Maths + Cancer

Episode 2: Communicating the evidence with Professor Sir David Spiegelhalter

Transcript

Vicky Neale:

My name is Vicky Neale, and I'm a mathematician at the University of Oxford. Since March 2021, I've also been having treatment, on and off, for a rare form of cancer. That's been very educational, I've been learning lots about cancer and the various treatments available. While I wish it was less personally relevant to me, I also find it fascinating. I take comfort and have great pride in knowing that I have colleagues in the mathematical community whose research helps to tackle cancer from prevention through diagnosis to treatment. In this podcast series, Maths + Cancer, I'm going to sit down with some of them to find out more about their research, and about the people behind the research. I'd love you to join me for our conversations to learn more about how mathematics and mathematicians are helping to combat cancer.

I'm joined today by David Spiegelhalter who is Chair for the Winston Centre for Risk and Evidence Communication in Cambridge. David career spans research in medical statistics and public understanding of risk. You might have heard him on BBC Radio or on his Risky Talk podcast, seen him on TV, whether a documentary or the BBC's Winter Wipeout show or read his book, The Art of Statistics. Among his many awards and honours, he's been knighted for his work in medical statistics, he's a fellow of the Royal Society, and he's appeared on Desert Island Discs. David, thanks so much for joining me online today.

David Spiegelhalter:

No, no, a pleasure, a pleasure.

Vicky Neale:

In the context of cancer, I think that we, or at least I, turn to statistics hoping for solid facts and clear evidence. But of course, it's much more complicated than that. Why did you choose The Art of Statistics as the title for your book?

David Spiegelhalter:

Oh, that's a good question. We took ages to choose the title, the whole thing was written, you know, finished off and everything, cover designs and everything, I kept on changing my mind and it was somebody else who suggested it because I was dithering around. You know, something to do with learning from data and everything, but the idea is The Art is that it tries to communicate that statistics is not some algorithmic automatic process. Data does not give up its secrets easily, and there's a nice quote I always use in the book, start the book with it, from Nate Silver from The Signal and the Noise, and it looks at sports betting and election forecasting and things like that. And he says something like 'numbers do not speak for themselves; we imbue them with meaning.' And I think you know, so it's an art, perhaps more of a craft to take data and to try to then say what can we learn from it. I mean, it's kind of the idea of turning information into knowledge or whatever in

statistical inference. But that sounds too narrow and too mathematical and the whole point about the book is that this is not just a mathematical process. The sort of stuff that I've spent years both learning and teaching is only of limited relevance when it comes to actually using data in our real lives.

Vicky Neale:

Yeah, I guess it's all about asking the right questions, not just kind of turning, turning the handle to get answers out. If you ask the wrong questions, then you're going to end up with junk at the end of it.

David Spiegelhalter:

Exactly, and the whole book is based around the data cycle, which starts with a question. You know it's all to do the problem solving, with question answering, starts with the question and then you know, then you go on to say, well, actually you know, can we even answer it with the data we've got? But if you think you might, or you can plan then to get some data and collect it and sort it out and clean it up, wrangle it, and then do some analysis and then go on to the communication and the visualisations and the interpretation. And so on. And the analysis is really only a small part of that whole thing. And yet it's what we all spend our time learning and teaching.

Vicky Neale:

That's really interesting. And I guess in the context of cancer, ideas and tools from statistics and the statistical numbers themselves are used in lots of different ways in trying to understand and tackle cancer, what aspects are you most excited about at the moment?

David Spiegelhalter:

See, well, I mean traditionally I've always worked as a medical statistician for decades and I suppose you know, medical statisticians are brought up on clinical trial data, and that's the most obvious way in which statistics have in the past been used I think for cancer, to determine treatments, and is staggeringly valuable. To the idea of a randomised trial so you have a proper control group that's randomly allocated so that any differences really should be, apart from the play of chance which you get over by having lots of people, should be due to the treatment you can actually quote a causal effect, and they've been enormously impressive in cancer. Led to huge advances and due to extraordinary, I don't know, the courage of the people who've been involved in it. I mean, randomised trials of mastectomy and breast cancer and things like that where women have volunteered to not know what treatment they were going to be getting up until the last minute, and it's terribly impressive that people have volunteered for this and given huge knowledge to people, and that's you know, I think this idea, the same thing happened with COVID is that enormous number of volunteers for clinical trials. Because everyone feels that if I'm going to have to go through this, I night as well, you know, what I experience should be of value to other people. So clinical trials have been enormously valuable in cancer treatments, but my main interest now is in prognostic models, and essentially what this means is that for people who have got cancer, trying to help them make a judgement about what treatment to have and actually just to have an idea of what their prospects might be.

Vicky Neale:

And I know that the Winton Centre, your team, have been involved in the Predict tools for breast and prostate cancers, which I think are designed to help clinicians have those conversations with

patients about possible treatment scenarios and what the consequences might be for patients and so on. Those don't apply in my case, but I had a bit of a poke around the Predict breast tool 'cause I was kind of curious how it works. So what principles were important when you and your colleagues were putting those tools together?

