Emily: I'm Emily Kumler and this is Empowered Health. Last week on Empowered Health, we talked about mammograms[1] and the efficacy of mammograms as a test for detecting breast cancer. We also got into this idea of over-diagnosis[2], which is something that's being spread around and becoming more sort of a popular debate in mainstream media and in obviously medical corridors. But I think one of the big takeaways for me from last week, and you should definitely listen to that episode if you haven't already before you listen to this one, is this idea of sort of population-based recommendations and how a lot of the recommendations that we get are based on huge cohorts of people, but that when it actually comes down to you, you kind of have to know your body and your genes and your predisposition for any given illness or disease or condition because you may be more prone to something than somebody else. And that's sort of up to you to advocate. So this week we're going to talk to somebody who's a radiologist[3] who is a very big proponent of mammograms. He feels really strongly that this effort to tell women not to get mammograms is misleading and dangerous and also you know, potentially you know, not to get conspiracy theory, but I think he feels like it's a war against women in some way. That's what he will tell us. I want everybody listening to be super alert to all of the statistics that are thrown around. This is definitely one of those episodes where we're going to break out some of the math for you guys so that you understand where people are coming up with such different numbers. This was a huge frustration for me when I started looking into this topic and trying to figure out for myself like should I have a mammogram, or should I not? Because both sides have really compelling numbers that they tout around and it's important to understand the difference between absolute risk and relative risk[4], which we'll explain more in the episode, but just as a sort of backgrounder on that: absolute risk is your absolute chance like you walking around as a person in the United States, population-based, what is the big picture? How likely am I to develop this? Or comparatively, relative risk is looking at two cohorts of people who have this and comparing them. That's always going to be a smaller and more significant number and something that people will throw around a lot because it makes the research look more valid. You really want to know your absolute risk because that's going to tell you where you fall in all of this and if it's significant or not. So that's an important sort of just disclaimer at the beginning of this. It's not a huge math episode, but it's a little bit, and I think those statistics are so easy to manipulate and it makes me really frustrated because I think we all want good information and we want to know that people are being honest with us and that is a really easy way to trick people in a very

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[1] https://empoweredhealthshow.com/mammogram-screening-breast-cancer/
[2] https://www.ncbi.nlm.nih.gov/books/NBK430655/
[3] https://www.acr.org/Practice-Management-Quality-Informatics/Practice-Toolkit/Patient-Resources/About-Radiology
[4] https://www.breastcancer.org/risk/understand/abs_v_rel

compelling way. So our guest this week brings up a lot of really good points and I think it gives us all a lot of food for thought.

Dr. Kopans: My name is Dr. Daniel Kopans[5]. I'm a professor of radiology at the Harvard Medical School and founder of the Breast Imaging Division at the Massachusetts General Hospital[6]. I've spent the last 40 years of my life trying to develop better ways to detect breast cancer at a time when it's curable.

Emily: Part of why I was so excited to talk to you is because there's a lot of confusion about mammograms in particular, whether they're the right thing to make as sort of like a mandatory screening for women or whether they're finding cancers that wouldn't spread. And I know you've spoken[7] a lot and written[8] a lot on this topic, so if you want to just start by, I guess making the case for mammograms, which seems to be the side that you're on in this, you know—I guess becoming a debate.

Dr. Kopans: It shouldn't be sides. All of the scientific evidence shows that detecting breast cancers earlier allows many women to be cured. Treatment has gotten much better over the years. But most of the treatments that have improved are those that delay death but don't actually cure the cancer. You can't at this time, unfortunately cure advanced cancer. So the discussion is about how important is early detection. It's been proven in one of the most rigorous scientific studies called randomized controlled trials that women who participate in screening have a much lower[9] risk[10] of[11] dying[12] from breast cancer than women who don't. I think the problem has arisen because unfortunately we don't cure everyone. And so the argument is made, well, you know, screening must not be that good because we're not saving everyone's lives. First of all, we found that[13] the Harvard hospitals that a large percentage of the women who die from breast cancer, over 70% are among the small percentage of women, 20% who weren't participating in screening. So that's additional information that early detection is critical. There's also the problem that there are some breast cancers that have already spread out of the breast into the rest of the body and that's called metastatic spread. They've gone to other organs like the liver or the bone or the brain. That can happen very early, fortunately fairly rarely, but it can happen early in some cancers even before you can find them. And there are some cancers that never spread. They get very large in the breast, but a woman dies, for example, of heart disease, and the breast cancer never bothered her. The problem is we don't know how to tell what a cancer has already done once

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[5] https://giving.massgeneral.org/cancer/honorees/daniel-b-kopans-md/
[6] https://www.massgeneral.org/imaging/approach/clinical-divisions/breast
[7] https://www.medscape.com/viewarticle/874713
[8] https://www.wsj.com/articles/daniel-b-kopans-mammograms-save-lives-1400800454
[9] https://www.ncbi.nlm.nih.gov/pubmed/11335897
[10] https://www.ncbi.nlm.nih.gov/pubmed/12209737
[11] https://www.ncbi.nlm.nih.gov/pubmed/17149701
[12] https://www.ncbi.nlm.nih.gov/pubmed/20512656
[13] https://www.ncbi.nlm.nih.gov/pubmed/24018987

we've found it unless there's obvious evidence that it's gone to other parts of the body. But oftentimes we have no way of telling that even though at a microscopic level there are cancer cells in other organs, we also can't tell if someone's cancer is never going to bother. I think the problem is that those two events, the woman who has metastatic disease very early in the growth of her cancer or never has metastatic disease or dies from some other reason, are at the ends of the spectrum. Most women who develop breast cancer, if they live long enough, and it's not treated properly and not caught early enough, will die from their breast cancers. But again, I think the people who would like to reduce access to screening, I think, play on the fact that we don't cure everybody even when cancers are found earlier. The bottom line though is that we've reduced the death rate in the United States since 1990 by over 40 percent.[14]

Emily: Well, so that's a relative risk, right? Cause I think it ends up, I mean, we just actually looked up some of these numbers and I think it goes from being about 20 per 100,000 tests to 26 per 100,000 deaths.[15] So that's an additional six people out of 100,000. Okay.

Dr. Kopans: So it's gone down. I don't know those particular numbers, but the death rate from breast cancer going back to 1940 was a flat line[16]. Nothing changed even as we got better at treating it in the years we weren't screening for it. And so the death rate had remained unchanged. And then in 1990, soon after screening began and treatment got better, no question about it. The death rate began to fall. So there are almost half as many fewer women dying each year of breast cancer than would have died, had that rate continued unchanged. And I'm not sure the numbers that you got I'm not sure what those represent. Everyone agrees the death rate from breast cancer has declined. The debate is, is it mostly due to treatment, or is it mostly due to early detection? I would argue based on all the scientific evidence that is mostly due to early detection allowing treatment to work. Something that we don't think about is that men get breast cancer. We get it at a much lower rate than women. There are about 2000 cases of male breast cancer every year,[17] whereas there over 250,000 cases in women[18], but breast cancers behave about the same in men, and they're treated the same way. Yet remember I said in 1990 the death rate for women began to go down, and in men it went up, stayed up for a few years, and then came back down to the 1990 level and it stayed at the 1990 level right through to the most recent data. It hasn't gone down, whereas for women, it's continued to go down. So again, men have the same access to treatment and the same treatments,

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[14] https://www.cancer.org/latest-news/report-breast-cancer-death-rates-down-40-percent-since-1989.html
[15] Actually it is 33 per 100,000 now
[16] https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2017-2018.pdf
[17] https://www.cancer.org/cancer/breast-cancer-in-men/about/key-statistics.html
[18] https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer.html

but we die at a higher rate than women do. And the only difference that I'm aware of is that men don't participate in screening.

