

Emily: I'm Emily Kumler and this is Empowered Health.

Dr. Kalager: I think we need to wind back and understand what our perception about cancer is. We have long learned that cancer is a deadly disease. It's devastating. It may kill you. And we have tons of examples of that. That's why we started mammography screening thinking hmm, if we could detect the cancer earlier, you know, we could save lives. But then we didn't realize that cancer could be a whole conundrum of different diseases. And by screening we have learned that [some of the cancers will not progress](#)¹. The way we have understood this is based on statistics, based on the numbers of tumors that we find when we do screening. So what we thought would be that, okay, we do screening, we find a lot of cancers earlier. Hence we prevent the cancers from being diagnosed at a later stage. So we thought that what we saw in the beginning was just what we would expect, that we find a lot more cancers with screening than we do without screening. [But then as the years progressed, we didn't ever see a reduction in the incidence of breast cancers.](#)² We started to think "hmm what's going on here?"

Emily: That was [Dr. Mette Kalager](#)³ who is a professor at the University of Oslo in Norway, but she's also a medical doctor and a former breast cancer surgeon. She is going to talk to us a little bit about how she came to study mammograms as an effective or ineffective tool in detecting breast cancer. So this topic is wildly misunderstood. In a 2014 New England Journal of Medicine article, they purported that American [women think that their risk is double of dying from breast cancer if they do not have a mammogram](#)⁴. So we wanted to really look into what do mammograms find, are they an effective diagnostic tool and why is there so much controversy about this? In the past few years, there's been a lot of talk about over-diagnosing breast cancer, which is something that I will take to task later in the episode because I think that word is actually not the right word. It's either the test is effective at finding cancer or it is not. And then I think a secondary question is, are we treating breast cancer properly or cancer in general, properly or not? And how do we differentiate between one kind of breast cancer and another kind of breast cancer? So we're going to get to all of that, but we're going to start by listening to Dr. Kalager explain how she came to be interested in this topic.

Dr. Kalager: So it goes way way back when I was resident in breast cancer surgery at a local hospital in Norway. So the hospital was part of a

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<https://www.mdanderson.org/publications/cancer-frontline/study-sheds-light-on-why-some-early-stage-breast-cancers-progres.h00-159220989.html>

² <https://journals.sagepub.com/doi/10.1177/0969141316668379>

³ <https://www.med.uio.no/helsam/english/people/aca/mettkal/index.html>

⁴ <https://www.nejm.org/doi/full/10.1056/NEJMp1401875?query=TOC>

[mammography screening program in Norway](#)⁵ and most of Europe has, in contrast to the U.S., we do have screening programs where every woman is invited to mammography in the age 50 to 69. And that program was implemented into the hospital where I was a resident a long time ago. Part of the [program in Norway was to organize breast cancer treatment](#)⁶. And the reorganization was that every doctor working with the breast cancer patients, all from the radiologists, pathologists, oncologists, surgeons, and the nurses involved in treating the patient we're having multidisciplinary meetings every week where we discussed every single patient. And this was a contrast for me as what we did previously because previously we didn't really talk to each other. Each specialty did their thing, and we never discussed it. And I was sitting there as a young doctor thinking, Hmm, this is very interesting. I wonder if this has any influence on life expectancy. So that's sort of how I got into it and got interested in the whole field of mammography screening. And then, with time, I was asked to be the head of the screening program in Norway. Part of my job was to evaluate the Norwegian screening program, and that's how I got into research on breast cancer screening.

Emily: So what have you found?

Dr. Kalager: So what we found in the Norwegian program is, first of all, we've found that these multidisciplinary teams actually save women's lives. So we found a 20% reduction in breast cancer mortality for all women who were treated by these teams of doctors instead of just single doctors working by themselves. So that is one part. And then, we evaluate the screening program per se, including these multidisciplinary teams, including taking mammograms. And we did not really find a great reduction in breast cancer mortality. So their reduction was 10%, which is a very difficult figure to understand what it is, and we've found a substantial amount of overdiagnosis. Most women ask me what is [overdiagnosis](#)⁷? I don't really get it. Overdiagnosis is really detection of breast cancer that you would detect by screening that would never progress to give you symptoms or to kill you if it were untreated.

Emily: So why don't we call it overtreatment?

Dr. Kalager: Because you detect it. So the difference between overtreatment is that you treat something, for example, ductal carcinoma, we treat it with too much, let's say radiation, that's overtreatment. But this is over detection means that these cancers really don't need to be treated. But since we don't have a marker, who can tell us whether this is an over-diagnosed cancer or not, there

⁵ <https://www.kreftregisteret.no/en/screening/breastscreen-norway/>

⁶ <https://breast-cancer-research.biomedcentral.com/articles/10.1186/bcr2331>

⁷ <https://www.ncbi.nlm.nih.gov/books/NBK430655/>

is no way of knowing that this is an over-diagnosed cancer. So we treat as it is a cancer that would progress.

Emily: And then you sort of retroactively look back at it.

