DANNY LENNON: As we mentioned, we're talking about fish consumption, and particularly points that you may hear at a variety of different places about how it may not be as helpful a food source as sometimes it is claimed or, in other cases, some people outright saying you should not consume fish or certainly not even rely on it for a source of omega-3, and these are all things that we'll get to in a moment. But as a way to perhaps tee this up, I want to play a short clip that was actually sent in by one of our listeners to me on Instagram a while back, of suggesting that some of these claims may be worthy of induction into the quack asylum. So I'm going to play that clip, I think it does a good job of highlighting a couple of claims that we're going to work through, and there's four that we'll work through after that, but let me play this opening clip, and we'll discuss afterwards. So this is the words from a medical doctor, Doctor Brooke Goldner, who I'm not familiar with her work, but from a quick look, it seems that she makes dietary recommendations as a way to cure autoimmune diseases, and this is from a video on her Instagram account.

Video Being Played Listen, where fish gets omega-3s is from algae or eating other fish that ate algae, all right? So

number one is you can get the omega-3 fatty acids you need from things like flax seeds or chia seeds. It's harder from algae, because it's hard to get anything that has a high enough dose in it to do the kind of work we're trying to do, without having the bad effects of eating the fish itself. So eating fish does not actually improve your health, and if that's news, I'm glad you're hearing it here. I've been saying for a long time that eating fish does not improve your health, all right? One is omega-3s are very – they're very sensitive to oxidation by heat, so cooking fish, you're already eliminating a lot of the omega-3; if you're buying it wild caught versus farm raised, so now they farm fish, farmed fish are not fed the algae that they would normally have, and instead of making omega-3s, they make mostly omega-6, and so they're actually inflammatory. On top of that, the FDA has actually shown that every sample of fish they pulled out of the ocean has PCBs or pollution, air pollution, chemical pollution from plants in their fatty tissue; so when you're eating fish, you're eating pollution, which is toxic, and that's going to cause more health problems; plus mercury, I've had people switch to pescatarians many times who came to me with mercury toxicity. So there's a lot of risks to eating fish, that can hurt your health, that are not available when you just get omega-3s directly from the plant sources.

DANNY LENNON: So within that, maybe why that's a good kind of starting point is it highlights four claims I want to work through here. The first claim is eating fish does not improve your health. The second claim made was by cooking fish, you're already eliminating a lot of omega-3. The third claim was that farm fish are not fed the algae they normally have, so instead of omega-3, they make mainly omega-6, so they're inflammatory. And then claim four is that when you're eating fish, you are eating pollution which is toxic. So maybe let's start with the first claim, and perhaps the most interesting, because I think it expands into a broader discussion around nutrition science

and how to appraise some of this stuff, and that first claim that eating fish does not improve your health. Maybe as a good jumping off point, I think it's maybe worthwhile revisiting some ideas that I'm sure we've shared with people before, Alan, around the context of even how to think about a statement like that – eating fish relative to what is the background diet or the baseline diet, what are we actually saying in terms of what improvements. So what is a good way, do you think, to maybe frame this when we hear something like a statement, eating fish does not improve your health?

ALAN FLANAGAN: Yeah, I mean, so there's a couple of layers that we could come at what we mean by, obviously, health, or indeed, health status. With any given foods, before we compare it to other foods, we could have its contribution to overall nutritional status, particularly if that food tends to contribute nutrients of interest that may be limited in the wider food supply in terms of their direct preformed form of the compounds in the diet. So that's one level of what's its contribution to kind of overall nutritional status, and is there any particular nutrients of interest in that food that might be uniquely contributed through the consumption of that food. And then the second is, well, if we're talking about health outcomes, what are the associations that we have and evidence that we have overall, not just associative, but intervention as well for the effect of that food on either intermediate risk factors or on outcomes. And then within that, we need to compare and think about, well, what's the frequency of this particular exposure, how do we see findings relative to different levels of comparison of the exposure which we've talked about before, what is the actual pattern of that food's consumption within the context of a wider dietary pattern, what are the characteristics of that dietary pattern, and what happens when we compare that dietary pattern to others, or what happens when we even look at the food itself, relative to other foods, so we can compare a diet pattern including fish like a

pescatarian or Pesco vegetarian diet, we could compare fish consumption to red meat consumption, for example; and we could look at the effects of fish potentially in terms of intermediate effects on, say, blood lipids, for example.

So the problem with those general statements is they don't even begin to get us to address any of those questions. I think with the first one that we teed up, I don't know that we should necessarily labor that too much, because we covered an episode previously on the conversion of ALA, the preform – or the omega-3 derived from the source. She mentioned, certainly, flax and other plant sources, which is an 18 carbon length polyunsaturated fatty acid, and we discussed at length issues in relation to conversion of ALA to both EPA which is the 20 carbon omega-3 found in fish directly and DHA 22 carbon length polyunsaturated fat also found directly in fish in a previous episode, which we can link to people; in effect, yes, omega-3 derived from alpha linoleic acid is important, a good contributor to overall omega-3 status; and it may certainly cover some of the bases for EPA requirements, but it certainly won't cover the bases for DHA requirements. So the contribution to nutritional status that we typically would look at to fish, and it obviously has other contributions, it has an overall good fatty acid profile, generally speaking; and it's obviously a contribution to protein, and then it has other select minerals, zinc and otherwise; but none of these are necessarily nutrients that are exclusive to it, but certainly EPA and DHA, fish would be one of the primary if not only contributions to status, and we know that the consumption of fish ties to measured levels of the omega-3 index, which again, we discussed at length in that episode, but specifically, it's an index of your status of EPA and DHA that reflects more of the DHA content of red blood cell phospholipid specifically. So there are nutrients of interest in fish that we cannot necessarily easily derive in other aspects of the

