* Perfect. So Hi, everybody nice to see you all. It's been a little while since we've had our cancer epi trivia. So we thought, we'll start with that. Then we're going to turn it over to Colleen Michelle, who are going to give a presentation about survival in cancer, both methodologic as well, some substantive work. And then, after that.

1:16

* Kresge 502 Cart: we're gonna discuss the article that was by welcoming day. We'll actually have you turn to your neighbors and have a little group discussion. First, we're gonna pose a few things for you to think about while you're talking about the paper, and then we'll all come together, and I know there's been some great comments already on the Harvard Canvas board which we're really looking forward to see, and then also kind of have that discussion.

1:38

* So why don't we turn first? And so I guess. Can you see the

2:03

* Kresge 502 Cart: where do you? How will they see that? Sorry?

2:10

* Kresge 502 Cart: Oh, my goodness, why don't.

2:18

* Kresge 502 Cart: did I? Okay.

2:20

* Kresge 502 Cart: maybe that's so strange.

2:24

* Kresge 502 Cart: Oh, maybe I'm just saying the meeting's pretty important. This is our sharing.

2:40

* Kresge 502 Cart: Oh, starts video.

2:48

* Kresge 502 Cart: yeah.

2:51

* Kresge 502 Cart: Desktop.

2:59

* Kresge 502 Cart: Do you know how to do it on a PC

3:13

* prostate cancer survival.

3:36

* So the question is among prostate cancer patients, what is the primary cause of mortality after a diagnosis of prostate cancer. Is it a prostate cancer?

4:01

* Kresge 502 Cart: Is it B. Death from other cancers? See Alzheimer's disease

4:12

* Kresge 502 Cart: and or d cardiovascular disease? And so now I can't see in. But then we can show the responses.

4:18

* Kresge 502 Cart: Ok. Got it so they can see each other. Got it. Ok? So 2 people who logged in

4:30

* Kresge 502 Cart: 6 people

4:39

* Kresge 502 Cart: 7.

4:43

* Kresge 502 Cart: So let's give it 15 more seconds.

4:47

* Kresge 502 Cart: 10 more seconds.

4:55

* So

5:01

* 5,

5:03

* Kresge 502 Cart: 4, 3, 2, and one. And then where is it? Sorry?

5:06

* Okay.

5:14

* Kresge 502 Cart: sit on the screen.

5:16

* Kresge 502 Cart: Oh, wow! All right. So 6% of people said, prostate cancer.

5:18

* Kresge 502 Cart: 18% said death from other cancers. 12%, said Alzheimer's. But in fact, the main cause of death is cardiovascular disease. And if you looked at currently today, all prostate cancer patients, about 30% of deaths, cohort is cardiovascular disease. But actually, death from other cancers is actually quite high as well. And then Alzheimer's disease

5:28

* Kresge 502 Cart: disease is kind of about the same as prostate cancer mortality is, it's different, depending on the stage of diagnosis. So if you have an asthmatic prostate cancer diagnosis, about 90% of deaths argue with the cancer itself

5:53

* Kresge 502 Cart: set

6:12

* Kresge 502 Cart: before we get started. Just a reminder. You are hosting an office hour related to the letter to the editor this afternoon, right after class. If you have any questions that is due on Thursday at midnight.

6:22

* Kresge 502 Cart: you are welcome to work on your own or up through groups of 3. If you don't need to tell us in advance. You can just submit it as a group of 2 or 3. Just make sure everyone's name is on it very clearly

6:38

* Kresge 502 Cart: any questions on that. If it's a collaborative letter.

6:53

* Kresge 502 Cart: yeah. And what person was submitted, we only need one copy as long as everyone's name is on it, and the total length of the one that a single person could do, or if you were to submit a real letter to the editor, it could be a solo effort. So we wanted to mimic that as close as possible

7:05

* course

7:30

* Kresge 502 Cart: any other questions.

7:31

* Kresge 502 Cart: and then we will hopefully turn back your descriptive of the individual assignments between tomorrow or before class on Thursday, and then you should have gotten your presentation assignments as well.

7:34

* Kresge 502 Cart: The text of the letter yeah. The header could be separate. Yeah.

7:53

* Kresge 502 Cart: Sorry, guys, it looked really weird.

7:57

* Kresge 502 Cart: And I did it from my laptop.

8:01

* Kresge 502 Cart: Okay?

8:05

* Kresge 502 Cart: Oh, it just didn't let me share. You couldn't see the slides. Well, yeah.

8:07

* Kresge 502 Cart: sorry. Someone created a separate desktop on this. And so we don't know how to close it on here. Thanks for bearing with us.

8:29

* Kresge 502 Cart: Okay.

8:39

* Kresge 502 Cart: And then are you sure your screen? Yes.

8:40

* Kresge 502 Cart: I don't think so. Yep, just like share on some.

8:46

* It's

8:57

* Kresge 502 Cart: quite so. Nope.

9:00

* I'll be

9:03

* Kresge 502 Cart: okay.

9:25

* No cause you can still see.

9:26

* Sorry guys.

9:33

* Kresge 502 Cart: please select the very specific.

9:37

* Kresge 502 Cart: Oh, I was selecting only the slides, but since it's plugged into my entire. Oh, okay.

9:39

* Kresge 502 Cart: I'll try it again.

9:54

* Kresge 502 Cart: So much.