Dr. Kalager: Yeah. And that's the difficulty. You sort of have to understand that when you accept going to mammography screening, your chances of over-diagnosis is a certain percentage and you can't avoid it. I don't think you can afterward say, well, I don't think I want treatment because we have seen that treating breast cancers will benefit your life or your life expectancy—will increase your life expectancy.

Emily: I feel like this is the crux of it. Right? And this is partly why everybody's so confused.

Dr. Kalager: Yes.

Emily: It is sort of one of those things where, how do you know? If we take one of the [ductal carcinoma in situ](https://www.breastcancer.org/symptoms/types/dcis)⁸, which we're going to just refer to as DCIS from now on, and we look at that, that does sometimes spread to invasive cancer. It's not like that's always benign. So how do you differentiate?

Dr. Kalager: So if you're talking about ductal carcinoma in situ, DCIS, that is not cancer, that is a premalignant lesion. It seems to be a risk factor of breast cancer later in life. So that's why we treat it.

Emily: And that's only found with mammograms, right? There's no other way to find that?

Dr. Kalager: Well, I wouldn't say only, I mean medicine is in the sense that you can never say it's just this, but it is mostly found at screening mammograms. But some women actually will also find them themselves. I have had several patients who have felt that, Oh I have something in my breast, I feel there's something there. And we have taken a mammogram, and we've seen that there is a ductal carcinoma in situ. So this is associated with mammography screening, but it's not only diagnosed at mammography screening. Another problem that we need to distinguish is that mammography screening is a test where you don't have any symptoms, you feel fine and then you go in and you take a mammography and you use the same technology, the same x-rays if you have a symptom. So everything is really mammography. So I think we need to distinguish between mammography versus mammography screening. And by mammography screening, we mean...

⁸ <https://www.breastcancer.org/symptoms/types/dcis>

Emily: So like I turned 40 and, you know, the first thing the doctor says is, have you had your mammogram yet?

Dr. Kalager: Right. That is screening

Emily: And so explain to me a little bit in terms of the statistics, why that's an important thing to separate.

Dr. Kalager: What you should do if you have a symptom in your breast is to get a mammogram because it can diagnose. That's the only way, or not the only way, but that's the first way that we would diagnosed a cancer. You could use [ultrasound](#)⁹ and you could use [MRIs](#)¹⁰ and you could do [computer tomography](#)¹¹, a different tests. You could use different tests to diagnose breast cancer, but if you have a symptom you should go and have a mammogram. But this is very different from if you're healthy and your doctor tells you, well, yeah just in case you should go and have a mammogram, because your risk of over-diagnosis, it's much, much higher when you do screening. Then when you do have a symptomatic examination of your breasts, let's say, let's just chat in general talk about the possible harms of mammography screening. One of the harms that has been emphasized a lot is [false positives](#)¹². False positives is when you have a mammogram and the radiologist says, well we found something on the mammogram, it might be cancer. It might not be. You need to come back for another mammogram or ultrasound or biopsy. So then after you have been examined with this test and evaluated, the test had been evaluated by doctor, you find that no there was nothing wrong. It was just something that we cannot explain what it was, but it was not cancer. So that's false positives. And then over-diagnosis is a diagnosis of cancer. So you're actually finding cancer, but this cancer will not lead to any symptoms or would not lead to your death. Meaning that just by calling it cancer, I think that's where we are confusing women and patients. Some have suggested to call this a insignificant lesion.

Emily: Well why don't we call it like a benign tumor or something that would be similar to other areas of the body?

Dr. Kalager: Yeah, that would be a good idea. If we had a marker, if we could by looking at it in a microscope or by testing it with some marker, we could say, Oh, this tumor is, it's an over-diagnosed or this is a benign cancer and another tumor is a malignant cancer. But we don't have that marker and that's sort of like a catch 22. So when you go and find a breast cancer, you cannot know

⁹ <https://www.nibib.nih.gov/science-education/science-topics/ultrasound>

¹⁰ <https://www.nibib.nih.gov/science-education/science-topics/magnetic-resonance-imaging-mri>

¹¹ <https://www.nibib.nih.gov/science-education/science-topics/computed-tomography-ct>

¹² <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/false-positive-test-result>

whether this cancer is what we've called today, over-diagnosed, or whether this is a real cancer.

Emily: In terms of this idea of over-diagnosis, you're finding cancers that would never metastasize theoretically, right. And not kill. How do you know that part?

Dr. Kalager: No. So you don't at the moment when you diagnose it, that's why when you find a tumor at a mammography screening, you have to treat it. So that's too late, then it's too late. Then you just have to let's say comfort yourself and say, okay, I have to go through this. I cannot not treat it. There are some studies, however, that will offer less treatment for the DCIS, the precursor of cancer. And to see whether that is one way of sort of minimizing the harms of mammography screening by treating the tumors less than you needed to before. But we do not have any data from these studies yet, so we don't really know.

Emily: And so how are we basing this information on this idea that we're not that theoretically, statistically at a population level, these would not result in deadly cancers.

Dr. Kalager: You mean how we studied it or how do we know or..?

Emily: Yeah, both. I guess.

