DANNY LENNON: Austin thanks so much for doing this. Appreciate you taking the time out.

AUSTIN BARAKI: Yeah, no problem. Thanks for having me.

DANNY LENNON: Before we get into the actual topic that we hope to discuss today, I'm just interested about your current work within the hospital. Can you maybe fill us in on what your day to day work looks like, what different types of roles you fulfill within the hospital, and some of that good stuff?

AUSTIN BARAKI: Yeah, yeah, sure. So basically, I work at a large kind of tertiary care treatment facility in South Texas. I am in the Department of Internal Medicine, and it's an academic center, which means that student doctors, PA students, as well as medical interns, varying specialties and residents kind of rotate through our services. And so what I do in the hospital medicine department is you know, somebody who's sick, who's an adult, usually non-pregnant adult with a medical illness shows up to the emergency department and they're deemed to have some condition or suspicion for a condition that would merit inpatient treatment. They call our team, we admit them to the hospital, treat them for whatever may be going on whether it's sepsis or a heart attack or stroke or kidney failure, liver disease or something like that, that any number of things that we commonly take care of, and I supervise and teach residents and students to kind of

guide them through their training process, which is usually takes a few years until they're ready to become independent functioning clinicians just the same process that I went through to get where I am after getting through medical school. And so I'll teach and lecture in that department and take care of patients and move them through the hospital and kind of get them hooked back up with their primary care clinicians on the other side of their acute hospital stay. So that's probably the big chunk of my work is clinical, patient care, as well as teaching which is what I really enjoy doing probably more than anything else in that environment. And then outside of that, I do a lot of other things outside of the hospital with the Barbell Medicine side of things and kind of science communication to the public and teaching about exercise, resistance training, lifestyle change, things like that, as well as where there is a rule for medical intervention, care, testing, treatment, things like that.

DANNY LENNON: The fact that you say that's one of your favorite, if not your favorite part of your various roles. Do you find that it's had an impact on your competency as a doctor?

AUSTIN BARAKI: Yeah, 100%. I mean, you get through, on the other side of getting through medical school, you can look back and realize that it's an enormous amount of information that you learned going through school, and then you graduate and you have a degree and you go to start your internship and you show up and you realize you don't actually know anything after four years of postgraduate education. Then you go through and you start treating patients and you learn stuff, you pick things up along the way and then by the end, you're expected to have at least enough knowledge and clinical competency to pass your board exams and things like that. And then you transition into being a supervisory role kind of attending physician and then you realize that I wouldn't say you feel like you don't know anything, but you start to recognize more of the gaps because now there's no backstop for you, like you're the person who's making all the decisions and now you might have students or interns or residents who are asking you, hey, why are we doing this this way? Or does this work? Or, or why don't we do this, and then you're like, oh, and so with my role and

responsibility to teach them and develop them into competent clinicians that forces me to be able to speak comfortably and intelligently on a whole variety of topics. And so I know that there are a handful of topics that come up every time I'm on the board service, and I know I'm going to teach about them. And so the more I've taught them, the better and more comfortable I've gotten with those topics. And then there are some things that I mean, every time I go back to work, I end up having a list of things that I've never seen before. That's one of the things that's really neat is like very odd, rare uncommon things, at least one or two come up every time and that provides a new opportunity for me to go down a new rabbit hole, get comfortable with a new topic and be able to teach about it. And so that's kind of what I find is like if I come across a clinical scenario where I'm like, if I had to teach about this, I probably wouldn't feel super comfortable about it and then that is my trigger to go and make myself comfortable and then to go test myself and actually teach it and see if I can get somebody else to understand it. And so that's definitely been a huge source of improvement. And it's kind of well known that between academic medicine and kind of more private practice side of things, working in the academic environment, I feel like tends to keep people sharper and more up to date with the evidence basis, because you kind of have to and you have in terms of residents who are learning the freshest stuff, and they kind of force you to stay up to date. Whereas in private practice, there's less of an incentive to stay super up to date with that, and it's easier to get a little stale with things plus, you don't have to teach anybody anything. You're just seeing patients. So yeah, it's definitely made me better to do that and is going to continue making me better.

DANNY LENNON: Let's get into our topic and there's probably some different subtopics throughout this that we'll bounce around between, but maybe to start off if we take the concept of screening, probably a good place to start the discussion as always is with some definitions. So how would you define the the concept of screening and what is a goal of screening essentially.

AUSTIN BARAKI: Sure. So the idea of screening is that we're searching for an unidentified condition in people who don't have

symptoms already, i.e. what we call asymptomatic individuals. So people who look and seem and feel fine, but we're trying to find evidence of either disease or a risk factor for disease or something like that, that could potentially increase the risk of down the line developing disease or premature death. And this is important to distinguish from diagnosis. Diagnosis is a situation where somebody shows up with a symptom and based on that symptom, we've launched an investigation to try to find kind of an explanatory process that can then be treated to mitigate their symptoms or risk of progression or death. So we're looking for people in, the conditions in people with no symptoms. And this can be applied both very broadly like across say, the whole population that would be like mass screening of the general population or it can be applied to like demographic cohorts. Obviously, there's some things that we only screen women for or some things that we only screen men for, for example, or you can apply much more selective screening to just members of a particular risk group. So people who share some sort of a, some factor that is shared among them, that itself is thought to increase their risk, maybe we target our screening directly at that group, to maybe increase our yield and to decrease or to better use our available resources. So the goal of this is to identify things that can increase the risk of downstream disease and death, what we call morbidity and mortality. And the big assumption and this is something that we're going to come back to kind of repeatedly and challenge the big assumption is that detecting these things earlier in the course, relative to when it would have shown up later with symptoms and treating it at that point is going to reduce that downstream morbidity and mortality, the assumption that early detection is always better. And it turns out not to be the case, which can be kind of a screwy thing. When people first learn it, it can be confusing, like how could it not be better to detect things earlier and treat them earlier? Well, yeah, it's complicated.

DANNY LENNON: I think a lot of people listening may be thinking, hold on, if there is all these tests we now have available and if they do, in fact, measure what they claimed to measure, why wouldn't I want to get certain tests on? Why wouldn't I want to do everything I possibly can

so I don't “miss anything” because surely if I detect it, then I can either do something about it or just like to know what's the best jumping off point for us to maybe start exploring that misconception?

AUSTIN BARAKI: Yeah, I mean, you kind of said it there in your description, the idea of I wouldn't want to miss anything. And the idea of not missing anything means you're going to catch everything, regardless of how consequential or not it may ultimately end up being which that is the underlying issue here. So I think probably the best place to start is talking about how do we decide what to screen for. And when we, look back the idea of screening really started to emerge in the 20th century, like the mid 20th century, they started screening for latent tuberculosis infection, and then that got broadened down downstream, including, like, you're familiar with the Framingham study, which introduced the concept of risk factors itself. And so then we started screening rather than just screening for diseases themselves. We started also screening for risk factors for disease and treating those risk factors as if they were diseases in their own right, like dyslipidemia, for example. And so in about the 1960s, the WHO published their principles of screening. These are known as the Wilson and Jungner criteria. These have been since modified with the advent of more modern technology, and there's a whole list of them, but the basic fundamental principles of screening hold that if you're going to screen for condition, the first thing is, it should be a prevalent health problem like. It should be somewhat common in the population. It should have an asymptomatic latent stage, meaning we don't screen for conditions that like all of a sudden strike at maximal intensity, because then you're either going to not find it or it's going to be too late. You wanted to screen for things that have this latent stage that develops over time during which there's no symptoms, giving you an opportunity to catch it during that period. And it should be a condition that actually causes significant downstream harm that you can hope to modify. So examples here would be like, we don't screen for incredibly rare conditions, like there's this condition called progeria, that's like premature aging. And there's like 100 cases in the whole world or it's not worth our resources to screen

