Numberphile Podcast Transcript
Episode: Statistics and Saving Lives - with Jennifer Rogers
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Professor Jennifer Rogers discusses coronavirus vaccinations, the media, and her own path to medical statistics.

Jennifer Rogers website, with links to all sorts of things

Jennifer's TEDx Talk

Jennifer has written about cornavirus vaccinations on the Phastar blog here and here

For some previous Numberphile chat and videos about coronavirus you can check these out:

Gondor Calls For Aid with Kit Yates

The Coronavirus Curve with Ben Sparks

Crystal Balls with Hannah Fry

Other links...

The Royal Statistical Society

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[gentle music box music]

Brady Haran [BH]: Today's guest is Jennifer Rogers, a statistician specializing in all things medical. In addition to her consultancy job, she's well known in the UK as someone who tries to increase public awareness and understanding of statistics. Now in a world of coronavirus and vaccinations there can hardly be a

better time to be talking to her. But before we get to COVID and clinical trials, I asked Professor Rogers a bit about her own statistical journey.

[gentle chimes]

BH: People who do the sort of things you do for a living, I like to find out what they were like when they were kids. Like were you as a girl, were you into stats and numbers and that? Were you always gonna be a statistician?

Jennifer Rogers [JR]: D'you know what? I actually was convinced that I was no good at maths and at school I really wasn't the biggest maths fan. It was my maths teacher who actually talked me in to doing an A level in it and it was really then when I did my A levels, so sort of college level, that I really fell in love in with mathematics and particularly that was the first time that I was ever really properly introduced to statistics and I really loved the application of mathematics and I loved the fact that you could see a dataset, you could plot it, you could, you know, mess around with it and that was when I really fell in love with mathematics and then decided to take it on further into university and always convinced that this was it. The last one, I'm not doing anything else after and then ended up doing more and more and more.

BH: Why didn't you like mathematics? Was it because you weren't good at it or was it because it wasn't… it wasn't cool and what the cool kids did? Like why weren't you into it at first?

JR: I think I potentially hadn't found my bit of maths that I loved and I'm… I'm a bit of a perfectionist and if I'm not the best at something I'm convinced then that I'm really bad at it. You know, it has to be all or nothing type of thing. And I think that when it came to some of the more, you know, trigonometry kind of subjects, there were people in the class who were better than me at it and I think I just then thought, oh that means I'm rubbish and I'm no good at this, and I… you know when I really found statistics I got a hundred percent in my first

exam and I was… I thought to myself, oh okay, this is what I'm supposed to do. This is what I'm good at.

BH: So what were you into when you were a bit younger? What would you have said when the adults said, whaddya gonna be when you grow up?

JR: D'you know what? I started out, I was actually gonna do a degree in maths and German. I really loved languages and really enjoyed doing German, went to Germany as part of my school course. So I think yeah, maybe, I'd have done Languages, whenever anybody asked me what I wanted to do for a living, I always said a teacher. And I did work in academia as a lecturer for a long time, so I do think there was that sort of teaching part always in me that I always wanted to do that.

BH: What do you think that maths teacher then towards your A levels saw in you or what did they say to you that persuaded you to do mathematics?

JR: I don't know what they saw in me, maybe a problem solving mind or something like that. But yeah, she… I picked my other A levels and I was just trying to think, ooh what can I do as my last one? So I picked, psychology, German and history and I know, it's a real random mix of A levels, and I was trying to decide what my last one should be and it was my form tutor who was my maths teacher and she just said, oh well, I think you're really good at maths, I think you should do it, and I thought oh well, you know, I've only gotta do it for a year, then I could drop it, why not, let's give it a go. My mum actually bumped into her in the shops whilst I was doing my PhD and said, you'll never guess what Jennifer's doing now.

BH: [chuckles]

JR: And she couldn't believe it, that I was now doing a PhD in statistics and they put me up on a little wall of fame in the school so… just to say, you know,

here's what can happen. [laughs]

BH: Ah that's brilliant. So if I raked over your earlier childhood, I wouldn't have found any clues.

JR: Probably not actually. Well… I say that, I was really into science and I was really into meteorology as well. I used to stand in the kitchen and do my own weather reports, but I used to collect data on the weather, you know, the air pressure and things like that and I'd take a little note of it and… I think my dad has a chemistry background and we used to do a lot of science experiments together and maybe now I think back on it I was more focused on the collecting of the data for it than actually doing the science itself but… yeah I've always been a scientists. My dad, when we used to go to bed at night, used to teach us how to recite the first twenty elements of the periodic table. So not your sort of typical bedtime stories [laughs]

BH: C'mon then! Do you remember any? I've got a periodic table right behind me, there I'm looking at one. [laughs]

JR: So, you remember it… if I… it's gonna sound really stupid but it's, H, H E, Libeb Cnofne [Knopf Knee] Namgal Sipsclar K C A*. That's how it is phonetically, and if you go through all of them then, you can actually recite the first twenty elements.

*[Ed. note: The first twenty periodic elemental symbols, H, He, Li, Be, B, C, No, F, Ne, Na, Mg, Al, Si, P, Sc, L, Ar, K, Ca.]

BH: Nice.

