DANNY LENNON: Welcome to the podcast.

KATHRYN BRADBURY: Thank you.

DANNY LENNON: Maybe just to set some context for people listening, how would you typically introduce the research interests that you have and where most of your research focus currently lies?

KATHRYN BRADBURY: Well, I started off with a background really in nutritional science, did a PhD in human nutrition, and I had variants and expertise in biomarkers of nutritional status and dietary assessment, and then I went to work at the University of Oxford for my postdoc in the cancer epidemiology unit there. So there I was really looking at the associations between diet and mainly cancer, but also cardiovascular disease, so really building on those skills and nutritional epidemiology. But I guess, now I'm back in New Zealand at the University of Auckland, and I have pretty broad interests, I'm interested in a lot of things. Generally, I'm interested in patterns of how people eat; obviously, the relationship between foods and disease; but also I have an interest in kind of meat and vegetarians and plant based eating, an interest in bowel cancer and digestive cancer. So yeah, a lot of things I'm interested in.

DANNY LENNON: One interesting way to navigate through some of this is to mention one of the papers you published from earlier this year. So for people listening in the future, that's a paper published in February 2020. This was on diet and colorectal cancer in UK Biobank, and published in the International Journal of Epidemiology, and I'll link to that in the show notes for people who want to go and get the full text to that. Before getting to some of the findings, just for maybe people who are just hearing about the UK Biobank maybe for the first time, I was wondering could we just set some context for that because how incredibly important and informative something like this is, how would you introduce people to UK Biobank?

KATHRYN BRADBURY: Yeah, it's a very unique cohort. It's fairly recent in terms of cohorts as well. A lot of these well-known cohorts like EPIC or the Nurses' Health Study were started quite a long time ago now. UK Biobank recruited around half a million people in the UK and the recruitment took place between 2006 and 2010, so that's fairly recent, which is interesting from nutrition point of view because it's recent, so it's what people are kind of eating now; whereas sometimes without results from older cohorts there's some criticism that, what we don't really – are those dietary intakes from a long time ago still really relevant. So that's one good thing about UK Biobank is it's quite recent, it's obviously very large; and everyone who participated in the study, so there was sort of middle aged people from the UK, 40 to 69 I think, and they went to an assessment center, so they actually went in and they did some questionnaires on a touchscreen, they had measurements taken, blood pressure but also height and weight, waist circumference, and they also all gave a blood sample which is really unique as well to have blood samples on the full half million. It's also a very unique cohort from the point of view that it was set out to be an open access kind of cohort. So any bona fide researcher who wants to do research that's for

the public good can access the data which has not really traditionally been the case with other cohorts as well, they're sort of set up by someone and that team around that person has analyzed the data from them.

DANNY LENNON: So for this particular paper, and looking at this diet-disease relationship between diet and colorectal cancer, maybe what are some of the important things to know about the particular methodology that might be of note for people?

KATHRYN BRADBURY: Yeah, so when people came into the assessment center at recruitment, they did a touchscreen questionnaire as part of – they sort of moved around these stations and one of them was a touchscreen questionnaire. And within that touchscreen questionnaire, so they're sitting at a computer answering questions, within that was a short, basically a short food frequency questionnaire. So asking to each participant how often, how frequently they consume things like meat, fish, fruit, vegetables. So it wasn't completely comprehensive, it was fairly short, but asked about key food groups. And then also the questionnaire asked about other things like, you know, a lot of other factors actually, alcohol, I mean, I think there was more questions just on alcohol than there were on other foods, so alcohol is really well characterized; smoking habits, physical activity, a lot of other things, so we have an idea about the lifestyle of each participant as well. And then the other interesting thing is everyone who left an email address at recruitment was emailed later on, a few years after recruitment, with an online dietary questionnaire, a different dietary questionnaire and asked would they fill that in; and they were emailed four times over the space of a year, so roughly once every season. And so that questionnaire just asked them to – it's a bit, I mean, sometimes we refer to it as a 24-hour, an online 24-hour recall, but I think the purists wouldn't really call it a 24-hour recall because you're not really free, if you're doing the questionnaire, you're not really free to recall