for something like that. We also don't do screening for like male pattern balding genes or something like that, because there's no morbidity or mortality, disease or death consequences from that. So like, why would we screen for that? And similarly, like I said, we don't screen for conditions that don't have an asymptomatic latent stage. So something like an embolic stroke that like strikes you with maximal intensity all at once. Why would we screen people for that, because there's no latent stage of that condition. It just like happens when it happens. And so those are examples of kind of the the subset of conditions that we would decide to screen for. Because, as you said, we have tests for so many things. And we could theoretically test for everything under the sun. But we have limited resources. And so we have to pick and choose more selectively. So once we have, say, a set of conditions that meet those criteria, it's a prevalent important health problem with a latent stage that causes downstream harm. It should be a condition that if we detected it during that stage actually has a treatment that can reduce long downstream disease and death, ideally, and like a cost effective way. So we wouldn't screen for things that have no treatment whatsoever, because it's like, you catch it and then what do you tell the person like sorry there's nothing we can do or you screen for a condition where you can treat it but the cost of treatment is like $10 million a year. What are you going to do with that information? And is it feasible to treat them during that asymptomatic stage? It may not be. So you want conditions that are important that you can detect over a period of time that have a treatment that can then influence the downstream consequences of that condition. And then finally, what you would want is, of course, you need to have a test for this condition. And the test needs to have a number of important kind of characteristics to it. It should ideally be a test that is relatively simple. It should be acceptable to the patient, meaning preferably, it should not be super invasive. So we don't go and like do open laparotomy is like opening up people's bellies to screen them for colon cancer. That would not be preferable to people. It should be a valid test. Like you said it should measure what we want it to measure. It should be reliable in terms of consistency of use. It shouldn't be subject to a bunch of like interpretation error, inter rater reliability

issues, things like that. It should ideally be somewhat economical. And most importantly and this is going to open up the next can of worms here it should be sensitive. And what we mean by sensitive is it should ideally be able to detect all the cases of this condition or as many of them as possible with minimal false negative rates. And so in this way, when we apply a screening test, a positive test would be useful to detect potential cases. But usually the downside, the trade off here is that it may come with the risk of false positives. And so a negative test that's very sensitive can be useful to rule out the presence of certain conditions. So if you go and you get tested, negative, you're like, cool. I don't, I feel fairly confident that I don't have this condition. If it's positive, however, then that opens up the next can of worms of I may have it or might that test be a false positive. What you wouldn't want is to apply a screening test broadly to a population that has a huge false negative rate. Because then it's like a negative test, it doesn't help anybody. So that's kind of the, those are the overarching principles of screening in terms of what conditions we choose to screen for and we want them to obviously have treatments that are accessible and available and cost effective. And then we need a test that is valid, reliable, and definitely pretty sensitive to detect the condition.

DANNY LENNON: And on that last point essentially, it's much more important for a screening test to be able to detect false negatives rather than false positives, at least at this stage of what we're trying to achieve.

AUSTIN BARAKI: Yeah. So I'll go into these concepts a little bit more. This biostatistics is kind of like the bane of most medical students existence when they go through the trading. So I think kind of going through it maybe a different way can also be helpful for people because ultimately, medicine and diagnosis is really much more game of uncertainty and probabilities than people realize. We use a lot of bayesian inference when we're actually in clinical practice where the goal is to either increase or decrease the suspicion of a particular condition. So in other words if somebody shows up to the clinic, and they present with either a particular symptom, or they show up and no symptoms at all, I have some sort of a pre-test

probability or a pre-test suspicion that they may have a particular condition. And I might do a test or obtain some clinical information by asking questions, by examining them or by doing medical testing that adds information to my like internal kind of calculus of probabilities. And that either increases or decreases my post-test probability. So it can say when they came in my suspicion that they have active colon cancer was pretty low. But then when they told me they've been losing weight, I found them to be anemic on a blood test and then I sent them for a colonoscopy and it found a tumor. Now my post-test probability is much higher that they have colon cancer. So it's all about probabilities and uncertainty. And this is really important to understand because all tests are imperfect. This makes the process really challenging. And this is commonly misunderstood publicly. I think there's a whole lot more faith and confidence put in a lot of tests, and imaging modalities and things like that compared to what they actually deserve. We overestimate the accuracy and reliability of the information we get from biomedical testing. So, this idea, the two fundamental concepts here are sensitivity and specificity.

Sensitivity is kind of like the true positive rate of our test. It's the fraction of people who have a condition who are going to test positive when you apply a test. So a high sensitivity test that is positive is going to catch everyone with it, but can potentially drag a lot of false positives along for the ride. So in this way, a positive test is not super helpful for ruling in disease, but it can be helpful For prompting further diagnostic evaluation. Conversely a negative test is pretty helpful to rule things out for people who don't have it. For example, you can stop your evaluation there. On the other hand, this concept of specificity, meaning a test that's very specific for a particular condition, this can be thought of as the true negative rate. This is the fraction of people who do not have a condition who ultimately test negative for that condition. So a high specificity test that's positive for a condition is helpful to rule it in.

Now, ideally, a gold standard test is going to have 100% sensitivity and 100% specificity. But of course, this is like pie in the sky hardly ever happens if ever,

because again, all our tests are imperfect to some degree. They don't, they tend to have a little bit less or potentially a lot less either sensitivity or specificity or both. And so there are some tests that have been discarded to the annals of medical history. And newer, more advanced high tech testing interventions are pushing the limits higher and higher on our sensitivity and specificity, which is sometimes a good thing, but sometimes ends up causing more false positives or over detection, things like that, that we'll get into a little bit later.

And so since these words sensitivity and specificity, they sound alike and positives and negatives and things like that can be confusing to keep track of when people are thinking about it. I think there's some, a whole host of good examples and analogies that I use when trying to explain this. And probably one that people can understand the best is when you go through security at an airport. They do screening when you walk through security? They send you through a metal detector, for example. That is a high sensitivity screening technique. It's very sensitive to catch all kinds of things both metal weapons, but it also detects your metal belt buckle, it detects your metal coins, it detects your metal watch, it detects all kinds of other stuff. And so after they detect everything, weapons, and a whole bunch of false positives that come along for the ride then there's a step two to the process, the high specificity confirmation. So we do the screening, step one, confirmation step two, this is kind of a classic sequence in biomedical testing, where they pull you aside, and then they actually look at you a whole lot closer to look more specifically for is it a weapon or was that just a false positive because this guy had some spare change in his pocket. And so that is kind of the fundamental idea. There are tons of other ways. I mean, I've also explained it in terms of like your motion detector light, say outside your house, if you set it to be really sensitive, you're going to catch any bad guys coming by, but you're also going to catch a leaf that's like trickling across your driveway. And then you actually have to go out and look to see is it a bad guy or is it a leaf, that's the confirmation with higher specificity for the thing that you're looking for. So, those are kind of the overarching concepts in

terms of detect screening and confirmation, but the one added piece of nuance here is that there are, the utility of these tests can vary. And these introduce some other concepts called predictive values; positive predictive value and negative predictive values that vary with how prevalent a particular condition is. And this is really important for people to understand these days in the setting of COVID, when they're trying to interpret their antibody tests or their PCR test or something like that, because even a test with good sensitivity and specificity like performance characteristics, it can have a pretty low predictive value if it's being applied in a population with a really low prevalence of a condition. So if we go back to our like airport security example, let's take a hypothetical example of like an airport that's in a city where there was just like a weapons convention or a gun show and like 10 million people came to the convention, and all those people are now leaving and your airport security screen is starting to go off, your predictive value of a positive test in that situation is going to be higher because there's way more prevalence of weapons in the city at that time, compared to that same screen being done in a city where no one has any guns where the prevalence is so low, almost any positive screen at that airport is going to be a false positive. And so that's important.