JR: [laughs] Really stupid random things. [laughs]

BH: Excellent. It's still there. Alright then, so you found this love for statistics

at A levels when you started doing mathematics and then that was it, like you did it at university and things like that, like it was just like… sounds like you fell pretty quick?

JR: Yeah, pretty much, I mean I did a… a maths with statistics degree, you know, I still enjoyed pure mathematics and I didn't wanna lose that part and I still think the number theory modules that I did whilst I was at university were some of the most beautiful modules that I did. I always think of number theory being this really beautiful language and these really surprising wonderful things about numbers coming out and I'd really glad that as part of my degree but very much statistics was always where I wanted to go and I think when I did my Masters in statistics it was really medical statistics that I was particularly drawn to. I've always had a love of medicine and this idea that… what I do for a living can help improve people's lives, improve their quality of life, help keep them alive longer, that's just always been something that I've been really proud of and really keen to pursue.

BH: You talked about seeing a great beauty in that different… that more kind of pure theoretical mathematics and number theory and that. Were you ever seduced by it? Could you have ever gone in that direction, like, or was it always just something on the side that you thought was nice and you were on this stats path?

JR: Yeah I think it was more the… the application path. I think I probably would've been quite happy doing some engineering as well as, you know, statistics. I think it was… any pure mathematician's probably gonna absolutely hate me for saying this but I always saw it as more sort of maths for maths sake and like it wasn't immediately obvious to me what the applications would be. Whereas in statistics it was very clear that this is what you could do with it and so I think with statistics I could very much see a path as to what my career trajectory could look like. I've always been a planner, and so having an idea of what I could do and that being very clear to me did appeal to me.

BH: You obviously rubbed shoulder's and probably still do rub shoulders with a lot of pure mathematicians. Is there a… a rivalry or a snobbery or an attitude that pure mathematicians have towards statistician within the field? Like what's the… give me the goss.

JR: Yeah… I mean… I don't wanna bad mouth any of my pure colleagues but if I had a pound for every time someone said to me, ooh, I don't like stats, I would be a very rich woman and… it does upset me sometimes that I think some people don't necessarily see stats as being… a proper maths or maybe it's the… the poor relationship of the maths world, you know, I get a lot of teachers saying, oh I hate when I have to teach my kids statistics. And… it does get to me sometimes, you know, you stand there thinking, but you know that I do this for a living, why are you saying this to me? Umm… so, yeah, I dunno, I really hope actually throughout all of the coronavirus pandemic, I think it's shone a light on statistics and the role that statistics has in society and I really do hope that a silver lining of the pandemic is that people may have a new… maybe not love but at least an appreciation for statistics and see us as being a credible part of mathematics.

BH: I don't think anyone could argue against like the utility and the importance of statistics but why do you think the pure mathematicians have previously had that sniffiness about it? Is it because it's so applied and accessible or because they think it's easier or… harder or…?

JR: I mean it might be some of all of those things. I think statistics is a very different way of thinking, not everything that we do is pure mathematics. I'm a methodological statistician, so a lot of what I do is developing new statistics models. So I have to do quite a lot of… pure mathematics and I have to do a lot of computer programming, but not every statistician would do that. You could just collect data and that would be classed as statistics. So I think there are some parts of statistics that are not as mathematically challenging as others. There's an

awful lot of thinking about designs, especially in clinical trials, you know, how do you design your trial. Trying to formulate hypotheses. So I think that sometimes if you are a real pure mathematician that loves your numbers, statistics can be a deviation away from that, at times, and so… maybe it's seen as a little bit of a black sheep and maybe a bit of a standalone within the wider field

BH: You said that you started drifting towards medical applications of statistics, what pulled you that way?

JR: I think I've always had a little bit of an interest in medicine. I sometimes wonder to myself, should I have done a medical degree sometimes? You know, I work with a lot of clinicians and I find myself just being absolutely fascinated by it and there's a really famous saying that, you know, that says one of the best things about being a statistician is you get to play in everybody's backyards and I think… the medical backyard is a particularly interesting one. You could find yourself getting lost in all the different areas so I've worked a lot in cardiovascular disease and just having that opportunity to learn about cardiovascular disease and heart disease and, you know, heart failure, has just been so incredibly interesting to me. My PhD was looking at epilepsy data and that fascinated me and then… when you start talking to people and you realize that a couple of your friends know someone that has epilepsy or one of your friends themselves has epilepsy and the work that you're doing can have a direct impact on their lives… that just makes me feel so wonderful about going to work everyday, knowing that I could be helping people. I remember going to a big cardiology conference and them talking about a new treatment that had been licensed and they put my work up on the big screen, so some of the plots that I'd produced and that was helping them decide, who should get the treatment and how it should be administered and I just remember sitting there thinking, wow, the work that I do, it actually matters. I think sometimes when we work with numbers, it's easy to just sit in our offices and plug away at our code or our calculations and not really appreciate that the work that we're doing does have a follow on effect and will end up actually having a big impact and… yeah I just…

I've always been really fascinated by medicine and just love the fact that I'm helping people. That being said though… my Masters dissertation was on extreme value theory and I do love extreme value theory. I find that really interesting.

BH: I don't know what that is.