Emily: Okay, I'm just going to stop Dr. Kopans there for a second because this is where we get all wonky with statistics and I want to make sure that we are really all on the same page and very clear about what he's saying and what I think so many people say, but maybe don't completely understand how the statistics work and I don't think that that's happening with Dr. Kopans per se, but I think for myself and for lots of other women out there, when we hear this 40% decrease since 1990 that sounds awfully compelling. But when I actually go back and we looked at the numbers very closely, what we found was, and I think this is such an important point to make because people often report relative risk values alone, which can be inappropriate and misleading for the individual and certainly for the public. So here's what I mean. When Dr. Kopans says that annual breast cancer deaths are down by 40% since 1990 he's reporting relative risk alone. If you're a healthy woman who wants to know what the probability is that you will die of breast cancer, a 40% relative decrease tells you the individual virtually nothing. Okay, so let's try to break this out so you can see what I'm saying and everybody can kind of feel confident in this because I feel a little manipulated by all of this. What you want to know or I guess what you need to know is the absolute risk and the absolute risk difference. Today, the age adjusted us death rates for breast cancer in women is 20 per 100,000 women in the United States in 1990 it was 33 per 100,000[19] going from 33 deaths to 20 deaths is in 40% relative risk reduction, which is what we just heard. But those 33 and 20 deaths were per 100,000 women. So let's see what happens when we look at these numbers. Per 100 women today, the age adjusted U.S. Death rates for breast cancer in women is 0.02 per 100 women in the United States. In 1990 it was 0.03 per 100 I hope you're still with me. In other words, while the relative risk reduction was 40% the absolute risk reduction was drum roll please. 0.01% which of these numbers sounds more impressive to you? Clearly the 40% number sounds better than what is pretty close to zero. Um, so I think we need to just take a second and let the thinkin imagine if Dr. Kopans had said the bottom line is that we've reduced the death rate in the United States since the 1990s by 0.01% keep in mind that those are annual death rates. So let's look at a lifetime risk of dying from breast cancer instead today, the estimated risk that a woman will die from breast cancer in her lifetime is 2.6% [20]in 1990 that risk was 3.7%[21] hope you're sticking with me. This is maybe boring, but also really important. So if we take these numbers at face value in 1990 the lifetime risk of dying from breast cancer was 3.7% today it's 2.6% this is a relative risk reduction of just under about 30% the absolute risk reduction is 1.1% over a life time, 1.1% over a lifetime. If you want me to tell you what the relative risk reduction was, that's fine, but it's only fine if you also tell me what the absolute risk is.

[19] https://seer.cancer.gov/csr/1975_2016/browse_csr.php?sectionSEL=4&pageSEL=sect_04_table.06
[20] https://seer.cancer.gov/csr/1975_2016/results_merged/topic_lifetime_risk.pdf
[21] https://seer.cancer.gov/archive/csr/1973_1993/breast.pdf

Otherwise, you're not really telling me anything meaningful. So here's an analogy that might help. Let's say there's a sale on a dozen eggs. Usually the carton of eggs cost $3 and 70 cents but there's a 30% off sale and we're going to take that 30% off the normal price of $3 and 70 cents and so now it comes to $2 and 60 cents but imagine that the grocery store didn't provide you with the actual price of the eggs. This is the same as not telling you what your absolute risk is. Why does that matter? Imagine another grocery store is saying we're also having a 30% off sale. So you rush over, you grab your eggs, you rush to the checkout line, hoping that you can get there before the sale ends. The cash register person rings you up for the eggs and cheese tells you that you owe $260,000 for your carton of eggs. That's a little shocking, right? But it turns out it's still the same. You still got a 30% off what the original price was, which was in this case $370,000 it's true that both grocery stores are knocking off the 30% off their eggs, but what we really want to know is what was the original price? Cause if you don't know what the original total number was, what are you going to pay, then you're obviously not going to, the price off doesn't make that much of a difference, right. That relative reduction in is a lot of what we're talking about here, but you need to know what the total numbers are. So for one store who's charging $2 while the other store is charging $200,000 this is pretty important to understand whether we're talking about eggs or we're talking about mammograms. So let's say that you knew your risk of dying from cardiovascular disease would go from 37% to 26% by getting an annual checkup. Your relative risk would decrease by 30% in this case, your absolute risk of dropped by 11% if your risk of dying from a disease goes from 3.7 to 2.6 your relative risk dropped by the same 30% however, your absolute risk dropped by 1.1% okay? I hope I haven't lost too many people. I really want people to understand that it is so much more effective to talk about really, really significant sounding numbers, like 30% or 40% but it doesn't tell you anything unless you know the total number because literally it's just telling you the relationship between those numbers, which is why it's called relative risk, right? Versus absolute. Absolute is a whole number. So with mammography, here's what might be surprising for you to learn if you're not already surprised or bored or asleep. Wake up because this is important for women. Between the ages of 39 to 49 that don't get an annual mammogram over the course of those 10 years, the breast cancer mortality rate per 100,000 person years is about 36. Another way to put this is 36 out of 10,000 women over 10 years will die of breast cancer. In other words, the 10 year death rate is 0.4% or four in 1000 or not even talking about one or 2% difference. We're talking about fractions of a percent difference, meaning less than one woman per 100. We're talking about fractions of women, not actual women, unless we Jack that number up, the number of women who are screened up to about 10,000 women over 10 years. One reason why the field uses terms like person years, which you have to really dig back and figure out what is a person year, right? So all of this stuff is made I think to make it, it feels like taxes are something that it's like literally makes you feel like you can't understand what they're talking about. So the field uses terms like person years and a denominator of 10,000 and not a hundred which is how we usually talk about

percentages and it's a little awkward to say that, right? Because it would be super awkward to say that we prevent 0.03 deaths from breast cancer for every hundred women we screen in this age group for 10 years, but this is factually what they are saying. Those are the numbers. So they jack the numbers up to 10,000 women so that they can get a whole number. Reportedly, mammography in this age group prevents 2.9 deaths for every 10,000 women screened over 10 years. How do you save 0.03% of one life? You don't. That's the point. That's why this is almost more like the lottery when, I don't mean to say the lottery. That sounds like a terrible analogy, but it's like really does sort of explain the point. You don't obviously win the lottery if you get breast cancer, but if we think about this, like the odds about the lottery, then you start to get the image of how insignificant these numbers are. Over 3000 women need to pitch in and get 10 mammograms over 10 years. So that one woman is saved from dying of breast cancer. Should I say that again? Over 3000 women need to pony up, pay the money, get their boobs squished in the machine and get 10 mammograms over 10 years so that one lucky woman is saved from dying of breast cancer. By the way, this is, if we take the numbers at face value, which I think is a big assumption considering how small they are. Right? So like the smaller the statistics are, the more there is room for error. And in this case, if there's any error at all, I mean like it becomes completely insignificant. So the report had relative risk reduction for women that get 10 years of screening compared to those that don't is about 8%. 8% relative risk reduction, but this is an absolute risk reduction of 0.03% so the example I just mentioned of preventing is 0.03 breast cancer deaths per 100 women screened over 10 years is not hypothetical. These are the actual numbers that are being reported. Even if you believe the 8% reduction in breast cancer mortality risk for 10 years of mammography is 100% accurate, it's virtually useless to know that this reduction exists without knowing what the absolute risk reduction is. Think about the costs, the financial, the emotional and otherwise of actually getting a mammogram every year for 10 years. Think about the costs financially, emotionally, and otherwise of actually getting a mammogram every year for 10 years. Keep in mind that on average there's about a 10% chance that you'll find a false positive reading each time you get a mammogram. In other words, a 10% chance that you'll learn the mammogram found something abnormal and you'll likely need to get a biopsy or this has happened to me. You get an ultrasound and then another mammogram and then another ultrasound and then they do a biopsy and then sometimes after that they want you to come back six months later and do it all over again and then after you've been put through all of that, it's determined that that's a false alarm, that there is nothing wrong but that takes an emotional toll on you. And for me, I had to miss like three days of work to go in for all the testing and do all this other stuff, which obviously if I have cancer I want to know and that's important. But the point of breaking these stats down, it's to show you that it's really highly unlikely that this test is going to find the breast cancer or that I have breast cancer in the first place. Before I go completely down the rabbit hole. I just want to remind everybody of this one thing which I think is a really important tip to keep in

mind. Anytime someone tells you about an increase or a decrease in risk, you need to ask if it's an absolute risk or if it's a number that she's comparing as a relative risk. Is she comparing death rates of 30 and a hundred people or 30% or three and 10,000 people or 0.03% This is absolutely, pardon the pun. Critical to understand. Okay, one more example to bang the point home. Let's say that there is a big power ball jackpot tonight and I asked my friend to buy me two lottery tickets. She comes back with one ticket and I turned to her and say, thanks a lot. You just reduced my risk of winning the lottery by 50% Relatively speaking, I'm right, but what are my chances of winning the jackpot with one ticket versus two tickets, one in 292,201,338 versus two in 292,201,338 Did you get that? I just added the two. That's the only difference. Otherwise the total number stays the same. So I went from having a 0.00000068% chance with two tickets to a measly 0.00000034% chance. But my relative risk reduction was 50% so I don't mean to make a joke of any of this because I also think a lot of times we're told this stuff in a way where we're already feeling vulnerable, right? So like you're thinking of going in for a mammogram or you got a mammogram and it's come back with some sort of funny result that you need to follow up with. Or you find out that you had cancer and you didn't get a mammogram and you're regretting that choice. This is usually when people look into this kind of stuff, right? Or somebody that you love is being exposed to this kind of testing? And I think you know what we'll hear and what we talked about a little bit last week too, is this idea of like you got to know yourself. I mean I, this is like ad nauseum, what I say every week you have to advocate for yourself. So if you have a greater risk of breast cancer, maybe some of this information changes for you. Maybe psychologically it helps you to go in for this kind of test because it allows you to feel relaxed. Even though we're trying to explain that the sort of efficacy of the test isn't great. But I also think like this is a conversation you should have with your doctor. Right? And it shouldn't be the kind of thing where like the doctor doesn't actually know that most of the risk being reported is relative risk and this idea that nobody seems to understand myself included until fairly recently. The difference between absolute risk and relative risk and what is always reported in the news is relative risk because it sounds way more significant and way more impactful and therefore it gets picked up in the media. I mean I've even seen stuff where they don't even say they say your risk without saying your relative risk, which is a massive difference, which I hope you all now understand. Okay. I'm going to get back to the interview. I just wanted to take that break to break out these stats and I think that Dr. Kopans is somebody who clearly cares a lot about women's health and as you'll hear when he and I get into the conversation more, he acknowledges this is not a great test, but it's again like the best we've got and I'm just frankly really fed up with all of this. It's enough. Women's bodies are important and we need to have testing, but actually helps find cancer and helps find cancer that will spread and kill us. And we need to have more research being done on the kinds of cancer that actually kills the metastasizing cancer. So

anyway, we kinda got into that last week. If you haven't listened to that episode, please listen to that episode. I'm going to stop ranting. Okay, back to Dr. Kopans.