These days, when we're using these COVID tests, for example, in a place maybe a place that has really low prevalence of COVID, because there's such high regional variability in terms of the prevalence of COVID. So these tests really remote rural country part of the US, most of my tests that I do, even if they had good sensitivity or specificity are going to be false positives. Whereas if I take that same test, and I apply it in downtown New York City, or in Italy, or one of these places that had horrible outbreaks, a positive test is much more likely to be a true positive than it is a false positive. So all of this stuff to summarize, makes testing and test interpretation a whole lot more complex than just drawing blood work and comparing the number that you get to the reference range that the lab provides.

And even these reference ranges themselves are a rabbit hole of their own in terms of how they're

established, where you set your reference range kind of cut off through a positive or a negative test. And so this is kind of drawing on the route of this conversation between us as far as like direct to consumer testing being an issue where people can just get a test look at a number compared to a reference range, and oh I have this disease. It's like not that simple. There's a whole lot of other things that go into clinical interpretation of these data that we can get from medical testing.

DANNY LENNON: Some of these things that are related to testing, whether that's sensitivity, specificity, their predictive value, they're not solely inherent to the test itself, but how we as humans interact with them. So the example you gave of the predictive value is not just down to the test, it's down to the context of where it's used.

AUSTIN BARAKI: Correct.

DANNY LENNON: Presumably the same thing applies with the specificity of a test if, as you mentioned, we could have different cut offs for or different thresholds we used identify to something that changes some of these things in relation to a test. So it's not an inherent characteristic of the test per se.

AUSTIN BARAKI: Absolutely. This is something that I teach a lot on when we're talking about it. So, for example, some of the listeners may be familiar with, like, say, some of the blood pressure cut offs that have recently changed in the past 5-10 years, where when I was in residency, which really wasn't all that long ago, high blood pressure, we really focused on treating folks who were higher than like 140 over 90. And more recently, that's cut offs have been kind of tightened up a little bit. And now we're kind of more interested in this kind of like pre hypertension phase of like higher than 120 for systolic and so moving these numbers around, is going to like if you decrease that blood pressure cutoff, or where you start calling it high blood pressure, you are increasing your sensitivity, you're going to catch a whole lot more people who have high blood pressure, but that's at the expense. There's always a trade off there of decreasing your specificity for that condition. Same thing goes for hemoglobin A1cs typically an A1c cutoff of greater than 6.4% is

used to diagnose diabetes. If tomorrow the endocrine organization said, now we're going to make it 6%. Well, now we're going to catch a whole bunch more people. We're going to make it more sensitive and less specific, which is especially tricky because a whole lot of these disease processes are not binary. They're on a biological spectrum, a gradient. So is there something inherent that happens when your blood pressure goes from 129 to 130, or 139 to 140, or A1c of 6.4 to 6.5, there is not like a distinct like switch that flips. It's a gradient, but we have to set these things somewhere. And of course, there are trade offs, there's potential for false positives and false negatives. And that kind of comes with the territory, so to speak, which makes this stuff complicated.

DANNY LENNON: It also relates in some way to a point you've just made earlier as well in relation to sometimes we're screening for risks factors as opposed to an actual disease process. And one of the things that I read in one of the papers that you sent me across on some of the sociological factors is how even having a certain factor that places someone now in at risk group, and even the communication of that to a patient as real impacts on them, definitely psychologically, and then maybe even physically, that may be we don't always think of when we consider these, not arbitrary but these cutoff points that can move around are essentially designed by humans.

AUSTIN BARAKI: Yeah. One of the other interesting things in those papers that I think I shared with you was that they looked at when the concept of harms from screening even emerged and the term harms of screening didn't even appear in the biomedical literature until like the mid 80s to early 1990s. And we had been already doing screening for like a few decades before that. So it's taken us a while to start to recognize the harms of screening and that's in the biomedical literature and then the real world tends to lag behind that quite a bit. And this is evident in the way people talk about testing. And I hear from patients all the time like they want to pursue something and when asked why they're like, well, I've always believed that more information is always better. And that just kind of like, makes me cringe a little bit when I hear that because it's like if you only knew how harmful this

kind of information has the potential to be from a number of different standpoints. Of course, there's obviously with screening using high sensitivity testing, there's a risk of false positives that themselves can have some downstream consequences.

So one that's commonly pointed out, for example, is in breast cancer screening. Women undergoing mammography. There might be obviously you want the test to catch all the breast cancers, if you want to have a good effective screening program, but there's going to be false positives, so they're going to get called back with their result saying, we found an abnormality and then suddenly this woman has very-very scary, so situation where she could be faced with breast cancer. Maybe she has family members who've had breast cancer or died of breast cancer, she knows. And this is such a commonly discussed issue with public health campaigns and things like that around breast cancer messaging. And so there's tons of anxiety, fear, psychological distress over this stuff. There can be in some, for some conditions, there can be stigma related to detecting a particular condition or risk factor depends on how it's perceived in society. There is definitely for many of these conditions, evidence of increased downstream healthcare utilization, even if it ultimately ends up being a false positive or in some cases, perhaps the more stigmatizing conditions, there might be health care avoidance, maybe somebody doesn't want to go back to get their blood lipids checked again, or their blood pressure checked again, or they don't want to go get their waist circumference measured because it's stigmatizing and embarrassing in the clinical setting or something like that. And of course, when you get a positive screen like I said, there's that screening confirmation sequence. Of course, there's now going to be increased downstream testing because you actually have to confirm whether or not that initial positive screen was true or false. That comes with its own economic burdens. There are potential complications. So for example, somebody screens positive for cancer screen, maybe they end up undergoing a biopsy. Maybe their biopsy has a complication of bleeding complication and infectious complication and the number of things that can happen. And then of course, all that can then lead to

treatment, potentially overtreatment, which we'll get to in a little bit. So there are a whole host of downstream consequences of screening that need to be taken into consideration when we're balancing; does this screening campaign, does this test, does searching for this condition in people who are apparently healthy and have no symptoms does it actually help them in the long run? And that's actually a tall order to achieve. There are relatively few conditions that we can search for on a broad scale. And people who feel fine that have a substantial ability to impact downstream morbidity, mortality and we have to be really careful about that.

DANNY LENNON: Later, we'll definitely get to the overdiagnosis, overtreatment, but from a look at what's happening within medicine and also have a screening plays a role there. But then almost a separate avenue not entirely separate, but the preponderance of at home self testing, direct consumer testing that's available that anyone can do. And for people who are healthy, asymptomatic people who are trying to be proactive in I want to stay on top of my health, and there's all these great tests are now affordable that I can go in and I can get maybe could you give people an idea of how that can actually translate into some of these pitfalls that you've mentioned already or these negative effects? Is there any kind of concrete examples to show them, hey, it's, these are real detriments that can happen.

AUSTIN BARAKI: Sure. Yeah. So there are a few that kind of come to mind off the top of my head. One might be there's obviously a lot of genetic screening services that are available. Nowadays people can get their genome sequenced and get supposedly information off of that; whether it's valid is debatable in some context. But one example might be somebody undergoes, goes and sends in their cheek swab gets their DNA sequenced, or something like that. And then again, with questionable, maybe validity to the testing and the information that's being provided, maybe they get a result that tells them that now they're at increased risk of early onset Alzheimer's disease or something like that. And they're doing this and they're like 40 or 45. And so now they're thinking that that would be within the next 10 years that they're going to start

developing dementia with, maybe not that may not be based on accurate or valid or reliable testing information. So now, I mean, it's hard for people to understand what that might feel like if you receive that kind of information. Similarly, if there are other kind of progressive, untreatable neurodegenerative conditions like Huntington's is a big one where once people start to experience some of the symptoms of it, like rates of suicide go way up in that population. And that's a condition that has definite it tends to show up in sequential generations. And so there's a lot of ethical and psychological and all sorts of sociological consequences to genetic testing for that condition and getting that kind of information.