9:56

* Kresge 502 Cart: That's interesting.

10:03

* Kresge 502 Cart: You'll switch to the screen.

10:22

* Okay? Yeah.

10:27

* Kresge 502 Cart: Oh.

10:29

* Kresge 502 Cart: thank you for your pat issues.

14:20

* Kresge 502 Cart: Hello. And. Mary.

14:40

* Kresge 502 Cart: we can use the team.

14:44

* Alright, we're gonna start talking about some considerations for studies in cancer survival and cancer survivorship and a brief overview of what we'll be talking about. So we'll provide an overview of the burden of burden of cancer survivorship in the Us.

14:46

* Discuss a proposed research framework for working with studies of cancer survivorship, discuss some potential biases and measures that you'll see in these types of studies. Michelle will talk about some next steps in this research space, and then we'll give you a very brief overview of our research, which is in this space.

15:09

* Kresge 502 Cart: So I'll start with an overview of cancer survivorship. Just so, you know, in our work. And in this presentation we'll be using the definition of a cancer survivor that is used by the American Cancer Society as well as other institutions like the Nci, which is that someone is considered a cancer survivor at the point at which they're diagnosed meaning they are a cancer survivor from the day. They're diagnosed onwards through their treatment and potential eventual remission.

15:27

* Kresge 502 Cart: So areas of concern in this research space is very wide in scope, but might include things such as the effects of certain treatments, comorbidities, as well as effects on homoridities that are incident because of treatments such as cardiotoxic effects, like laurel, said about cardiovascular disease and prostate cancer survivors

15:54

* Kresge 502 Cart: as well as disease, progression, quality of life, metrics concerned with the well being of cancer survivors, both physical psychosocial as well as specific symptom burden. And then, of course, mortality, which is what we see in our survival studies.

16:14

* Kresge 502 Cart: So just to put a figure to what we're talking about the current estimates are that there are over 18 million individuals in the Us. Who are considered cancer survivors and comparing that to our total Us. Population that makes up over 5% of the total population. It's projected that this group will increase as well with an estimate of over 22 million by the year 2,032 and 26 million by the year 2,040.

16:31

* Kresge 502 Cart: So this figure just puts it on the same statistics that I just outlined, but breaks it down by age group. And of course we can see that the older age groups are where we see the greatest proportion of individuals who are considered cancer survivors. But I'll just highlight here on the very bottom. This is our group of individuals who are younger than the age of 50, and you can see that there has been an upward trend in this group contributing a larger proportion of cancer survivors, and that's projected to increase through 2040 as well.

17:01

* Kresge 502 Cart: So as noted, the number of cancer survivors is expected to grow. This can be attributed to a number of different things, including screening and diagnosis and potential over diagnosis as well as treatment advances.

17:32

* meaning that we're able to treat and manage the disease a little bit better in individuals. And hopefully, this makes sense of the figure tending to increase. If we go back to our Fb. 201 basics of what a prevalence is, it's a function of incidence which we have from increasing hypnosis as well as duration, which comes from both diagnosis where we're hopefully able to diagnose individuals at earlier stages as well as treatment advances where

17:46

* hopefully able to extend the survivorship period within reasonable burden.

18:10

* Kresge 502 Cart: So when we're talking about survival of cancer patients. Typically, you'll see statistics of the 5 year survival. That's kind of the standard metric that you'll see in population based studies

18:16

* Kresge 502 Cart: and across all cancer sites. It's estimated that the five-year survival is around 69, and that goes down when we're talking about more extended survival periods upwards of 18 for 20 year survival hopefully, that makes sense, though, since, as we talked about, most individuals are older age over 2 thirds of cancer survivors are over the age of 65 in the Us.

18:28

* Kresge 502 Cart: It's really important to consider that these statistics that we have are across all cancer sites and the site specific statistics are really important to look at individually as we looked at last week. There are certain cancer sites where the majority of diagnoses are in stages, 3 or 4 where individuals have advanced disease, and therefore the prognosis is a little bit shorter and more grim. And so, looking at site, specific statistics is really important.

18:52

* Kresge 502 Cart: This is just a graph that I included in case there was some interest of consideration of the differences, and how different cancer sites and demographic characteristics are contributing to the prevalence of survivors.

19:23

* Kresge 502 Cart: And so, as alluded to all of the cancer sites, we're contributing to some of these statistics. There are specific cancer sites where we have the much more cancer survivors who are living longer because these are sites that have greater treatment options and have screening programs that allow individuals to live longer beyond their diagnosis. So the majority of cancer survivors in the Us. Are breast cancer, prostate melanoma and polar rectal cancers.

19:38

* Kresge 502 Cart: But you can see this in perspective to some of the other major cancer sites of what groups are really contributing to that figure of 18 million individuals.

20:07

* Kresge 502 Cart: Stage is another really important factor to consider individuals who are diagnosed in their earlier stages might have better treatment options potentially curative treatment options. If cancer is diagnosed in Stage one and it's confined to this specific organ of interest, and the tumor is able to be removed from surgical procedures. There might be greater options for extending survival

20:20

* as opposed to someone who essentially has stage 3 or 4 disease. And we need systemic options that are trying to target each and every cancer cell in the body. But this represents a really important group of individuals who have advanced disease and specifically metastatic disease, who have potentially unique needs and contribute a large portion to the cancer survivorship population. In the Us. The current estimates are just over 600,000 individuals are metastatic cancer survivors specifically, and this figure itself has also projected to increase.