JR: So it's dealing with extremes, so extreme weather… extreme sort of flood levels and so the idea is, you know, we think about statistics or probability a lot of the time in terms of relative frequencies. If you roll a dice lots of times you get a number six about a sixth of the time and that's how you work out your probability. What extreme value theory thinks about is how do you try and generate probabilities or predict something that doesn't happen very often or indeed has never even happened. And so that's when you're really heavily relying on underlying models that give you an idea of what the shape of the curve could look like and you can sort of then, you know, take that, extrapolate that out into the future and I found it, yeah, I found it really really interesting to think about that so I did a Masters dissertation, I think it was on different flood levels.

BH: Cool, so you're predicting when the next Noah's Flood's gonna happen?

JR: Exactly! Exactly. And you sort of…

BH: [chuckles]

JR: …talk about it in terms of… sort of once a… one in a century event and things like that and, you know, people who were looking at offshore oil rigs and things would use all that information when they're trying to decide where to put them and also, you know, how to build them.

BH: That sounds pretty cool.

JR: Yeah! Really cool. [laughs] Like really cool. [laughs]

BH: Yeah. [laughs] So after you've got your PhD, can you just give me like the short summary of the jobs you've done and the path you've followed to get us to where you are right now?

JR: Yeah so I worked at the London School of Hygiene and Tropical Medicine for a few years, that was my first job out of my PhD. Really enjoyed my time there. I got a research fellowship whilst I was working there as well, for the NIHR, which is the research arm of the NHS. Then I took the last year of my research fellowship with me to move to Oxford University and I worked there for… I think it was probably about three or four years in total. Once my grant had finished I actually took on a role building and running a consultancy unit within the statistics department and that's where I really developed a love for consultancy work. So working with sort of small biotechs… a lot of them within the university who had new treatments or new devices or new AI models that they were wanting to develop and commercialize and they didn't have any statistics expertise and so they would hire me as a consultant and I would help them with all of that. And… was really really enjoying that work and last August decided to make the move into the big bad world of industry and have been working for a company called Phastar since last August and they are a clinical trail consultancy company. So we work with lots of Big Pharma, smaller Pharma, again the tiny biotech type of companies, helping them with their studies. It might be a randomized clinical trial, it might be an observational study. Just, yeah, helping them all the way through from designing them, all the way through to analysis and final regulatory approval. And yeah I really enjoy it, so my role there is to direct the research strategy within the company. They decided that they wanted to really start investing in research 'cause it would, you know, put them right at the edge of all methodological advances and I manage all the sort of smaller consultancy projects that go on within the company, too.

BH: How do you find that… change of culture going from sort of academia and, you know, universities to that different world of medicine but also, you know, big bucks and money and I dunno, there's probably also a lot of more… I would imagine more secrecy perhaps and things like that? Like… what's the culture change like for you?

JR: It was a little bit of a shock to the system. We do quite a lot of regulatory work so, you know, the way all our folder structures are, version controls, QC systems, standard operating procedures, all of that sort of thing took a little bit of a while for me to get my head around. All the acronyms that get thrown [laughs] around took a long time to figure out. I spent a lot of time Googlin' every time someone said something on a call to try and figure out what it actually meant in real terms. But, yeah, it's been interesting, it's been really interesting. And it's been interesting the fact that, you know, the pandemic's thrown up all of these sort of working from home issues and I think it's been a bit of an interesting eighteen months or so but really exciting and I've really really enjoyed it.

BH: You talk about focus on research and I've, you know, I've read stuff about you online and, you know, we read about breakthroughs and new developments in statistics. I'm perhaps gonna betray my own prejudices about statistics here but… what do breakthroughs and progresses look like in statistics? Because I thought… I did think the mathematics of statistics was simpler and most of the mathematics was known. We known how to add and divide and do percentages and plot graphs. What do breakthroughs look like in statistical research? What's there to learn and find out?

JR: That's a really good question and it is one that I get asked quite a lot, you know? I get asked how can someone do a PhD in statistics? Surely all your methods are already developed. The thing is that the world is constantly changing and the way clinical trials are run are constantly changing. So let's think for example about heart failure, that's where I've done a lot of my research. Heart failure, when people first started treating it, the main thing that people

were trying to prevent were deaths. We wanted to stop people dying from it. It was a bit of a death sentence when people first started looking at it. As our treatments have improved we can actually keep people alive longer, so when we want to try and decide whether or not a new treatment works, we might not necessarily be just interested now in whether or not it prevents them from dying because we can keep people alive longer we might also be interested in, okay, well… does it stop from them dying, or dying sooner, can't stop someone from dying, but does it stop them from dying sooner but also does it prevent them from having to go to hospital more often. And as our studies get more and more complex, standard statistical methodology fails to be adequate for analyzing it. So one of the things that I looked at for my PhD is sort of recurrent event modeling. So, you know, in heart failure it's these repeat hospitalization. Can we analyze these repeat hospitalizations through time for individuals, yes there's methodology that exists for that, but in heart failure you've got this complication that the more hospitalizations you have, the more likely you are to die. So people dying within your study is really important and so it's can I analyze hospitalizations and deaths at the same time in some way and that's where standard methodology, that just doesn't exist, so you have to come up with a new way of analyzing it. And so when you come up with a new way of analyzing it… it's a new method and I said you have to do all the background in mathematics of how do you get the numbers our that you need but also then, you know, there's no code for you to be able to run it, how do we do all of that, and so there's a lot of statistics that's still be discovered and really is just in response to the world evolving and the world of clinical trial evolving.