And that holds for a whole host of different conditions is there can be those sorts of harms that may prompt certain behaviors that may either be harmful, or they may not be helpful, ultimately, because what if the information that you got maybe you ended up with a false positive because you don't know how to accurately interpret or confirm this information or there may be no confirmation for it like there is with early onset Alzheimer's, that's like a clinical diagnosis that you can't really, there's no in-vivo confirmatory testing that you can do. Other ones that could be common would be a lot of hormone endocrine related testing that people may then go and choose to act on. They might start taking various supplements that may have more harm than benefit to them based on a certain hormone test and interpreting endocrinological testing is way more difficult than people give it credit for particularly when there are no symptoms. There's all kinds of diurnal variations. You'd probably be into the circadian biology of a lot of these kind of endocrine pathways and so people not knowing this, they might just check a spot hormone level, a spot cortisol level, something like that, and then do all kinds of things based on that because they read about some condition or adrenal fatigue or whatever the case is, that may be unnecessary, may be a waste of resources, maybe more harmful than beneficial. Another one that comes to mind is a PSA screening. That one is one that is historically, was used a ton for prostate cancer screening. It's called a prostate specific antigen despite it not being particularly specific for prostate cancer, and that has,

the rabbit hole that PSA testing has opened up is enormous, particularly due to the nature of prostate cancer itself being most commonly, though not always a relatively slow growing kind of indolent process, that detection, pursuing maybe you end up getting a high level and then you get a biopsy and the biopsy can have complications, bleeding, infectious, neurological injuries, erectile dysfunction, things like that. And then you end up getting treatment for prostate cancer if it's detected that may have never caused you any problems. You may have died before the prostate cancer did anything to you. You may have died of something else and treatment for that may involve hormonal therapies, chemo therapies, radiotherapy, radiation, therapies, all kinds of things that may have never been necessary in the first place. So those are just a few examples of things that are quite commonly discussed and people might choose to pursue. I guess in our lifting world where I sometimes spend half my time with the Barbell Medicine side, lifters are always interested in their testosterone levels. If they start to feel tired, maybe they'll go and get their testosterone level checked. Perhaps get it checked at the wrong time of day or not get it checked properly without confirmation, not checking the subsequent tests that would need to be done to confirm it. And maybe they have a hard time getting the TRT that they might want more than they might need prescribed to them, they go to the black market and get testosterone. That way there's all kinds of ways that this can go that can ultimately cause more harm than good.

DANNY LENNON: And I think, for example, when you bring up the PSA, it's everyone believing well, I've heard like, early detection of cancer is has to be a good thing, right? Because if I catch it early, as opposed to late, how can that not be a good thing? But as I was reading some of the stuff you sent me the same, that there was like data showing, even in places certain doctors ordered a ton of people PSA tests would have a lot more like positive cancer detection. But there is no difference between them and other clinics that in terms of deaths of cancer later on.

AUSTIN BARAKI: Yeah, this is this is basically the concept of overdiagnosis, which is the diagnosis of a disease

“that will never ultimately cause symptoms or death during a patient's expected lifetime.” And it can occur just from the screening interventions that can happen just from getting more advanced, higher tech testing modes that allow us to find increasingly subtle or milder disease. And this gets even trickier because when you detect more subtle or milder disease that improves your apparent success rates, because then you're like, look at all these cases we detected and now they're all doing better, where it's like, well, maybe we're detecting cases that were never destined to cause problems. And there are if you look through the history of screening and all the various things that we have tried, there's a whole graveyard of conditions that we have screened for that ultimately proved not to be beneficial. One of the most dramatic of them was thyroid cancer screening. And again, people hear the word cancer and they're like, that has to be bad, earlier detection has to be better. And so there was a period of time where thyroid cancer was fairly aggressively screened for most of all in South Korea, they screen so aggressively that their incidence of thyroid cancer increased about 15 fold, pre and post once they started doing the screening, and there was no change in mortality. So that's the key point of what you want to look for. Again, where we started out, I said, it's a tall order to take people who look fine, feel fine, have no complaints and ultimately impact their long term risk of disease and death. And this is a situation where we found “all kinds of problems” without actually having any impact on their well-being or risk of death. And so ultimately, that screening program was abandoned.

Prostate cancer screening is still kind of in controversial waters. There's there's an active debate going on. around it. There was just a paper published on the topic in the New England Journal last month that kind of gets into how complicated this is talking about the future of PSA screening and kind of what direction we're heading in. But the problem with this overdiagnosis piece is when you find something on a screening test, we don't know whether it's been over diagnosed at the moment when we find it. When you find something, whether it be a pre malignant lesion, whether you find a tumor or something like that, what's the patient going to assume? Oh, this test just

saved my life because I had this cancer and I didn't know about it the test found it. My life is saved. Because now I can get treated. Again, this may not be the case. There are some very interesting aspects of this some biases that can affect our interpretation of the effectiveness of screening. So one example is the idea of lead time bias. And this is a situation where say patients are going to die at the same time, regardless from a particular condition, but you institute a screening program and you start detecting it earlier. Well, now all of a sudden in the patients who you screen now they appear to survive longer from the time it was detected until the time they die compared to how long they survived previously when they would just present one symptomatic until the time they die. So now your screening intervention looks good, even if it has no effect on their ultimate morbidity and mortality. And similarly, there's another bias called the length time bias. And this is where in cancers, there's a huge heterogeneity in terms of cancer biology. Some tumors are really, really aggressive, rapid progress and kill people really quickly. Others are much more slow growing indolent, they last a whole really long time. If you institute a screening program, statistically, you're going to catch a whole bunch more of the slow growing indolent ones that are around for a really long time whereas the people who have a really aggressive fast growing cancer, they're going to get killed more quickly than you may have time to catch them with a screening test. You're going to miss them that way. And so all of a sudden you do a screening intervention now all the people you catch with screening wow, they look like they live a really long time we're saving lives with screening, when really you're just catching more benign indolent biology and missing the more aggressive cancers. And there's a host of these sorts of biases that influence how we should interpret the efficacy of screening programs that we don't necessarily have all the time to get into all of them. But that's just a couple examples of how we can be fooled by this stuff. And how earlier detection while it may seem better, may not actually be better.

DANNY LENNON: I did a bit of amateurish digging around just to try and read up some more on this. And there was a couple of papers I think, actually, both were in the Lancet one

was on aortic aneurysm, one was on breast cancer, but essentially the similar type of finding that on a large degree of screening that for every one death that avoided due to this advanced screening, there was between three to four people who had essentially been over diagnosed. So diagnosed with something that we've never caused an issue or maybe never been diagnosed in their lifetime. And so that kind of brought me to the question I wanted to ask you, when we know that there exists this ability for there to be overdiagnosis, but at the same time there is some people that are being able to be saved their life. At what point do we have like an acceptable ratio? If that's such a thing. As in would it make sense to screen everyone if we were only saving one person for every 10,000 overdiagnosis? Probably not. But at the same time is there a certain amount of overdiagnosis that's acceptable to save a certain person's life and this gets very strange language, I guess, when we're talking about saving people's lives or not. But how do we view that problem of what is acceptable from a large scale screening perspective?