20:43

* Kresge 502 Cart: This is hard to see the difference in colors on here, but this is a breakdown of that group of individuals broken down by whether or not, they had de novo metastatic disease, or presented with metastatic disease or diagnosis versus recurrent metastatic disease.

21:17

* Kresge 502 Cart: And with that, then I'll transition over all right. So now we're going to talk about cancer survivorship research framework.

21:34

* Kresge 502 Cart: so in collaboration between Bergmann Woman's Hospital, Harvard Medical School and Ci experts, policymakers, advocacy groups and cancer survivors. The cancer survivorship care quality framework was created. And this framework is an interplay of individual interpersonal organizational community and policy factors. Of course. But today we'll be focusing on the

21:43

* individual level factors. So this framework serves as a foundation to define 5 domains of cancer survivorship care as well as general needs for this patient population. So the domains are interrelated and codependent on each other, of course. But consideration of these domains can help us think about research questions and developing ideas that we want to do research on improving the quality of life.

22:09

* improving care, access to care and overall outcomes for cancer survivors.

22:33

* Kresge 502 Cart: So let's get started. So the first one is reoccurrences and new cancers. So cancer survivors are at an increased risk for reoccurrence of primary cancer. But also the development of new cancers as well due to their genetic predisposition. So hence there's a need for surveillance for subsequent cancers, such as through repeated physical laboratory tests

22:40

* Kresge 502 Cart: and imaging. So if you recall from a couple of weeks ago, when Dr. Eliison came and spoke about breast cancer, hormone, receptive, positive breast cancer is the most diagnosed subtype of breast cancer that we see.

23:04

* Kresge 502 Cart: and for hormone receptor, positive breast cancer endocrin therapies used as a adjuvant treatment to reduce the risk of reoccurrence, and that's also to reduce the risk of death.

23:18

* Kresge 502 Cart: However, for a lot of populations, especially vulnerable populations, such as individuals of color, individuals who may not have insurance or speak different languages. Adherence can be so optimal, so assessment of adherence, of adjuvant or risk reducing strategies can help identify populations who are at higher risk and who may need additional interventions as well.

23:29

* Kresge 502 Cart: Next, we have physical effects. So cancer survivors are at risk for physical effects of cancer as well as treatment. Of course, this depends on what type of cancer individual diagnosed with and the type of treatment that they're treatment plan that they're going through. So this requires assessment of symptoms, conditions via medical history and physical examination. So, of course, there are various treatments and different combinations of treatments.

23:57

* Kresge 502 Cart: But some of the side effects that can come with this, for example, with chemotherapy, include nausea, fatigue, constipation, diarrhea, hair loss, chemo induced neuropathy. Amongst many others.

24:26

* Kresge 502 Cart: Next, we have psychological or psychosocial effects. Sorry so similarly to physical effects, psychosocial effects, the type and extent of surveillance will depend on the cancer type and treatment. Of course. So this can be done via assessment of symptoms and conditions using validated questionnaires and instruments.

24:43

* Kresge 502 Cart: So some examples of psychological effects include anxiety, depression, cognitive changes, fear of reoccurrence, and then, on the other side, some social effects include financial toxicity, loss of work, productivity, return to school change in insurance status, interpersonal issues, such as with family and caregiver relationships as well.

25:05

* Kresge 502 Cart: Next, we have health promotion. So just because someone has a cancer diagnosis, this does not mean that. And an individual will change their health behaviors at the drop of a hat.

25:32

* Kresge 502 Cart: So, in fact, a lot of research research shows that cancer survivors tend to be more obese, less active, and have higher levels of smoking than those who do not have cancer. So assessment of live self behaviors is needed when we're talking about cancer, survivorship care. And this can range from asking questions about physical activity, smoking, cessation, age and sex for chronic conditions and vaccinations as well.

25:44

* Kresge 502 Cart: And lastly, we have chronic conditions. So so far, we've noted that physical effects and psychosocial effects after treatment are some of the domains that we want to focus on. But it's also important to acknowledge that there are some high prevalences of front conditions both before and after diagnosis of cancer and some non-related non cancer-related conditions include hypertension diabetes, cardiovascular disease. Copd, amongst many others

26:13

* Kresge 502 Cart: this week. Yeah, go ahead. Last point I would just mention, because

26:46

* Kresge 502 Cart: chronic diseases. Today, we know that all these exposure to chemotherapy causes changes in the deep, and we call them today.

26:53

* Kresge 502 Cart: And there are changes in it that occur with age which is interesting to the last couple of years. We now know that

27:01

* Kresge 502 Cart: the modification of all these work, or a lot of these modifications and chronic conditions, go through all these modifications in the DNA. So there's actual pathogenesis of the DNA changes that makes cardiovascular toxicity higher calculation. And there are papers on copd immunological diseases.

27:12

* Kresge 502 Cart: So we know another piece of that, not just association, but also the part of physiology.

27:34

* Thanks.

27:44

* So care for cancer survivors is complex. And in the Us. We have a very complex health system. So aspects of getting care for cancer survivors includes primary care, oncology, survivorship, clinics, the type and availability of providers offering care overall access to care, communication and decision making cancer treatment plans across health teams.