Dr. Kalager: So as I said, we cannot, on the [?] tumor level, we don't really know whether it's an over-diagnosis cancer or let's say benign cancer or malignant cancer. We don't know. That's why we treat everyone. So when it comes to the population, and the reason why we know there is such a thing as over-diagnosis is because we see the explosion of cancer incidents. Once you started screening, it happens with mammography, it happens with [prostate cancer](#)¹³, it happens with [thyroid cancer](#)¹⁴. It has a [study of neuroblastoma in Japan, in children, they found the same thing.](#)¹⁵ So that's why women need to be informed about this concept and women and people, I guess, this doesn't only apply for women because you have the same problem with prostate cancer as well. So people need to understand that there is a risk with breast cancer screening that you can find cancers that would never have progressed to give you any symptoms or cause death at all. You'll find lesions that are benign, but it looks like cancer.

Emily: But I had a patient level and as a surgeon yourself, I mean like that becomes so difficult, right? Because there are cancers that are found early

¹³ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3540879/>

¹⁴ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5470703/>

¹⁵ <https://academic.oup.com/jjco/article/48/3/214/4825045>

that are treated, that do save lives. And so how do we, on a patient level, sort of make this distinction.

Dr. Kalager: So once you're a patient once and by patient is that once you have the breast cancer diagnosis, you need to treat that woman. I've had several of these patients and I always have to comfort them saying, well you know, when people are worried is this an over-diagnosed cancer? And I said, you cannot really think about that now we need to treat you. So you need to make a choice before you go to screening. Once you've decided that the benefit is higher than the harms for me, you have to forget all about over-diagnosis.

Emily: And so when you're talking about patients making this decision for themselves, you know, obviously things like family history are probably important, right? Are there other things like that that you would weigh more heavily towards saying, you know what, you probably are somebody who should be regularly screened versus somebody who should not.

Dr. Kalager: Well, there are genetics. Some families that have some genetics, like your [BRCA genes](#)¹⁶. These women are recommended to undergo screening. I would never recommend against screening for these women, but I would like us to be more informed about the benefits and harms before we screen the average 40 to 50 or 50 to 69 or 60 to 69 to 70 year old women. So we need to inform people so that they can take or make their own choice. And I know that sounds very like, I don't care as a medical doctor, but I think here we are in a very complex area and where we have had for several years we have been informed that screening helps, you know, early detection helps and just the recent maybe 10 to five years that we have started to focus on, okay, there are harms besides the false positive and false negative tests and psychological distress or whatever you think is a harm. And its the harm of over-diagnosis. What is interesting when you look at the randomized trials, which is sort of the best evidence that we have, we find that although mammography screening reduces deaths from breast cancer, it does not reduce overall death. So I keep wondering what are we doing? Are we saving people from breast cancer but we are killing people because of treatment and let's say they die of heart attacks or something because of treatment. Since we do not find a reduction in the overall death between those who have undergone mammography screening and those who have not.

Emily: Well I was also, when we were sort of crunching some statistics over here and looking at the specificity and sensitivity and all that stuff, which I generally get very confused about.

¹⁶ <https://www.nationalbreastcancer.org/what-is-brca>

Dr. Kalager: Yeah that's hard.

Emily: But it seemed like about one in six people who get a mammogram who have cancer will not find it with that test, which also seems pretty outrageous. And so when you look at those statistics, just the numbers, it's about the same percentage of the general population. So like if you were to take a hundred random people and have them, you know, walk into your office and say, okay, two of you have breast cancer, it's about the accuracy of the test being unplugged. Right? So we could unplug the machine, which sounds nuts, right? That this is the gold standard screening test. And from a statistical perspective, it's incredibly, I mean it's like, you know, it seems to me like this is really poor in terms of the results that it finds. Then on the patient level, you think, well everybody I know who's had breast cancer has found it on a mammogram. So that then anecdotally kind of clogs my statistical brain.

Dr. Kalager: Yeah. And then you have to remember that, well a lot of these women will be over-diagnosed and they will be the living example of how good the health system is and they will survive their breast cancer, you know, because they would never die from it in the beginning. And that's the stories that you hear. So by doing this test, you increase the incidence rates. A lot more women will have a diagnosis of breast cancer and you will hear success stories because these cancers would never have bothered you in the first place. And of course then you're going to survive the cancer. So you have to remember when you hear about all these women who have been saved by mammograms, you could also think that, I wonder if that was a cancer that was over-diagnosed or not. So when you look at a thousand women who are screened for 20 years, 15 of those thousand women will be over-diagnosed. So you will find 50 cancers altogether among those thousand women and 15 will be overdiagnosed.

Emily: It's significant.

Dr. Kalager: Yes, it is significant. And then you save two from dying from breast cancer and you don't save a life in the sense that you would think, but two less would die of breast cancer. But if you look at the statistics, you do not prevent people from dying. They just die of something else. Meaning that two more will die of something else.

Emily: Right. And unfortunately we do know that chemo and radiation causes cancer. Right? So like the treatment is causing the thing you're trying to stop or prevent. So I think that harm is not well understood either.