David Spiegelhalter:

Well, the first thing is that we didn't do the statistical analysis, Paul Farrow really has been in charge of developing, and colleagues, been in charge of developing the statistical models, but it is the kind of thing I could do, and the principles are to try to take factors that are available at the point at which a decision has to be made, essentially in breast cancer about adjuvant treatment, and prostate cancer about whether one is going to do essentially a radical intervention or not. And using just that information, using the best prognostic factors you can, to predict really essentially just what survival might be.

Vicky Neale:

So in the case of the breast cancer tool the clinician or the patient can enter data about the size of the tumour, and a few kind of factors about the patient and explore the possible scenarios for various different types of drug treatment. Is that a kind of quick summary?

David Spiegelhalter:

Yeah, exactly, so it would be you know, age and size of, you know, the number of nodes involved and various things that one would normally be able to have available and then looking at the survival if there was no treatment given apart from any initial surgery, and then on top of that would be the effect of chemotherapy and various other treatments one might give in terms of survival and using the best data that's currently available.

Vicky Neale:

And one of the things that struck me as interesting about that is that the tool presents this survival data in a number of different ways, so it's not just a single way, and I suspect that that's the result of a lot of discussion and thought about the advantages and disadvantages of different approaches.

David Spiegelhalter:

Yeah, I mean the one thing it doesn't do is say how long someone is going to live. It doesn't give any number at all for how long, 'cause I think those numbers always grossly misleading to say, oh, how how long have I got doctor a year or 18 months? Because the crucial thing is that we don't know. And actually, if you say to someone a year, it's very unlikely they'll live a year, you know, they'll either live a lot less or considerably more, and so it much more emphasises the idea of the uncertainty. The fact that we could, we could say, you know about what proportion of women like you might be alive in 10 years, 5 years, 10 years, 15 years, and there's lots of different ways to present that data.

And so because there's no correct way of doing it, some people just like the numbers, some people like little icons, little images, although we we've learned lots of things like don't use images of people and the choice of colour is important, we're trying not to, trying to make it as a sort of emotionally ah, we want it to be engaging and vivid, but not emotionally powerful, we want to actually de-emotionalize the whole thing so we don't put great big black icons or great big red ones or anything like that. And we're not making a judgement about anything. We use tables and bar charts, I like

survival curves and some people like survival curves, so we put them in there. Some like like it, some can understand it. There's no correct way to do this, and so we do it in lots of ways.

The other thing we're really keen on is that we never say this is your risk. This is the risk of the woman, it's not. Everyone is individual, everyone is unique, the most we can say is that, well out of 100 people who ticked those boxes, essentially we're saying, this is what we'd expect to happen to them in 10 years time. And we can base that on the data that we've got, and so that's how it's always represented. Because everyone's unique, there's always factors that we don't measure that the doctor might very well know about, and so it only provides a ballpark figure for the actual conversation to be had, between the clinicians and the patient, and that's how it's used. In multidisciplinary team meetings it's there all the time. It really is, you know, like an expert system. We don't call it AI, but it is AI, it's treated like that. It's treated as a, as an expert in the corner. They bash it through, see what Predict says and then they say, well, yeah, we think it might be a bit higher bit lower. This patient's got some extra factors involved and that's how it should be used.

Vicky Neale:

And do you have a sense of how widely used these tools are now? Have they been kind of taken up in lots of places?

David Spiegelhalter:

Very roughly, Predict for breast cancer is used around 30,000 times a month across the whole world, so that's about 1000 times a day around the world, right around the world. It's translated into 8 languages now I think. So it's seemed to be extremely valuable and I can understand why, because it sort of levels the playing field, as I say it doesn't say what the woman's risk is, but it gives everybody a common basis from which to work from. It gives a ballpark figure that puts things in perspective and gives an idea, and particularly what the benefit is of things like chemotherapy, where, which is going to be tough.

Vicky Neale:

And one of the things I think is really interesting about it is that idea of empowering patients to be able to engage in that conversation with clinicians in a meaningful way. I know from my own experience as a patient it's really hard 'cause I'm not an expert in this stuff, but also I want to understand these decisions. I want to be part of these decisions and I guess this provides a mechanism that clinicians can use as part of that conversation with patients.

David Spiegelhalter:

Absolutely. I mean, that's the whole idea where we are, although it can be used just by the clinicians, our hope and our experience is that very often it's used with the patient as well. It can be used just by the patient if they've got the information that's completely publicly available, and there's no, there's no patient version and clinician version we ruled that out immediately. Everyone gets the same, and so it should be part of that conversation, so a triangular conversation so they can explore things. We haven't got side effects in, we've got the side effects in prostate, not in in breast yet. They're almost ready to go in, and I think that's also incredibly important.

Vicky Neale:

Yeah, I'm so reflecting on my own experience. Side effects are really important in terms of making a decision, but it's so difficult to build into these things.

David Spiegelhalter:

Otherwise, you'd just, everyone would go for maximum intervention, but no, you don't necessarily want to do that. So, I mean talk from my experience, I've had prostate cancer, but I was diagnosed, it was 2016 or so, and I wish prostate Predict had been available then. I really do. I could have put myself into it, got an idea and it would have helped the conversation hugely, I think. So I really, really wish I'd had it available.