BH: Is it using… a well established tool set and just using those tools in different ways and aiming them at different targets within… in the world or is it coming up with whole new pieces of mathematics? That's what I don't quite understand.

JR: Yeah you kinda use the same sort of fundamental tools, so when you're at university you learn topics such as statistical inference which is if you've got a

dataset, how do you pull out, you know, what the average is and things like that. How do you pull out what is the effective age on this outcome? Or gender on this outcome? And you learn those fundamentals and those fundamentals are constant throughout but the intricacies of the individual models is what changes and you then have to sort of apply these fundamentals to these new models that you developed to pull out the different numbers that you need.

BH: In areas like mathematics there are famous unsolved problems. The classic one that I always talk about is the Riemann Hypothesis or Fermat's Last Theorem and that… is there something in statistics? Is there a problem or a thing that statisticians wanna be able to do, that you're waiting for some brilliant mind to come up with the tool or the algorithm or the equation? Is there a deep burning problem in the back of every statisticians mind?

JR: I don't think there is, you know, I've never really thought about that. But I don't think there is. I think it is more that statistics evolves and it's little steps each time and it's little steps in response to the world changing. You know the world of Big Data and AI, you know as computing power increases that changes what we're able to do and how much data we're able to process and that then leads us in a direction of where we need to go with our future, you know, future research and I think it is these sort of small incremental changes rather than any big burning questions that are yet to be discovered.

[gentle string section music]

BH: Obviously we had this pandemic at the start of 2020 and all of a sudden every person and their dog was an expert on curves and infection rates and flattening curves and R numbers and things like that. As a statistician and a statistician who I know has a real interest in the public perception of statistics, do you think that all went really well? I mean obviously no one's glad coronavirus happened, but do you think this was like people were doing it well? It was being reported well? Or was it a big fat mess? Or how was it at the start for you,

statistically, watching the world suddenly become obsessed with medical statistics?

JR: Yeah it was interesting. I don't think it was a big fat mess but I don't think that everything was perfect. For example when we first saw the case numbers, you know, the daily case numbers that we are so used to seeing. Those plots to start off with didn't have the averages on them, so you would just see this noisy data all fluctuating which is normal for data of that type and I think, you know, it was interesting to see quite early on people trying to educate and say, you know, if you take three day or seven day rolling averages that gives you a better idea of what the curve really looks like and you kind of saw these things evolving. There's still somethings that I'd like to see maybe being done a little bit better, so for example when the… remember when they had the exponential growth curve where they said if cases were doubling every seven days by the middle of October we'd have fifty-thousand cases and they'd showed that curve. That wasn't presented with any kind of uncertainty or anything like that, you know, projections into the future they're not shown with uncertainty and confidence bars or anything like that so I think, you know, there's still somethings that we could do to better communicate with the general public but I think… I think it's been okay, I think at some point we saw too much information and I think we were showing information for the sake of it, so when we were in the first lockdown and we had the daily briefings… did we really need to see every single day how many people were traveling by car or by bus or by train? I'm not sure that we really did… I think one of the lessons that I hope has been learnt is, you know, only present information that's really useful and actually telling you something that is useful. Don't overwhelm people with it, but I have been encouraged by the fact that people have been engaging with statistics, you know? There's been a lot of couch statisticians, they may not always be doing it right, but at least they're engaging with it and it means that someone like me, I've got a great opportunity to talk to people about it and talk to people who may in the past been completely shut down by it.

BH: Pulling back to the bigger picture then about the media and statistics, because just before we started recording I watched your TEDx talk in New Castle which is excellent and I recommend anyone to go and watch it, and I will put a link to it in the notes. I really enjoyed it. I think it would be fair to say… there was some… good natured but well deserved media bashing in it where you like, you know, you point out classic mistakes, bad headlines, bad reporting. And not only is that entertaining, it's important to know about it. But it felt like the issue you didn't talk about in your fifteen minutes you had for your talk, was… who's to blame for it? Because like… it comes across that these are dim witted journalist who… or opportunistic journalist who are just latching on to a good statistic and a good number for a cheap headline and they're not telling the true story. But there was no talk whatsoever about the source of those statistics or who put them out and I know that… and often there are companies and statisticians and business who are putting these numbers to be consumed by the media. When it's being done badly, who do we blame?

JR: Yeah, and I'm not sure I even really know who I'm blaming. And I think that's why always sort of tee it up as I'm giving the public the tools they need to be able to ask the right questions of what they're seeing. Umm… I think that sometimes an editor will want a grabbing headlines so that they get, you know, they get the page views or they get the newspapers sold. I think sometimes press offices are a little bit to blame, you know, they want the newspapers to pick up their work and report about it and so they make the results seem as sensationalized as they can to try and get people to pick it up. You know, universities as well they come under so much pressure for their work to have impact so they themselves, you know, they want to have their work picked up because, you know, if you're thinking about if you're gonna get future research funding, well if the last thing that you did got covered by the BBC, that's amazing, you know, that's great impact and so there's a pressure on researchers to have their work published, there's a pressure then on press offices to make sure their work gets picked up and there's a pressure from, you know, within the journalistic world for their work to get page views and I think that it's maybe a

real deep rooted problem that we're maybe not ever gonna be able to solve and so that's why I do really like having the opportunity to try and educate people of the things that they're seeing because, you know there are, I mean, I think things have got better and I definitely get more calls from journalists now saying, we've had this press release can you just talk me through it. So I think there is a little bit of a change and I do genuinely really appreciate that. But I think there's probably gonna be someway to go and I think we're probably will get a hundred percent there, so I think… there is still a space for me to give these talks and hopefully educate people a little bit into asking the right questions.