Dr. Kalager: No. And I agree. And we haven't really studied this. And this is very hard conceptually. When I first heard about over-diagnosis, I thought, no, no, no, this is cancer that this is insane. This is just playing with statistics. or the

numbers. I mean this is just, it can't be true. And then I started looking into the numbers and I thought, Hmm, I don't understand. The only explanation I can find that can explain this huge increase in incidents is over-diagnosis. And then you saw a pattern for prostate cancer as I said, and for thyroid cancer as also as I said, and then for malignant melanomas. And then you see this, this whole industry finding and trying to find cancers earlier. And what I've landed on for myself is that screening cancer with tests that detect cancer early have all the problems with over-diagnosis and then over treatment because you are treating the over-diagnosed cancer and then you might die over the harms of chemotherapy or radiation. And then you have another test, let's say you use for colonoscopy or for cervical cancer, where it's like a more preventive test where you find a precursor of the cancer and you remove the precursors. So as a result, you reduce both the incidence and the mortality from cancer. What I've seen on the statistics so far is that those tests, the preventive screening tests may have a very good benefit/harms ratio, meaning that the benefits outweigh the harms. But for most early detection tests, I'm now talking about the general population, not specific. If you have a family history or not a family history, I'll come back to that. But if you have a gene like say the BRCA gene, I'm not talking about those people. I'm talking about the average risk person. So when you said family history, so if you have had mammography screening, let's say for the last 30 years and you have 15 out of thousand people who are over-diagnosed of course that's going to be also influencing the family history. So just by that.

Emily: Oh yeah, that's, I hadn't thought of that.

Dr. Kalagar: No. Your mother and her sister who had a cancer that was over-diagnosed detected by screening and then people say, oh your risk is probably increased. So they will recommend you to undergo even even more screening. So this is like a vicious cycle that's very hard to stop and when you look at the whole industry behind this, you know this is people are bread feeding their families.

Emily: We talked to [Dr. Kopans](#)¹⁷ who was at MGH in Boston and you know is a Harvard guy who is very pro mammograms and he is obviously been involved in screening and he really pushed me to say think about the people and ask them what their funding is and all this stuff about people who are saying don't get screened because he was like they don't want to pay for it, they don't want to save women's lives. Do you have any conflicts of interest or any funding sources that we should know about?

¹⁷ <https://connects.catalyst.harvard.edu/Profiles/display/Person/11351>

Dr. Kalager: So my mammography screening, that I do, was funded by the [Cancer Registry in Norway](#)¹⁸ who is responsible for the screening program, who is really pro screening, really recommend screening. For other studies that I've done it's been financed through the [Norwegian Research Council](#)¹⁹ and I've been working as a breast surgeon. I haven't done that in some years, but it's always been a public healthcare system without any incentives in how many I do, how many operations I do or treatments that I do. And I've been the head of the mammography screening program in Norway and now I'm a professor at the University of Oslo and I don't have any associations with any industry financing.

Emily: Yeah, no, it's just so hard because I think, you know, from the lay person's perspective, it's like he would probably say about you that like, well the government doesn't want to pay for this. Right?

Dr. Kalager: But it does in Norway.

Emily: But it does in Norway. And I just sort of think like if we, again, it's like that's why statistics are so important, but then you look at the statistics of different things and you realize that there's a lot of manipulation that can go on. Right. And the all cause mortality stuff becomes kind of fuzzy because as you said, people get treated and then they die of other things.

Dr. Kalager: Yes. And then you're not counted in the statistics that you're looking into. So if you're only looking at breast cancer death, you are not counting everybody who dies everything else.

Emily: Even the person years stuff drives me crazy. It all feels like, why can't we just talk about the raw number?

Dr. Kalager: And some researchers tried to make it simple. I mean, you have the New England Journal for the last, I don't know, five or ten years been publishing studies where they really look at statistics that's not manipulated. You see the raw rates where you see over time what's going on. And I think it's hard to say that there is anything manipulated in those statistics. And that's why I think that's very valuable. Then maybe something that when you are a laypersons should look into. So what is the statistics? What does it say? What does it mean? And there are some good papers in the New England Journal [evaluating trends in breast cancer incidents and mortality from the 70's until today, published in the New England Journal of Medicine.](#)²⁰

¹⁸ <https://www.kreftregisteret.no/en/>

¹⁹ <https://www.forskningsradet.no/en/>

²⁰ <https://www.nejm.org/doi/full/10.1056/NEJMoa1206809>

Emily: We also wanted to see if there were any really good sort of longitudinal studies that compared one cohort of women who got mammograms to a cohort of women that didn't get mammograms, which sort of sounds crazy cause the idea of randomizing women and saying to one group like you're not going to get a mammogram is something that I don't think we could ever do in the United States but it turns out they did this in Canada, so from 1980 to 1985, 89,835 women were divided into two groups. One group got mammograms, and one group did not, but they did get annual physical sort of checkups or self-exam. They were told to do sort of self exam, breast checks. That study was followed up 25 years later, which was 2014, and so we wanted to talk to the senior author on that study which was called the [25 Year Follow Up for Breast Cancer Incidence and Mortality of the Canadian National Breast Screening Study](#)²¹, which was a randomized trial screening.