Vicky Neale:

So has that, your own experience informed the way that you kind of go about thinking about these tools?

David Spiegelhalter:

Hugely yes, and my enthusiasm for these things, I think everyone should have these available for as many conditions as possible. We've now got it for transplantation and other conditions as well. So, because when people see it they, largely clinicians largely say, well, I want one of those for my cancer, I mean they're not always so, you know, it's much so much easier when, terrible thing to say, but with the really common cancers 'cause you've got lots of data to build these things on so you can build more refined models.

But the basic idea, I think of it, you know, helping with the conversation, I think it is definitely to do with patient empowerment. Not you know, patients can choose how much they want to be involved in their decision, but in the end it is a shared decision. And then there's the patient has to take the consequences, and so they have to feel that, they should feel that, actually whatever decision has been made that they have been engaged in it. And you know, lots of studies have shown that this kind of thing doesn't actually change, may not change very much, what anyone does, it's not intended to try to reduce or increase treatment or do anything like that, but it increases decision satisfaction when people feel they have been engaged. They have been consulted. Their feelings have been taken into account and this is hugely important because regret you know, is an important emotion that one would like to avoid.

Vicky Neale:

And I think this this interplay between the statistics and the humanity is such an interesting aspect of your work in this area.

David Spiegelhalter:

Yeah, I mean that's why I work with psychologists almost exclusively because this idea of the fact that you know these are difficult, difficult topics, people are in a very vulnerable state because this is for people just after, essentially just after diagnosis, so this is, uh, as I know, and you know, this is a really, you know, you're in an extraordinarily fragile state at that point, and so it's got to be done carefully. And it's got to be done with consideration and care and yet it can, it can be done. And people really appreciate it, but we've done so many interviews and focus groups and individual and conversations with patients. I don't do them, but we've got trained people who are incredibly good at it.

Vicky Neale:

My sense is that there's an increasing emphasis on empowering patients to be involved in these conversations.

David Spiegelhalter:

Oh, if you look at the Personalised Care Institute that's going on, SDM, that's Shared Decision Making. It's been around for donkeys years, but it's being taken a lot more seriously and well the other thing we've just prepared and published for the NHS are 10 decision aids in a range, they're actually paper based at the moment, that's what patients wanted, but on a range of difficult topics and which take the predict approach and play it out for topic after topic after topic, and difficult things in which one looks at you know, what are the options? What are the treatment options? What are the potential benefits and harms?

You can't be so personalised because it's, so it's not, and I don't even like calling Predict personalised, it's stratified. Because it otherwise it sounds like it's your risk, it's not your risk, so it's stratified. I like that term, but and the paper ones really have much more general, although they can obviously stratify into very broad factors and they talk about the benefits, harms or relative treatments, and what you may want to think about. And, particularly about the side effects and things like that and what your prospects might be, so it's less refined. But it's got all that ethos there and these things again and again have shown to be popular and useful. But they take a lot of time because you've got to test them. The language we want to put in pictures. You tend to often have things at multiple levels. You have something at a very high level, then more detail, and then always let people, give people sources. So, if they want to go on the web and find out more, they always can, so there's no single way to do this. There's no single level that's right. So when you're catering for multiple audiences with multiple sophistication, multiple levels of numeracy, multiple interest and engagement, you have to allow for this, yeah.

Vicky Neale:

Well, one project I know you were involved with was to do with developing information provided to people when they're invited for breast screening to help them decide whether or not they want to do that. So I guess this is slightly different from the person who's just received a cancer diagnosis and is making treatment decisions. But maybe there are some similar principles there, of do I want to do this or not, what are the advantages.

David Spiegelhalter:

Those principles are exactly the same and I was on the committee that drew up the breast cancer screening leaflets, and in particular, this business of being clear that everything has got benefits and harms. And that was the first time, and that the information is not there to persuade you to do something. So that was the first time that a breast screening leaflet was published that didn't recommend breast screening.

Vicky Neale:

I think that's such an interesting shift, isn't it? That change from, well, the medical people have decided this is what we think you should do to here's the information to help you make a choice.

David Spiegelhalter:

The policy is to offer breast screening. That's quite reasonable that part, but it's not the policy to persuade people to get breast screening. And so it was quite fairly clear about the benefits and harm, potential harms, of breast screening in particular. I mean, there was the, you know, there are multiple things with breast screening, that you might get a false mammogram and we just, you

describe how often that happens, but that instance can be countered quite quickly through further checks, but the biggest, the biggest problem is overdiagnosis.

And you know, and overtreatment. Because, uhm, you know, while the breast screening programme is estimated to save 1300 deaths from breast cancer every year, it's at the cost of 4000 women being treated unnecessarily for a cancer that would never have affected them, so that's the trade-off over the whole programme. But at an individual level, you decide, well, you know am I prepared to take that, to want to do that sort of trade-off? And some people will, and some people won't. So the crucial thing is that there's no right decision at the end of this. And what, I've seen some very good articles written where, about somebody saying, well, I got two friends given exactly the same information and they came to different decisions. They're in exactly same situation, same information, different decisions, yeah, absolutely fine.