27:48

* access to research participation and patient caregiver experiences within just the health care system itself. And of course this can differ based off of how individuals may identify. So across race gender identity, socioeconomic status just to name a couple.

28:15

* And of course, then, comes into question, how do we measure this in the spatial population? So, of course, some of these outcome measures are not necessarily distinct for the spatial population. But these measures can help researchers identify gaps in care and survivorship experiences.

28:35

* So outcomes include health related quality of life, including physical, mental, emotional, social functioning, healthcare utilizations, specifically like emergency care, hospitalizations, critical care, use.

28:52

* Kresge 502 Cart: cost of care, including those to the patient health care, system and mortality. So all cause mortality and cancer specific mortality. So an example for health-related quality of life measures that we use.

29:05

* Kresge 502 Cart: Me and colleen are the er Tcg. 30, which is a validated questionnaire for health, related quality of life among cancer survivors, and is applicable in over 100 languages, which is a functional assessment of cancer therapy questionnaire. And that questionnaire also has extensions for specific cancer sites as well.

29:22

* Kresge 502 Cart: Ok, great. So transitioning to specific considerations for epidemiologic studies of cancer survival. Specifically.

29:53

* Kresge 502 Cart: we wanted to just flag a few measures that you'll see. Commonly some of these will be very familiar, hopefully, and just a caveat that we're talking in the probability framework here, but of course, these can be extended to event analyses, and so measures. You'll see, as Michelle alluded to include all cause mortality, where we're looking at the total number of deaths across the population as well as cause specific mortality. We're concerned with death due to a specific cause, say cardiovascular disease.

30:04

* Kresge 502 Cart: And then there are some other measures that might be of interest. For example, overall survival within the cancer population where we're looking at the number of patients that are alive after some period of time. Like, I said, a lot of the time we'll see metrics of this five-year period among the total cancer patients for that site. There's also relative survival, which is a comparison of the overall survival for a specific cancer

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* site and a comparison of that overall survival among a similar but cancer-free population to try to deduce the effect of the cancer on survival.

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* Kresge 502 Cart: And then also, we, of course, have cause specific survival which is related to that specific mortality measure. Again, an interest of not dying of a specific cause. Among the total population of patients

31:07

* Kresge 502 Cart: there are a number of potential biases that we think about often when we're designing studies of cancer survival. These are not unique to cancer, epemiology, or even chronic disease equity. But we do see them in this space fairly often, and this is not any means to try to tell you how to fix a study. If you have these issues, there's whole chapters on some of these or whole classes on some of these issues

31:22

* Kresge 502 Cart: here. So this is just a brief overview, so that you're familiar, the first of which is competing risks. So to define a competing event is something that inhibits our ability to observe the event of interest.

31:47

* So, for example, in our studies of cost, specific survival, say, breast cancer, specific survival or breast cancer specific mortality on the flip side. If someone died of cardiovascular disease that would be a competing event that precludes our ability to have seen them die of breast cancer. To handle this, there are a number of different modeling frameworks and decision to make as someone who's designing this study.

32:00

* including using a cause, specific hazards approach or a sub distribution hazards approach. You can learn about that in Biosat 223. There is probably a month's worth of lecture on that.

32:24

* Kresge 502 Cart: Another issue that you might see is immortal time. Bias so immortal time can be defined as a period of time where it's not possible for study participants to have the event of interest, such as a death, for example. And that's why it's quote unquote, immortal.

32:36

* Kresge 502 Cart: I'm just going to hopefully see great that work. There are a bunch of different ways that a mortal time bias can come up in our studies and function as a specific type of bias. But it's really a nature of the determination of an individual's treatment status or their exposure status involves some delay in between the time that they're enrolled and your time of starting follow-up and their actual treatment received

32:53

* Kresge 502 Cart: depiction. There's this exposed group on the top, and an unexposed group on the bottom follow up, started, but we did not observe anyone have their first prescription, which made them exposed of this study of, say, a prescription drug use

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* Kresge 502 Cart: until this time point, but because we observed that we know that they didn't die any time before that, however, they weren't exposed at that time. So it's kind of misclassified person. Time there again. This is a really complex issue, and if you want to learn more about it. You can take bias at B 203, where you'll have a great Tf. Next semester. We'll talk about this Michelle

33:34

* Kresge 502 Cart: and if you want to learn more about mobile time by his colleague is linked this paper that goes way more in depth, with different types of moral sign bias

33:58

* Kresge 502 Cart: and describes different types that can occur and what to do in your study design to prevent it, maybe. Can you talk just very quickly? If you were designing the study differently, or could you to get rid of the immortal times? Example?

34:09

* Kresge 502 Cart: Yeah. So the kind of way to make sure that you don't have a mortal time bias. One of the ideal ways is to emulate a target trial which a lot of the folks in the causal inference space here talk about B 289. If you're in lab right now, and F 207 will talk about that extensively. But the ideal way to do that is that you choose a time scale at which you can align the time 0 where you start, follow up the eligibility of being in the study, and then the exposure determination, so that you don't run into this issue of potentially

34:25

* Kresge 502 Cart: and having misclassified for some time is one option. Yes, alternatively. You could also take that period of time where your treated individual is not being exposed at that point in time, and just consider them unexposed for that period of time as well.

34:56

* Kresge 502 Cart: All right. So the next bias that we would raise is lead time bias, lead time bias as well as length. Bias are particularly relevant in studies of cancer screening, which is what we're going to talk about a lot more today.