BH: A message I took away from your talk and from things you say in general sometimes, is you're trying to say… you're trying to equip the readers and the consumers of media with the information that they know to be more cautious but that just seems such a huge demand on me with my cup of tea and my toast when I'm reading the Times in the morning, to have to be second guessing and thinking, oh is this the relative numbers to this and that like, I almost feel it's a bit unfair like to make the readers have to do this. Like there must be another solution. [chuckles]

JR: Yeah, and I… yeah… I mean I can appreciate that and you know we work a lot with journalists, so I do a lot of work with the Royal Statistical Society and we have a course for journalists and I think we are starting to see more the headline may still be the big relative risk, the, you know, the impressive sounding figure but you're starting to see the absolute risks now sneaking into the actual text and the same with uncertainty. You know, you might get just the one single figure point estimate in your headline but if you go on and read further you might see a confidence interval. So I think those sorts of things are starting sneak in. Not sure that they'll ever make the headlines but… hopefully they make the text a lot more than they used to.

BH: What do you think it takes to catalyze that change though and make the journalists more responsible and ring people like you up? Is it the occasional bit

of public shaming like you sometimes do? [chuckles]

JR: You know what I… [sighs] yeah, I mean maybe my public shaming makes people think a little bit more. But I think… well sometimes you know as statisticians we also do try and… award people who do well. So, you know, my work with the Royal Statistical Society, this is my last year of chairing the journalism award so we do actually award excellence in journalism and people are really proud when they get one of these awards and they see it as a really good thing, you know, this stamp of approval from the Royal Statistical Society that I do good statistical reporting. And so I think maybe a… a mix of giving people a slap on the wrists when they do it really badly but also making sure that we really highlight the people that do it well and use them as an example for the people and something to aspire to.

[gentle violin music]

BH: Okay, I wanna ask you about coronavirus, COVID, and vaccinations 'cause at the time that we're recording we've just come off the back of a few weeks of what has felt like a real glut of reporting about statistical trials and medical trials vaccinations, this is good, these are numbers, percentages and now we're starting to get some of these vaccinations approved and being rolled out into our communities. And like, I don't think I'm… stupid or mathematically illiterate but I have to admit I've been a lot more bamboozled during this reporting of vaccinations then I was when the reporting started about the coronavirus itself. And I kind of don't know, what I should be listening for or what I should be looking for, what I should be accepting, what I should be… can you help me? [laughs] What do we do?

JR: I can appreciate that and, you know, clinical trials are a lot more complicated than just seeing a daily count on a, you know, on a plot on your screen.

BH: Hmm.

JR: You know, there's also the intricacies of, you know, they've had different trial designs, and the designs have been called into question and things like that and it is really complicated and I do, you know, I'm trained in this so I understand it more but for anybody else I really do feel for anyone trying to… work their way through all of this because ultimately at the end of the day, everybody has to use this to decided whether or not they want to put this vaccine in their bodies, so it's a… you know it's a big decision and… you know, one that anybody shouldn't take lightly. I couldn't believe it, I gave a webinar yesterday and it was the 9th of November so just a month before was when we got the first announcement from Pfizer from their interim analysis and in that month we had, you know, interim analyses from Moderna, interim analyses from AstroZeneca Oxford, we had final analyses from the Pfizer BioNtech, final analyses from Moderna and we had the first vaccine being put in someone's arm. It's been an absolutely crazy crazy month.

BH: Big picture, you've looked at lots of these stats and these numbers that have been reported, are you impressed? Are you happy? Are you happy to put this in your arm, no questions asked?

JR: Yeah, I am.

BH: Yeah?

JR: I've been absolutely astounded by the results. The results have been amazing. If you look at all the study designs and all of that in a lot more detail what they were hoping they would achieved compared to what they did actually achieve is actually quite astounding. We've got three vaccines right now that not only work but seem to work really really well and so much better than we ever could've hoped for and I think that that's just absolutely amazing in such a short period of time. Yeah, I mean, I'm happy with all of the safety assessments that

have been done to date. You'll never gonna be able to say with any brand new treatment or vaccine that there's zero risk. I mean [sighs] there's not zero risk every time we take a Paracetamol, you know? There's nothing is ever zero risk, but I'm confident that every thing that should've been done has been done and everything that we could possibly know, we do, and I am confident as well that the monitoring that's going to carry on in the future is going to be very sound and, you know, the system will work as it should. And I'm more than happy to put this vaccine in my body, and you know, I have a… I've got three grandparents left who are over the age of eighty and will be in that first wave and I've told all of them to please go get this vaccine as soon as its offered.