diet, and we know that the contribution of that to nutritional status is reflected in measuring these biomarkers of omega-3 fatty acid status in the body. So even at that level, certainly fish contributes to health if we're defining health, just at that initial point of departure as a contribution of important nutrients in the human diet.

DANNY LENNON: Yeah, so I think the phrasing, at least how it was put in that clip, is quite vague and doesn't really say much. So if we were to maybe take, what a steel man version of it and try and be as most charitable, what's probably being referred to is the claim that, well, if you are eating a diet with zero fish, but that has an omega-3 intake that is sufficiently high from ALA, so that in chia, flax, and other plant sources, then the addition of fish to that diet won't necessarily improve health outcomes. That might be a claim that someone may get. And, as you said, we discussed that specific idea in much more detail in the DHA as a direct source episode, which we will put in the show notes here, but that might be the most charitable way to view that; but even at that there's probably a few issues that you just highlighted there in relation to conversion. And then there's the next step to saying, well, if you're putting out the statement that it doesn't improve your health, therefore, at a kind of broad level, it's kind of suggestive to people that if you just stopped consuming fish or you didn't add it into your diet, there's no potential downside or there's no difference between people who do consume fish or don't. And maybe that's more of a pertinent question that we could get better answers to by looking at the epidemiology around, say, fish consumption or dietary patterns that do contain moderate amounts of fish versus none, etc. So, maybe that's an avenue that we should explore.

ALAN FLANAGAN: Yeah, I think so, I think that’s really independent, you know, obviously, the contribution to nutrition status is one aspect, but we know that total dietary patterns are

important, and we know that certainly the whole food matrix can be also an important factor. And we do have a fairly wide body of epidemiology and, in this regard, across populations in some large and well conducted prospective cohort studies – the Adventist Health Study-2 in the US, in what is quite a unique population to study; we have the European wide EPIC cohort, and then specific sub-cohorts within that, particularly the Oxford EPIC cohort; and we also have the UK Biobank study. And if we're looking at diets where, and there are operational definitions within these characterizations of diets that are accepted as not necessarily a complete limitation, but as a factor to consider, so these diets are often defined by arbitrary presence or absence of a particular foods, and there's obviously a limit to how much we can make an inference. If we're studying dietary patterns, then the conclusion is in relation to the total dietary pattern, and we can make inferences as to the effect of any specific food within that pattern. However, within that, where we look at dietary patterns that are defined as either meat based or meat inclusive, and then differentiation to non-vegetarian diets, so we can have kind of semi-vegetarian where people might consume meat but irregularly as far as a frequency, we have pescatarians, Pesco vegetarians, or vegetarians that include fish but don't necessarily include dairy maybe or eggs; and then lacto ovo-vegetarians who would include dairy and or eggs; and then, obviously, we have vegan dietary patterns as well.

And so, when we actually start to zero in on some of these bigger cohort studies that are kind of generally well conducted, what we typically tend to see is that the Pesco vegetarians, the dietary pattern that includes fish, tends to fare the best, in terms of overall risk reduction associated with all-cause mortality, and then cause specific mortality, particularly, for cardiovascular disease, ischemic heart disease, and other cardiovascular related outcomes. And we've

seen that in the pescatarians, in the Adventist Health Study-2; we've seen it to a lesser extent in the UK Biobank where the overall categorization was slightly different to the way I've just described as far as the AHS-2 study went. So they had regular meat eaters, low meat eaters, fish eaters, and vegetarians, and in that, the order went from vegetarians to fish eaters as far as kind of overall risk reduction, and this was looking at total cancers. So, for example, for the fish eaters, this broad categorization of fish eaters, there was a 10% lower risk compared to regular meat eaters; and in the vegetarians, it was a 14% lower risk; so they were kind of similar-ish magnitudes of effect sizes for both of these kinds of dietary patterns in the UK Biobank study. We can look at the total European EPIC cohorts, where they were looking at red and processed meat, poultry, white fish, fatty fish, milk, yogurt, cheese, and eggs, specifically, in relation to a IHD as an outcome, and again, white fish fairly null, fatty fish was not statistically significant but the direction of effect was toward lower risk. And this again is observed in some of these specific sub-cohorts, particularly the EPIC Oxford cohort, which also used a similar definition to the Adventist Health Study-2 in terms of kind of vegetarians, Pesco, you know, the definitions of pescatarians within it, where we typically see that again the fish eaters or the kind of pescatarian, Pesco vegetarians tend to show benefits as far as lower risk of heart disease go.