AUSTIN BARAKI: Yeah, there are multiple layers to this obviously and there is a related conversation going on right now as far as like COVID interventions and things like that as far as what we're doing, what's worth it per given life that may be saved or something like that. So it's definitely gets into some murky ethical waters. I think the way that's typically addressed in the biomedical literature is well, first of all, you need to show that your screening program actually or intervention actually works. That should be kind of the foundation of the discussion. If you're in a situation where that thyroid cancer screening situation in South Korea, where you're detecting a whole bunch of cancers, and nobody's life is saved, that just like throw the whole thing out up front. If you do actually have the potential to save some people's lives, the discussion, at least as it goes in literature tends to focus around the quality adjusted life here as one example of a metric where if you can kind of save or preserve a certain number of those quality adjusted life years then that's kind of where you might tip the scales in either direction. And just like with testing cut offs or cut offs for what number of quality adjusted life years is worth it that itself is a, it's somewhat arbitrary

cutoff, it's a difficult conversation. And it's probably going to be variable even region to region or country to country based on the available resources, economic resources and things like that, at least that's how it's commonly discussed in that context. Face to but all of that stuff is like really like 30,000 foot public policy like overviews. The trickier thing because I'm not in a position to make those decisions. I'm instead sitting down at the bedside next to a person and talking to them about this. And so really where those kinds of conversations end up going is attempting to get as much of an informed discussion on the topic as possible with a given person as far as what is the likelihood that they are going to be benefited by undergoing this screening intervention and that conversation should be had before you go down that rabbit hole not once you have a positive results you try to now dig yourself back out of did I just overdiagnosed somebody or not. Ideally you'd go into it with a plan from the very beginning. We are suppose to like clinicians were taught to try to think at least two or three steps ahead. If I do this test and I get this result, what am I going to do with it, rather than ordering a test and then getting caught with your pants down with the result that you don't know how to act upon. And so there are a bunch of kind of clinical decision tools that have emerged based on some of these data. So one that I like to use when I'm teaching some of this stuff to residents, the University of California at San Francisco, they have a website, the UCSF e-prognosis tool, and that website, it basically, there's a section on there specific to cancer screening with respect to like colorectal cancer and breast cancer screening. And you can go through and you can input a whole bunch of individual patient characteristics into that tool. And then ultimately, using the models that have been established, it tries to give you a sense of what's the likelihood that this patient is going to be helped, compared to what's the likelihood that they're going to be harmed, and you can use that in a conversation with the patient to try to come to a shared plan with the understanding that we're going to do this. We may find some Something if we find something, it may be real, it may not. But once we find something, are we going to act upon it? If the answer is yes, then we can go down this path. If we found something and you would say, no, I wouldn't

act upon it. And even if we did find something, then we probably shouldn't start going down this rabbit hole at all with this screening intervention. So that's kind of some of the different layers as far as how it's discussed in the literature, public policy level, individual patient level and how kind of I approach it day to day because obviously in my specialty, I end up seeing a lot of older folks multi morbid geriatric patients, and the conversations still are going to come up about should I continue getting this kind of cancer screening, and maybe I have somebody who is like maybe approaching 80, maybe they have chronic heart failure, advanced kidney disease, maybe they're on anticoagulation therapies for various other things and things like that, COPD, home oxygen, all these typical things that I might see and the conversations like alright, so are we going to screen your colon cancer? Not only there are a whole bunch of hurdles that we have to jump through to get you screened. But if we find something, are you even a candidate for surgery or for chemotherapy or is the oncologist is going to say, no, he's way too sick, he's not using it wouldn't even survive going through treatment. Okay, in which case, should we be doing this at all. So these conversations need to happen pretty early to have a good plan in place when you're moving forward with an individual patient.

DANNY LENNON: That discussion and collaboration with the patient brings up an interesting idea in that something we've talked about in the podcast before is that people in the general public at large tend to be pretty poor at probabilistic thinking. In fact, you could probably say a lot of professionals in various fields have also the same issue. But when they hear something like, oh, we've detected a certain issue or you're at higher risk of X, being able to think of that probabilistically as opposed to in a binary fashion is difficult for a lot of people to do and it reminded me of I think it was a case study, you actually shared your Instagram story about a particular case that someone had been screened for something in the abdomen, I think. And there was this whole kind of sequence of events that arrived from but the kind of punchline being that at the end, they just weren't aware of the probabilities of what was going on. Could you maybe just recount that case just for people? Because I think it's pretty

interesting number one, and to illustrate this point really well,

AUSTIN BARAKI: Sure that the paper where that came from was from JAMA. I think it was last month. The title of it was the $50,000 physical. And basically, it's talking about the role of the routine physical exam. And this is something that most people we've had kind of ingrained in our minds that everyone should go to their doctor annually and get a routine physical exam done or a routine physical, your annual for example, and people expect to have their heart and their lungs listened to. They might expect to have some other physical examination, somewhat poke and prod on their belly, things like that. And really, it turns out that outside of measuring somebody's blood pressure, and I would argue perhaps their waist circumference, but that's just my bias, that really there aren't any other elements of the physical examination that are evidence based from a screening perspective. In other words, things that we can find by looking, listening, poking, prodding at people who have no symptoms or showing up feeling fine looking fine, that can ultimately improve their long term risk of disease or death.

Now, of course, there are certain specific risk cohorts, certain people with certain demographic factors or other health related behaviors or conditions who, once we detect that then we might look further for something. So if somebody has an elevated waist circumference, maybe I might look more aggressively for signs of insulin resistance or something like that. But again, and people who are apparently healthy with no symptoms, if I listen to your heart in the clinic, if I hear anything, I'm more likely to consider that oh, I think that's something in my ear, probably a false positive rather than something useful that I heard in your, from your heart or if I put the stethoscope on your back and listen to your lungs and I hear a little crackle, but you have no symptoms, you're not complaining anything, no cough, your vital signs are fine. Your oxygenation is normal. We like, okay, just a false positive sound that I heard, right? I interpret that same finding very differently compared to, if I have an inpatient in the hospital who has sepsis from pneumonia and their oxygen saturations is 80%.

And I hear the same kind of crackle. I interpret that very differently based on the context. That's kind of the overarching theme we're talking about with our testing and screening concepts, and so I also not immediately remembering all the details of that particular article, but I think it had to do something like he poked and prodded on this patient and felt something that felt like a mass in the belly and thought it was a abdominal aortic aneurysm and that led to a downstream sequence of testing and interventions and of course, aneurysms are potentially life threatening, dangerous depending on the size and rate of growth and he, may have undergone surgery and the surgery may have been complicated and you can have catastrophic complications that's like vascular surgery is probably among the highest risk kind of surgical interventions that you could have done. And you could potentially die or have a pretty catastrophic complications from something that perhaps never needed to be intervened upon in the first place. And so that's kind of that situation that illustrates something that most people assumed to be really useful as the annual physical, when I think that the there's nothing necessarily wrong with seeing your doctor regularly, of course. But I think that the interventions and the things that we do and those sorts of visits to actually should all actually be evidence based with respect to reducing downstream risk of disease and death. And there are again, relatively few interventions that have demonstrable benefit for that purpose and just like looking and listening and poking and prodding at people who look and feel fine is not one of them

DANNY LENNON: With over diagnosis I know you already clarified but I think it's worth going back over just to make people clear there's the difference between overdiagnosis and an actual outright misdiagnosis.

AUSTIN BARAKI: Yeah. So an overdiagnosis means the diagnosis is actually correct. You actually found the thing that you're saying it is, but that thing is irrelevant to their prognosis, meaning it would have never caused them any problems if it hadn't been detected even though you did, in fact, find the correct thing. And that, of course, may result in treatment to address that condition that itself does not provide benefit, because

again, the condition was never going to cause harm. Therefore, the treatment that you administer only has the potential to cause harm in those situations. Another potential possibility of this kind of testing is a false positive. And this is like in the airport. It's a false alarm. The test suggests that there is a disease but the disease is not truly present. And that's why we do the subsequent confirmatory step. That's why the TSA agent comes in actually takes a look at you to see if you have a gun on you, rather than just assuming that you have one because the metal detector went off and then a misdiagnosis is a diagnosis of a disease that the patient doesn't actually have. And that, of course, is potentially really bad because it results in inappropriate treatment for the wrong condition that doesn't even have the potential to help at all and can only have the potential to harm.

DANNY LENNON: It kind of reminds me of previously we're talking about direct consumer testing where a healthy asymptomatic person is going to order these whole list of tests and try and pick up something, go hunting first that's wrong.

AUSTIN BARAKI: Yeah.

DANNY LENNON: There's the other side of it, then that people can also use that testing where they're sitting at home, and they actually have a symptom. I'll test for these things. And they may get a certain test result back that they're then going to interpret and say, oh, well, this explains why I had this symptom. But then that may be very different to what would happen if you are their doctor, let's say and they'd be gone to you for testing.