every food and drink that you've ever – that you've eaten in the last 24 hours, so it's not like an interviewer 24-hour recall. But what it is, is a questionnaire which starts by food groups and it might say, did you eat fruit yesterday; and if you say yes, then a whole bunch of fruit items drop down and then you select from the list of however many fruit items there are, you ate one apple, half a banana, that sort of thing. And then you move on to the next food group. So there's over 200 food and drink, and they're the most common food and drink items consumed in the UK. So it asks about, you know, it aims to capture all the food and drink that someone's consumed in their last 24 hours in an online format, and it's a very simple questionnaire to do which is why it's very good to do on a large, large cohort. So quite a lot of people did that, did at least one of those online questionnaires. So therefore we have a sort of remeasurement, we were able to remeasure dietary intakes on a large sub sample of that UK Biobank cohort.

DANNY LENNON: Comparing that to maybe a study where there is no real measurement of intake, what are some of those inherent advantages to doing that?

KATHRYN BRADBURY: There's a couple of things, one thing is that your true intake might change over time, so it is good to remeasure. And the other thing is that really having, you know, using remeasured intakes really does reduce your measurement error, which is really important because generally in nutritional epidemiology, if you're measuring diet, there is some measurement error there. I mean, it's not unique to diet, it's error if you're measuring – asking questions about how much physical activity someone does or even if you're doing a blood sample and measuring something in the blood there's laboratory error. But there is error in dietary assessment when we're trying to find out what people are eating. And so being able to do a remeasurement actually helps to reduce that error. And generally, measurement error kind

of adds noise and tends to weaken the association, so if you're able to reduce it, you will often see a stronger association, and that's what we tended to see in our paper and that's one of the reasons why we think it was stronger is because we did have – we were able to remeasure dietary intakes.

DANNY LENNON: With a prospective study like this, we have a certain amount of follow-up that we're having with those participants, and then we're tracking colorectal cancer. Can you maybe just again clarify for people what we're talking about with follow-up and then disease occurrence when we're trying to measure diet-disease relationships?

KATHRYN BRADBURY: Yeah. So I mean, a lot of the cohorts work in the same way. So after recruitment for the participant, really they just carry on living their normal life except if they get invitations to do other questionnaires as part of the study, but they will have consented at the start of the study to be – to have their data linked to health records. So basically, the participant just goes about their normal life, but we are following them up via linkage to health records. So in the UK, there's very good cancer registries and there are good cancer registries in lots of countries actually. So what we do is because the participants have given us permission, we can link their data to the cancer registries, so that we can figure out who out of our cohort has been diagnosed with cancer. So we follow them up and we might get the cancer data. At a certain point, we get all the cancer data, and we know, okay, up until that point, we know in the cohort who has been diagnosed with cancer and who hasn't. So it's via linkage to their health records which the participants have given consent to do, and we have ethical approval to do that.

DANNY LENNON: What, from an overview level, are some of the most important things that you think came from this particular study?

KATHRYN BRADBURY: Well, one thing that we wanted to do is quite often you see with papers from cohorts and nutritional epidemiology that they might look at one factor in relation to one disease, and we really wanted to just try and look at really the whole – a lot of different dietary factors, really all that we could look at in one paper in relation to colorectal cancer. And I can kind of see why other people don't do that because it does make it difficult to write about in one paper, it's quite a lot. But yeah, so we looked at a lot of things and I think that is good because we did it all in the same way, and it was just all in one paper. So it's nice from that point of view. We found that people who said at recruitment that they eat red and processed meat quite often, they had a higher risk of developing colorectal cancer. Also, the same for alcohol, so those who drank more alcohol were more likely to get colorectal cancer as well.

DANNY LENNON: With that particular finding, I don't think it's that surprising for people who have looked in this area that there is this association with increased intakes of red and processed meat and colorectal cancer. I think that's kind of relatively consistent finding.

KATHRYN BRADBURY: Yeah.

DANNY LENNON: However, one of the things that was interesting from your paper is, and I'll just check the numbers that I have, so I think the comparison of 76 grams per day of meat consumption versus 21 grams per day had a 20% higher risk of cancer. And what was interesting about that is that that higher number of 76 grams per day still actually fits in with some of the government guidelines.