BH: When you open one of these reports or documents about these trials, can you tell me what some of the like… like the column or the category or the number or the word you first look for are? Like what's like… what's the important thing that you turn straight to and you've gone, yes, or wow, that's impressive?

JR: So it's the… it's the vaccine effectiveness or sometimes it's called the vaccine efficacy.

BH: Hmm.

JR: So these are the… it tells you how well does this vaccine work, so for the Pfizer BioNtech, we saw a ninety-five percent vaccine effectiveness. What that means is if you had a hundred people who got coronavirus this vaccine would've prevented ninety-five percent of them. So if that same one hundred people had been vaccinated, only five of them would have got coronavirus and that's the number that I really look for to start off with. Now when all of these studies were being designed, they said that they wanted to be able to get a vaccine that had a vaccine effectiveness of greater than thirty percent.

BH: Oh.

JR: That was the number they were targeting. If they had a vaccine effectiveness of great than thirty percent then this would be a good result. And to have a vaccine effectiveness of ninety-five percent, that's huge! That's so much more than we ever could have hoped and it's such, you know, a big result, you know the other studies have also had really good vaccine effectiveness estimates.

BH: Thirty percent seems really low to me. That seems like… that almost seems like, is there much point… like do we use many vaccines that have only a thirty percent efficacy?

JR: So, [sighs], so it would have been… they wanted a true underlying efficacy of thirty percent. What that would have meant for the clinical trials, when you take into account, you know, the uncertainty and the confidence bars, they were actually an estimated vaccine effectiveness in the studies of fifty percent. That's what they were looking for. The flu vaccine that's got an effectiveness of between forty to sixty percent. There was one year a few years ago where it went down to about fifteen percent. So, 'cause you know they do slightly different flu vaccines every year because of the different strains and things like that, so yeah so thirty percent to me, I agree with you it does seem… quite low, I guess, there is also the question of though if we've got something that is gonna help, it's better than doing nothing at all. You know, especially when we're in this situation.

BH: I do agree but if I had a thirty percent vaccine in my arm, I think I'd still be locking myself in my room and be scared of getting the virus.

JR: Yeah, quite, exactly, yeah, you definitely feel a lot more confident about a ninety-five percent effectiveness than thirty percent. [chuckles]

BH: As someone who works in this field and you were in impressed by the numbers. How do you explain that, then? Is it just because they've just thrown so much resources at it? Did it just turn out this was an easier thing to make a

vaccine for than we thought, like, how can we explain that after all these years of diseases and things that we just can't crack or it takes ten years to make a vaccine that they were able just smash it out of the park so quickly?

JR: Yeah, I know, well [sighs] I mean I'm not a virologist. I don't know the ins and outs of vaccines but I know that, you know, the Pfizer BioNTech and the Moderna, that was using the genetic sequencing and I believe that that's the first time that this has ever been used. All of that work that's been going on in the background for, you know, tens of twenties years has now come to fruition and we're really seeing perhaps this is you know a new world of vaccines and it's a new way of doing things and we're just really lucky that actually this new way of doing things turns out to be really good. But yeah it [sighs] you can't statistically explain these big numbers. The numbers are what they are because of the vaccines being so good. Yeah it's just… it is astonishing, that you know we've had three from three and they've all been really impressive.

BH: You said when you open a report the thing you look to first is the efficacy and you were like ninety-five percent, you were like, oh that's awesome. What else do you look at though? And what do you look at on the negative side of the ledger? Is there like a side effects column or an uncertainty column? What's the sting in the tail?

JR: Yeah, so, uncertainty becomes less an issue when you've got such a big effect because it's so far away from that sort of thirty or fifty percent, you know, target, so when you've got such a big effect you don't worry as much as confidence intervals because they could still be quite wide and you'd still have a really good result. But I do look at that, you know, you try and look at what are the actual numbers behind, you know, how many did get it in each group? What's been interesting to look at is how many people got severe COVID in each group. So they've not just been looking at cases of COVID but they've looking at cases of severe COVID. Yeah I look at the safety events. So for example in the AstroZeneca Oxford study there were, you know, two… [pauses] they're called

grade three side effects. So a grade three side effect is what we would class as a severe side effect but it's probably severe definition wise, rather than it actually being a severe side effect. So the two grade three side effects that happened in more than two percent of people were fatigue and headache. So in real terms they're quite mild side effects but, in sort of clinical trial world they're classes as a grade three severe side effect. So I start looking at, you know, what were the safety profiles of them. So, you know, you don't wanna have an amazing vaccine that does all these wonderful things if it also causes a lot of harm. You've got to weigh up the benefits and the risks associated with them. It's not just, you know, one story to tell there. You've gotta look at it, you know, in its entirety. So I start looking at all of those sorts of things. It's been interesting looking at the different ways that they defined COVID cases and trying to then get an idea of, ooh what else? What might we be able to get from this study? So for example the Pfizer BioNtech, their definition of a case was twenty-eight days after the first dose and the Moderna study, their definition of a case was fourteen days after the second dose. So the Pfizer BioNtech because it looked at people after the first dose, it meant you'd be able to have a look at that data in more detail and see if just one dose provided some protection and then two doses provided full protection. You wouldn't necessarily be able to get that information from the Moderna study because they only classed classes if they happened after the second dose. So I start looking at all these little intricacies and think, ooh what could we look at when the full data comes out, that you know, and what's gonna be really interesting to try and also explore?