And so, we're looking at different populations, we're looking at varying degrees of health status in those populations, so Oxford EPIC has generally been thought of as an example of a health kind of use, healthy user bias cohort, i.e., there's an overall high demographic, a high health profile in the demographic; but actually, Oxford EPIC typically has a higher socioeconomic demographic bracket, you still see higher prevalences of things like smoking or alcohol than you might otherwise expect from a healthy user cohort. Whereas in the

Adventist Health Study-2, you don't observe those characteristics, because the Seventh Day Adventist lifestyle is usually defined by abstinence of both smoking and alcohol, but it has other health promoting characteristics as well. And yet, in these differing populations, in different regions, and again, there's French cohorts which show the same outcome, there's obviously Japanese cohorts which show the same outcome as well as far as fish and specifically oily fish go, so this association, as far as a benefit compared to usually the comparison or the reference group is meat eaters or regular meat eaters, and compared to that group, dietary patterns that include fish or are Pesco vegetarian, are consistently associated with a lower risk of, certainly, cardiovascular, and then, certain cancer outcomes, colorectal in particular. And we see that across populations, we see that that association is fairly consistent; and certainly on the basis of the epidemiology, it's difficult, I think, to men to claim, you can start to get more into the specifics of the magnitude of the effect and all of this, but if we're literally just starting at a baseline of does the evidence show a benefit or not, well, then that benefit is evidence, and that benefit is evidence in different cohorts with different background diets, different ethnic and genetic compositions. We've seen some of these associations even independent of genetic mediators, like, for example, Apo B or Apo E4 gene alleles, and some of the analyses in relation to fish and Alzheimer's and dementia, have survived adjustment or mediation by those potential very important genotype risk factors for that particular outcome. So, yeah, I think, overall, the body of observational evidence that we have, particularly from well conducted cohort studies with very large sample sizes that have the ability to kind of consider different factors in adjustment, have a consistency in showing a direction of effect that we would call beneficial to health, because it's compared to other dietary patterns associated

with a reduction in risk of various disease endpoints.

DANNY LENNON: Yeah, and you've mentioned a number of things there that I think highlight that question of, well, first, we have to be clear on what are we comparing it to, and how do we place this question of whether adding fish to someone's diet will lead to some sort of measurable health improvement. And so, first of all, there's number of different ways by which a food or a diet with a certain amount of a food or food group can have its effect. Right? So we can look at just omega-3 status as a one particular line, but then, as we've noted before, there's other ways in which the inclusion of this food group could have effects. So if we're thinking of heart disease, if someone now on an individual level starts adding fish in place of processed or red meat, now, you're not only getting the addition of this one food, but you're now getting removal of a food that could have negative downsides, you're getting a change in maybe the amount of saturated fat in that person's diet, etc. So there's all these different changes that are going on when we have this substitution going on. And then one of the other aspects of why it's important to consider that background or baseline diet is, again, if we're comparing it to someone that has no intake of fish, and now you start including fish within a diet, within these modest intakes that are typically recommended, one to two servings a week, and some of that is going to be from oily fish and you're therefore getting a change in EPA and DHA that's coming to the diet, that in itself has been shown to have potential benefit. And one of the interesting things to consider then, of one of these thinking of the demographic that's been looked at, you mentioned these different cohorts that we see it in, and we see, for example, there seems to be a threshold effect. Right? So if you look at the Japanese populations that you mentioned, where there's less of an impact of adding fish or omega-3 to the diet, is because you have a population with a very high background diet, or

a high amount of omega-3 in their background diet, and so, therefore, most of those people are probably above the threshold from which they're getting this disease risk reduction to some extent. So these are all just these big questions that need to be answered before we can start saying, okay, does doing X have a neutral or beneficial impact, and then, when you do all that, like you say, kind of, the general conclusion we'd come out with is probably that it's a net benefit, which seems to be reflected in most kind of guidelines, whether you're looking at dietary guidelines from the vast majority of countries where you're looking at the EAT-Lancet report, whatever, most of it seems to have one-two servings of fish as a relatively beneficial part of an overall healthy dietary pattern. So it just seems like a very big claim to outright state eating fish does not improve your health, without qualifying that in some very specific way.

ALAN FLANAGAN: Right. Exactly. And we see this, kind of, look, I guess, we see this type of broad based claim consistently in the domain of quackery. We'll see it with LDL denialists, for example, they'll just simply kind of hand away a statement, LDL isn't associated with heart disease, let's kill this myth or some kind of profound statement like that, that tends to accompany those very declaratory beliefs. And they're often being published to an audience of fellow believers. So it's not like those statements are going to be met with any sort of kind of critical inquiry, or indeed even pushback. So they're able to get away with making throwaway statements absent any context or perspective whatsoever, and it's often going out to a receptive audience that are willing to take that statement as the truth of the entire evidence base or whatever indeed the question in particular is. So yeah, it's the operational definitions are really important to actually hone in on what is it we mean by that statement, and then, if we can put a definition, like you said, or a steel man version of that question in place, we can actually then begin to move forward there, and

think about that evidence. And again, if we are steel manning it, and being open about where some of the limitations lie within this literature, one of the one of the gaps, unfortunately, is that while we have observational – and this reflects a principle, I guess, that has been at play in nutrition science that we have talked about before, a paradigm of viewing things that where we see observational associations between a food and specific nutrients that that food provides, what tends to translate into randomized control trials is an isolated supplemental version of that nutrient of interest. And we've discussed this before with the vitamin E example, it's like we get these observational associations, and then we get interventions, but they're not food based interventions targeting a certain milligram per day amount of vitamin E that would have been observed as beneficial in epidemiology, they're just packaging alpha tocopherol into a pill and giving it to people and expecting to see the same outcomes. And we see the same with fish and EPA and DHA consumption, where the bulk of the evidence from intervention studies is from supplemental EPA and DHA studies, not necessarily always interventions deliberately just targeting fish consumption. And so, that is something to just consider when we're thinking about the translational relevance of some of the findings that we've thought of, we need to actually work harder to parse together the various experimental lines of evidence from the different research designs that we have.