KATHRYN BRADBURY: Yeah. Well, that's right, I mean, the UK recommendation, I don't know – I did look up and it is still worded in quite a strange way. It says if you consume 90 grams of red and processed meat, you should cut down to 70 grams. So if you consume more than 90 grams, cut down to 70 grams, so it's a bit of a strange

recommendation, there's not really one number. But yes, what we found is that those who ate the most amount of red and processed meat at baseline, when we remeasured them, they were eating – the people in that group who did an online survey a few years after recruitment, they were eating on average 76 grams of red and processed meat a day, and they did have a 20% higher risk of developing colorectal cancer compared to those who are in the lowest group who reported that that remeasurement on average consuming just 21 grams of red and processed meat a day.

DANNY LENNON: When we look at the whole body of evidence across different types of populations, if we kind of stick to, I suppose, westernized populations that may be relatively similar to the UK but maybe slightly different, so US cohorts or Australia, New Zealand, and so on, do we see differences in those level of intakes or even the disease occurrence because sometimes there tends to be different rates we see depending on which population even though we might presume sometimes that the diet patterns are very similar?

KATHRYN BRADBURY: Well, I think the associations are really pretty consistent just in terms of direction, that's for sure. So maybe not in sync every single study, but certainly when you put them all together you definitely see that both real and processed meat, or if you put them together as read and processed meat, that there is a higher risk of colorectal cancer for those who eat more red and processed meat. The magnitude of our association was stronger really than probably what has been seen generally, although I'm not sure that that's anything to do with being in the UK per se or anything, I think it's more to do with the fact that we were able to remeasure intakes where some of the studies haven't been able to do that. And that really does, because it – yeah, it reduces the measurement error, and so it does tend to give you a stronger association.

DANNY LENNON: One of the talking points that often comes up in this area is looking at this summated effect of unprocessed red meat and processed meat versus looking at those separately, and I think the processed meat issue seems to be incredibly clear, like, it seems to be cut and dry that we know that this is going to increase risk where some of more of that gray area where there's more debate is to what magnitude we see with unprocessed red meat. What type of findings do we see when those are analyzed separately, and then also what challenges from a research perspective are there from actually being able to accurately delineate between those?

KATHRYN BRADBURY: I think that's a really interesting question. I think with processed meat, another thing that comes into it is just when you look at the composition nutritionally of processed meat. There's really nothing that is really, it's got going for it. I mean, it's kind of high in saturated fat. No one's really defending processed meat as a great thing to eat all the time from a nutritional point of view at least. But red meat is different because it is high in iron, other minerals and things. So I think people from that point of view want to be a bit sure that if there is a risk with red meat before we go recommending people don't limit it or reduce it. So I think that there's that sort of context to the whole argument as well. People, overall, have found stronger associations for processed meat as well, and the red meat association has been a bit more borderline. So there is a bit more uncertainty, although, if you look at mechanistic work and looking at what are the potential biological mechanisms that might underpin this association, the mechanisms for red meat are quite, I mean, it's not completely clear, and I wouldn't say we know all the answers and we've got it completely sorted, but for red meat there are kind of stronger mechanisms. So I think it's good just to not just look at one strand of evidence, but everything, you know, the biological mechanisms, the lab based studies as well as the nutritional epidemiology, and look

at the whole picture as well. I mean, there has to be a biological mechanism. But I wouldn't say we've worked it out completely. There are definite things that we think might be important in terms of red meat and processed meat like the heme iron actually is probably leading to the formation of N-nitroso compounds which are probably carcinogenic; and there's some other things as well about perhaps cooking meat at high temperatures or open flames leading to again potentially carcinogenic compounds. It is important to do the work on the mechanisms, but at some point you've got to make a recommendation or we do make recommendations on the evidence that we do have. And although it is always good to have further research and really figuring out finer points and whether things are important or not, at some point you think, well, there are potential biological mechanisms which seemed plausible, there's a very consistent body of evidence from epidemiological studies.

DANNY LENNON: Yeah, we still have to make decisions about this every day.

KATHRYN BRADBURY: Yeah.