35:17

* So the lead time is the time between which a cancer is detected by screening versus the time between which it would have been detected by symptomatic presentation and going to the doctor and diagnosed.

35:29

* And so I have a graphic here that shows that as well. I believe the paper where this is from, as well as a very technical source. If you want to get into the math behind this, which I don't want to. But you can see here, if we attribute that the null hypothesis is true that screening truly doesn't have an effect on prolonging someone's survival. The patient would have died at the same period of time.

35:43

* Kresge 502 Cart: Whether they were screened or not, you can see that being diagnosed by screening in this upper group. Here they appear to be surviving longer than the group that was diagnosed, based off of their symptomatic presentation. So it looks like screening is effective for survival

36:07

* Kresge 502 Cart: moving on to length bias. So length bias is another concern in these studies of cancer screening or other screening across disease areas. Probability of being in your sample is proportional to some characteristic. And in the case of cancer screening.

36:27

* Kresge 502 Cart: If that works great. It might be related to the screen detectable period in which we are able to observe that tumor, and if more indolent tumors have a longer screen detectable period than, say, an aggressive tumor where they have symptoms starting sooner, we are more likely to observe individuals that have this longer period of potentially being detected by screening. And again, this can overestimate the effectiveness of screening

36:53

* Kresge 502 Cart: great. And the last issue we wanted to raise was on prevalent users. So this is a bias that occurs. If you are looking at a study where you're not looking at an incident exposure meaning something that is starting new, but rather something that individuals could have been doing beforehand, say, taking some drug versus not taking some drug as your comparison, but they have been taking it

37:24

* all along before they were even thought to be in your study. So this is an issue that arises where, if the exposure was truly harmful and you include these prevalent users. Anyone that would have been harmed by that might not be in your population, there might have been a depletion of susceptible individuals, in which case the people in your study might not be representative of the true effect of that exposure and outcome relationship.

37:47

* Kresge 502 Cart: This is just a kind of overview of all of this again, not meant to be comprehensive, but just to provide you with some things to think about. If you're designing these studies.

38:12

* Kresge 502 Cart: Okay?

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* So now we want to talk about some next steps in cancer, survivorship, survivorship research.

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* Kresge 502 Cart: So we can use research to improve clinical care, quality of life and understanding of adverse effects of treatment to improve the health and well-being cancer survivors and caregivers.

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* Kresge 502 Cart: So we can do this by defining population needs for various cancer sites and systematically evaluating evidence gaps when it can inform where needs are not being met. So another thing that we can see is standardizing outcome measures. So, as I mentioned previously. For health related quality of life. There are a ton of different ways that we can measure a health related quality of life for cancer survivors, including the Ertc. In fact.

38:46

* Kresge 502 Cart: but having a standardized method that is commonly used, can allow us to compare more studies that are looking at the same outcome being measured. We can also use methods from implementation, science to disseminate and implement interventions with shown benefit, but also de-implement interventions that have shown no benefit or have been seen to be harmful for cancer survivors as well.

39:12

* Kresge 502 Cart: So we just wanted to share some funding research opportunities that are currently available for research work into cancer survivors, including an Ro one. We're looking at research to understand and address survivorship needs of individuals living with advanced cancer. Uon, looking to address the primary care needs of cancer survivors, and another Uon

39:37

* looking at a multi-level approach to conducting underrepresented populations in clinical trials.

40:01

* Kresge 502 Cart: So the Nci office of cancer survivorship actually posted this on their twitter yesterday. And we wanted to share this graphic where it shows the number of cancer survivorship brands that have been funded by the Nci. As of 27 since 2,017. So, as you can see, that number is increasing, and hopefully continues to increase in their patriotism.

40:09

* Kresge 502 Cart: So we can also think about power research methods that we develop can also be used in the clinical setting to improve care for cancer patients. So we can think about how and when clinicians can actively measure quality of life metrics, for example.

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* Kresge 502 Cart: quality of life metrics for their patients while also ensuring that we're not overburdening patients, providers, and medical systems when trying to measure these outcomes.

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* Kresge 502 Cart: For example, this could mean implementing patient navigators who may ask questions while patients are at their visits. Also, we can look at optimization of tools and collecting patient outcomes and processing measures to prevent provider burden, designing effective evidence-based clinical survivorship care providers, practices and health care systems

41:07

* Kresge 502 Cart: to systematically understand patient needs. And lastly, we can think about how we can implement full cancer survivor care quality framework in the clinical setting. So this might be easier to do in a comprehensive cancer center and a lot more difficult to do for smaller, independent oncology, clinics, and consideration of what's more feasible in those settings is also necessary as well.

41:32

* Kresge 502 Cart: And then, lastly, we can think about next steps in policy. So

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* Kresge 502 Cart: our research and what we do in this betting also impacts the policies that are implemented in the United States. So professional guidelines, training, reimbursement and health coverage for post-treatment. Care is definitely necessary and needed. And the research we conduct

42:03

* Kresge 502 Cart: can impact the community level to the Federal level, not to mention policies that impact insurance, professional organizations that promote cancer care and further support advocacy groups as well.

42:21

* Kresge 502 Cart: Umhm. And then we do have 2 slides on our research. But maybe in the interest of time. We'll leave that up. You can come to chat with us if you're interested in what we're working on. We're always happy to talk about it. We both asked our Pq. 2 very recently, so we're happy to chat about it whenever.