DANNY LENNON: Yeah, and the final thing I'll say before we maybe move on to the next claim, it's something just to reiterate that I think we mentioned on that episode related to do we need a direct source of DHA. Is that the correct question here is not can someone be healthy without consuming fish or not, because quite clearly compared to, let's say, the standard Western diet, someone that consumes a, for example, a plant exclusive diet that has no fish within it, is probably going to have better

health or improve their health by making that switch, and can probably have long term health as well. But what the question we're actually asking is would that person in that situation see any measurable benefit from also the addition of a direct source of DHA as we discussed in that podcast, or as we're discussing here, the inclusion of a fish overall. And then beyond that then, we have to take the next step of saying, well, in general, do people benefit from the inclusion of certain food groups or not, in a way that we're going to discuss in a dietary guideline.

ALAN FLANAGAN: Yeah, absolutely. I think one factor, like a way of thinking about benefit or risk with nutrition can sometimes be to think about the dose if we want to consider food exposures in that kind of biomedical way, the dose and the duration of exposure, and one of the things I see sometimes in debates about that question of whether you need, quote-unquote, fish or not, was like, that's not the question really to ask in relation to any foods, irrespective of its source, whether it has eyes or not. It's more a question then of actually thinking about, yeah, in the overall context, it's not necessarily a need, obviously, people can get nutrients from any given food from other sources, people can supplement, and there are all these options available. It's more about not really focusing on that and asking the objective question of whether there is actually a potential benefit, or what the evidence says as far as associations and benefits do go. And with fish, one of the kind of reductionist arguments that get made in relation to it is, well, what if you compared fish to olive oil, for example, or what if you compared it to nuts, and I find these kinds of, like, let's distill foods into these one to one comparisons and compare their relative risks to be a really asinine approach to assessing nutrition research. But I notice it's a pretty common tactic, and the reason it's asinine is because people might consume 60 mil of olive oil a day, people might consume fish once a week or twice a week; and so if you're getting a

15 to 20, or 10 to 20% relative risk reduction from an exposure that is one to two servings per week, and the dose response with fish is inconsistent, you do find some studies that suggest that even like slightly more servings than that, say, four compared to one, will yield a greater magnitude of effect; and you find studies that find a ceiling effect with to give or take servings a week. If you're getting that relative risk reduction, compared to a food that's consumed daily, then the idea that, for example, that other foods might have a stronger relative risk reduction, and therefore, we're saying, aha, like, that's a superior food, it's probably not a great way to think about the relative contributions of both of those foods to help because the actual frequency and dose exposure required to obtain a benefit is completely different between the two. And there's nothing to stop a dietary pattern actually including both, so I find those one to one comparisons quite an obfuscation of the question over whether there's a benefit.

DANNY LENNON: Indeed. So, but maybe let's work our way through some of these other claims, because I think the first one is such a broad meta point that we could probably spend the whole time discussing it. The second claim is much more specific, and this was a claim stating that by cooking fish, you're already eliminating a lot of the omega-3, and so, therefore, the premise being that, well, if you want a good amount of omega-3 in the diet, don't rely on fish, because once you cook it, you're eliminating the omega-3, so therefore, don't bother, and just rely on plant based sources is the kind of thrust of this particular video. Now, in relation to trying to look into this, there's maybe a couple of studies that I'll mention that I came across, and I'm sure there's a few that you have to point to, but they seem to show a relatively consistent picture. One of those studies that I found was by Bastias and colleagues, 2017 that appeared in PLOS One, and they compared raw salmon and mackerel to four different types of cooking method. So oven baked, steamed, microwave

and canning. And when you look at this for the salmon first of all, compared to raw salmon, and then you look at each of those methods I just mentioned, the amount of omega-3, and this was reported as a percentage of fatty acids, and when you look in the table here, you can see that, basically, none of them are lower in the amount of omega-3, and, in fact, a couple of them were statistically significantly higher, but at least they're all in around the same amount for the salmon, there was no change in their omega-6 content. And you basically see a similar story for mackerel there as well, so again, going down to that results table, and I'll put this in the show notes for people, you see that compared to the raw mackerel, once you cook it in any of those methods, there's basically the same or more omega-3 as a percentage of total fatty acids. And then another study where there was a slight difference that I can maybe point to is Zotos and colleagues, 2013. They looked at the impact of omega-3s in baked sardines, and then also in fried anchovies. So for the sardines, they oven baked them for 20, 40, 50, or 60 minutes, and the omega-3 content of all those sardines samples was basically the same. Where you do see a difference and that kind of might be could be used as a cherry picked example to back up this claim that we're discussing is that for the anchovies that were deep fried, so they deep fry them in either sunflower oil or olive oil for two, three, four, or five minutes, there was a significant drop off in the omega-3 content for those. But what that means is that we could say from one study, it seems that, at least in this case, if the cooking method is high heat, deep frying, then anchovies specifically can lose a decent amount of their omega-3. But the bigger question, and something I mention to you is, number one, is that replicated across other studies; and it seems, from what I could find, not really. And then the bigger question is, if you were to use that as a support for saying, once you cook fish, in general, that it's losing, or you're eliminating most of its omega-3, then that will just not