Vicky Neale:

And I read some of the, I read about some of the work that had gone into designing this leaflet about breast screening and so on. Has there been follow up work to see what the impact has been on the number of people choosing to accept the invitation or turn down the invitation? Or is it too soon to say?

David Spiegelhalter:

Yeah, the numbers, uh, they didn't go up. And I don't think they had a huge influence actually, as far as I remember, the trend numbers in people actually screening and they have, you know, held up, held up well but didn't go up. It wasn't intended...

Vicky Neale:

So that that ties in with what you were saying earlier that often it doesn't make a difference to the decision.

David Spiegelhalter:

It's an interesting thing, but it's not a performance indicator 'cause if it went up or went down isn't, you know, it is not the point. But as you said for me the really interesting thing was the fact that there was, there was a, it was more than a focus group, it was a, you know, major sort of citizens' jury essentially was set up. Now which we went to address, I think it's about 25 women really covering a wide range of, you know, within the age range of being screened, but very different sorts of people. And we got to present to them, which is, I think, unusual. They had an oncologist there and their statistician and we weren't, we warned you know about different ways to present the information and we prepared all sorts of graphics and things like that. And we went, and we were told under strict, you know, you must not say which one you like, or that research suggests is the right one. You mustn't do that. You must just present these as we're thinking about these options and then go bugger off, go away and leave these on the tables for the women. And so it was very, it was quite, you know we had to just do this. So yeah, just like this this this this, here you are, and we left them on the tables, the women sat around and make their decisions, and they chose exactly the ones I wanted them to choose.

Vicky Neale:

Oh perfect.

David Spiegelhalter:

I was so pleased. It's lovely, just the ones. It's all to do with what does it mean for 100 people, blah blah blah. And things like that. So again, it was what we would call technically an expected frequency representation. Nothing to do with probabilities or chances or rates and percentages and nothing to do with that. Just, what does it mean for 100 people?

Vicky Neale:

So this is the sort of diagram where maybe you have a hundred stick figures and then they're coloured in according to consequence.

David Spiegelhalter:

Something like that or it's a sort of tree diagram showing you start with 100 people in this many, go down different branches and things like that. So, and that you know, research has shown that's a very good way to do it. But no matter what the, but there's two things, there's the visual representation, but before that there's this choice to do it in terms of an expected, um, outcomes for a group of people and you know, you think when you do it, people say oh that's obvious and you realise there's lots of other ways you could do it which are not so clear at all. You can start talking about false positive rates and stuff like, oh no, no. God, no.

Vicky Neale:

Yeah, I'm a mathematician, I'm highly numerate, I feel like I'm good at data, I really like these, kind of frequency-based diagrams. I just, the ability to see the whole picture in one go in such an immediate way, I think is really profound.

David Spiegelhalter:

Exactly, you can do the part to whole comparison, and especially if it's visualised like that so it's not just concentrating on the bad events or the good events, or something like that, actually you should be able to see them both. They should be both be given equal emotional salience in terms of the colour and the representation and things like that. So, these are you know, they're all, it's all in a sense, common sense. But it obviously hasn't been common sense all the time because of how I think a lot of poor, a lot of communication has been.

Vicky Neale:

I think, I think this might be common sense with the benefit of hindsight.

David Spiegelhalter:

Yeah exactly, yeah, yeah and a huge amount of work.

Vicky Neale:

Absolutely and related to this communication of risk I suppose. Over the years you've commented on lots of media stories of behaviours that do or don't apparently cause cancer, I mean apparently conflicting responses on consecutive days and all of these kinds of things, so I suppose as an audience we have to have a questioning approach to such stories. But what advice do you give to, to journalists and researchers when they are telling such stories, which are sometimes built on important research? How do they go about communicating that, those ideas in a meaningful and accurate and not too alarmist way?

David Spiegelhalter:

Yeah, I think we just say use both relative and absolute risk, so that, most studies the study designs that are used in a lot of, a lot of medicine and a lot of reporting, is in terms of what you call relative risks. What's the relative comparison between two groups of people? Say, give them one treatment or another, you get one treatment oh but that increases or decreases the mortality rate by 20% or you know, eating bacon increases your risk of bowel cancer by 20% or something like that. So it's done by, in terms of the change, the relative difference between.

But it doesn't tell you actually, well how big are those risks? Is it 20% of a lot or 20% of almost nothing? Because a 20% increase on almost nothing is still almost nothing and you may not care a jot about it, particularly if they're telling you to give up your favourite food. So you're, the only way to get an idea of the importance of something is do the absolute risks. And so it's not only us, I mean everyone recommends this, it's guidelines in journals, they're mainly ignored, and that they should be reporting absolute risks and in terms of what does it mean for 100 people. So you know, we always do the thing of 20% increased risk of bowel cancer over your lifetime if you eat bacon every day, well, you know 6% of the population get bowel cancer. So that means that that you know 6% goes up to about 7%, so that's, that's that relative increase applied to an absolute number percentage. Best to call it 6 percentage points goes up to 7 percentage points. A bit like that. So that means that 100 people have to stuff their gob with bacon every day of their lives in order for one of them to get bowel cancer. And if they eat that every day of their life, they might not live long enough to get bowel cancer.