42:36

* Kresge 502 Cart: thanks.

42:52

* Kresge 502 Cart: I wonder if you could. Just I think that examples of lead time bias in particular, and as well as the other biases, are interesting as we talk about paper. I wonder if you might have an example of a cancer kind of talking about how long a link bias can be

42:57

* Kresge 502 Cart: like in screening. For example. like prostate cancer. Maybe. Yeah, I mean, prostate cancer would be a good example, potentially of length. Bias where we have these slower, growing, indirect tumors that probably would not have caused severe harm in patients or caused them to die of that. And so it's possible that we're kind of observing more of these individuals that eventually would have been fine as well.

43:13

* do you have an idea for lead time? I have a nice example.

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* Kresge 502 Cart: Think of like metastatic disease, like someone who's

43:46

* Kresge 502 Cart: like there's no potential

43:52

* Kresge 502 Cart: like next steps like in a very extreme case. So maybe they decided to get strained for some reason, before symptoms appeared. But the disease had already progressed, and then comparison to someone who just waited for symptoms to come. But both individuals died at the same time anyway.

43:54

* Kresge 502 Cart: and prostate is interesting from a lead time. Perspective. Is it like moved the diagnosis 7 years earlier to 10 years. So if you think about

44:16

* Kresge 502 Cart: 5 years survival or even 10 years survival for prostate cancer, people will say, Oh, it's 99%. Nobody died. But actually, it's the second reading. So it's interesting how big of an effect. And then, as you mentioned all these other cancers, that all of the burden that comes from

44:27

* Kresge 502 Cart: over diagnosis, too, of anxiety and then unnecessary potential

44:51

* Kresge 502 Cart: treatment. So you might hear sometimes people talk about with I can't feel like we talked about thyroid cancer, prostate cancer, even some breast cancers, maybe, where right here a term called pseudo disease, or actually 2 cancers physiologically. But cancers, people think, would never have progressed, never have caused harm.

44:57

* Kresge 502 Cart: Hi, so so I put a slide deck, and so I think the thought was that we'll give people like little time to just discuss we'll come up

45:24

* discussion. So to put together

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* Kresge 502 Cart: a few slides. So I think, you know, hopefully, everybody's had a chance to read

45:42

* Kresge 502 Cart: article. And just while we're pulling it up I can, just for things we'll be thinking about. So first, I kind of talk about why did Welch and Day even write this article? What was their motivation? Significance was, look at the figures and think about what's your interpretation of their findings? Do you agree with them? Disagree? And why are there anything

45:49

* Kresge 502 Cart: the cancers you've studied colorectal cancer? We haven't talked about prostate cancer yet. But are there things that you wouldn't know about? Cancers that make you think they might have missed the mark a little bit?

46:15

* Kresge 502 Cart: Yeah. And then I think I had a question about Oh, yeah, do you think the the I'm so assumptions that made were reasonable? Why or more, why not so? But really talk about whatever you wanna talk about anything that really resonated with you anything that gave you a little bit of pause and talk with your your neighbor, and then we'll we'll come together, maybe at 30'clock for for discussion.

46:30

* Kresge 502 Cart: Okay, perfect.

46:53

* Kresge 502 Cart: Put some questions there.

58:57

* Kresge 502 Cart: And I know some of you already sent some some good comments on the chat. So okay, let's start. So does anybody want to? Just let's.

59:26

* Kresge 502 Cart: it's always easy to begin, like what was the stated significance of the article.

59:38

* Kresge 502 Cart: Yes, the owners are supposed to attack screening costs so much economic work on their government, and so they want to question that their screening gets helpful. In the first place.

59:45

* Kresge 502 Cart: Ok, that's a good point. So there is economic burden. Any other burdens or other reasons. Yet

59:57

* Kresge 502 Cart: I think that the concept of are we actually saving life? Or are we going to do it? Done at the same time with other conditions, anyways.

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* Kresge 502 Cart: And in that case, isn't it competing on all the other life? Is it just really good causes?

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* Kresge 502 Cart: Right? So yeah, so there's economics. And then how many lives actually save, I guess.

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* Kresge 502 Cart: Okay, any other thoughts?

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* Kresge 502 Cart: Oh, I can see something big. Oh, I'm sorry. I was Ok, a little bit later in the origin. But is it actually hurting people to be undergoing this process?

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* Kresge 502 Cart: Right? So right? So some people may get safe. But they're you know, downsides, like

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* some people can. Can. Actually.

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* Kresge 502 Cart: you could even die from unnecessary surgery. Or, as Laurel mentioned.

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* Kresge 502 Cart: You know, side effects and treatment stress

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* Kresge 502 Cart: things like that.

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* Kresge 502 Cart: Okay? So

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* Kresge 502 Cart: they also differentiate between cancer-specific mortality and all cause mortality to propose looking at multi-cancer screening and alcohol mortality, to get at whether screening is saving lives, I think, is reductive.

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* Kresge 502 Cart: That's one of the arguments. Yeah, III think you have to add some useful.

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* This one here?

1:02:00

* Kresge 502 Cart: Right?

1:02:02

* Kresge 502 Cart: Yeah, could someone want to basically describe what you? I think? That's basically your point.