Emily: Now if we are going to sort of go to this idea that these in situ tumors[22] may not ever metastasize, then you're catching tons of cancer the person would never have died of—potentially, that's the theory. So if we go with that as a thought experiment, then we're also going to say, well the survival rates should be better because we're catching all of these cancers that never would've killed anybody. So those two sort of factors of like how do these numbers actually compare to the overall denominator. As well as, there's a much bigger pool of people who are being screened. So your total population of people who are going to be found to have cancer, whether it spreads or not, is much larger. Right? So this is why a lot of times, you'll hear people compare breast cancer screening to prostate cancer screening because there is reason to believe[23] that if you were to do an autopsy on every man over 80 most of them would have prostate cancer. That's not what's going to kill them. So this is really, really, really fundamental to this topic because we're going to go back to the guest and he's going to sort of explain this more, and I'm going to try and challenge him a little bit. But it's one of these things where I feel like people are so mired in their own data sets or in the statistics that they believe are the most significant rather than looking at the overall picture. I mean, I feel like it's really important to unpack a lot of the stuff that you're talking about. And some of our listeners will be sort of aware of some of these things. And some of them won't. So I feel like it's really important for us to try to explain these things in as simple ways as possible. But I think one of the most important things, which I like to say over and over again on this podcast is whenever a woman goes in to see her doctor and the doctor is recommending some treatment or medicine or whatever, the most important question for her to sort of ask is have there been randomized controlled trials on this intervention with people who sort of look like me. Now in this case, that makes it a little bit easier because mostly women are having mammograms and that does it have an impact on all-cause mortality? And so you're saying it does that there has been a clinical trial that has looked...

Dr. Kopans: No. All right, let me interrupt you for a second because you're going to throw out all-cause mortality. You have to realize that only 3 percent of women who die each year die from breast cancer. Even though it's the most common cancer in women. Lung cancer still kills more women unfortunately.[24] Well I guess for women with breast cancer, I guess it's fortunate. The point is to reduce all-cause mortality in a randomized control trial would require almost two and a half million women just by reducing breast cancer deaths. So the people who argue it

[22] https://www.breastcancer.org/symptoms/types/dcis
[23] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4485977/
[24] https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf

hasn't reduced all-cause mortality are just they're making it up. It's a fantasy. If I reduce breast cancer deaths by 30% that would mean I'm reducing all-cause mortality by 1%. Remember breast cancer makes up 3% of all deaths in a population, so looking at the randomized control trials for all women, mammography screening clearly reduces deaths from breast cancer, but the trials aren't big enough to show that its statistically significantly reduces all-cause mortality. If you look at all-cause mortality among women with breast cancer in those trials, which is more like in treatment trials; all-cause mortality is brought up mostly in treatment trials because you want to be sure that your treatment isn't killing women even though it's saving them from breast cancer. For example, the radiation treatment trials caused heart disease in some women. And so if they hadn't looked at all-cause mortality, they wouldn't have known that. But remember, in treatment trials, most, all the women have the cancer.

Emily: Right. But I think that the reason to bring up the all-cause mortality, at least from my perspective, and certainly correct me if you don't agree with this. But that maybe, there are these cancers that are being detected with a mammogram that wouldn't have necessarily spread, right? Which obviously hindsight bias is wonderful and we don't know if they would spread or not until they do. Theoretically, if you're treated with chemo and radiation, you are put at a higher risk for developing cancer again. Right? Or having a cancer come about.

Dr. Kopans: So what you're bringing up is a different point from all cause mortality. It's over-treatment. I completely agree with you. I mean we over-treat everything in medicine because we don't know how to predict who is really going to benefit from treatment. For example, if you get a pneumonia and let's say it's a bacterial pneumonia, not viral pneumonias[25] we know you really can't treat but bacterial pneumonia, those we have antibiotics for. So if you have a bacterial pneumonia, everyone gets antibiotics because it could kill you. Now many of those people will get better on their own. We don't know who they are. So that's why we treat everyone with antibiotics. But some of those people are going to be harmed by the antibiotics. They're going to have an allergic reaction. The antibiotic could cause an overgrowth of a new bacterium, which is going to be even more deadly. You can even respond to the antibiotics and have a severe lethal reaction. But for the most part, you treat all bacterial pneumonias because most people benefit. We end up in all of medicine over-treating. In breast cancer there are huge studies that show that for women who have real cancers, if you will, only a small percentage of them benefit from systemic, you know, from chemotherapy. And yet they're still treated because there's no, we have no other choice. You don't know who is going to benefit and who isn't. I would argue though, that's not the fault of mammography. You know, that's not the fault of screening. That's the fault of a pathologist[26] who can't differentiate which

[25] https://my.clevelandclinic.org/health/diseases/4471-pneumonia
[26] https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/the-pathologist

cancers are going to be potentially lethal and which aren't. And it's the fault of oncologists[27] who haven't figured out how to best treat things. It's like saying, well, you know, seatbelts save lives, but they also get in the way and they can kill people. People can get hurt by the seatbelt. They can get trapped in a car. I mean, this gets to be a little ridiculous, but we wear seatbelts because for the most part they save the most lives despite the fact that there are downsides. So over-treatment we can talk about that in more detail. I don't treat breast cancers I find but over-treatment is not the fault of mammography. It's the fault of our inexact medical system.

Emily: I think that my concern is that if we, if we're reliant on an, you know, a test, right? Let's just call it mammography, a test. The test is far from perfect. Right? Because there's a lot of times that people get called back. So 10% of the time you will have a false positive test.

Dr. Kopans: No, that's not a false positive test. It's called false positive because that's used to make you get nervous. No one is told, oh you have a breast cancer, you have to come back. They're told we need to get some extra pictures. Go ahead, finish your thought and then I'll jump back in or did I destroy your thought?

Emily: No, no, no. I mean I think there's a couple of things. So like we had our resident statistician just like sort of run some numbers for us to try to figure out statistically like is this a test that is, you know, a sound measure for predicting whether you have cancer or not. Right. And I think it's about 2% of the population that has cancer or breast cancer or that will be found to have had breast cancer in a year in the U S population. But it seems like when we look at these numbers like to find a true positive, which would be somebody who we know has cancer and the test has found that they have cancer versus the false negative, which is somebody who does have cancer, but the mammogram misses, it ends up being 84% that it finds it.

Dr. Kopans: Yeah no one is—I'm the last person to say this is the ultimate answer to the breast cancer. We don't have an ultimate answer to breast cancer. Treatment is not the ultimate answer. 40,000 women are still dying every year in the United States[28] despite treatment and at the Harvard hospitals. And there was a huge study in Sweden.[29] It showed the vast majority of those women, were probably not participating in screening. And even if they all did, screening probably reduces the death rate by 50% but that's tens of thousands of lives each year. You know we don't—no one has ever said that screening saves everyone. But if you don't get screened, you're at a higher risk of dying from breast cancer than if you do.

Emily: So this is what I need you to explain to me because this is where I get confused. Like I look at these statistics and I'm like, this test looks terrible. Like I want to follow through on this because I know you have a different point of view and I want

[27] https://www.cancer.gov/publications/dictionaries/cancer-terms/def/medical-oncologist
[28] https://www.breastcancer.org/symptoms/understand_bc/statistics
[29] https://www.ncbi.nlm.nih.gov/pubmed/12209737

to make sure that I'm not missing anything because when you look at the negative predictive value, right? Which is like...

Dr. Kopans: Oh, the negative predictive value is way above 87%.

Emily: Yeah, I know it's 99.8[30]

Dr. Kopans: Right. Okay, I'll accept it.

Emily: What we have, and I think these numbers are from 2000.. Up to date. That was in 2017 so they're not maybe the most current. And so, I mean I sort of feel like if you were like, this makes me feel like if we were to unplug the machine and have people walk in the door and we say like, okay, 2% of the people that come in—we're going to say you have cancer. Or like you know, like it doesn't feel, it feels like almost the same as just randomly assigning value.