Dr. Miller: My name is [Anthony Miller](#)²². I'm a professor emeritus, that is retired from the Dalla Lana school of Public Health at the University of Toronto. I am a cancer epidemiologist. I've done a great deal of work on cancer epidemiology, causes of cancer. I have advised the [U. S. National Cancer Institute](#)²³, the [World Health Organization](#)²⁴ and served on a number of committees and working groups of the [International Agency for Research on Cancer](#)²⁵. I became interested in the possible ill effects of radiofrequency radiation because I did some studies on electromagnetic radiation, [the effects of electric and magnetic fields in the occupational circumstances in the 1980s in Toronto](#).²⁶ We did a study of childhood leukemia at that time and we found increased risk for workers of those who entered a strong electric field and [we found increased risk of childhood leukemia in children who had poor wiring in their homes](#)²⁷, which caused exposure to magnetic fields. And then in 2011, I was an expert advisor to the [International Agency for Research on Cancer](#)²⁸ and I reviewed all the data that had been collected for the [agency's review of radio frequency radiation in 2011](#)²⁹ and I decided this was something I had to be involved in. Since then, I have become an expert advisor to the [Canadian Association for Safe Technology](#)³⁰ and the [Environmental Health Trust in the U.S.](#)³¹

²¹ <https://www.bmj.com/content/348/bmj.g366>

²² <http://www.dlsph.utoronto.ca/faculty-profile/miller-anthony-b/>

²³ <https://www.cancer.gov/>

²⁴ <https://www.who.int/>

²⁵ <https://www.iarc.fr/>

²⁶ <https://www.ncbi.nlm.nih.gov/pubmed/8172168>

²⁷ <https://www.ncbi.nlm.nih.gov/pubmed/10454069>

²⁸ <https://www.iarc.fr/>

²⁹ <https://www.ncbi.nlm.nih.gov/pubmed/31457001>

³⁰ <http://c4st.org/>

³¹ <https://ehtrust.org/>

Emily: Talk to me a little bit about what you have sort of come to learn or come to realize about the impact of mammography on death, I guess on cancer deaths specifically. We have your, which we'll link to in our show notes, [BMJ article](#)³², looking at this longitudinal study that you were a part of.

Dr. Miller: Yes. Well I initiated that study in the 1970's there was a great deal of discussion in Canada as well in the U.S. at that time of the possible role of mammography. I served on committees in Canada and the U.S. reviewing what was going on at that time. And I decided that we needed to do a better study. The U.S. decided to do what they called a [demonstration project of breast screening in 28 centers across the country](#)³³, but they used cancer control funds and they were not able to turn this into a research project, although at one stage, other epidemiologist [Alan Morrison](#)³⁴ who unfortunately subsequently died, his colleagues tried to evaluate what happened and decided there may have been a reduction of breast cancer mortality as a result of the screening, but they were not certain. So we decided to evaluate in Canada the role of mammography screening over and above breast examinations.

Dr. Miller: Recognizing that at that time in Canada, treatment had substantially improved compared to the previous decades. We followed these ladies, nearly 90,000 for 25 years, although we evaluated the impact of the screening, which went on in each women for four or five years. Yeah, seven years after initiation of screening, 12 years after initiation of screening. And then 25 years after initiation of screening, we could find no evidence that mammography reduce breast cancer mortality and when we compared our study with the major study which has influenced most countries in introducing a breast cancer screening that is the [Swedish Two Counties study](#)³⁵. It was immediately apparent that the major difference between our studies was that at that time in Sweden they we're not using modern adjuvant chemotherapy after breast cancer diagnosis, whereas we were in Canada, as the leaders of breast cancer in Canada had all participated in the U.S. Studies, which had established the value of adjuvant chemotherapy.

Emily: Meaning that that has a real impact on survival rates.

Dr. Miller: Absolutely. When you look at the mortality from breast cancer, it's apparent that after the introduction of adjuvant chemotherapy in both the U.S. and Canada, [around 1980 there's been a major reduction in breast cancer](#)

³² <https://www.bmj.com/content/348/bmj.g366>

³³

<https://dceg.cancer.gov/research/cancer-types/breast-cancer/detection-demonstration-follow-up-breast-cancer>

³⁴ <https://academic.oup.com/jnci/article-abstract/80/19/1540/929498?redirectedFrom=PDF>

³⁵ <https://pubs.rsna.org/doi/full/10.1148/radiol.11110469>

[mortality](#).³⁶ But this in my view, is not due to screening. Though many radiologists would like to believe that it is due to the good modern treatment adjuvant chemotherapy after breast cancer surgery.

Emily: So I'm so glad you've brought this point up because I think some of the confusion, certainly that I have had, and I'm sure some of our listeners will also relate to is the word over-diagnosis is sort of a complex idea. Right? For me, I sort of feel like a test is positive or negative. It's black or white. It's there or it's not. And so how can you over-diagnose something? To me, the more that I've gotten into the research on this, the more I feel like, it seems like it's an over-treatment. Like we are treating cancers that maybe don't need to be treated.