make any sense based on any data you have around regular fish eaters or people who include more fish in the diet, and we can see a marked increase in their omega-3 status, as an example. Why would that happen if it's getting eliminated anytime they consume food? So that was my line of thinking based on not only these couple of studies, but then generally just thinking through that problem a bit more. I'm wondering what have you seen in relation to this particular question of any data you've came across, or any useful studies that might highlight some answers to this?

ALAN FLANAGAN: Yeah, I thought the Bastias paper was interesting. There was another one that I came across, which looked at freshwater fish from the Great Lakes region, Neff and colleagues in 2014, and basically, they looked at a number of different cooking methods, so broiling, baking, and then also frying. And there's, again, two questions, like, what's the effect on long chain omega-3 polyunsaturated fatty acids like our EPA and DHA; and then what's the effect of cooking method on potentially the kind of wider nutritional content of the fish itself. And ultimately, the cooking treatments themselves, as far as the various methods go, had basically little to no effect on the omega-3 fatty acid content, and that seems to me to be pretty consistent across the evidence that I've seen. But as far as nutritional changes go, yes, there may be some decrease – there may be some changes in lipid content that relate to cooking duration, and the temperature that it's exposed to, they seem to be relatively minor overall. With frying, what you would typically see is that there's a higher omega-6 and potentially higher monounsaturated fat content as a result of frying, and that's what the Neff paper showed, however, that's because to fry it, they used canola oil. So the act of frying is not altering the fatty acid composition of the fish per se, it's altering the overall fatty acid of what would be the meal, because it's been cooked in rapeseed oil or canola oil as it's called in North

America, which then contributes MUFA and omega-6 to the actual fish that was cooked.

So as far as the various cooking method goes, it's the choice of oil that would influence more greater alterations in the fatty acid content of the subsequent meal than, from what appears from the literature that I've seen, cooking method influencing an alteration of the kinds of specific fatty acids that were interested, and their content in fish, independent of these slight changes we could see to cooking method can sometimes affect the protein content, which some of the studies show. And yeah, there can be this slight change to the total fat, total lipid content, as a result simply of lipid oxidation that occurs from exposure to heat, and the two major factors there are temperature and duration. So, like you say, yeah, super high heat and long duration of something like deep frying may have an influence, but I really, ultimately, A, can't imagine too many people cooking anchovies in that way in 2022; and, B, just the other general cooking methods that are observed, you know, that have been tested just seem to have such a negligible impact on the overall nutritional content, and certainly have little to no impact on the actual omega-3 fatty acid content.

DANNY LENNON: Yeah, and then, just to kind of reemphasize a way of thinking through this type of question, if someone was doing this as a practitioner, and is wanting to do evidence based practice of, okay, I've got this question about either wanting to include dietary sources of omega-3 in a certain person's diet to therefore, presumably, impact their health outcomes by improving their omega-3 status, that must be the line of thinking that you'd have this premise for. And so then, if someone is saying, well, if you consume fish, it's not a good way of doing that, because you're eliminating that omega-3 when you cook it. Well, you can easily kind of think through this in a practical way of what happens when you go and look at diets that are high in fish, and that people are going

to be consuming in normal dietary patterns, what are people's omega-3 status, so you could look at something like the omega-3 index, and then what are the health outcomes from that. They're much more important questions of, can I find one research paper where you have a certain drop in omega-3 from a certain cooking method, right? That's kind of hyper focusing on the wrong question, at least to me that'd be the wrong way to go about it.

ALAN FLANAGAN: Yeah, definitely.

DANNY LENNON: Cool. Let's get to the third claim, which was that farm fish are not fed the algae they normally have, so instead of omega-3, they make omega-6, so they are inflammatory. So here, there's probably two separate questions; one, we can ask is farmed salmon low in omega-3, and, say, much higher in omega-6, because if the presumption here is they're not making omega-3, they're going to make omega-6, I think that's the specific claim. That means that if you look at farmed salmon, they should surely be low in omega-3, so that's the first thing to investigate. And then, second we'd have to ask, even if there was more omega-6, does more omega-6 make this now an inflammatory food, and I think that's a broad question that we've discussed before. But first, if we talk about the first question, is farmed salmon low in omega-3 – again, based on what I was able to find and look through this, it seems that not only does farmed salmon not have a low intake or low amount of omega-3, it's actually much higher than many other types of fish, and, at least from one set of data, I think this is from Mozzaffarian paper, they pull data from the USDA, FDA, and EPA – so EPA in this sense being the Environmental Protection Agency, not the omega-3 fatty acid. And in this for the farmed salmon, I feel like the farm salmon had 4500 milligrams of combined EPA and DHA per serving, so for six-ounce serving, whilst the same size serving from wild salmon only had 1700 milligrams. So that immediately would suggest this idea that

farmed salmon are not containing omega-3, because of the algae they're fed, seems to be contradictory before we even consider how much of that would be a problem. I'm wondering, does that kind of fit in with what you've been able to find on the general picture around farmed fish, omega-3, omega-6, and just this broader question generally?