Dr. Kopans: mean, listen, we're in a world of numbers and they're very important. But the point is breast cancer there are what, over 250,000 new cases of breast cancer each year[31]. But as you point out, we've got a huge population of women in this country so that amounts to, I don't know what it works out, but it's probably between two and six cancers per thousand women this year. Well that's tiny. Why are we worried about those few women and all the almost a thousand women aren't going to have breast cancer. And you could make that argument. If I were a woman I'd be a little annoyed by it cause if I have breast cancer it's me. It's 100%. There's cervical cancers at even even a lower rate and yet we test for cervical cancer. I mean all of these things are low probability.

Emily: That you're going to find it.

Dr. Kopans: Well low probably you're going to have, forget about finding it. It's a low probability that you're going to have it. I mean the vast majority, vast, vast majority of women are diagnosed with breast cancer each year. But I would say 250,000 is not a trivial number. And if you're one of those women, it's very important to you. So I think the problem that I see, and you're sort of explaining it to me, is the people who oppose screening, not you, but the people who are arguing to oppose screening, don't want to pay for it, but they don't want to say we don't want to pay for it because you'd be telling women, we don't want to pay to save your lives. And I suspect, I could be wrong, women would take offense of that and say, Oh really? You know, what's my life worth? And so they don't say, we don't want to pay for it. They say, Oh, we looked at it, it doesn't work. Or look at all these women who are going to be made anxious because they're called back for additional evaluation and so on. Listen, every woman should make her own decision. And it's not just women 40 to 49 it's all women. No one is forcing anyone to be screened. My argument is

[30] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2224070/ - Some studies say **99.6%**
[31] https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer.html

that women aren't being told A: the truth and B: all the facts. So for example, the United States Preventive Services Task Force[32], and if you read them, but they said carefully, they said you save lives by screening starting at the age of 40. It says that right in there in their piece they use the National Cancer Institute, CISNET modeling group[33], these are computer models at the National Cancer Institute supports, and by the way, the National Cancer Institute is not a supporter of breast cancer screening. The CISNET models all show you save the most lives by annual screening starting at 40. If you use the CISNET models, and this has been published[34] and women who are now in their thirties wait until age 50 to be screened every two years instead of being screened annually every year, almost a hundred thousand lives will be lost. That could have been saved by annual screening starting at 40. That's the National Cancer Institute.[35]

Emily: But how do they know that?

Dr. Kopans: Well, they don't know that. Its computer modeling, but it's based on the scientific evidence of the randomized control trials. And then there's huge data that show that when you introduce screening into populations, the death rate goes down for women who have access to screening. And it goes down even more for women who participate in screening. A huge study out of Sweden[36] just published within the last six months showed that the incidence of death, in other words, if you'd go out and see, okay, what percent of the population is dying from breast cancer, the incidence of death for women who participate in screening.

Emily: Death at any time?

Dr. Kopans: Well, so yeah, 10 years after a diagnosis, the incidence of death is 60% lower for women who participated in screening. And at 20 years it's 47% lower. Now, that still means that, that it's not perfect. It doesn't save everyone. And no one's claiming that. I mean I've looked at mammography, which I got involved in in the 1970s, and I thought, well, I'll do this for a couple of years and they'll find a cure for breast cancer and I'll go do something...

Emily: I like your optimism.

Dr. Kopans: Well, unfortunately that shows you how much I know because we clearly don't have a cure for breast cancer and I'm still stuck in this very important

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[32] https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/breast-cancer-screening1

[33] https://www.uspreventiveservicestaskforce.org/Page/Document/modeling-report-collaborative-modeling-of-us-breast-cancer-1/breast-cancer-screening1

[34] https://www.ajronline.org/doi/full/10.2214/AJR.10.5609

[35] https://www.cancer.gov/

[36] https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/cncr.31840

field, I wouldn't say stuck. I think it's a critical field. But the arguments, I mean if you go back and see, I actually wrote a paper on this a couple of years ago. It's been one false argument after another that's been used to try and reduce access to screening. We went through the radiation scare in the 1970s oh it's going to cause more cancers and it's going to cure. It turns out that's not true at all. Then it was, well, it doesn't work for women in their forties. That was in the 1990s. And then the data proved that that wasn't true. And now you know, so the latest, I mean there are many, many others, but now it's, oh, it finds all these cancers that would never bother anyone. But let me just make a point about that. The people who say, wait until 50 and get screened every two years, that's fine. That's safe. They don't tell you that would only be true if there were fake cancers. All right, now I'm going to say, all right, let's say they're fake cancers. Yeah, but it would only be true if the fake cancers disappeared. The ones that were going to be in, in your forties would disappear by the time you hit age 50. There've been papers in the New England Medical Journal, which is an outrageously compromised journal based on screening. They are completely biased, which claimed that in 2008 alone, 70,000 breast cancers found by mammography[37], although they had no data on which cancers were found by mammography, they, as they said in the article, guessed 70,000 would disappear if left alone. Well, 70,000 in one year you'd think someone would have seen a breast cancer disappear. No one's ever seen it. I've pulled at random, informally, over 4,000 breast imaging radiologists. Have you ever seen a breast cancer found by mammography disappear? No one's ever seen it happen. And a study published[38], I think a year or so ago where the in in about 40 centers across the country, they asked what's happened to women whose cancers were detected by mammography, but for some reason they didn't get treated. Not only did none of them disappear, none of them even regressed. So if you're going to say wait until 50 to reduce over-diagnosis, the fake cancers, they got to go away. If they don't go away, they're still there.

Emily: Right? So they're not resolving themselves is basically what you're saying.

Dr. Kopans: But you haven't accomplished anything by waiting until 50 except you've got to let 100,000 women die unnecessarily. I think the counterpoint would probably be something like over intervention, which we started talking about earlier also comes with you know, harmful side effects. Right? So from a very outside perspective, for me, I feel like there's just sort of this general, we don't really understand cancer, right? So like we just did a big episode on the Pan Mass Challenge[39], which is the number one donor to Dana Farber[40]. You know, when I was looking up information about how cancer research is funded, it's like 90% or

[37] https://www.ncbi.nlm.nih.gov/pubmed/23171096/
[38] https://www.jacr.org/article/S1546-1440(17)30145-X/fulltext
[39] https://empoweredhealthshow.com/pan-mass-challenge-cancer/
[40] https://www.dana-farber.org/

something crazy, I don't want to misspeak, but the vast majority of cancer funding goes to localized cancers rather than metastasized cancers. And then most of this is done in rodent models, which, you know, don't necessarily translate to humans. So I feel like there's a whole swath of stuff that we clearly don't really understand about this disease. And obviously people are excited about immunotherapy[41] and these other kinds of treatments. And I don't want to waste your time talking to you about the treatment part because I feel like that's...

Dr. Kopans: Well, no I didn't. In fact immunotherapy has been, was thought of back when I first started out. I had a good, good friend who was working on it at Mass General. There's a lot of optimism, but no, I agree with you completely. I think the human body is way more complicated than we ever, certainly that I ever expected. And even the people in genetics who, you know, everyone is saying, well, we're going to be saved by, we know the genome now and we can do all these analytical studies. They say, now it's even more complicated than that. The point is that while we're waiting to unravel this, what can we do to save lives? You have every right, I would never say to you, oh, you've got to go get screening. I would say, here are the facts and you have to decide. Every one of us decides for him or herself how to participate. My concern is that I think women are being fed misinformation, alternative facts. Breast cancers don't disappear. I shouldn't say that. There have been some reported cases of very large breast cancers that were clinically, you know, you could feel them and see them that it was claimed, went away on their own. Now some of those women still died from breast cancer, but the breast cancer in their breast went away on its own. But these are a handful. I mean, in the literature and none of them were detected by mammography. So if you wanted to say, well, breast cancers can disappear on their own, then the ones you should be leaving alone are the ones you can feel cause those are the only ones that have ever disappeared on their own, now I would never say that, but I'm trying to point out that people misuse information. So they say to women, Oh yeah, there've been cases of breast cancer disappearing on their own and the mammographically detected cancers will disappear on their own. They don't. No one's ever seen it. There's no data to support it. And the data that the claims are based on, I'd be happy to take you through them, are nonsense. They're scientific nonsense. The point is mammography screening is not the ultimate answer to breast cancer. We've never said that. We're waiting for the answer. You said cancer, there's no cancer. There are multiple types of cancers and a breast cancer in one woman that looks exactly the same by all criteria may behave differently than a cancer in another woman in her body may respond to it differently. These are all, you know, the immunotherapy issues. And so on. The point is how do we reduce deaths from breast cancer? And the answer is your best chance is to find it early. You just pointed out that all the money, by the way, the money never goes to early detection. That goes to the Dana Farber. I never got a penny for the research that I was doing in early detection from

[41] https://www.cancer.gov/about-cancer/treatment/types/immunotherapy

either Mass General or the Harvard system. It all went to treatment. I don't denigrate the importance of treatment, but there's no one cancer, so you're not going to find a cure for cancer. You're going to find and we are finding cures for some cancers and some very good cures for cancers, childhood leukemia for example. But the point is if you'd prefer not to die from breast cancer, there is a test that can reduce your risk of dying. It's not 100% but it's pretty big. 40% decline in breast cancer deaths primarily due to early detection is you know nothing to, as we say, sneeze at, but it's not perfect. What I hear in your, in you is the frustration that you know, we're not curing everybody and screening is not going to save everybody. I would completely agree with you but it's saving a lot of women and if we put more money into screening and finding better ways to find cancer earlier we might save most women from breast cancer for example, magnetic resonance imaging[42], which is very expensive and you have to inject a women with an intravenous contrast agent called gadolinium[43].