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* Kresge 502 Cart: You or anyone can describe, what's the main point? I mean, I think this is really the main point of of the slide of the paper.

1:02:14

* Kresge 502 Cart: So we think even common cancers. like, you know, we think, yeah, that they're common breast cancer prostate cancer. But when you consider the number of people who who die from them.

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* Kresge 502 Cart: it's a relatively small percentage of the total. So an easy way to think of it is, I think Colon, cancer is a common cancer. Spend a lot of time studying it.

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* Kresge 502 Cart: But it's still 10% of cancer, just cancer deaths or colorectal cancer deaths. And then that's of all cancer and cancer is only a percentage of total deaths. So when you get down to it. You actually, even for pretty common cancers, seems kind of small. But

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* Kresge 502 Cart: I mean.

1:03:18

* Kresge 502 Cart: do you think this is a good way of looking at it? I mean it is in some respect. But you think it's missing something? Or is this the only way to look at it? Or is there a counter argument. If you're saying screening is actually more important than you're making out on this?

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* Kresge 502 Cart: Or do you think it's a pretty compelling argument?

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* Kresge 502 Cart: I just had a quick question. Yeah,

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* it wasn't clear to me if panels C and D are real data.

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* Kresge 502 Cart: or is it just a hypothetical suggestion? They didn't really talk about that in the method. So there's no really methods of the same

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* Kresge 502 Cart: if I had. So I know there's no screening trial to our knowledge that has 30 years of follow up after a moment. So I do think, they said, in 30 years, given the age, this is how many deaths we would expect. So I think that's okay.

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* Kresge 502 Cart: They got that gem.

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* Kresge 502 Cart: Yeah, it's interesting for the Colonel, I mean, it's hard to see. But

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* Kresge 502 Cart: I think the columns are about the same pipe. It's just so. They're actually

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* Kresge 502 Cart: like, you know. Yes, so so the screening is probably saving some lives. But is that offset by the I don't get breakfast. Normally. I'm sorry. I think the grabs normalized. That's why the cones are the same height.

1:04:40

* Kresge 502 Cart: So it's like among all people that die, which percent would be due to death. So the world would be like all people that die. What's the risk of death?

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* Kresge 502 Cart: But after 30 years of follow up, you're saying 70% of the people would have died. So I don't think they realize that. And they just said, We expect, based on the outdate of these trials and 30 years of follow up that 70% of the population to be dead based on

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* Kresge 502 Cart: basic demographics. I think that's what they've done.

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* Kresge 502 Cart: Yeah. But you're right. There's no methods also. So it's hard to say exactly where they got these data from.

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* Kresge 502 Cart: Yeah, II think they really don't say

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* Kresge 502 Cart: where they got it.

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* Kresge 502 Cart: It's probably, but I think the point is still valid in a sense that it is true, because you do have data from the trials that have been done like prostate cancer trial

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* Kresge 502 Cart: for the the European study. What was

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* Kresge 502 Cart: like? How many do you remember roughly how many deaths from prostate cancer than total deaths. Yeah, you know, it was interesting because they didn't, even in that first publication, to even talk about total death

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* Kresge 502 Cart: at the first publication. No? Well, actually, I recall that the numbers I could be a bit off. But this is a trial that showed a benefit from screening on prostate cancer.

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* Kresge 502 Cart: They had something like

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* Kresge 502 Cart: like 70 deaths in the screening trial. And, like, let's say, around 100 in the control arm. But like there.

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* Kresge 502 Cart: the total numbers of deaths were almost identical. because I remember, these numbers may be off, but it's something like this. So this is total exams.

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* Kresge 502 Cart: So there were. So you know you have minus 30

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* Kresge 502 Cart: debt. So 30 30% reduction sounds impressive. But then, when you looked at the numbers now, you know.

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* Kresge 502 Cart: it was hard to tell like were there like 30 other deaths here. But that's out of 1,730. That's at least chance. So it's impossible to chance. But that's the main point. I think that if you're trying to do a trial to show

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* Kresge 502 Cart: a reduction in total mortality, even if there were like 30% reduction in prostate and no other death. So the trial was successful. The number is going to be too small for the total number

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* Kresge 502 Cart: to, you know, to look at a small reduction for the total. So so that's the main point, I think. Why.

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* Kresge 502 Cart: they would have to do like a humongous trial. But to get the numbers. But

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* Kresge 502 Cart: like so for colorectal, they estimated. Was it like 5.9 million?

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* Kresge 502 Cart: Here we go. Oh, yeah, this is.

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* Kresge 502 Cart: were anybody surprised by these, or having thoughts.

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* Kresge 502 Cart: the numbers they came up with here.

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* Oh, so

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* Kresge 502 Cart: one of this may equal other screen points. First, I think he talks about about Floss

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* observation studies. That's

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* Kresge 502 Cart: how how does 5 year over survival is not the accurate circuit marker how that is not accurately assessing, attributable to cancer screening cancer

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* Kresge 502 Cart: procedures that are associated that are also attributable in those studies. But

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* Kresge 502 Cart: one of the main things that I do from this table that he placed is that we want to show that maybe with all cancers or a movie cancer approach, we can lower the number

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* and get

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* Kresge 502 Cart: lower numbers that are maybe more rational to achieve certain

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* Kresge 502 Cart: period of time.

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* Kresge 502 Cart: Personally, Leon, I think that's wrong.