Dr. Miller: That's absolutely correct. As we increasingly for many different cancer sites use screening tests, we discover cancers that in fact were quiescent. They are true cancers. That's what they look like when you take them out and they're examined under the microscope by a pathologist. But in fact, they are not, they're just staying there. There is a sort of quiescence of the cancer as if the body is keeping these cancers under control, they're not growing and they would not have grown and killed that person in that person's lifetime. And so essentially we are screening tests which are increasingly sensitive, are finding these cancers which are not, were not destined, if untreated, to kill a woman in her lifetime. And we have the same phenomenon in many other cancers, prostate cancer, particularly in men.

Emily: But so I think part of the reason that this so confusing or complex is that it's based on a sort of a retroactive analysis, right? Like how do we know that the cancer wouldn't ever metastasize?

Dr. Miller: Well, the reason we are able to determine that is that we find all these cancers in excess in the screen group compared to the control group. And in our study, there was no difference in breast cancer mortality, but these excess cancers which were found, you can quite readily determine, analyze the, comparing the groups the extent to which they comply with the definition of over-diagnosis. In fact, pathologist's don't like over-diagnosis cause they say we've seen it and it's a real cancer. In fact, what they prefer is the term over ascertainment. But over diagnosis is to become really too common in parlance to ignore. In fact our analyses of over-diagnosis- in the Canadian national British breast screening study demonstrating that a large number of the cancers found by mammography that were not detected by the breast examinations are over-diagnosed. So that if a cancer is found by mammography and you cannot detect it by a good breast examination, there's

³⁶ <https://www.nejm.org/doi/full/10.1056/NEJMoa050518>

a very good chance that's over-diagnosed and doesn't need treatment. Though, of course, the mere fact that you've found it means you've taken it out.

Emily: Yeah. Well and so that would be like the DCIS kind of cancers, right?

Dr. Miller: In a sense. Yes. It's an extension of DCIS into what pathologically appears to be an invasion, but in fact it's not going to kill the woman if it hadn't been removed.

Emily: But it does sometimes, right? I mean, DCIS does sometimes turn into invasive cancer.

Dr. Miller: Well, it's not at all clear whether we're talking about just the development of DCIS or the fact that in another part of the same breast, another form of cancer arises and becomes invasive and it's very difficult to distinguish this.

Emily: Yeah, no, I know. And I think that's sort of part of what we're struggling with in terms of trying to accurately get the information to women so they can make their own choices about these kinds of screenings. But, so just to go to your study for a minute, it sounds like during the course of the study there were 3,250 women in the mammography group and 3,133 in the control arm that both of which had breast cancer diagnoses during the course of the study. And I think that's really interesting because that's very, I mean that's a kind of beautiful in the perspective of doing a study where it's very or close to being equal in each group. And so I was just curious like how did that work? Some portion of the population in the study were told, okay, you're going to get regular mammograms and the other group was told you're just going to do self-exams. Is that correct?

Dr. Miller: Essentially what we did was by various means, we contacted women in the population and we invited them to attend screening centers and then we put them through a process called informed consent. This was largely administered by the nurses who explained to them the study, explained to them that whether or not they would get a mammogram would be determined at random. They had no role in that. But if the woman agreed to come into the study, they had a 50/50 chance they would get a mammogram. Otherwise they would not. And everyone would be followed. And we followed the women who did not get mammograms through their family physicians. We had good collaboration from the family physicians as we had from the women. And then we have good records in Canada of women who develop cancer and also good records of deaths. We should collect it centrally. It's statistics Canada. So it was not difficult for us to link our records to those as statistics Canada to determine which women had developed breast cancer and which women had died of it.

Emily: And it was about 500 and then 505 from each group that died. So I'm mean again, very, very, very close. You know, I was so excited to find your research because I feel like, you know, you always sort of want to have this control group that doesn't have the intervention. And in the United States right now, it seems like you turn 40 and your friends toast you with a glass of champagne and ask if you've had your mammogram yet. So I don't know how you would do a study of women who didn't have mammograms because it's just so pervasive.

Dr. Miller: It would be very difficult now in the U.S. to do that. You can evaluate different forms of mammography and that has been done and that is informative. But to compare women who have mammograms with those who do not it would not be possible to do a study like that anymore in the U.S. nor would it in Canada because unfortunately the authorities, when we completed the screening and the study, they had a meeting and they decided to initiate screening programs without waiting for our results.

Emily: So, interesting. How did you feel about that?

Dr. Miller: Well, when you spend a lot of time and effort doing a study and then people ignore it, you don't feel very happy, I can assure you.

Emily: Well, what do you make of that? Because I feel like there is this, you know, there seems to be a real backlash against the research that is coming out against screenings. And I as a, you know, reporter sort of become curious in anything like that because you think, well, you know, are these people all wrong or is this misunderstood in some way? Is this a threat? Right? Like financially or otherwise? What is your sort of takeaway? Have you had any kind of backlash against you or your work?

Dr. Miller: Not very much in Canada, but a great deal for the U.S. When we published, we had a great deal of hate mail from the U.S. being accused of killing women and such like, and some of it in fact came from the people who were essentially earning a lot of money doing mammograms.