So this, so I, you know, I tell this story with lots of images of little people and things like that. You can do it. It is a very powerful, very powerful technique. Obviously, I tell it deliberately the other way to make it look a completely mundane risk. Although you know I've been influenced, I don't eat as much processed meat as I used to. I mean, for me, a bacon sandwich is a big treat. At least I used to stuff them down, so you know I do vote with my feet to some extent, but you know I try because you know it is a real, I'd like my risk, that's why I take statins. You know it, it makes a fairly small risk, reasonably smaller so, so why not do it? So, so you should use absolute risk. And we've got our, plug plug, software RealRisk for journalists and press officers where they can put in these relative risks. And it expresses in nice language and draws pictures of changes in absolute risks. What does it mean for 100 people.

Vicky Neale:

I was really struck that you said these are kind of standard guidelines and yet people are ignoring them. Do you think that's because they're not aware of the guidelines, or because they feel like they get a more dramatic story and a better chance of a headline with the big numbers for the relative risk, or?

David Spiegelhalter:

There's quite a lot of storytelling there, and I think, I again talk about this quite a lot, it goes right back to I think, it often goes back to the scientists themselves, who quite like coverage and newspaper headlines. But then the press officers can want to milk the story, that's their job and then the journalists want to get their story accepted by the editor and then worst of all, even if they do quite well, it's the sub-editors who stick their headline on and then it really that's the most the most infuriating thing when people have made an effort all the way through and some crass sub-editor sticks clickbait headline on that suggests that something is going to kill you. I mean I, I see them all, every day I get sent these things and I, don't know, almost you know, long for the days of COVID when at least you weren't getting these cats cause cancer stories coming into your emails every day.

Vicky Neale:

I'm just going to interrupt briefly to let you know that if you're enjoying this episode of Maths + Cancer, then please do head to ox.ac.uk/cancer to find the other episodes in the series, in which my amazing guests tell us about some of the many intriguing ways in which maths and stats are helping us to understand and tackle cancer.

True story, early in my experience of being diagnosed with cancer, I knew there was something going on, I was waiting to find out exactly what. So of course, I went and looked up the stats and you know the sort of percentages describing the different kind of scenarios here. And then I thought, well, actually, this doesn't really mean anything because either I do or I don't, or either it's this or it's that, there's no randomness in my case, there's no probability associated with this, it just is or it isn't. I just don't know and at that moment I thought I'm sure I went to this talk by David Spiegelhalter in Cambridge where he was tossing a coin. And you will explain this much better than I do.

David Spiegelhalter:

Basically, there's two forms of uncertainty. Put very simply, you've got what you call aleatoric uncertainty. I'd prefer to call it chance, which is before you toss the coin. You don't know what's going to happen in the future, the weather tomorrow, and all these things. They're just unknowns and we can't know them until they happen. We can talk about probabilities of the coin coming up a half, coming up heads whatever, and then you got the other form of uncertainty which is after you've tossed the coin but you cover it up. So, if I can't flip a coin now and I cover it up and I say heads or tails, what's the probability it's heads? Well, you know it's either heads or tails. It is decided and so what does it mean to talk about the probability? And I think it is meaningful to talk about the probability, and it's what it's called epistemic uncertainty. It's an idea dating back centuries that you could put probabilities on your lack of knowledge, essentially your ignorance. It's a number that expresses, you know, what we don't know, so that as you said, when you're diagnosed, when you take a test for COVID either you've got COVID or not and you don't know whether the test is going to be positive.

When you're waiting for a diagnostic test to come back, it's epistemic uncertainties, there or not, we don't know what it is. And I's say it is quite reasonable to think about what's the betting? You know it's like when someone's pregnant, you don't know if it's a boy or girl, all these things it is reasonable. I mean the main way to think about it, if it's something reasonable that someone might put a bet on it's reasonable to talk about the probability. I doubt anyone was betting on your diagnosis, but mentally you are betting on your diagnosis and so therefore it's reasonable to put odds on it, or probabilities. And they're based on, maybe based on judgement, and experience and things like that, but eventually you will find out the truth.

Vicky Neale:

Yeah, and I guess that ties in with what you were saying earlier about the distinction between, with the Predict tool, for example, being able to present kind of population level, for 100 people like you type things, versus a prediction for an individual person, the one person whatever happens, happens. But you can say something meaningful and useful and informative about the population level.

David Spiegelhalter:

Yeah, whatever I mean, in the end, everything collapses down, it will happen, but the other way of thinking about it, I think, is that for this individual their future is aleatoric, it's chance. We just don't know, we cannot know what's going to happen. But what we can say, in other words, we switch it to epistemic, you know, to a model of the past. We can say well in the past, or you know, we would expect 100 people like you, this is what we would expect to happen, so we're making a judgement about their chance from observation, I mean, that's how statistics works. Of course, you know it uses you know, history to try to say something about the future and it does this in this case by embedding that individual in an imaginary group of 100 people. It's not actually 100 people. We made that mistake. Can you imagine? People said, oh, we've got some response saying, well, we don't think much of this tool, it's only based on 100 people. I said no no, and that was our fault because, you know, we draw 100 people. We don't mean this is what actually happened to 100 people in the past. This is 100 fictitious people like you.