ALAN FLANAGAN: Yeah, it seems to be there's kind of two elements to what could be compared or nutritionally different based on wild or farmed fish. One study was from a group in Norway, looking specifically at wild caught versus farmed salmon in Norway, and what you would typically see, it appears in this comparison is the overall fat content of farmed salmon is much higher than the wild counterpart. So that in this analysis certainly was the most noticeable difference between the source of the salmon, it was just in its total lipid content, and that typically reflects the fact that they just have a more abundant supply of feed, and potentially, obviously, like other factors like reduced actual activity levels overall compared to wild salmon. And so that's total lipid content per se, and then in relation to the fatty acid content specifically, interestingly, there are differences at this level, but they don't appear to be of such a magnitude that you would worry about the difference between farmed versus wild caught salmon, if your concern was deriving long chain omega-3 fatty acids. So there were differences in, say, for example, farmed salmon, the difference in EPA and DHA in this particular study in Norway, which compared these sources was between 5 and 8% for EPA, and between 2 to 4 or nearly 5% for DHA. And so, that's not an enormous difference, and it still means that farmed salmon makes a substantial contribution to omega-3 in the diet, and importantly, the context that they put the difference into was, would you still meet your weekly recommended amount of long chain omega-3 fatty acid intake from consuming farmed salmon, and yes, you would. There is a concomitant difference

because total fat intake – the total lipid content is higher. Yes, you do get a higher content of both linoleic acid omega-6 and alpha linolenic acid, ALA, omega-3 that we talked about at the start. And so, yes, you would see, so you see this higher total fat content, you see slightly lower EPA and DHA content, and you would get relative to wild salmon, a higher amount of both omega-6 LA, and omega-3 ALA, the 18 carbon ALA, and certainly the amount of ALA difference was significantly higher. So in both LA, they were orders of magnitude higher than the wild salmon, so because of the total lipid content is greater, everything is gone up; but the actual nutritional, I think, evaluation of this really wouldn't necessarily change dramatically one's decision to consume one or the other. And then, of course, on the other side, I know we'll talk about this next, if wild salmon exhibits certain nutritional and specifically lipids and fatty acid compositional differences to farmed, well, then compared to farms, they also exhibit higher levels of compounds that we would determine as contaminants, environmental contaminants like dioxins or PCBs or otherwise. So I know that's the next question, but it's not necessarily just that the uniform or that the nutritional differences yield a conclusion of their inherent superiority to wild versus foreign salmon.

DANNY LENNON: Right. So just as a recap there, if we're thinking about, is there this shift in the amount of omega-3 and omega-6 in farmed salmon versus, say, wild salmon, there's kind of two ways then to look at that. One is there an important difference then in the total amount of omega-3 left, or that you're getting per serving, let's say. And then the second question would be, are you getting much more omega-6, and is that a problem. So on the first question, as you noted, we can maybe see a case where on a percentage basis, there is this slight shift that there is maybe a slightly lower percentage of the total fat is coming from EPA and DHA, let's say, in a farm sample; but in that case, the farmed salmon has much more total fat, so on

an absolute level, the amount of omega-3 from EPA and DHA that you're getting in, say, a serving is going to be, let's say, the same or maybe, in some cases, could be substantially more than that wild salmon. Then the second part of that is, okay, well, but does that mean the farmed salmon has an increased amount of omega-6, and if there is that kind of shift to more omega-6 in farmed salmon, plus it has a total amount of more total fat so that in an absolute sense, you're getting much more omega-6, does that mean now it's an inflammatory food? Is this a problem that there's this increased shift of omega-6, because omega-6s are inflammatory or at least that's the claim? Again, we don't need to maybe rehash everything we've said about this particular issue, but given that that was part of the claim, what would be the kind of take away line about omega-6, and therefore, the conclusion that farmed fish are more inflammatory?

ALAN FLANAGAN: No, it's flat out no. Ultimately, we're dividing benefit with benefit, and I think that's the way we should start to kind of view the composition of fatty acids in the diet, like, what we're seeing is that, yes, the total fat content is higher; and then, yeah, there's the slightly lower levels of EPA and DHA and higher levels of LA and ALA; you're still getting a food with a very health, kind of, promoting nutritional profile as it relates to these fatty acids. Omega-6 in the form that it would be in salmon is linoleic acid. There are studies that can overfeed people in linoleic acid by 500%, relative to where they were at baseline, and see no alteration in circulating levels of arachidonic acid, which is considered the precursor for these inflammatory pathways. And we certainly see no effect of, or change in the actual profile of these inflammatory mediators or pathways or cytokines from – so we basically, at this point, and we have talked about this before, have all but zero human evidence that altering linoleic acid levels in the diet will lead to some sort of dramatic change in someone's inflammation.