DANNY LENNON: Hence why we got to use what data is there. One thing that you said earlier that was particularly important was the idea that you, in this study, didn't want to focus just on one very small aspect of diet, maybe in a too reductionist of a manner and look at many of these different factors. So for example, you looked at fiber intakes within the diet, and I'm wondering, depending on what the fiber intake is for someone, can that act as a potentially moderating factor for some of these other nutrients or foods that may have an impact on risk?

KATHRYN BRADBURY: Yeah, and I think fiber is nice in that it's the other way around, it's something that you can probably do that's probably protective. And I think we found that fiber from whole grains, we didn't measure whole grains, but those kinds of

foods and what other studies have found as well is that's the whole grain or it's a cereal fiber as well that people who eat more of that, do have a lower risk of developing colorectal cancer as well. And again, there's pretty good biological mechanisms that probably explain that in terms of reducing fiber, reducing transit time through the gut, diluting potential carcinogens and yet increasing stool weight. So it all sort of makes sense that fiber would potentially protect. So again, yeah, I mean, it's not just one thing you eat, but probably a combination of things. I mean, we don't just eat one food. And although, in nutritional epidemiology, quite often – I mean, there are people who are really looking at dietary patterns, but although we are often in nutritional epidemiology trying to look at one food at a time but it is true that we do eat a whole diet, and people who are eating lower meat and lots of fiber obviously have a lower risk. But if you're doing one of those things and not the other, you might be sort of in the middle somewhere, yeah.

DANNY LENNON: What sort of impact do we see for other animal foods whether that's fish or dairy products or so on, what type of associations are we seeing?

KATHRYN BRADBURY: Yeah, fish is kind of interesting, it's not really consistent. I think in the WCRF, the World Cancer Research Fund, I think they find a small, you know, a lower risk with fish. But if you remove one study, it's not there. So it's not really, I wouldn't say it's really convincing that fish might protect against colorectal cancer. And dairy products, I mean, we didn't find this but our sort of dairy variable was very crude unfortunately because in that short food frequency questionnaire touchscreen, it didn't really ask about milk. We tried to kind of make a variable based on how many bowls of breakfast cereal that they ate and tea and coffee, but we had to make a lot of assumptions, and we didn't see anything with milk. But generally, and I think there's probably just quite a lot of error in there, so I

wouldn't take our word on milk as the final – put too much into that. But other studies that have looked at milk and when you synthesize them and look at them all together and look at that totality of evidence, they do seem to show that milk is actually – so higher intakes of milk, people who drink a lot of milk have a lower risk of colorectal cancer, and I find that really interesting as well. And that does seem to be pretty consistent.

DANNY LENNON: Is there any clear suggestions why that is the case or is there a frontrunner in terms of the mechanism as to why milk or dairy can have that benefit?

KATHRYN BRADBURY: I think there's a couple of sort of mechanisms again, but I don't know that we've really – it's interesting because it also can be seen with calcium, so it's a question of whether it's the calcium or if it's something in the milk, so there are still questions about that. And then also people have looked at other dairy products and yeah, I mean, I think it's strongest for milk. But no, I don't know that it's that clear what exactly there is, although there's differently proposed mechanisms.

DANNY LENNON: You mentioned one of the other components of diet, namely alcohol that was looked at – what were some of those findings and what we can conclude from at least this study?

KATHRYN BRADBURY: Yeah. So we found that people who drank more alcohol had a higher risk of bowel cancer. And again that's pretty consistently shown as well.

DANNY LENNON: Is that a dose response kind of relationship or is there a certain threshold of alcohol that seems to be problematic?

KATHRYN BRADBURY: It seems to be a kind of dose response, yeah. So for every 10 grams of alcohol, so that's sort of ethanol, not 10 grams of beer or anything, 10 grams per day, there was an 8% higher risk. So that's about 10 grams of alcohol a day is about a standard drink.

DANNY LENNON: Yeah, that would be roughly equivalent to a unit or standard drink depending on which country we are talking about...

KATHRYN BRADBURY: Yeah, it's a bit different depending on the countries that you count, but yeah.

DANNY LENNON: The UK, maybe is around eight maybe for a unit.

KATHRYN BRADBURY: Yeah, I think it is, yeah.