Emily: Which stays in your brain for a long, long time.[44]

Dr. Kopans: Well that's the latest curveball. I agree with that and it makes me nervous but assuming the gadolinium is harmless, I'm just saying if it is, MR is finding many cancers at a time when they can be cured and it's entirely possible and more than mammography. It's entirely possible that if MR screening can be shown to be safe and if we can make it affordable that we could almost eliminate breast cancer as a cause of death. That said, I'm not optimistic that's going to happen and I'm very concerned as you are about the gadolinium part. But the point is that early detection is actually the only way that you save lives from breast cancer. As you were pointing out. Why isn't more investigation going into women with metastatic disease because no one's been able to figure out how to cure it. They have very few clues. There's all kinds of hope, but nothing is curing metastatic breast cancer at this time. The, the way you cure it is to prevent it. And my frustration is that I haven't been able to figure out how to cure, how to prevent all of them. In other words, find them all early, but we've done pretty well. Again 50 years of no change in the prognosis for breast cancer. And now it's down by almost 50% is not perfect, but it's way better than it was back in the 1960's and 70's. I appreciate your frustration. I'm more frustrated than you are cause I've been doing this for 40 years and we're much better than we were, but we haven't got the magic bullet. But I would just urge that you be careful because there are people out there who are making up arguments like, Oh, it doesn't have any effect on all-cause mortality. That's just a completely specious argument. And the argument that the breast cancer would disappear if you left them alone. Totally not true. And yet they're out there and they're misleading women. I have no problem if you want to give accurate information. But the U.S. Preventive Services Task Force didn't tell women how many will die if you wait until 50. They said it's

[42] https://www.nibib.nih.gov/science-education/science-topics/magnetic-resonance-imaging-mri
[43] https://www.insideradiology.com.au/gadolinium-contrast-medium/
[44] https://www.fda.gov/media/116492/download

okay to wait until 50, but they didn't say, oh, and by the way, almost a hundred thousand of you will die as a result. Even though that's, they used the data to say you can wait until 50 that came from this CISNET models.

Emily: I sort of am just curious from your perspective as somebody who has really been in this for a long time and has seen the change, I mean the imaging has gotten better too, I think that's sort of an important point to make as, the technology comes along. We do obviously hope that there will be a new test that is developed. But when you look at interventions like this, do you have anything that would be helpful for us to have as a sort of benchmark when you're looking at this kind of, whether it's positive predictive value or negative predictive value or like the specificity, all these kinds of things. Are there gold standards for you where you say like, okay, if we can see these kinds of numbers and we can know this is a reliable test?

Dr. Kopans: Well, so here's the problem. And I don't know if in your research you found out, but I actually invented digital breast tomosynthesis[45], which is the latest thing to cause a stir in the media because the companies are promoting it vigorously and everyone thinks they just want to make money. Tomosynthesis is just a—do you know what it is? Or should I give you a quick background?

Emily: A little bit, but yeah, please give a background.

Dr. Kopans: Okay. So a standard mammogram that a woman would get today in the United States is an image of all the tissues in the breast from one side to the other and they're actually shadow pictures created by having the X rays go through. Just like you'd hold your hand up in front of a bright light. You can cast a shadow on the wall and when you can look at and say, oh that's a hand I can tell that. But if you put your other hand in the way or something else in the way you go, Hmm. Is that a hand with something else in the way or is that some weird new thing that's in the beam. So on a standard mammogram, everything from one side of the breast to the other, is superimposed. So I liken it to a book with clear pages with print on them, but the pages are clear. You can hold the book up to the light and see all the words from one side to the other, but you can't read them very easily cause they're super imposed one on top of the other. What a digital breast tomosynthesis does is allow us to see the pages through the book and what it's shown now in hundreds of thousands of women who participated in studies that we unmask more cancers than would be seen on standard two dimensional mammography, but called three-dimensional mammography. It's really not, it's a quasi three-dimensional study, but unmasked cancers that are hidden in normal tissue and it has the additional benefit of reducing the false recall. So you were earlier, you were worried about

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45 https://www.massgeneral.org/imaging/programs-and-services/breast-imaging/development-of-breast-tomosynthesis

women being recalled for so called false positives. They're not told they have cancer when they don't. They're just asked to come back for additional evaluation. But DBT, digital breast tomosynthesis, reduces the recalls[46]. So it addresses one of the complaints about mammography. And yet people are now criticizing tomosynthesis and it increases the cancer detection rate. Now you're asked the question, well, how do I know if that's good, bad, or indifferent? And the answer is we don't know. The only way of knowing whether you really have an impact on breast cancer is if you reduce deaths and that requires a randomized control trial. We have a huge number of women, cause we don't know who's going to have breast cancer in a given year, and you're randomly assigned them to one group or the other. So that every group, every woman in one group has a twin and the other group, now that sounds kind of silly, but if you have large enough numbers and this takes tens of thousands of women in the study, each woman in one group will have someone in the other group who has a very similar history that goes forward. So for example, a woman in group a develops a breast cancer and it's going to grow at a certain rate. If there are large enough numbers, there will be a woman in group B who had, does exactly the same thing. So the principle is that if you have large enough numbers and you do a test on one group and the other group doesn't get the test and there are fewer women who die of breast cancer in the group that got the test, and if the numbers are large enough, so the statisticians say this is a significant result, then you can prove that your test actually makes a difference. Without that you can always make arguments that any test, and most tests have never been subjected to randomized control trials. Cause as you can imagine, they're very expensive. As I said to you earlier, to do a randomized controlled trial of mammography screening to show that the 30% reduction that was shown in the trials for women who the 30% reduction in breast cancer deaths, if you wanted to show that that was statistically significant for all cause mortality, you'd need two and a half million women in your study. No one's going to do that. But the point is that you kind of do the best you can. And what the randomized control trials of screening have shown is that any way you can reduce the size and even better the stage, although even just the size of cancers at diagnosis saves lives. So for example, back in the 1960's it was a randomized control trial of clinical breast exam plus mammography compared to women who just got, you know, usual care[47] if you feel something in your breast come in. And the combination of clinical exam and mammography reduced deaths by 23% now the mammography in the 1960s was terrible, but it had some influence on that. But the clinical breast exam was sufficient to reduce the size of cancers in the screening group such that they reduced the deaths for the group. Some screening is better than no screening and then as you get better and better at finding small cancers, the death rate continues to go down, which is what we've seen in the United States.

[46] https://www.ncbi.nlm.nih.gov/pubmed/26971428
[47] https://academic.oup.com/jncimono/article/1997/22/27/2952590

Dr. Kopans: It's continued to go down as we've gotten better and better at screening therapy has gotten better. But again, therapy only saves lives when you apply it to early breast cancers. If you want absolute proof that, for example, the DBT, digital breast, tomosynthesis saves lives. There will never be any absolute proof cause no one's going to do a study with a death as the end point. They're doing the TMS trial, which is to look and see, we reduce the rate of advanced cancers and there are all kinds of problems with that trial and I think it's a waste of money. But the fundamental concept that earlier detection saves lives has been proven over and over again.

Emily: Yeah, and I think one of the other things that's important to point out is that one of the things that I find just generally on this podcast is that people seem to be better and better at manipulating statistics and maybe they always were, but now it seems like we can really sort of go back and look at like all the p-hacking[48] and all this stuff that's been happening.

Dr. Kopans: They've always been good at that. There were books written on it in the 70's I can tell you about it, but go ahead.

Emily: I think it's important to also just mention that a lot of the success for things like cancer have to do with survival rates at three years, five years, or one year, three year, five or 10 years.