AUSTIN BARAKI: Yeah. This is a a situation I mean, diagnostic evaluation is a situation where I feel even more strongly that a trained clinician can be involved and of course this does not eliminate the possibility of missing diagnosis all together because clinicians are people too, we make mistakes. Looking back over the course of medical history we've done some preposterously stupid shit over the centuries. So not excusing things from that standpoint, but doing it by yourself as an untrained lay person is even crazier in my opinion. And so a common example from the lifting world that I'm involved in somebody might feel

tired. Fatigue is obviously a super common symptom. It's arguably a part of life but sometimes can represent an underlying medical issue that's going on. And maybe they're a power lifter, and they're like they associate that they're like, oh, I must have been developing low testosterone. I'm going to go get my testosterone checked. And so they go and they get their testosterone checked. And maybe it comes out lower than they wanted to. And they end up pursuing and maybe even getting treated with testosterone replacement therapy or something like that. Perhaps all along their fatigue may have been more related to a symptomatic anemia or something like that, and maybe their anemia was due to a colon cancer because colon cancers commonly caused slow bleeding and you can get anemic and that's a very common presentation of colon cancer. And that was missed altogether, because the person who did their own self testing doesn't know the differential diagnosis and clinical approach to evaluating fatigue, for example, or they miss hypothyroidism and they started themselves on treatment with the wrong hormone treatment. And in fact, it can be even more complicated because it's common that somebody who has cancer may have low testosterone because that's a chronic inflammatory state that can have consequences. So this is just one I just made this up, but it's a completely plausible scenario where somebody may on their own hunt for I mean, maybe they Google fatigue and they see this that confirms their bias of what they want to test for, they go and they get the testing. Maybe they interpret it either accurately, or inaccurately and then end up going on to pursue treatment or self treatment or supplementation or something like that all along missing the actual issue or potential broader set of issues that may be going on for for them.

DANNY LENNON: From a nutrition standpoint, again, I was trying to think of like, what are some very simple examples people may be using, someone starts going on like a plant based diet, and they hear about vitamin B12 deficiency is common.

AUSTIN BARAKI: Sure.

DANNY LENNON: I've been actually very tired lately. And then they go and get their B12. tested, which on the surface seems

like well, that is inconsequential. I'm not testing for disease. I'm just testing my B12 levels. Maybe they come back low and that explains this fatigue, that could be due to a number of things and potentially something super serious.

AUSTIN BARAKI: Sure. Yeah. And then B12. I mean itself, if we want to go down that example, there's subsequent issues there. Maybe they actually detect a low B12 level and that can arise from a number of different issues and maybe they start supplementing vitamin B12 by mouth, but of course, there are some conditions that result in B12 deficiency where oral B12 supplementation won't work. You need parental or injection B12 therapy due to certain kind of autoimmune conditions and things like that. So they might go on self treating this condition to no benefit for a long time before they ultimately end up pursuing evaluation that gets them the actual treatment that can stand to help them. So overall, I definitely agree that particularly I mean, screening itself is a thorny topic to wade through, but diagnostic evaluations for symptomatic individuals, I definitely think get pursuing that with a clinician is wiser than trying to do it on your own for sure.

DANNY LENNON: And the other thing that you just touched on was also people can identify, let's say symptoms that are maybe fairly generic, that may actually not be a symptom of anything, like you mentioned, tiredness could be just due to being tired in your normal day, but I think a lot of people may be sensitized to that from the term you mentioned around disease mongering that they were that somewhere on the internet, someone's told them about, oh, be on the lookout for these certain symptoms, it'll tell you adrenal fatigue, or whatever it is. And usually it's a raft of general symptoms that may not actually be symptoms of anything. Can you first maybe explain that concept of disease mongering? And then how that kind of fits into this conversation?

AUSTIN BARAKI: Yeah, sure. There's there's a few different ways that this has been described. But basically, it's the idea of expanding definitions of disease to encompass more things. And they may be encompassing more things that don't actually end up relating to downstream

human suffering, which is what we actually care about in the context of medical evaluation and interventions. We want to reduce human suffering and premature mortality and things like that. But we may be expanding these disease definitions to encompass things that don't have any impact on that. Over medicalizing them is a phrase that you'll see used to describe this. Pathologizing them disease mongering that one has a more negative connotation obviously, and it's more sinister. And that one is more often attributed to like pharmaceutical companies that tend to go on, at least in the US put TV ads on for are you experiencing this like insert benign symptom that's part of human life, talk to your doctor about this drug that we just released that can treat your benign symptom that's part of human life. And so that's definitely an issue where it can come from a whole bunch of different sources. I mean, obviously, as our medical knowledge expands, and our understandings of like the mechanisms of certain physiologic processes and disease grows, then we can start to suggest the various mechanistic reasons why somebody might feel a given way and turn that into a disease in and of itself. But the idea, again, is that we're starting to separate like this idea of disease and illness from the actual human experience of suffering, and finding more ways to turn people into patients, particularly when we have a treatment available to offer for a particular condition that incentivizes us to make it into a disease which is problematic obviously.

DANNY LENNON: You can definitely see that in almost a marketing strategy of some people I've seen on the Internet of let's create a blog post about this issue that doesn't exist and then suddenly a few weeks later, we now have a product that actually takes care of this for.

AUSTIN BARAKI: Yeah. There are lots of people doing this and people who I think would merit induction into your and Alan's "Quack Asylum" thing for sure. People send me links to videos or articles all the time about some guru who recommends getting this thing tested that thing tested or worrying about something that they never knew they should be worried about, basically.

DANNY LENNON: Yeah. With relation to overdiagnosis it seems logical that overtreatment can often follow that but not

necessarily always in that manner. They don't have to exist together. Can you maybe explain why that's the case or how they may be divorced from one another?

AUSTIN BARAKI: So this idea of overtreatment and overdiagnosed it ties into the problem up front that when you screen somebody and they screen positive, you don't necessarily know if they've been overdiagnosed in the moment. So then you're faced with a difficult decision, we found something, what do we do about it? Should we actually go on with treatment? And this is it. It can be a difficult conversation with patients, especially in the realm of cancer because cancer is just such this big scary thing and people assume of course, if I have cancer, I want to treat it, I want to cut it out, I want to chemo it, I want to do whatever I can to get rid of it. Because I know so many people who die of cancer, for example, even though there's this enormous heterogeneity in cancers. There are even cancers that, like I said, there's some that are so benign and slow growing, that they never cause harm. They're even some cancers that actually regress. And that's part of the issue of increasingly sensitive testing modalities is catching more and more and more of these things, some of which were bound to actually regress on their own or we're catching pre-malignant cells, who had the potential to go malignant but our immune system, the miraculous thing that it is, can actually go and clear it out. And we ended up resolving without the need for treatment and the risks and complications of things like chemotherapy and radiation, etc. So the problem is, again, that we don't know in the moment, and so you have to have a conversation with the patient, or some people don't necessarily have that kind of, that level of nuanced conversation, say, oh, we found cancer, we should, we should treat it. And committing to treatment for whatever this condition is, can come with its own risks. And so in the case of a condition that was over diagnosed, again, it was never going to cause harm, therefore treating it has no potential to offer benefit. And so it can only cause harm. And these can be potentially serious risks, including death in certain more aggressive, more morbid, more invasive treatment interventions. And so there are some situations like in the prostate cancer world where if somebody decides to get screened, then something maybe they undergo biopsy and it's

confirmed and it's detected, there is a clinical approach of active surveillance, or just simple observation that somebody may elect to undergo under the care of their physician, i.e to deliberately not pursue therapy, but just to kind of watch and wait as a way to mitigate the risk of unnecessary treatment. And then maybe you finally cross some threshold in the future that prompts treatment or you never do, and you never end up suffering as a result. But that itself is a tricky thing because as a clinician, you have your own concerns about the patient, their well being you have medical legal concerns, what if you tell them, we don't need to treat this right now we can just watch and wait and then it ends up spreading or causing something really bad or catastrophic. There's inherent risk there. But the problem is that at the front end, you don't actually fully know the risk ratios of treatment versus no treatment. So you're having to make a judgment call either based on big data, information, epidemiological stuff, or models or something like that, that you're trying to apply to a single patient. So there's a whole bunch of things you have to take into account in these conversations, including patient's values and preferences and things like that. But of course, like you said in numeracy, or a numerical statistical equivalent of illiteracy is very prevalent and it's difficult to understand some of these concepts and it makes it even more difficult to make some of these decisions when they're so emotionally loaded with fear of disease and death like around cancer, for example.

