his best known developments and is still at the cutting edge of the scientist's search for certainty.

## **Anthony Edwards**

Any method of estimation in statistics such as the method of maximum likelihood is a method to teach us how to extract information from data, to find out what we don't know from what we do know in the form of data.

#### Voice-over

At the British headquarters of the Human Genome Project, the Sanger Centre in Cambridge, Richard Durbin leads the team of statisticians.

#### **Richard Durbin, Sanger Centre**

Ideally in science people want to establish the truth conclusively. Often we only have partial sorts of information and one of the challenges is how to put together partial information that may not be completely conclusive in itself to give as much certainty as possible. The human genome contains the information that is inherited, that creates a human being from a fertilised

egg, and we can think of that as a parts list and an instruction manual for putting together those parts to make a complete human.

## Voice-over

Scientists now know the complete human genome sequence but the code needs to be translated into a usable form. This means analysing the individual genes which make up its component parts.

## **Richard Durbin, Sanger Centre**

When we look at the generic sequence it's a long string of a, c's, g's and t's, just three billion letters long. Within that we know there's around 50-100,000 genes and these are comprised of small segments of the sequence.

### Voice-over

Using statistics Durbin's task is to investigate the nature of unknown genes by applying data from genes which are already understood.

## **Richard Durbin, Sanger Centre**

What we want to do is use all the information and evidence that we have to help us find and characterise genes in other parts of the genome where we haven't yet done any experiments. The way we do that is by fitting parameters to a model, using maximum likelihood or related techniques, and really the theoretical foundations for this sort of approach were set earlier in the century by Fisher and his colleagues.