Dr. Kopans: There's a name for that. It's called lead time bias[49] that that you can screen. I use the example, I don't know if you've got my book, I'd direct you to the third edition, which has all this in it and I do make money from that. So please buy my book. The point is that if you have two women, the twins A and B, and they're absolutely identical twins, more so than even identical twins, they both got to develop a breast cancer on the same day in the same breast and it's going to grow at the same rate. Twin A five years after her cancer starts growing, gets a mammogram, we find her cancer and she survived 10 years. Twin B doesn't want to have anything to do with mammography. She doesn't believe the data. And so on. Waits until she can feel her cancer. Seven years after it started, gets treated and dies eight years later, she delayed two years. So it looks like women A survived 10 years woman be survived eight years. Clearly mammography is better. No, if you kept up with me and I'm sorry, I usually do this with slides, what both women died 15 years after their cancer started. So finding cancers earlier doesn't mean, and having women look like they live longer for that reason doesn't mean you did anything for them. So I completely agree with you. The problem is that the only way to eliminate the biases that we have by just looking at survival is randomized control trials. They have proven there have been randomized controlled trials that prove it has nothing to do with just finding it earlier and making it look like they lived longer. There were fewer

[48] https://fivethirtyeight.com/features/science-isnt-broken/#part4
[49] http://sphweb.bumc.bu.edu/otlt/MPH-Modules/EP/EP713_Screening/EP713_Screening8.html

deaths. I mean I think we'll agree death is pretty absolute. So if you look at reduction in deaths, it can't be fudged by the statistics. Oh you just found it earlier. No, you didn't die from it. And that's the bottom line. So there are ways of getting around what you're saying. And that's why I only argue from the scientific evidence. So the proof was randomized controlled trials. There are observational studies which suffer from what you're saying, where women's survival, women who participate in screening survive longer than women who don't. Well, is that because you found it earlier because you just, it looks like they survived longer, but they really, it didn't affect the date of death, but that's additional information. And if they survive much longer for much longer period of time, the lead time bias falls away because, you know, two years difference, once you're out of 10, 15 years has little influence on the ultimate survival. And then there are studies, as I mentioned earlier, where you look at, it's called failure analysis, which was used in looking at airplane accidents. We look at the women who died. We can't argue that death can be fudged. I mean, they died. So if you look at women who died at the Harvard hospitals from breast cancer,[50] the vast majority were not participating in screening. Does that prove that screening saved the other ones? No. But it's more the proof comes from the randomized control trials. And then you add on top of that, cause you have no other choice because no one's going to fund all these randomized controlled trials. And then you have the data from Sweden which look at deaths in another way, the incidence of death after a period of time. And that also shows that women who participated in screening have a lower incidence of dying from breast cancer then the women who didn't. So you're completely right in terms of proving all this, most of your healthcare, most of what we do in medicine has not been subjected to a randomized controlled trial. I would be delighted if we could do randomized control trials on everything as well.

Emily: Me too.

Dr. Kopans: And I don't know how rich you are. Maybe you'll fund them.

Emily: Not today, maybe later.

Dr. Kopans: Yeah. They're incredibly expensive and they take years. So you know, fortunately women don't die immediately from breast cancer. You know, pancreatic cancer would be easy to look at because unfortunately everybody dies so quickly. But breast cancer there are women who live with metastatic breast cancer for 20 or more years. People don't want to do randomized controlled trials with death as the end point because it takes so long. That's one of the recent TMS looking at digital breast tomosynthesis is just going to look at advanced cancers, which I would argue is not a good surrogate, but that's what they're going to do because we can't do the randomized controlled trials. The important thing for your audience to understand is A: it's your decision. Each woman makes her and no one is going to

[50] https://www.ncbi.nlm.nih.gov/pubmed/24018987

force anyone to be screened for breast cancer. And I would, I would say absolutely not. You can't force anyone to be screened for anything but be aware that you're being misled and your position is that those of us who are in the field may be misleading and over making unsupportable claims for breast cancer screening. I appreciate that. I don't do clinical imaging anymore so I don't make any money from breast imaging. I do get a tiny royalty. I developed wired to direct surgeons to lesions[51] they can't feel and I still, the company's been sold. I don't know if I'll still get—I used to get a small royalty from that. That's the only money that I get. My arguments are based on the scientific evidence. And the problem is that you've been actually pointing out to me how effective the campaign creating alternative facts has been. I mean, citing all-cause mortality when the people who say, oh, it hasn't had any effect at all-cause mortality don't know what they're talking about. It's complete nonsense.

Emily: I mean, the thing, I think the big sticking point for me is how effective the test is. Right? In detection.

Dr. Kopans: I can tell you 10% of women are called and on average, I mean it varies, are called back for additional evaluation[52]. So that's a hundred women out of a thousand and of those women about 20, will be asked to have an imaging guided needle biopsy. So that's, you know, call back for a few extra views and an ultrasound is anxiety provoking and inconvenient. But I think most women don't get too upset by that. But having a needle put in your breast is not much fun. Although it's done with local anesthesia, it's very safe. So about 20 of those women will be asked to have that and about 20 to 40% of those women will be diagnosed with breast cancer. And that's actually, you know, if you're waiting to have a lump, and if we, back in the days when there was no imaging, only 15% of the women who actually had surgery for their lumps, only 15% actually had breast cancer. So 20% is, 20 to 40% is doing a lot, a lot better. But yeah if you want a perfect test, don't get a mammogram. It's not a perfect test. In terms of over-treatment and over-diagnosis or over-diagnosis and over-treatment cause one follows the other, don't blame the mammogram, blame the people who are making the diagnosis pathologists and the people who are treating the surgeons and the medical oncologist who are treating. The problem that we've got is that there's a lot of misinformation out there. Unfortunately it's coming from papers that should have never been published. They should have never gotten past peer review, but they did. And unfortunately the misinformation is out there. And let me just give you another sad anecdote. One of the major sources of the misinformation comes from the Dartmouth Institute for Health Policy and Clinical Care.

Emily: That's Welch or–

[51] https://pubs.rsna.org/doi/abs/10.1148/radiology.134.3.7355235
[52] https://pubs.rsna.org/doi/full/10.1148/radiol.13121487

Dr. Kopans: That's Welch[53]. Now, I don't know if you know Welch was found guilty at Dartmouth for plagiarism[54] and he left Dartmouth as a result. He's[55] written[56] four[57] papers[58] in New England Journal of Medicine claiming massive over-diagnosis that are just not based on the evidence. He just, he actually said in his first paper, his best guess as to what the incidence of breast cancer would have been in 2008. Well, it turns out he didn't have guess they were data going back to 1940 and they showed that his claims were wrong, but they got published in the New England Journal so of course they have an impact. There was an obituary on Dr. Schwartz[59], female doctor, who was at the Dartmouth Institute worked with, well, she and her husband and their campaign was to do exactly what you're doing, make people aware of the issues and in their situation claiming that screening was not doing much at all. It was a hoax. You can look up her obituary. I forgot her first name her last name was Schwartz.

Dr. Kopans: She, in the obituary, it said she was diagnosed with cancer seven years earlier and died at age 54. So she was 47 when she was diagnosed with breast cancer— I'm sorry, with cancer. They didn't say breast cancer in the whole obituary, they never said—they just said cancer. But in the obituary they talked about how she and her husband had run meetings at Dartmouth to educate the media on all these issues. I have no problem educating the media. The problem is when you're giving them misinformation, then they go out and I think as you probably are, you're a little skeptical of this guy Kopans cause you know, he used to earn his living reading mammograms. Of course he's going to support mammography. Well, that's not true. I've argued against all kinds of imaging tests that don't work. The point is that her obituary didn't mention that she died from breast cancer that was diagnosed when she was in her forties and she'd been arguing against screening for breast cancer for women in their forties and that wasn't part of the obituary. And I would argue that, and I wrote to the Boston Globe, it would certainly be newsworthy to say that she died of breast cancer when she'd been fighting against early detection. You know, I hate to bring that up cause it's a sad story that she died prematurely and maybe mammography wouldn't have saved her, but I know she wasn't getting screened.

Emily: So I mean I think there's a couple of things that you're bringing up for me. One is I tend to just be skeptical of everybody. Right? And that's my job.

Dr. Kopans: You should be and I am too.

Emily: But I also think like, you know, this is actually a really good example of something that we don't talk a lot about but that comes up frequently, which is when

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[53] https://faculty-directory.dartmouth.edu//h-gilbert-welch
[54] https://www.statnews.com/2018/09/13/gilbert-welch-resigns-from-dartmouth-over-plagiarism-dispute/
[55] https://www.nejm.org/doi/full/10.1056/NEJMoa1600249
[56] https://www.nejm.org/doi/10.1056/NEJMoa1206809
[57] https://www.nejm.org/doi/10.1056/NEJMp1510443
[58] https://www.nejm.org/doi/full/10.1056/NEJMe1008369
[59] https://www.nytimes.com/2018/12/06/obituaries/dr-lisa-schwartz-dead.html

you look at something on a population level and you can sort of see some of these statistical things, you can say like, okay, so one out of six women who has breast cancer, it's not going to be found on a mammogram or you know this percentage of people are going—10% are going to be called back.[60] We can go through all those numbers and I think that's really important and it is important because I really believe women have to be their own advocates and they have to know what they're getting themselves into and that all of these things come with problems, right? That there is no unfortunately machine you can walk into that's going to scan your whole body and tell you what you're going to die from eventually.

Dr. Kopans: I mean I completely agree. You have to make your own decisions. And yes, we all need good, accurate information. And if you say to women, look, here are all the issues and you may not want to participate in screening or if you do you may want to wait until 50 and get screened every two years because that reduces your recall rate, that anxiety and inconvenience. But then you got to tell them however, almost a hundred thousand of you will probably die as a result. I have no problem tell people that. I think they'd be, you know, a lot of women will still say, I'll take my chance.