DANNY LENNON: We've talked, mainly looking at from the perspective of the patient, but I'm also interested as to this from a doctor's perspective, to think about psychologically how it may impact the doctor in their own self evaluation of their competency, let's say either positively or negatively through the case of whether there's too much screening done and they're flagging up all these things and how they may appraise themselves versus the opposite maybe they do everything right but some patient gets unlucky, like you said, and something develops. How this is something that you would advise doctors to be aware of, but also how it may play out both towards the positive and negative end of that self appraisal of their competence.

AUSTIN BARAKI: Yeah, I mean, for physicians, you really don't have to be in practice all that long before you start seeing what we call like I intergenic harms related to medical care itself. This isn't something that you need decades of experience to be able to see. We see it all the time. And there's definitely a bias among most clinicians and this is a it's been termed the commission bias. And it's basically a tendency towards action rather than inaction. A tendency to do something rather than not. There is a good series of papers, I think, from some Australian physicians, where they call they described the art and value of deliberate clinical inertia, which is like one of my favorite phrases. The idea of I'm going to deliberately not do anything, watch and wait observe in a particular scenario, but that can be really hard to do. So I tend to work more often in like the inpatient acute care setting. So an example of this might be I have a patient who has bad sepsis. They have an infection, and we have them on antibiotic treatment that we think is going to cover their condition. But maybe despite being on antibiotics for a couple days that they're still on, maybe they're still having fevers. And so my, like, students are in terms of like, oh, we need to change the antibiotics, we're not getting what we're getting. And sometimes that's true. Whereas other times, I'm like, no, we need to give it a few more a little more time before we carry on and continue treating this, this just happened like two weeks ago, where ultimately they just need a little more time and then they stopped having fevers and everything ended up getting better. And that was a situation where I could have done something rather than not done something but my judgment was to not do something and it end up being okay. Of course, that could have gone the other direction. Maybe they got sicker. And that would have prompted me to then change my therapeutic approach in that context. But there's definitely an overarching bias to do things rather than to not in a lot of scenarios and this is both expected and reinforced by the general population, I think. I mean, there's a perceived, there's more of a perceived value from doing things. So how many times you hear somebody who says, I went to my doctor, and they didn't do anything for me? It's like, what are they supposed to do for you, they're supposed to give you

recommendations as far as your health, they're not supposed to just do things to you for the sake of doing them maybe you're in great shape, and there's nothing to worry about. There's nothing to do. That's, that's great news, that was the result of your consultation. So it's kind of like this perception of value that can affect things from how the expectations that are placed on us in a clinical setting, as well as our own biases to do things. And as you mentioned, this can come from medical legal concerns, defensive medicine, defensive testing and ultimately, this can result in these things that have been termed diagnostic cascades or cascades of care. There was a good article in JAMA about this last fall, where they surveyed a bunch of I think, was internal medicine physicians basically like raise your hand if you've been involved in one of these cascades of care that like made you hate everything about what was going on and like everybody raised their hand. I mean I experienced it all the time where I might have to perform an imaging test to rule out some dangerous life threatening thing and of course, that test ends up revealing some other incidental finding. And now I'm forced to, maybe forced or I may elect to have a discussion with the patient say, we found this other thing on the test that we didn't mean to find or to look for in the first place. This is what it could be, this is what it might not be, etc. And sometimes we're forced to keep chasing things and that can be really, really frustrating from a clinicians perspective. And one other thing that I've noticed I mean increasingly in the age of electronic medical records is that a lot of these computerized medical systems that allow physicians to input their orders that way, they come up with like suggested orders and like default orders and things like that when you input like say you put in a symptom and it like suggests a bunch of orders to you. And that itself I feel like incentivizes uncritical behavior from a clinician standpoint. Maybe you input like back pain and then the first suggestion is like X-ray. And it's like, wait. That's not what we're supposed to do for like new onset nonspecific back pain, but it comes up and you might just like say, oh, yeah, sure, let's do an X-ray. That way. I'm like doing something about this, rather than saying, like, let's watch and wait, for example. I mean, in general, this has also been well established in the literature that most

clinicians, and this is not just physicians, this is people across all the healthcare professions, we tend to overestimate the benefits from our interventions, and we underestimate the harms from them.

DANNY LENNON: Yeah, there's almost that pressure to act probably comes from multiple areas that you've outlined. There's probably an internal pressure of I actually want to help this patient. I don't feel like I'm doing nothing. But then there's the patient themselves who tend to go I mean, I don't know how many people that have heard that have gone to their GP or I suppose a family doctor and complained that I went and I have these like symptoms, a common cold, essentially, and he refused to give me antibiotics. And after paying him this money. It's like, so they're going there with this idea of what they want from the doctor before even getting any sort of diagnosis. And then there's always the other layer of legally what may look differently on paper is how someone acted versus didn't act. And it may be that a good decision can still end up with a bad outcome or a bad decision gets rewarded by a good outcome. And unfortunately, people don't make that connection too often.

AUSTIN BARAKI: And sometimes patients obviously get better regardless of what you were going to do anyway. And given our own inherent biases and our own observational experience, maybe we pat ourselves on the back and say that was a job well done. Every patient who I've seen who has ever had a cold got better with antibiotics, and it's like, yeah, no shit.

DANNY LENNON: Alright. But just to pull this back then for what we discuss right at the outset, particularly when it comes to common forms of screening that those of us who are not suffering certain symptoms or maybe would be relatively healthy may look at on an ongoing basis. So I think the most common we'd see in routine blood tests would be going and getting your blood lipids checked, for example, or your doctor takes your blood pressure and so on. If you were to give people some takeaways of the most common tests you see people going and pursuing themselves, which ones are useful to look at on an ongoing basis, which ones they probably shouldn't waste their time with?

AUSTIN BARAKI: I would say upfront again, that taking people who look fine, feel fine aren't experiencing symptoms and searching for problems. It is a tall order to find things that which when you intervene upon them, you can materially alter their downstream risk of disease or death. There are a few of those. And so this applies when I'm talking about just mass whole population screening. So there are very few things that I'm going to say everybody, all sexes, all ages, etc. should get done. Most of the things that I would recommend are going to be somewhat more targeted to certain demographic groups or certain risk groups. And that's just a way of as I said, the predictive values are going to change based on the prevalence of these conditions in the population. So there's a reason why we don't routinely check blood lipid levels in somebody who is like six days old because the prevalence of major atherogenic dyslipidemia in that population is going to be low, maybe one day, they'll do a study and maybe recommendations with respect to lipid screening at birth will change. But that's just an example of we want to target these things to places where the prevalence is sufficient, such that our screening tests are more likely to generate true positives rather than a whole bunch of false positives. And so the place to go for people who are interested in learning about where is the actual evidence on a particular screening intervention, at least obviously, I work in practice in the US and so we follow those guidelines, but the US Preventive Services Task Force source, the USPSTF their website, they have the that's where all this analysis and data are found. And in particular, there's a tool on that website called the Electronic Preventative Services Selector EPSS. And that tool basically you pull it up, there's a web browser version of it, you put in age, sex, smoking history, sexual activity or not. And I think wonder I can't remember if there's anything else just like three or four basic demographic factors. And it spits out all the available screening things stratified by the level of evidence for their use, like level A, B, C, D, I for insufficient data to support or go against screening for that particular thing. They have a phone app and things like that too. And so I recommend that to students and medical professionals as well because that is basically the current clinical guidelines on the matter. Now, you'll find if you look that there are a