Vicky Neale:

I'm imagining now like on the BBC Show Pointless where they say we asked 100 people.

David Spiegelhalter:

Yeah, yeah.

Vicky Neale:

It's not that you asked 100 people.

David Spiegelhalter:

This is based on tens of thousands of people and their history, so that was our point. We never, until you listen to people you don't realise how they might interpret something. I've learned so much from that, you kind of think it never crossed our minds that anyone would think that, and yet this was you know it's not just one or three, yeah?

Vicky Neale:

It's so interesting, isn't it, those fine subtleties of the language.

David Spiegelhalter:

And this is the kind of thing that when you've done it, nobody really realises it, they don't realise the care and work that goes into just the wording of a simple thing. We spent a oh, I know, can I tell you a story?

Vicky Neale:

Please do.

David Spiegelhalter:

We did one on, a really serious one, for parents of children with congenital heart disease, talking about the mortality rates in different hospitals for uh, for congenital heart disease. And we published this is because it's public data and it produced, you know, allowing for the variability and things like that. But you know when you start talking about, you know, let's say 95% survival rate. You know. So five out of 100 babies like this, we would expect five to die. You know how do you talk about, what's the word you put on that uncertainty? You can't say binomial variation or something like 'cause we can put an interval around this. We can talk about the in the sense of what was the

underlying risk for a child in that hospital if they had so many deaths. So you can't say, you know, you can't call it random error, all these technical terms are so totally unacceptable, and you can't for an individual you can't call it, you know chance or fate or providence, whether they are one of the ones who survive or die, we just know there's a probability, we don't know in your case, which one it's going to be.

What words can be, and we struggled for ages, and then to somehow get a term for unavoidable unpredictability. You know, we cannot say whether you're going to be one of the 95 who survives or one of the five who dies. There's no more we can say. All we can say is one or the other will happen in roughly in these proportions. There's unavoidable unpredictability, but that's too clumsy a phrase. So, and somebody suggested, who wasn't even a native English speaker suggested, you could use, we predict who will live or die because of unforeseeable factors. And not unforeseen factors, unforeseeable factors, and it is true actually, because actually a lot of it's do, with when the surgeon actually opens the baby up. You know what they'll find, exact details, really fine morphology that could affect the operation, so it's unforeseeable whether the baby might survive the operation or not.

So that went in there and we checked it with the parents and that was fine. And now that's in there and it's a fact I now always use that if I have to communicate to anybody, say well, why don't we know who's going to live? If after the scene, oh right, you know, surely you've got good, I mean, why can't we tell? Unforeseeable factors.

Vicky Neale:

That's so interesting, finding that right phrase.

David Spiegelhalter:

Finding the right, not random error.

Vicky Neale:

Definitely not random error. You've talked about the fact that these tools are not built on 100 people, but on tens of thousands of people and the, I guess maybe one reason that the Predict tools were created for breast and prostate cancer first was that they are, sadly, common cancers, relatively speaking. I've been being treated for a rare type of cancer, so I look at these kind of tools and these data and I have data envy 'cause there's not very much research and there's not very much data 'cause, I mean happily, there are not very many people. But there are still statistical tools and techniques that are important in the context of small sets of data, sparse sets of data, I think. I wondered whether you could say a little bit about that?

David Spiegelhalter:

Well, I think what it does it, it means that there's even more, I think, responsibility on the profession and the medical establishment to collect data on rarer conditions by, you know, synthesising from, you can't just do it in a few centres or something like that. You have to make a really special effort to set up registries, to collect that data, to inform, to provide everyone with a common baseline, so that when this occurs wherever it occurs, you can refer to a wealth of experience and you're not just reliant on who happens to write a paper about their group of patients, what they did, or anything like that.

And so, I think, and of course this is done, and I'm not sure how much has been done with your condition, but yeah, it's a incredibly valuable thing to do, as for example in congenital heart disease,

which is, uh, you know, really, terribly important, but fortunately not very common. And they've, they coordinated data collection, they built a risk model for congenital heart disease. Really rare stuff, but they've got a really quite sophisticated risk model there because of, essentially every single patient goes in. Every patient in the country goes in. So that's the way to do it, I think, that you have to set up these things because so, even if something is rare you do have sufficient, you have as much data as you could have. And again, everyone loves the idea of their experience contributing to future knowledge.

Vicky Neale:

I absolutely, that really resonates with me. I have carefully ticked that I want to be, please use my data for research, if I'm going to go through this, please do something with it.

David Spiegelhalter:

Yeah, exactly. That's one, in a way, good thing that could come out of all this, is if you can help people in the future.

Vicky Neale:

I was reading a little bit recently about an area I think called experimental design, which seems to be about using interesting, I guess, kind of mathematical and statistical tools, maybe where you want to carry out a clinical trial, but you have very few patients potentially to be able to use, and how you can kind of control for those different factors you were describing earlier, and so on. It's, yeah, it seems like some interesting maths in that.