Emily: Well and this is what I mean by like you look, you can see trends in a population, right? So we can see that the death rates have gone down by a certain amount or we can see... But when it comes down to the individual making their own choice, it's really hard to be the one to raise your hand and say, okay, I'm not going to do this.

Dr. Kopans: Do you wear a seatbelt? I do only wear it because it's the law?

Emily: No, I mean, I, my point is like, I think most women are in favor of mammograms because of the off chance. Very small percent of women get breast cancer, period.

Dr. Kopans: Over their lifetime though, don't forget it goes up. So it goes up each, you know, it goes up each year. But you're right in a given year, you can roll the dice and that you're going to, you're going to win the vast majority of the time, you're not going to be diagnosed with breast cancer. The only point is that if you are diagnosed with breast cancer, your chance of being cured is much higher if it's detected earlier. That's the point. And again, you're completely right. I mean, most of us don't have anything happen. Fortunately, anything bad happened to us in a given year. You don't get into car accidents where the seatbelt saves your life. I've never had a seatbelt save my life. It saved my kids cause they were hit from the side in a car accident a week or so ago.

Emily: Oh no, was everybody okay?

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[60] https://pubs.rsna.org/doi/full/10.1148/radiol.13121487

Dr. Kopans: Unfortunately, my daughter-in-law got a concussion, but you know, the car ran a stop sign and hit him broadside. The point is you wear seat belts cause it makes sense. And yeah, my granddaughter got a burn from her seatbelt, but it probably saved her from being thrown at the window or out of the car. So yes, you're absolutely right. You can, the odds are you're not going to get breast cancer this year and in fact the odds are you're never going to get breast cancer, although it's pretty high risk. But it goes up with age. And so if you're young, you can say, well, I'm young. My odds this year aren't very high. But the question is, if you would prefer not to die from breast cancer and it's not a very pleasant way of dying not that there are any pleasant ways of dying.

Dr. Kopans: But mammography screening is the way to save your life. Therapy by itself is not going to save your life. Therapy only saves lives if your cancer is detected early. The people who argue against screening say, Oh, but be aware of your breasts. Now they also argue against self-examination, but be aware of your breasts. So when you're washing, if you feel a lump, you know, bring it to your doctor's attention, that's fine. But there's no proof that that saves any lives. There's never been a randomized control trial of being aware of your breast saving lives. And in fact the only two randomized controlled trials of breast self-examination one was done in Russia[61] and it was questionable whether it was worth doing in the first place, didn't show any benefit and one was done in China[62], which was probably better done. But you know, my understanding is Chinese women have smaller breasts for the most part, so they're more likely to feel a lump washing than they would doing self exam. The point is that breast self awareness its insane to say that. I mean, it's clever. You know, we just have to be aware of your breasts. But if you're worried about science, I mean that's just an outrageous, a recommendation in lieu of being screened with a mammogram. So I completely agree with you, but I argue you need all of the information.

Emily: Right. I know, I completely agree with that. Absolutely.

Dr. Kopans: We do. And I'm telling you there's a huge amount of propaganda out there. And one of them is what I call delusional nihilism, which is what you've been saying to me. Well, if you look at all the women in the United States and you screen, all these women and you know, you'd call back 10% you know, that's a lot of women who are going to be made anxious and it's money. I agree with that. But for the woman who has breast cancer, it's 100% so you know, you can go to both extremes. I would just say, here are the data. If you want to say, Hey listen...`

Emily: Well, but also, I mean I feel like it's important to just add in there. It's not catching all of it. So even if you have, like your anxiety about having the test may

[61] https://europepmc.org/article/med/10443229
[62] https://academic.oup.com/jnci/article/94/19/1445/2519925

extend beyond just that, right? Because you might think, Oh, I'm fine, and then you find out you're not.

Dr. Kopans: That's right. Well, but don't forget in a thousand, women say average age, maybe find four to six cancers, let's say six cancers, and we may miss two. So that's two out of a thousand. So take away this six that, that's eight. So 992 women were legitimately reassured they don't have breast cancer. I mean, you can look at it—I don't, I wouldn't say that's a great reason to get screened—but you know, if you want to do the numbers game, you're reassuring all those women.

Emily: As a patient, I'm clearly conflicted about this, right? Like I don't want to not get a mammogram and find out that I have breast cancer. And yet at the same time, I now have an awareness that the breast cancer that's being found may not be the kind of breast cancer that would ever metastasize as well as the fact that the test isn't that great. So I might have breast cancer, go in for the mammogram and find out that the test comes back normal. So I was sort of curious if I'm struggling with this decision so much, knowing all these statistics and having rerun all the numbers, how does a doctor decide what to recommend and I know there's this idea of like the standard of care that you kind of have to toe the party line and do what ACOG is recommending. Well, at the same time I wanted to know if a doctor really understood these statistics the way that I feel like I kind of do now. How do they possibly tell women like this is a great test?

Dr. Conti: My name is Dr. Jenn Conti[63] and I'm an OB-GYN that's based in the Bay area. I treat women for all kinds of women's health-related conditions and sub-specialize in family planning, which is contraception and abortion care.

Emily: Great. We are excited to have you back. We did talk to you once before on our abortion episode[64] and I'm sure we'll have you back again, but I wanted to talk to you this week about mammograms.

Dr. Conti: Yes.

Emily: Because you know, there's a lot of confusion, and myself included, about the efficacy of mammograms and we've dived pretty deep into this and talk to researchers on both sides. And I wanted to hear as a practitioner, I mean it's like, so basically we could have, we probably should have sent you the stats and whatnot before, but you may be familiar with this. The mammogram itself as a test is not a great—it's not a great test. Right? The efficacy of finding cancer in the woman is not great. The sensitivity and the specificity are pretty bad. Right? And so without getting into all of that, it does find cancer.

Dr. Conti: Right, right.

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[63] https://stanfordhealthcare.org/doctors/c/jennifer-conti.html
[64] https://empoweredhealthshow.com/abortion-access-united-states/

Emily: And I think when you look at those studies, or those stats rather. So when you look at those stats, one of the things that's really hard from a patient perspective, and I would imagine from a doctor's perspective, is this idea of, that's great on a population level, but if somebody comes into your office and the, you know, standard guidelines are everybody gets a mammogram at 40 but you know, the test isn't that great. How do you make that decision?

Dr. Conti: It's really hard. It's not even just breast cancer that this issue comes up with. And I would say that it actually comes up even more and in a worse situation with ovarian cancer. And I'll get into that in a sec, but we have this idea that if a disease is prevalent enough in a society, so like breast cancer, we know that by the time a woman reaches, the older part of her life, like one in eight of us is going to have breast cancer, which is you know, pretty significant. And if it's that prevalent then we need to, as a population, come up with a way to screen for it and try to prevent it. Right? Cause that's the end goal just to try to prevent this. The best that we have is mammogram, right now. And they're coming up with all these different ways to like improve the mammogram, whether you do like a 3-D mammography or tomosynthesis, all these other things that can sort of improve on the baseline mammogram. And they've looked at a bunch of other things too. Like does an ultrasound give you better imaging? Does an MRI give you better imaging? Does just feeling your breasts give you a better sense of what's normal and what's not and whether that's you feeling your breasts or your clinician feeling your breasts. There's a lot of different ways to sort of screen for these conditions, but unfortunately nothing's perfect. And so when you look at all of those different modalities right now, at least for the general population, mammogram seems to be the best. But the problem is it's not a one size fits all. So if you are a younger woman or if you're a person with really dense breasts, which I tell people is actually a compliment, it just means you've got young breasts, mammogram is not going to be the best. Ultrasounds tends to be a little bit better. I find the best approach is to really just give as much information without overwhelming the person as possible and then come up with a shared decision making process about it. If you come into my office and I tell you, hey look, we don't really have anything that's, you know, 100% good or effective at finding breast cancer, but this is what I can tell you. Then we come up with a decision, you know about starting at age 40 how often to start screening someone for breast cancer or do we start at age 50 or you know, we would go off of all of the different recommendations out there and try to come up with the best decision for that person. Where I think it gets really tricky is if a person has a family history of breast cancer, whether it's like a first degree relative or not, and they're just, you know, so they have like this heightened level of awareness and fear that is helping to drive that decision.

Emily: And potentially risk.

Dr. Conti: And risk. Yeah. Specifically risk because I mean without delving into that sidebar as well too, we don't even know about all of the genes that cause breast cancer. We know that the BRCA or the BRCA genes definitely put you at an increased risk[65], but the majority of women who get breast cancer don't have that genetic predisposition. It just comes out of nowhere.

Emily: Right. And I think it's about 50% of people who do have that genetic condition do not develop cancer.[66] So it's not 100% either. Right?