Emily: The point of the whole podcast is really to get women information so that they can make the best choices for their bodies. And one of the things that I'm struggling with with this episode is this idea of sort of looking at something from a population level and seeing what the trends are. And so we looked at the [specificity and the sensitivity](https://www.ncbi.nlm.nih.gov/pubmed/12558355)³⁷ of mammogram testing and we sort of crunched some numbers to sort of understand the positive predictive value and all that. And the test itself seems pretty terrible, right? I mean it doesn't seem like it's actually a great predictor to the point where the comparative analysis reveals that it's basically about the same as the general population

³⁷ <https://www.ncbi.nlm.nih.gov/pubmed/12558355>

statistics. So if you were to just randomly pick a little bit less than 2% of the general population, it would be about the same as what the mammogram is doing.

Emily: So like just unplug the machine basically and randomly select women who have breast cancer and you might be pretty close to the same results. Now that said, on a patient level, it does seem like, you know, everybody I know who's had breast cancer, they found it through a mammogram. And so that becomes sort of hard to reconcile, right? Where you sort of are like, okay, I understand that there's this over-diagnosis, we know the treatment in this case causes the disease, right? So you do want to avoid that if possible. And we know the standard of care is like you find it, you treat it. Do you have any women in your life and like what do you sort of, how do you explain this to them on an individual level?

Dr. Miller: Oh, well there's a number of women in my life. I have three daughters, I have 10 granddaughters and so on. I've even got two great granddaughters. Though they're nothing like the age which they would consider mammography. No. And that when we talk about it, I tried to explain to them that well, what we believe is more sensible than doing mammography is not to do breast self-examination, as used to be taught on a regular basis, but to be aware of their breast, to be aware of the consistency of their breasts. I mean, if they feel anything at all, they compare that area of their breasts with the opposite breast. And if they're all concerned, they'd go to see a physician who is an expert in examining breasts. And one of the things that then happens usually is a mammogram and mammography is good for diagnosis, but it's so happens particularly in younger women that mammography will not detect all breast cancers that need to be treated in younger women.

Dr. Miller: So if they find an abnormality which appears possibly to be breast cancer and even if the mammogram is negative, they probably should have a surgery and have a small biopsy and then make a determination as to whether that is breast cancer, allow the pathologist to make the determination as to whether that's breast cancer or not. It's important that we are aware that this is what is now being recommended worldwide. I mean we know that mammography is really only possible in a country which has good health services and the people are afforded or can afford it or the government in our case in Canada affords it. In many countries in the world breast cancer is still the most important cancer in women, but they can't have mammography screening. And what the world health organization is trying to teach is this form of what we now call breast awareness. Being aware of the structure of their breasts and if they find a change, see someone who is competent to examine breasts. And not all physicians, unfortunately, family physicians have been taught to the standards to enable them to determine whether or not a woman

has breast cancer. But as I say, then other diagnostic tests can then be put in place.

Emily: And your study looked at women who were 40 to 59 years old.

Dr. Miller: That's correct.

Emily: And does that, does your feeling towards any of this change when women get older?

Dr. Miller: I don't think there's any evidence to suggest that there's any particular difference. There was one analysis which tried to combine the various studies that were done in Sweden, which seems to suggest that the benefit of mammography was largely restricted to women ages 60 to 69. But as we have concerns over most of the Swedish studies, I don't think that should be applied, generally. We recruited women age 40 to 59. Largely because we felt this was the age group where there was a priority to investigate. We didn't want to ignore all of the women, but we did find that the older women were even within this 40 to 59 age group, the less they were prepared to consider volunteering for our study. So I don't think we would have had much success if we'd had an older age group.

Emily: And how do you see the landscape changing from, you know, sort of back in the 70's when you started looking at this to today?

Dr. Miller: Well, what's particularly changed has been the way the radiologists have adopted different forms of mammography and the way people have decided many people, not everybody to accept these, I mean types of mammograms that were given in our study what are now called [analog mammograms](#). [Digital mammography](#)³⁸ came in later then. Now there is a form of [tomography](#)³⁹ which evaluates breast cancer. But when I look at the studies that have reported on these, it seems to me that what's happening is yeah, detecting more cancers that would not have progressed. In other words, they're increasing the extent of over-diagnosis. And I don't see any evidence from the population studies that people are doing that mammography is responsible for reduced death rates. And there've been a number of studies and to be compared different areas of Europe, somewhere, mammography has been introduced, others have, they hadn't. And these tend to show no particular benefit for mammograms.

Emily: And again I feel I just want to make sure that I have this really very clearly explained and understood. This idea that there are cancers that would

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<https://www5.komen.org/BreastCancer/Table31Digitalmammographyversusstandardmammographyforbreastcancerscreening.html>

³⁹ <https://www.fda.gov/radiation-emitting-products/medical-x-ray-imaging/what-computed-tomography>

not have developed into metastasized cancers that would kill the woman is based on looking at overall death rates of women who have died of cancer, of breast cancer versus women who have not, or women who have been treated for breast cancer versus women who have not.