David Spiegelhalter:

Yeah, well, I mean, experimental design has been around for donkey's years, and it started really in Rothamsted with agricultural plots. And you know, standards of Latin squares where you, where you arrange your crops around the field so that everything is balanced and up to an element of randomness. And the simplest experimental design is a simple randomised trial where you essentially flip a coin to decide which treatment someone going to get in two treatments, and that means that the two groups are comparable even in ways you don't know they're still comparable because you've done it at random, you haven't matched them according to their characteristics, so they're matched even on things you don't know are important.

That's the crucial thing about the randomization. But then, that's very blunt instrument, and it works you know, if you've got huge trials. With smaller studies, people are using increasingly adaptive studies where you might start off, where you kind of, because if it's something fairly rare means that you know quite a big proportion of the people with the condition are being experimented on, and you would like to minimise the number of people getting the inferior treatment, so the sort of adaptation that can happen is that you might, for example, start with a whole lot, with lots of different treatments, lots of different ideas, four different ones or something. And then you do so many and then the one that starts looking, starts dropping behind, at some point you drop it. It's like, so it's not gonna, you've got a conclusion. And then you concentrate on the others, or you can, might, move change the randomization proportion so more people start getting the one that looks better, the most extreme is play the winner in which you know, you just, just give the treatment to the thing that looks best at the moment, but that's a very extreme example. People, you usually keep some randomization going for as long as possible until you're pretty confident. But it's good.

So these study designs, which are aimed to, as I said, minimise the number of people getting the inferior treatment. A lot of work on that, you can do all sorts of simulations to work out how powerful they are to make sure you can get a firm conclusion at the end. And extensively used now. That's become very very, much more popular as a a way to do. The idea has been around for donkey's years, but it's taken quite a long time for it to become accepted because it was so much easier just to do 50/50 and keep going until you've done masses of them. And then, because there's quite a strong argument, I think, because people were doing studies that were too small and so that they weren't convincing enough to change practice. And so, some very influential people, led by Richard Peter, I think they had the idea that, when you do a clinical trial, it should be the last clinical trial.

Vicky Neale:

That's a really interesting phrase.

David Spiegelhalter:

You do the last, so you make it enormous, and you don't stop it early. You don't stop it until you're absolutely sure that, and that it will change practise, and that's it, you never have to do this again. Because otherwise people do lots of small ones. You put them together in a sort of what's called a meta-analysis and combine them. But actually, the blockbuster study, and there was a period of doing those, I think they're, I think they're not quite so popular now because they were, they established some really important treatments, streptokinase and aspirin you know other, other things, statins, you know, it's quite a rare event heart attacks and strokes, so you've gotta do a lot of people, so I'm really grateful. I take statins and I know tha, I don't know, I have no idea whether they're going to help me or not, and I never will know whether they help me or not, but I know on average they reduce heart attacks or strokes.

Vicky Neale:

And you know that thanks to really robust clinical trial.

David Spiegelhalter:

Thanks to tens of thousands of people with some really huge studies, yeah.

Vicky Neale:

You were a maths undergraduate here in Oxford. At what point did you decide to go into medical statistics?

David Spiegelhalter:

Ah, that's a good story. Oh well, I did, I like the pure maths and I got about halfway through the second year. And frankly, as I said, I banged my head on the pure maths ceiling. I think everyone's got their ceiling of abstraction, beyond which they really struggle, and I started struggling, and I thought I loved it and, but it got really too difficult. And I was very fortunate, my tutor at Oxford was Adrian Smith, now president of the Royal Society, and a convinced Bayesian statistician, so not just a statistician, a Bayesian one, so he both got me interested in statistics, but also the philosophy of statistics. What it means, this idea of the uncertainty, the epistemic against the aleatoric uncertainty. I was learning that 50 years ago when I was 19. And got totally indoctrinated about a particular way to think about probability that if you give me a chance to, I will go on about for about 2 hours, so I'd be wary about asking me.

So, but and then, what I found that it was still very mathematical statistics the sort of stuff I've been teaching as well. But then I got a job. I was interested in going into doing a PhD, again in mathematical statistics, no real applications. But then I got a job and I thought I'd quite like to do some applications. My first job was in computer aided diagnosis, essentially in the 1970s it was kind of AI in medicine. It was writing, you know, working out algorithms for diagnosing patients, and building prognostic models in head injury. So I was doing that in 19, late 1970s, and that got me really interested in the whole business. And so, but I what I managed to do throughout most of my career was combine the more mathematical methodological work in with real applications and so for me the whole career has been an utter joy, utter joy and I always said, well, I'd do it even though I wasn't being paid and now find out that's true, 'cause I don't get paid anymore and I'm still working just as hard.

Vicky Neale:

You touched on this a little bit earlier. You talked about your own experience of prostate cancer. Can you say a bit more about how that's changed or not changed the way you go about your work?