DANNY LENNON: Yeah, and if people want a deep discussion of diet and inflammation, we did a podcast episode titled diet and inflammation, so go back and you can find that, I'll also link to it in the show notes, if you're interested in that type of conversation. The final thing that I'll say here before we move on to the final claim that is more about, again, at a population level if we are noting, there's potential benefit to including, let's say, oily fish within the diet on a weekly basis in a certain amount, is that it's also worthwhile considering the cost effectiveness of getting those target amounts of EPA and DHA from something like farmed salmon versus wild caught salmon, and there's going to be kind of clear differentials there that might be a consideration for people from a cost perspective; and so, there's going to be the cost per unit of omega-3 is probably lower from farmed salmon than some of these wild caught sources.

ALAN FLANAGAN: Yeah, I think one of the nice things that was quantified in that last paper from the Norwegian group was, if we think about the per day amounts, it's generally like 0.25, so about 25 milligrams, if we were to distill it per day of EPA and DHA, is what we'd aim for, as far as current recommendations. And that would add up to about kind of 1.8 to a little over 2 grams a week, right? Both wild and farmed salmon would give you that if you were consuming just 20 grams a day, you'd hit the daily portion, and 150 grams a week would meet the weekly portion, and you would easily cover that bases from both sources. But it would be more cost effective to opt for farmed salmon to achieve that, because wild salmon is substantially more expensive.

DANNY LENNON: Excellent. Let's get to our final claim, which was when you're eating fish, you're eating pollution, which is toxic. So maybe let's try make this more specific, and again, maybe to try and steel man this by rather than just saying, oh, you're eating pollution, this is toxic,

what we could probably think of is a couple of things. One that was actually mentioned was PCBs and maybe dioxins, we can come to those, but maybe the first one that we should discuss in relation to fish consumption is mercury, which I'm sure many people will have heard at least discussed in some amount. And there's probably a few aspects here of mercury is something that we should be aware of, it's something that most food regulatory bodies will look at, whether that's the EPA or EFSA which is in Europe here, the European Food Safety Authority have published a bunch of stuff around this. And the idea being that when we have mercury, at least, the form that it gets into when it is in water, so once it makes its way into lakes and oceans, it can get converted into methyl mercury by microbes there, and this methyl mercury is readily absorbed and transport into tissue, and so, therefore can actually accumulate in the tissue of fish. And so, this brings up concerns about, well, is there a potential toxicity from fish consumption, one of the things that is probably unsurprising is that the levels of mercury are going to depend based on the species, typically, its highest in these kind of larger predators with longer lifespans, and then, smaller fish that are more short lived species tend to have much lower amounts. So, I suppose, the real question then again, becomes, like you mentioned a moment ago, as much of the things in nutrition are is one of dose. So what is the dose that is problematic? And then, what is the dose that we're typically getting from different sources of fish? And therefore, based on that, does a certain amount of fish consumption lead to negative health outcomes via this mechanism of increased mercury and maybe mercury toxicity? So there's probably a few jumping off points here. I don't know if there's a particular good place that you think maybe we should start around the whole mercury-fish health kind of discussion.

ALAN FLANAGAN: Well, I think where do we potentially see levels of mercury that would be of concern and, by

concern, and we've discussed these concepts a little more in the Sigma statement on the organic foods question, and it relates to, well, if we're going to define, if we're going to say there's higher levels of X, mercury in this case, or dioxins or even artificial sweeteners, for example, if we're going to say there's higher levels of this in this food or this product, well, what does higher mean, and is this something that is of concern based on concentration levels and thresholds that have been established by food safety research. And obviously, those potential standards might differ relative to jurisdiction, so in the US, it would be administered by the FDA, the Food and Drug Administration, and then, Europe, it's typically the European Food Standards Agency or EFSA. And so, we could think about, well, are levels of mercury, for example, in commercially available fish higher than what we might have, like higher than the thresholds that we've set. And certainly, there is evidence that some, as you said, like particularly predatory species can, but there's an analysis, a 2014 paper in America which looked at a range of different fish across multiple different regions, six regions of the US – king mackerel, salmon, tilapia, catfish, cod, pollock, yeah, so like different, ultimately, I think there were 77 different species of fish included in this analysis; and the only ones that were above the FDA kind of threshold level for concern for mercury were swordfish and king mackerel. And so, this is something, obviously, that then allows us to distill down, well, this isn't something that is broadly a claim we can make against fish, as a category overall. I mean, it's clearly confined to some specific instances, and, as a result then, it's pretty easy to make and navigate one's food choices with these kind of considerations in mind. So at that level, and again, I've seen some European research, again, suggesting similar, although interestingly, it seems to be more prevalent in the predatory species that are Pacific based, and so, overall, it would appear that the potential for consuming really high mercury

fish, and based on European fishing, might be kind of overall lower, and indeed, the Norwegian study that I referenced previously had the mercury concentrations and the salmon in that study were nearly 10 times lower than the EU maximum level. And that American analysis, again, every other species examined, but those two were lower than the FDA levels, so it's not just the presence of the compound itself, it's relativity based on established thresholds that we have for food safety with any given compound.

DANNY LENNON: Yeah, and that, as a more general point, is worth considering how some of the safety levels are often set, so I think, particularly in the case of mercury, it's something like they take the 95% confidence interval, take the lower limit of that, and then, there's like a 10-fold safety factor below, which then you actually set kind of a safety intake...