substantial number of things one that is commonly discussed and debated is screening vitamin D levels, for example. Lots of people want to do it, what's the harm, etc. As of now, the evidence they report is that there's insufficient evidence to show that there is a clear benefit in like mass population screening for this stuff. And there's insufficient evidence on the harms of it either. Now, of course, there are certain clinical subpopulations in whom I might check the vitamin D level, people who I'm more potentially concerned about bone mineral density issues or chronic kidney disease issues, nutritional deficiencies, things like that I might be more likely to check vitamin D level in those people but you know, as of now, in my current practice, if I had somebody who looked well, felt well was at a healthy body, composition, body mass, waist circumference, good blood pressure, like everything checked out. I wouldn't feel particularly compelled to go and check vitamin D level on that person, just as an example. And again, that evidence is subject to change in the future. Now the things where we have probably the most evidence you were right blood pressure is if we could get more of the populations blood pressure under control, that would have an enormous impact on population wide morbidity, mortality. And of course, we have multiple ways of doing that through exercise, nutritional interventions, medications, etc. The blood lipid one is also a bit interesting in that the current recommendation is that you either check it in men or women who are thought to be at increased risk for coronary heart disease that may be due to say, family history or something like that. Or if there don't seem to have increased risk factors, then you check it in men starting at 35 or older women at 45 or older. Now, in my mind, knowing a bit more about lipidology, as you do too, we share an interest in that I could see that there maybe an argument for checking things earlier given what we know about kind of the the role of the lifelong exposure to these atherogenic lipoproteins over the course of life and there's even a growing discussion in the lipid world for a one time LP(a) screening in life. But that, of course has not yet been incorporated into official practice guidelines. I would definitely be more inclined to check blood lipids in people, for example, who had an increased waist circumference who came in with elevated blood pressure, things like that. And I think that was

probably reasonable to check earlier if you wanted to. But of course, that's where the guidelines stand right now.

There's some other interesting ones. Depression is in the guidelines, but there's even controversy about overdiagnosis and overtreatment of depression here too, meaning diagnosing it and people who don't come in complaining of symptoms but rather they end up screening positive when you go and search for it. Substance use issues, waist circumference measurement, I think probably have value. There are certain risk groups in whom screening for HIV, Hepatitis C infection is recommended. Certain cancer screening so cervical cancer, for sure would do. Colorectal cancer has pretty good evidence for benefit, breast cancer and lung cancer, those start to have decreasing evidence of benefit and more controversy around them. And so those involve important discussions with with the clinician when you're trying to make decisions about am I gonna get screened for this thing or not? But on the flip side of this, as you mentioned, there's tons of these things that we can screen for that, the question is just because we can screen for them, should we. I mean, most people probably don't know that just routine labs like what we call complete blood count CBC or a complete metabolic panel, we don't actually have evidence to support routinely measuring those things in people like I can count on it's unlikely that I'm going to spontaneously discover an asymptomatic leukemia in somebody that's going to be of significant clinical consequence. So that's just one example of something where people tend to order those labs kind of indiscriminately without realizing like is there benefit to checking these things or not. PSA, as I mentioned, is a whole really-really thorny rabbit hole to go down. So I would be very cautious with that and do that with the clinician if you're going to. I think that most nutritional markers as we talked about earlier, the vitamin D1 that one I suspect the evidence is going to be evolving pretty rapidly on in the near future, at least. I hope we get better evidence as far as is it beneficial to screen more broadly for it but a lot of other nutritional markers, like if you're checking folate levels or other things like that most of them don't really have much clinical utility. And there are

definitely some gurus in this space. Some who maybe write entire e-books on how to test yourself for various nutritional deficiencies and things like that. And again, nutritional deficiencies particularly in the developed world and people who have not undergone bariatric surgery or have malabsorption issues, the prevalence of real legit nutritional deficiencies is so low in that population, that the predictive value of your test is poor.

Other things like inflammatory markers, and people who again look well, feel well have no symptoms checking ESRs and CRPs on people not useful outside of select clinical scenarios usually where people have some sort of a symptom or complaint. Similar with hormone testing, genetic screening. My nightmare above all else is people who sell like full body MRI screening for people. That is like the worst possible thing that you can do try to find every like incidental like variant of textbook norms in people and pathologize them. So they're worried about like their every little tissue in their body. So do not pursue those kind of things.

DANNY LENNON: I remember *Scrubs* did like a whole episode on that concept.

AUSTIN BARAKI: Yeah. It's just awful. Most and as we said earlier, like most things from, like a functional medicine practitioner, they tend to go way overboard with tests that are either lacked validity, lack reliability, or are essentially uninterpretable, particularly in the context of a patient who looks well and feels well. I mean, the temptation to want more information and more data is really strong. And so I generally recommend against most I'd say all direct to consumer testing services for screening purposes. For diagnostic purposes I think that you know, it would be wise to have a clinician at least involved to reduce the risk of missing things as much as you can. But when it comes to screening, we really want good data on the intervention to demonstrate that they can actually reduce morbidity and mortality, reduce human suffering, hit away that outweighs screening related harms. The difficulty here is that that kind of data typically requires fairly large cohorts. And obviously, it needs to be relatively long term. The larger it is, maybe you can get away with

making it a little shorter and vice versa. But if you want to demonstrate effectiveness on all cause mortality, it usually needs to be pretty big or pretty large or both and and our data on those things is limited. And so in the face of that limited data, with significant potential for harm in many conditions, we ought to be pretty careful and pretty selective with just like indiscriminate medical testing, especially in people who seem fine. So I would just tend to I get a lot of patients outside the hospital setting who come to me and they say I'm really into optimization and then is like a red flag for me that they're going to want to like test and search for everything. And so that usually prompts this conversation is hey, are you meeting like, you know, I wrote an article on our website about like, what our priorities should be for health. Are you meeting these health priorities? Are you meeting physical activity guidelines? Is your waist circumference body fat at a good place? Are you sleeping well? Things like that. If you're not meeting those things, then don't worry about all this other stuff. Focus on those things. And then we can discuss what is worth or isn't worth looking for. But really, like, I think it's best to stop searching for problems. When you feel fine, and you're doing fine outside of this, again, small set of things where we have good evidence that high blood pressure doesn't tend to cause many symptoms outside of super extremes. But that's a situation where if we can detect real legit high blood pressure, like if we detect your resting blood pressure is 150 we have a huge potential to decrease morbidity mortality. But again, that comes with tricky things of its own. So you know, the measurement of it is trickier than people think. The risk of false positives is trickier. Like if we if we sat you or Alan down in a clinic to check your blood pressure and in walks Dr. Malhotra [PH] to check your blood pressure, like we're going to get a false positive reading you guys blood pressures are going to be sky high. So the interpretation is going to be tricky there too. So this stuff is rife with potential potholes and places where people can go wrong. So that's my caution.

DANNY LENNON: So before we get to the very final question for people looking to find you on the internet, Austin, where can they go on social media, the internet and all that type of stuff?

AUSTIN BARAKI: Yes. So probably the easiest places that are a Barbell Medicine website, barbellmedicine.com. I'm on Instagram Austin_Barbellmedicine. I'm on Twitter, at AustinBaraki my name and yeah, that's probably about it.

DANNY LENNON: Awesome. And so with that we come to the final question that I always end the podcast on can be completely outside of anything we've discussed so far today, and it's simply if you could advise people to do one thing each day that would have a positive impact on any area of their life. What would that one thing be?

AUSTIN BARAKI: Train. Yeah, I'm a big proponent of regular exercise and and probably, I'm more biased to that even over a lot of other things that maybe even have more evidence for benefit than that. But that's my bias; train.

DANNY LENNON: Yeah. Thank you so much, man. It's been an absolute pleasure. And also thank you for helping me learn more about this particular area. I've really enjoyed it and I've really enjoyed this discussion. So thank you for being so kind with your time and information.

AUSTIN BARAKI: Yeah, no problem, man. Happy to help.