BH: There's obviously vast amounts of money involved here and so much at stake for these companies, and that's not something you know you'd necessarily have if it was just like, you know something being done for academic purposes or it was your PhD or something. What sort of safety mechanisms and checks are in place for the public to feel confident that all the data we're seeing and the reports and the studies being done are absolutely… legit and aren't being corrupted by those stakes.

JR: So everything would have to go through an independent regulator. Whether that's the Food and Drug Administration, so the FDA out in the US, or for example we heard from the MHRA earlier on last week, so the Medicines and Healthcare Products Regulator Agency in the UK or the European Medicines Agency, the EMA. So we have all these independent regulators and regulators get involved in every single stage of a clinical trial. So, there's lots of different phases of clinical trials, so phase one is your first in human studies, so it's the first time that a human gets it. And you're really just looking at the way the body reacts to it. Then your phase two is your sort of dose finding study where you try and figure out what's the optimal does that you can give someone whilst taking into considering the toxicity issues and then you have your big phase three study. And regulators are involved in all of those phases and they're involved in all stages of those phases. So when you're designing it, that has to… you know signed off by the regulators and say, yep, that's a good trial. You've designed that properly, we're happy with your outcomes, your sample size is big enough, you can go ahead and you can do it. Then when trials are running there's independent monitoring boards. So I sit on a few, so we would be independent from all of the pharmaceutical companies and we monitor the safety data as it comes in. So we're making sure that people and the trials are staying safe. We might do, interim analyses so we might take little looks at the data whilst the study's goin' and that's all done independently and just yeah to make sure people stay safe and everything's working as it should. And then at the end the full results all have to be approved by a regulators and they're the one that gets the final say as to whether or not they're going to license it. Because, you know, you can publish the results but it doesn't mean that necessarily it's gonna get licensed. All of that information has to be looked by someone who's independent.

BH: Do these independent regulators have like boots on the ground and referees in the room or are they just looking at the spreadsheets that are being supplied to them and saying, yeah those numbers check out. Like, is there someone in the room, like when they're taking the results or you're doing

random spot checks and things like that? Or are you just taking their word for it when they supply all the numbers and say, this is who we gave it to, this is what happened, this is what we did?

JR: They don't just submit the final results. You have to submit all the data, you have to submit all of your code. These big pharmaceutical companies they may analyze the data but they have to have somebody independent also analyze the data so my company, that's a lot of what we do. We are independent and we reanalyze the data. Academics get used an awful lot for that as well. So you would have to make whether or not they all matched up and they were all verified and yeah all of that gets sent to the regulators. They don't just get the final sort of spreadsheet of you know, effectiveness numbers and confidence intervals. They have to see absolutely everything. You know, we save the minutes from every single meeting that's happened and the regulators would review all of that, so they really do go through all with a fine tooth comb. And that's why there's a bit of a delay, between the results coming out and getting approval.

BH: I mean I don't wanna be like flippant about it but I guess what I'm saying is like, you know, if you put a vaccine in someone's arm and their turned green and their arms fell off, you might say, oh let's not put that one in the results because that's gonna look really bad. Are there every people in the room saying, like, just making sure like the recording of the data is happening correctly?

JR: Yeah so, you know, a lot of the time when these studies are happening they're all done blind, so, because people don't know whether or not people have got the treatment or not, that kind of takes away that motivation to fudge the numbers and things like that so people are well trained in what they should be doing and things, so and I think ultimately people, yeah, they want vaccines that works but also nobody wants to have the vaccine that really causes harm to someone, you know, that's negative press that nobody wants. So, I think, people sometimes think, oh it's everybody's best interest to just get a vaccine out there really quickly and that's not the case. It's everyone's interest to get a vaccine out

there as quickly as possible that is safe. Because, yeah, nobody wants that negative press. Could you imagine what would happen those share prices if there was some major side effect, you know, we don't just want to put a vaccine out, we wanna put a safe vaccine out.

BH: There is a subset of… the world who are saying, the vaccine, don't take the vaccine, the vaccines are dangerous. I'm not saying those people are well informed, but there is that kind of chatter going on for better or worse. What are those people latching on to? Do you know? Have you got a sense of what they've seen or what they've read or what number they've possibly misinterpreted that has led to this sort of section of the community not in favor of the vaccine?

JR: I think these people who are saying these things are a little suspicious of the time scale. And they're a bit suspicious of the fact that this seems to have happened so quickly and so corners must've been cut. And that absolutely isn't the case here. When we run trials normally all these different phases, so I was talking about the phase one, two, three, the design of them, the analysis of them, it tends to happen in a sequential manner. And the reason that happens is, you don't wanna start designing your phase two study if it turns out that your phase one failed. You know, it wouldn't be in anybody's best interest, it'd be a sort of a waste of time or money, but because, you know, with coronavirus, every single day is however many deaths, we've really want to do everything that we can to speed up that process and you know, everybody's just been able to throw as much money and as many resources at these things as possible that people have been designing their phase two study whilst their phase one study is already happening. And those sorts of efficiencies have all filtered through.