ALAN FLANAGAN: The toxic equivalence, yeah.

DANNY LENNON: Right. Yeah. And so... Yeah, go ahead.

ALAN FLANAGAN: Yeah, I was going to say, and then even if we're saying, okay, that even some fish species might still have mercury and someone might be like, well, I'm still not comfortable, there's these thresholds have been set, you're telling me that mercury is lower than that, but surely no mercury is better, well, interestingly, if we're shifting that emphasis to outcomes, there was a 2016 paper from Martha Clare Morris, the late Martha Clare Morris research group in Chicago which looked specifically at seafood consumption, levels of mercury in the brain, and neuropathology of Alzheimer's in older adults. And so, this was from a project, the cohort study they had conducted in Chicago, a subgroup of which had consented to brain autopsies on passing away. So a number of their studies have been brain autopsy studies, comparing the brains of deceased participants who died with dementia or Alzheimer's to participants who died disease free. One of the

really interesting things about this study was that seafood consumption was associated with significantly less dementia and Alzheimer's neuropathology, but the seafood consumers who died without disease had higher levels of brain mercury. And there wasn't a significant correlation between the levels of brain mercury and the dementia and Alzheimer's neuropathology, and the kind of message was, well, if you're concerned about the mercury content of fish as a feeding into a decision of I will not consume seafood and oily fish, then that might be actually somewhat shortsighted because the conclusions from this study certainly suggested that it's actually just better to eat the fish rather than worry about some accompanying mercury levels. So I always thought that was quite an interesting study.

DANNY LENNON: Yeah, and that's interesting, because I think that, in a relatively similar fashion, relates to what we talked about at the very start of in some of those epidemiology that, yes, there can be some potential downsides, say, including mercury, but on the net effect of completely avoiding fish may actually be detrimental, if you're doing it for that reason. So sure, you're avoiding the potential negative of mercury, but you're also then not reaping any of those benefits from a risk reduction. So in, at least at a population level, what might be that effect, it might be a net harm of avoiding it altogether on that basis. So yeah, and then with the mercury thing, I think, when you look at where the evidence, and certainly, where the guidelines are most focused, tends to be on very specific groups, so it's not really a population wide recommendation around avoiding certain amounts of mercury containing fish species, for example; it seems to be focused in on pregnancy, breastfeeding very young children, and within that, there's actually a really nice simple table made for the general population that the EPA put together, and you can see that the way they've broken it down is for your servings of fish, you can still get your usual one, two, or three servings a

week type thing; they have then different seafood options broken down by best choices, good choices, and then choices to avoid; and you can see like there's this whole massive list of like best choices that aren't going to be problematic at all, some that have maybe a bit more mercury, and then those big larger fish like shark and swordfish and king mackerel, those ones that you mentioned, to avoid. And then basically yeah, have your two servings a week from the best choices list, or if it's from the good choices list, you would pick one, but it's like really quite nice and intuitive for people that is targeted at kind of childhood pregnancy and breastfeeding, which is where most of the concern tends to be and where probably most of the data and therefore the advice tends to center around.

ALAN FLANAGAN: Yeah, absolutely, and the Japanese cohorts have clearly shown that maternal fish consumption as far as cognitive outcomes in offspring goes, would be preferable to no fish consumption, and that is obviously something then that would, yes, there can be erring on the side of caution, and it might be that the same results can be obtained from fatty acid supplementation in pregnancy, but perhaps a more, like you say, a more kind of rational and nuanced consideration of to consume fish or not to consume fish can be guided by these kinds of actual known knowns that we have as far as potential contaminant levels go.

DANNY LENNON: Yeah, and that was actually there's a nice review paper, again Mozzaffarian & Rimm were the authors, and they kind of make that point of not only in relation to avoiding fish on this basis can be problematic for adults, say, in terms of coronary heart disease risk, but then also in this suboptimal neurodevelopment of children, which is one of the main kind of aspects that I know you discussed in relation to DHA, and particularly through pregnancy, and that kind of early childhood period of why it may be beneficial. So again, the advice is not to avoid fish out of fear of mercury, it's about just

being aware of what choices there are to avoid, and then which ones are fine to consume. So yeah, I think that does the mercury thing. And I think that pretty much does us, unless we want to mention a small bit around PCBs and dioxins, because I know they were mentioned in that claim.

ALAN FLANAGAN: Well, I mean, the conclusion would be similar, like, as far as the research, I've seen, the toxic equivalence, which is set by European standards, which is expressed in toxic equivalents per kilogram body weight per week, and again, dioxins or PCBs were all, by orders of magnitude, seven times plus lower than the EU thresholds for concern for any of these compounds, even though were you to compare wild fish to farmed fish, yes, you would see higher concentrations of these compounds in wild salmon compared to farmed salmon, but those levels themselves in wild salmon do not appear to be any cause for concern relative to the food standards that we have for these compounds and are all significantly lower than would be of any kind of concern, I think.

DANNY LENNON: Yeah, and particularly, again, when we balance that out the potential net benefit for most people of consuming this or having a dietary pattern that has certain foods, is likely beneficial relative to completely eliminating them.

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