DANNY LENNON: But then we tend to go a bit higher in Ireland for obvious reasons. With colorectal cancer specifically, if we just take a step back from diet a moment, who seems to be at highest risk?

KATHRYN BRADBURY: There's a lot of variation in colorectal cancer incidence around the world actually. So different populations generally have different rates. New Zealand, where I am from and where I am now, has a very high rate of colorectal cancer actually, one of the highest in the world. And New Zealand and Australia, some parts of Eastern Europe as well, and the US, UK generally have fairly high rates; whereas other populations have lower rates, in Asia they generally have much lower rates of colorectal cancer. So there is quite wide variation across different countries and populations. Men do tend to have higher rates than women. And also there's other things, so that's interesting, I think for our paper we adjusted for all of that, but we actually use waist circumference as an adjustment because in our main analysis, because there's some thought that it's probably abdominal obesity, particularly, that's important, yeah.

DANNY LENNON: What are the next number of questions you think that still need to be elucidated, what are kind of research questions that groups – this could be outside of your own group – that may be a focus over the coming years that would be good to get answers to?

KATHRYN BRADBURY: Well, that's a good question. Well, I think a good thing to do generally, and I think more and more this is happening, is to be able to combine the results of several studies. And people do this in a metanalysis, but the best way to really do it is if you actually get the investigators of the different cohorts to agree to pull their studies together and either get someone to centrally analyze all the studies or they agree on an analysis plan and do it separately but in exactly the same way. And I think that's really important, and it's best if you can get everyone coordinated on that because it means you're all adjusting for the same things, you're doing it in exactly the same way, so it makes it very compatible. And I think that's good as well because some, there are some cohorts out there that haven't reported on this that could, you know, they have the data, and so it would be good to be able to just try to, yeah, try to collate all the data in the world that is available that could answer these questions on diet. And then, yeah, I guess, that would be interesting for something like fish as well where I don't know that we're completely clear yet what is happening with fish and is there a potentially, is it, you know, if you eat more fish, would that potentially lead to a lower risk of colorectal cancer or not. So it might help answer some of these questions if we have really all the available data collated together. So I think that, yeah – and that is starting to happen for certain things. I think cancer is kind of hard because there's not intermediate things that you can measure really. I think with cardiovascular disease, we have blood pressure and we have LDL cholesterol, things that you can measure that are sort of established risk factors for cardiovascular disease. For cancer, we don't really have that luxury, there's nothing we can really measure that says, oh yeah, that means in the blood, if we measure that, that means you're at high risk of cancer. So we are kind of reliant on these long term cohort studies in that way. RCTs are an option but they're pretty difficult really to do a largescale randomized trial on diet and follow up for

cancer. I mean, it's being done at the Women's Health Initiative, but it's very difficult.

DANNY LENNON: Just maybe to summarize some of the components that we've discussed so far, Kathryn, on this particular topic for maybe people who are practitioners, what would you say now is the kind of safest evidence based conclusions that we can come to around some of those dietary factors and how they relate to colorectal cancer risk, are they those that have a strong negative effect, some that seem to be beneficial, and then if we wish we can discuss broader dietary patterns, but what are some of the main things we have the strongest evidence for?

KATHRYN BRADBURY: I mean, I think what we found was pretty consistent with what other people have found. I think the strength of our association might be stronger, but generally, alcohol has been consistently showing that people who drink more alcohol do have a higher risk. So I guess, alcohol is important. In terms of red and processed meat, I mean, as we said so, I think the world cancer – is it the World Cancer Research Fund they say that, try not to, you know, very little, if any, processed meat, and try and cut down to three servings of red meat a week. So I think that's a reasonable kind of recommendation. And I think if everyone in the population, you know, the actual risk we're talking about here is kind of small in a way, like, it's much smaller than if you were looking at something to do with smoking cigarette, smoking and lung cancer – I mean, that's a huge risk. So we're not really in that league with processed meat or red meat and colorectal cancer. But if everyone in the population – if red and processed meat really does cause colorectal cancer and everyone in the population cuts down a bit on red and processed meat, then you should see an effect in the population numbers, so you would see a reduction, and then fiber again, something on – and I'd say milk as well, I would include that, not particularly strong in our study, but I think

it is pretty consistent that milk and fiber, on the other hand, higher intakes seemed to be protective.