Dr. Conti: It's not, it's enough to scare you and maybe drive your hand a little bit with the decisions you make around screening or even removing your breasts. But it's not enough to say for sure whether or not you're actually going to develop it, which is terrifying. And I find it also like when I have women coming in from different countries, maybe you know, they're coming to the U.S. Having received some of their women's health care in a different country before where they do the screening differently. It can be especially confusing for them because for example, a lot of European countries will do ultrasounds as their routine screening. But in the U.S. we don't do that. And the reason why is because it doesn't make sense on a population level. Like you're saying, I think it gets down to a bigger issue, which is are we making this decision because of money? Because what makes sense to test, you know, the biggest amount of people or cast the widest net at the cheapest rate. Does that make more sense or does it make more sense to do the more expensive tests? You know, cause maybe it's more expensive to do MRIs for each person. It certainly is, but maybe catch something a little bit more. It's a really, like the question is not as simple as it looks at face value. It's not just like what is the test that's going to find the most disease in the most number of people? Certainly that's a factor. But money is a huge factor in this as well.

Emily: Yeah. And I think, you know, as a patient or as the doctor, it's always so interesting to me and especially on this podcast where it's like we're talking to all these, you know, brilliant researchers who are really looking at large populations. A lot of cases they're using epidemiology, right? To sort of come up with a hypothesis. And then hopefully do further testing on it. But you know, you do see different things so you can find trends. And so one of the things that I was frustrated with in reporting this episode is there's this word that everybody uses that's over-diagnose.

Dr. Conti: Yes.

Emily: So we're over-diagnosing breast cancer and like as a word person, like what does that mean? Over-diagnose—it's either there or it's not—you diagnose it or

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[65] https://www.nationalbreastcancer.org/what-is-brca

[66] https://www.nationalbreastcancer.org/what-is-brca - "It's estimated that 55 – 65% of women with the BRCA1 mutation will develop breast cancer before age 70. Approximately 45% of women with a BRCA2 mutation will develop breast cancer by age 70."

you don't. Yeah. The more I peel that back, the more I'm like this isn't about over diagnosing. This is about not knowing how to treat. So it's like in situ tumors, which there's a big debate about, right? Like when do you treat for that? Should you treat for that? Would it ever spread? Would it not? For me that's actually sort of removed from this mammogram issue. Yeah. Mammograms may find it because it's there. Right. And that's the job—to diagnose or to not.

Dr. Conti: There's this idea in medicine that if you go looking for something, be prepared for what you're going to find. Just because we have the technology and this comes up today in this day and age too, with like, especially in the Silicon Valley, we've got all these amazing tests that can answer these questions. But what are we going to do with the answers? So just because you have the imaging to find something, doesn't that you should go looking necessarily if you don't have a baseline elevated risk and that answers the question of well that's why we start screening in your 40's or 50's. Because at that point there's a baseline elevated risk enough in the population to be screening without, you know, additional risks. But you face the challenge of what would you do if you found one of these incidentalomas[67] that's sort of like the, you know, joke name for it I guess. But you know, like it's something you found incidentally, but it's an oma like something that ends in OMA is usually a tumor, so incidentaloma and that you find this thing, you don't know what to do with it. What are you going to do? And for some people, like you're saying, it is reassuring or you know, beneficial to know that because more information is better and at least I know it's there and I can decide what to do about it and I'd rather know than not know. But for other people it's more anxiety provoking to know that there's something there that you don't know what to do with. And a lot of people would just prefer, I'd rather not know. You know, that's really anxiety provoking, especially if it is probably just benign and the actions that you might take to go in and find it that it's benign or to prove that it's benign might cause more harm. You know, people going under surgery, it's such a fine line to walk.

Emily: Yeah. And I also think, you know, this idea of like cancer, the word cancer is so scary and it's like these are all very different kinds of things, right? So like these are different kinds of dangers, but they're all called cancer. And that's also really confusing to the patient because it's like, wait, what? I have cancer. I mean I have somebody in my life who literally was just while we were working on this episode, diagnosed with in situ. Yeah. She of course like talked to me and my husband about like what you know, what is this all about? And like what's the research behind this? And it was so hard because her doctor was like, well we're going to do radiation, we're going to do chemo and that's a tough call.

Dr. Conti: Yeah, exactly.

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[67] https://www.aafp.org/afp/2014/1201/p784.html

Emily: You really don't know if it's going to spread. And you do know that chemo and radiation causes cancer. This is a tough, tough thing, you know, I'm never one to say like don't know your body as everybody listening knows. Right? Like you want more information, always more information, arms you—you can make better decisions. But in this case it's like step one is do you do the test and then step two is if the test comes back as positive, how do you move forward? You know, once you've confirmed all of these things and then what do you do? I also think like the way that breast cancer sort of treatment is set up is that it is like pretty universal, right? I mean it's not like there's a huge amount of distinction between these. Like it's like there's just a standard of care and that's what you get. Right, and that's tough.

Dr. Conti: It's so tough and I see the benefit, right? The benefit is cast the widest net so that you don't miss these, these cases that can be stopped in their tracks essentially or cured, but there's so many moving variables that that play a role in that decision about like, do I test? When do I test? How often do I test? For example, if you're an 80 year old person, you might have a different answer to that question. Do I even test? Because what if they find something and you're 80 and going through chemo and radiation, like you're saying is so hard on your body. Maybe it's not worth it at that point. Versus definitely if you're in your twenties Oh my God, yes. Pull out all the stops, do everything you can. It's easiest and most financially effective to just cast a wide net and set like a standard screening modality for everyone, right? We need to have rules. In reality, it's a conversation with the person, you know, what else is going on in your life, what is, what's the risk that you're bringing into this? And just, you know, with your family history and your lifestyle and then what do you want to do? How do you want to screen?

Emily: And so do you do that with patients?

Dr. Conti: I do. So not on this level we're talking about right now. Cause this is, I mean I think I would just freak everyone out and we don't have time for that. I think everyone, most people, come to screening with a baseline knowledge that not everyone is recommending the same start time and frequency. I mean that's out there in the media enough, I think. The conversation that I have with them goes something like this. There are many different governing bodies in our country that recommend breast cancer screening at a certain age and a certain frequency. So, for example, on the very, very conservative side of that is the American Cancer Society. They recommend offering breast cancer screening or mammograms starting at age 40 and then doing it annually even all the way up through your 50's or older.[68] And then you have on the very liberal side of that, the USPSTF or the U.S Preventative Services Task Force and they recommend starting at age 50 and they say actually

[68] http://www.cancer.org/research/infographics-gallery/breast-cancer-screening-guideline.html

that you can go every other year[69], you know, have this discussion with the person. And then the people that are right in the middle, ACOG or the American Congress or College of OB-GYNs, they say, you know, you can offer it at age 40 but definitely don't start any later than 50 and you know, have a conversation with people.[70] And it can be every year, it can be every other year. So it's so confusing when you have these big governing bodies saying pretty much mumbo jumbo. All of this stuff is, you know, very confusing. But I kind of lay the groundwork with those three governing bodies. I say that what I like to do is sort of a combination of, I can meet them both in the middle. Most of these are all three of these organizations and say we can start age 40 and do it every other year, but please start by age 50 and do it every year in your 50s but again, that may be totally different to the people listening right now than what their own OB-GYN says.

Emily: Right. I mean like just anecdotally like my OB and I had this conversation, I mean she obviously has to deal with me knowing and questioning all the research that she was just like for a little love of God, Emily, like a lot of people in New England have breast cancer and we don't know why. Like just get your damn mammogram. And I was like, really? But it's like a little bit of radiation. And she was like, okay, yes, you're right. You're right, you're right. But I still say go do it. And so I did it. For me, it's also like, it's so hard to be like, oh you know like like the idea that like I could have breast cancer and like not have done the mammogram and like die in whatever. That hindsight bias drives me nuts. But I know on a statistical level this is not actually the best predictor.

Dr. Conti: I have a background, a Master's in epidemiology. I'm trained to look at the public health aspect of it as well, but it is sometimes a little sad to think that we make really important decisions in people's lives. A lot of times those are driven by what makes sense at a population level. Medicine is an art. I know that's a cliche, but medicine is such an art and so you have to have, like you have to harness the understanding of why it's important on a population level, but you also have to take the person sitting in front of you, you know, at face value in their lived experience and what's important to them, what's terrifying to them and make that decision with them.

Emily: And I think this is why everybody wants a doctor who can actually spend the time with them to do that.

Dr. Conti: I know, I know. My God, I know

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69 https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/breast-cancer-screening

70 https://www.acog.org/About-ACOG/News-Room/News-Releases/2017/ACOG-Revises-Breast-Cancer-Screening-Guidance--ObGyns-Promote-Shared-Decision-Making?IsMobileSet=false

Emily: I'm Emily Kumler and that was Empowered Health. Thanks for joining us. Don't forget to check out our website at empoweredhealthshow.com for all the show notes, links to everything that was mentioned in the episode, as well as a chance to sign up for our newsletter and get some extra fun tidbits. See you next week.