David Spiegelhalter:

Oh for my work, it's just given me a real enthusiasm for, just what we're discussing, the empowerment of patients, the providing them with balanced information that's not trying to persuade them one way or another. And so they're not totally dependent on just the people around them, either family or friends, or the particular doctors they see. Because one of the things we do, you always think somehow, it's like you know people think oh science says like there's some consensus in science. People think oh the doctors think that or so, and they don't realise that if they went to a different hospital and maybe just a different clinic in the same hospital, they might get a very different opinion. There is a big variation from place to place and person. So the idea there is a monolithic body of knowledge which decides this is the right thing to do is, is, I think, is not the case. And actually there is a big variety of opinion. I mean, that's why the multidisciplinary team meetings, the MDT's, are so valuable and as I said, that's the point at which tools like Predict are enormously valuable at providing a level playing field across the country, if not the whole world.

So yeah I, I think that for me, it's just giving me an enthusiasm for empowering the patients who want to, to engage with the decisions being made about them. They may not want to, and that's completely their right, say I'm sorry, thank you for telling me that, like many will say, thank you for telling me this and, you know, what do you think I should do? And I'll do whatever you think is best. And that's totally fine, but that should not be the default, otherwise it's pure paternalism. So, I think that I mean apart from being of course a legal obligation to get a proper informed consent now since the Montgomery judgement in Scotland from the Supreme Court, did you know about the Montgomery judgement?

Vicky Neale:

I do not.

David Spiegelhalter:

Few years ago, and it was, and it's to do with the fact that consent, when someone consents for a medical intervention, it shouldn't be on the basis of the issues that are perceived by the medical profession. It should be on the basis that takes into account their own perceived anxieties and concerns, so it shifted the responsibility that, to the doctors to actually find out what's important for that patient. And not just to consider what the medical profession think is important. So it's given a

big responsibility for that. So they have to bring, yeah, they're supposed to do it legally, to listen, this sort of thing, so it's almost made really shared decision making or some aspect of that, you know, a legal requirement.

Vicky Neale:

That's fascinating. And so having the tools to do that is even more crucial. You mentioned multidisciplinary teams, I guess you have your own kind of multidisciplinary team. You mentioned you spend lots of time working with psychologists, for example, professionals with a range of expertise. How do you find those collaborations?

David Spiegelhalter:

Oh, I love it. I love it. That's what I've done now for years since I had this more public engagement job. And now when we got the funding to do our Winton Centre, I'm the only statistician essentially. So, because we don't do data analysis apart from the experiments we've run, so it's a multidisciplinary team meeting of science communicators, of web designers, and psychologists. And, who are extraordinary, god, I love them. They're so brilliant. And they, you know, so we're both designing things and doing some beautiful design. We do use outside designers as well for some for our things, but a lot of it is in-house designs, then testing them on individuals and in the end doing randomised trials, and the big difference between a medical randomised trial, you know where you might spend years to recruit, you know a few hundred or a few thousand people, these trials they spend ages to plan because you've gotta, like good psychologists, they pre-register the design, have to get ethics approval and things like that. And then, you run them overnight. So, you know, on 5000 individuals on, you know there's also, the number of different data places you can go to run these things where people get about 50p a time, and they do a study on which visualisation they like. Or do they understand that you give them something, can you answer questions about it, so you test people, and you test their numeracy, things like that. So we've done workshops where we're designing different interventions with the group running them over night and coming back in the morning with the results of the randomised trial. So I mean, you know, doctors eat your heart out. This is the way to do it. So I'm so impressed the people who can do this, yeah.

Vicky Neale:

We're going to have to wrap up soon. Final question for you, what advice would you give to somebody early in their studies now who has an interest in using statistics to understand, prevent, or treat cancer?

David Spiegelhalter:

Oh, do it. I mean, we've only talked about a couple of ways. I mean, there's vast amounts more things if you start getting into genomics, into genetics, and there's so many other ways in the development of treatments and so on, so many other ways. So we've only hardly scratched the surface on the role of quantitative methods in treating and exploring cancer. But I've always been personally interested in the, the real sort of, oh I think it's a kind of sharp end, the, you know, the stuff that's dealing with patients, with humans. And I have, that's always been vivid for me, got me engaged. But there's a vast amount of, the science of cancer, all this, the understanding, and you know, again, just trying to, a great industry of people doing this work. I've never found that quite as you know, engaging. I like the pointy end I like, I like the human bit.

Vicky Neale:

It's absolutely my privilege in this podcast series to be able to talk to people doing a whole bunch of these kind of quantitative techniques and different aspects of maths and stats applied to cancer.

David Spiegelhalter:

Yeah yeah, the real stuff, yeah.

Vicky Neale:

David, thank you so much for a fascinating conversation today, for all your statistical research, and also for being such an energetic and articulate champion of clear communication of risk and evidence to benefit cancer patients and so many more. Thank you.

David Spiegelhalter:

No, it's been a pleasure. Thank you so much for letting me ramble on.

Vicky Neale:

Thanks for listening to this episode of Maths Plus Cancer. I hope that you found the conversation as interesting as I did. There are more episodes of Maths Plus Cancer, as well as features about Oxford's research into cancer, at ox.ac.uk/cancer . If you're enjoying exploring how maths and stats help us to understand and tackle cancer, I'd love it if you'd tell your friends about the podcast. And please do join in on social media using the hashtag #MathsPlusCancer. That's plus the word, not the mathematical symbol...