BH: So there's nothing wrong with doing that, it's just normally an expensive thing to do, but in this case, okay, hang the expense.

JR: Exactly, and well… it's an expensive thing to do if it turns out that it doesn't work 'cause you've wasted a lot of time. You know, they were

manufacturing the vaccine before they even knew whether or not it worked. Usually that's a big risk. That's a huge waste of money if it turns out it doesn't work. But because it's, you know, coronavirus, sod the money, let's just try and get this as quickly as possible. You know I… I use the analogy of building a house. When you build a house you could do everything sequentially, or there's somethings that can be done at the same time without damaging the integrity of the structure. And that's the same here, we can do some of the things at the same time without you know damaging the final integrity of the study at the end of it. And that's just what's been happening. We've been throwin' all this money, all these resources to try and get things done as quickly as possible but absolutely no corners have been cut. Every single step that needs to be taken in order to license a new drug, a new vaccine, any kind of new treatment. Every single step has been taken the way it should be taken. I think some people are worried about the fact that, you know, we don't have enough safety data, we haven't been watching people long enough… but we've been watching people as long as we would've done even if we'd have done these things sequentially. You know, the total amount of time that people have spent in the studies is exactly the same, just because it's not been as long, you know, calendar length, everybody's been in the study for the amount of time that they would be when it would normally get licensed and one of the things that I'd also like to stress is, once a vaccine is licensed that's not the end of the story. We don't just then, you know, let it out into the world and that's it over and done with. We have phase four studies which are surveillance studies and confirmation studies where they wanna check, okay that effectiveness or efficacy that we did see, do we still see it? And, are we continuing to see side effects? You know, if you've got a side effect that's a one in a million person event, you're never gonna see that in any clinical trial and you're gonna need to, you know, carry on monitoring people afterwards before you see it. You know, there's never gonna be zero risk in… any vaccine or any new drug that gets brought onto the market but everything is being done the way it should be done and everything will continue to be done post, you know, post approval to make sure that people are staying as safe as possible and as I said it's not in anyone's best interests to put an unsafe vaccine out.

[gentle chimes]

BH: Finally, as the professor who's like, you know, known for having an interest in how well reported and conveyed information is, how do you feel this's been? This second half of the year? The vaccination stage compared to the outbreak stage, in terms of that relationship between statistical people like yourself and laypeople out there trying to understand what's going on? It feels like it hasn't been quite as… [sighs] good. [chuckles]

JR: No. And I think I would agree with you there. One of the things that's really frustrated me is [sighs] we've had this sort of science by press release where we get this press release and it's got very limited information in it. And… people have been fillin' in the gaps with hypotheses of what could happen, so for the Oxford AstroZeneca study, you know we had this… there was a low dose given by accident and then we had this low dose, standard dose group compared to a standard dose standard dose group. And, you know, people were asking questions of the design of the study before we'd even seen the design of the study and I think sometimes trying to fill gaps with speculation can be quite damaging or quite harmful because we do have skeptics out there. We do have people who are uncertain about whether or not to take the vaccine and filling the empty spaces with this potentially unhelpful noise, I don't think has really been that fantastic. You know, I mean I've done a lot of interviews. My phone hasn't stopped ringing and I'm just… I feel like… now I've got a real role to play in this and I've got a part to play in trying to communicate to people what is the clinical trial process. Can they be certain that what they're putting in them has gone through all the proper procedures and, you know, can they have confidence in what they're putting inside their bodies and I… yeah, I think I've just gotta keep pounding the pavements and really just trying [laughs] to help do as many interviews as I can.

BH: Well, you've done more than your bit today. What did you call them?

Sofa statisticians or armchair statisticians?

JR: Yeah. [laughs]

BH: [laughs] I like that term. I can't remember what it was, but you said it earlier. I'm gonna use that in future.

JR: [laughs]

BH: One last last question then, when all the dust settles and hopefully life returns to normal, what's all this gonna mean for your field? Medical statisticians and that? It feels like this could be a real… shot in the arm. [laughs] For your industry like it feels like it's really like a big deal now. Everyone's really interested in it.

JR: Yeah it is and I think statistics suffered a little bit for a while because, you know, artificial intelligence and data science and machine learning, they were all cool and classical statistics was a bit, you know, in the dark ages and it wasn't very cool but you know, we've had a brand new disease here where there's been no data and we've had to rely on classical statistics, you know, you can't do big data analysis when you don't have big data and right at the very beginning of the pandemic we didn't have hardly any data, and I think this really been an opportunity for the statistician to show their worth and really put us right under the spotlight and I do hope that a silver lining of all of this will be that people will have an appreciation for statistics and statisticians and really value the work that we do and… [music fades in] yeah maybe we'll have more budding statisticians join the field which would be amazing, it would be a really good thing to come out of a really horrible and tough year.

[music fades up and continues]

BH: That's all for today. I've put some links to Professor Rogers' work, her

TEDx talk, and some writing she's done about coronavirus in the notes for this episode, so do go and have a look. [music continues] Thanks for listening today and please feel free to go back and listen to some earlier episodes if you're new to the show or you haven't hear them. Maybe even subscribe to the series if you're so inclined. I'm Brady Haran and you've been listening to the Numberphile podcast.

[music fades up and cuts out]