Dr. Miller: It's actually not based on death rates. It's based on looking at the occurrence of breast cancers in women who have not been screened compared to those who have and seeing that there is this great excess which persists once you stop screening there still this excess as a result of the over-diagnosis from mammogram.

Emily: So just to explain that, I'm sorry to harp on this point, but I feel like it's so important that we understand this. It's that if you look at one group of women who have mammography versus the other group that does not have mammography, you see there is a lot more cancer detected in the one that does have the mammography. That's correct. Right?

Dr. Miller: Yes.

Emily: And then step two would be that that cancer that is detected and then treated—probably, Right? In the mammography group—doesn't progress because it's been treated. So that's where I get sort of fumbled up. I don't understand how you can say it would have progressed versus it wouldn't have progressed.

Dr. Miller: It's not looking at individual cancers. It's looking at the totality of cancers and the occurrence of the cancers over time. And what happened subsequently, I mean what screening does, even if there's no over-diagnosis, is to bring forward the time of diagnosis of the breast cancer. So a cancer that might have progressed being detected by the woman herself say at the age of 52 may have been found by a mammogram at the age of 48 so the time of diagnosis is being brought forward four years. Well, when you compare women who've been screened with women who have not been screened and look at the pattern, the incidence of breast cancer, the rates of breast cancer occurring in those women, it becomes apparent there's an excess in one group, which isn't mirrored over time with the other group. So there's an excess in the screened group and the other group not screened never catches up. So you've got this excess as a result of screening.

Emily: So just so as a hypothetical, let's just say you screen a thousand women and five of them have breast cancer that they're treated for. And in the other group you have a thousand women and two of them find lumps in their breasts. I mean this is not based on like actual statistics, right? But just as a sort of thought experiment. And so your point is the fact that you found more in the mammogram group is symptomatic of finding rather than something that

would cause a problem because the ones that are self-diagnosed or found through other means besides mammography have progressed...

Dr. Miller: It's not on an instantaneous basis. It's done on the basis of a long term follow up. Because we have a long term follow up, were able to do this, do this sort of analysis, longterm followup where initially that was screening and then it stopped and later some of the women came into the mammography programs in the country. And you could see that in terms of the trends and incidence when there's still this major excess in the screened group, the control group never catches up.

Emily: And so if you're not looking at death rates, then how is that determined? Because it seems to me like you'd find this and then the women would be treated in one group and then the other group they might find it or they might not. Right?

Dr. Miller: I mean, essentially what is collected in Canada is not just the death rates, the deaths. It's also the cases and the cancer registers and so on. Its essentially counting the cases year by year and filling them year by year and can determine the cumulative numbers and the cumulative numbers in the screened groups they're always in excess of the control group.

Emily: And your study that that had very little impact on death.

Dr. Miller: It had no impact.

Emily: And then what about other screening like ultrasounds or MRIs? Do you find those to be similar in the, in the regard of over diagnosing?

Dr. Miller: I don't think so. We don't have the evidence for MRI or ultrasound in terms of screened group vs. controls. While they're essentially doing for MRI is largely those women who are known to have inherited risk factors, genetic changes, a BRCA I and II. They are providing them with the benefit of earlier detection. Whether or not they are doing any good in terms of reducing their death rates. We have no idea because that's just never been tested. Ultrasound is useful to distinguish between, you know, those lumps which are essentially cysts and therefore not cancer. And they can also help in resolving some issues in women who have [dense breasts](#)⁴⁰. This has become quite a problem in the U.S. And Canada. But there still no evidence that either of these approaches reduce death rates for breast cancer.

Emily: One of the things that strikes me about this mammogram episode is something that we come across fairly frequently, which is that we look at these population based studies or huge statistical analysis and we can see that

⁴⁰ <https://www.mayoclinic.org/tests-procedures/mammogram/in-depth/dense-breast-tissue/art-20123968>

there's an effect, but when you're actually thinking about your own treatment or as a doctor, you're thinking about how you're going to treat your patients. This becomes something different. And I think this is probably why people refer to medicine as an art form because you have to sort of look at the whole person and think about what are their risks of developing breast cancer. And if you're really at a high risk, whether it's genetic or some other environmental exposure that you've had, then maybe you're going to decide that a mammogram is worthwhile. If you're at a really, really low risk, then you might come up with a different conclusion. And I think for me it's really interesting when we look at these kinds of big trend models and we can see that there is an effect. Albeit very, very, very, very, very, very, very small. Then how do we translate that into our own lives? And I think you might feel super stressed out not getting a mammogram because you might be worried about it and then in that case then you might lean towards getting one. But as far as the efficacy of it being a good test, I think we can pretty conclusively say it is not a good test. It misses cancer and it finds things that are not cancer. And then it leads people down a path where they're treated for aggressive metastasis kind of cancers when maybe it's not. So we're going to continue to explore this and next week we're going to talk to a radiologist who was the head of radiology for Mass General Hospital here in Boston, which is a Harvard teaching hospital and he thinks women should have mammograms and we're going to explore this farther to sort of give you guys all the information that we can so that you know when you go to get your mammogram—or you decide to not—what's involved. 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.