DANNY LENNON: From your own perspective, going forward over the next few years, what are some of the areas you're interested with your research that can be completely separate from what we've discussed today, what are – or maybe even what you're most excited about in nutritional science more generally?

KATHRYN BRADBURY: Yeah. Well, it is going to be different, I mean, I'm still interested. I think I'll always be interested in nutrition and cancer, it is interesting, but I'm back in New Zealand now and I'm kind of in a different, you know, obviously working with different people, although I still have my connections with, and my colleagues who I was working with. But New Zealand's, you know, I'm really interested in it New Zealand data. We don't have big cohort studies with lots of dietary data in New Zealand. And unfortunately, we don't have a good rolling program of nutrition surveys either. Our last one for adults was 2008. So we have a real lack of data on what New Zealanders are actually eating. So I'm kind of interested in describing what New Zealand is really eating, so very kind of basic descriptive epidemiology, but we have data on purchases and we also have very good data on processed foods that are sold in supermarkets in New Zealand. So just sort of describing what our food supply is in New Zealand, I'm kind of interested in that. And the other thing I'm interested in is also the sustainability aspect whether, because I'm interested in meat from a health point of view, but also environmentally it's – and I'd say from an environmental point of view, it's actually just really clear that red meat has a very big environmental impact. So I mean that's kind of just very clear. So from that point of view as well, and I think it's good to cut down, and it is interesting, you know, hardly any of the dietary recommendations around the world really talk about sustainability,

maybe a bit more now, but traditionally they've just not really mentioned it or discussed it, it's been a bit neglected. So yeah, I'm also interested in sort of trying to figure out the sustainability of our food purchases in New Zealand as well.

DANNY LENNON: Yeah, I was recently on the podcast talking to Rebecca Leech who's over at Deakin University, and she's been doing work on eating patterns within Australian populations, but just noting how there's actually very little of the evidence that's done in a way that we'd ideally like to see that there's a lot of room to do really good epidemiological work and to have really tighter methodology of capturing some of these dietary patterns in specific populations where, because diet choices are always going to be specific to that region or the context which people eat.

KATHRYN BRADBURY: I was looking at bowel cancer, you know, colorectal cancer, and I was particularly interested in that because it's really high. New Zealand has a really high rate of bowel cancer, and I wasn't able to really look at that in New Zealand because we don't have cohorts in New Zealand, you know, really large cohorts that people have the dietary data from. So it was a way to kind of look at something that's important for New Zealand.

DANNY LENNON: For people who are interested in learning more about your work, where they can find you on the internet, those types of things, where's the best places for them to go?

KATHRYN BRADBURY: Well, I'm at the University of Auckland now, so I have a little page there. I am on Twitter, but I'm not – I'm sort of more of a lurker on Twitter, I kind of watch but I don't really get into big diet debates on there.

DANNY LENNON: That's a very good decision I must say.

KATHRYN BRADBURY: Yeah, I think, I kind of stand back from that, I can't really cope with it.

DANNY LENNON: Yeah, there is a very strong correlation between people who are most prolific and actually doing proper nutrition work and little Twitter use. So I think that's a very good decision, Twitter's not a good place to hang out.

KATHRYN BRADBURY: Yeah, I mean, I think on my university page, you'll have – it will have links to my papers as well.

DANNY LENNON: So with that, we come to the final question I always in the podcast on. This can be completely outside of what we've discussed so far today. If you could advise people to do one thing each day that would have a positive impact on any area of their life, what might that one thing be?

KATHRYN BRADBURY: It's funny, as a nutrition, you know, as someone who studies nutrition epidemiology, you do really realize that smoking is really important as a single risk factor. So I think that my advice would be if you smoke to really concentrate all your efforts on giving up smoking, that would bring about the biggest benefit to your health I think.

DANNY LENNON: Kathryn, let me say, thank you so much for taking the time to have this conversation, I've really enjoyed it; and also more so for the work that you've done and continue to do, it's been very informative and helpful for me, so thank you for that.