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* Kresge 502 Cart: Just because, as you mentioned, most of the patients with prostate cancer would not die of prostate cancer. Most of the patients with leukaemia would die with leukemia perspective to find everything in place, everything in the same basket for me. I've shown

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* Kresge 502 Cart: next step for a brief way to evaluate that

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* Kresge 502 Cart: But that's another. That's my advice.

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* Main problem with all at least putting everything in one basket

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* Kresge 502 Cart: and trying to decide that. I mean, he concluded.

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* Kresge 502 Cart: maybe we should do Rcts with multi-cancer studies to evaluate whether it is

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* Kresge 502 Cart: really beneficial

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* Kresge 502 Cart: or not. I think the result for that for prostate breast cancer or

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* Kresge 502 Cart: so, I'm not sure that's what I mean. That's what I do from this table, and I don't agree with it. But that's online.

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* Kresge 502 Cart: That's quite reasonable. Any other people that agree or have other.

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* Kresge 502 Cart: If people are not dying of pastures, they are going into fire. Another reason.

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* Kresge 502 Cart: Ok, so even though it be at all those deaths in together. Actually, the difference of dying cancer is really really small compared to

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* Kresge 502 Cart: countless of other reasons, whether it's like a disease or even an accident, because you have all class mortality. So also, that's why you would need such a big number of patients with cancer to actually test that. And it would be kind of similar to

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* Kresge 502 Cart: he rarely diseases. So it doesn't mean that because there's a really small number. And you're definitely gonna have enough power. But it doesn't mean that it does not exist. It does not benefit the patients

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* Kresge 502 Cart: and come up to your point also, though around the timing of death, like for colorectal cancer, you'd expect those to happen when, if you live to 5 years after diagnosis, you have a really good probability of surviving, whereas the other deaths might be 1020 years later. So it's also when you die, not only we're all going to die like we know for certain it's going to be 100% in that group at some point. But the timing of when you die in your life.

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* Kresge 502 Cart: Pretty similar.

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* Kresge 502 Cart: like statistics. And if you're going to throw all cosmetics, cancer is just like a small percentage. So you're gonna like, reduce your effect size in comparison to the population. And then you need more patients. But it doesn't like for me. Make the argument that you're not saving lives anymore.

1:13:04

* Kresge 502 Cart: stronger. It's just like, as I said, like, everybody's gonna die. So of course, the difference that we have because everybody's gonna die and cancer. Especially prostate that happens later in life. So of course, people are going to be exposed to a greater risk of death.

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* Yeah. similarly, I think

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* Kresge 502 Cart: this paper just made me question a lot like, what is the purpose of screen? And it's in the name itself. It's like to screen for cancer. And so like when I saw the mortality, I immediately other people like government policies will say, like this is saving lives like the actual intention of cancer screening was to identify

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* Kresge 502 Cart: the cancer, and hopefully the quality of life and assigned treatments are clear afterwards. The whole point was to save lives that were like from

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* Kresge 502 Cart: the cancer, and not just

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* Kresge 502 Cart: more generally. I'll know if that makes sense. But

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* Kresge 502 Cart: I would love that to be debated as well. Yeah, no, that makes sense. Yeah. yeah. Sorry if I missed that.

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* Kresge 502 Cart: If you want to go identify.

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* Kresge 502 Cart: I may be missing this sense. It's also my hearing is better than I've left.

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* Kresge 502 Cart: you know, when they generalize. Oh.

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* Kresge 502 Cart: it may not be worth it to screw you with cancer, because you may just die in 10 groups. Anyway, I feel like it's a big ask of a patient to accept this uncertainty, but it may or may not impact your total lifespan would scare me a little bit high-risk groups that would be especially stressful.

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* Kresge 502 Cart: Yeah, there was little discussion on risk. Stratification

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* Kresge 502 Cart: makes sense to capture the cancer-specific mentality through measure. That is all caused

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* Kresge 502 Cart: just somewhere, like the idea that should be a different view

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* Kresge 502 Cart: where it's like death isn't beautiful. And the timing.

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* Kresge 502 Cart: please, that can be happy. And so why can I do so

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* Kresge 502 Cart: focus on other activities

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* because of cancer?

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* Kresge 502 Cart: Because you missed, for example, in a subgroup analysis. So if you were to do a whole cause mortality, and you assessed it.

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* Kresge 502 Cart: reveal enough effect. But if you were to look at it more specifically, you might have different groups that are hierarchy.

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* Kresge 502 Cart: This by doing this like very generic type of stuff.

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* Right? Yeah, yes, I actually had a question. So I realized that they proposed an Rct

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* Kresge 502 Cart: for the multi-cancer color test. And I was wondering, this doesn't seem very invasive. In the first place.

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* Kresge 502 Cart: doesn't seem like it's going to harm people. So why are they so focused on mortality

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* Kresge 502 Cart: it didn't. I don't see how that could hurt you.

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* Kresge 502 Cart: for the

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* Kresge 502 Cart: could do a lot greater. So you're saying that if it's not invasive. Yeah.

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* Kresge 502 Cart: like. And it's not going to impose harm on.

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* Kresge 502 Cart: Why is are they looking at all cosmetology

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* Kresge 502 Cart: on cause? Mortality is really a measurement that we look at. If procedures are in places

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* Kresge 502 Cart: you know. What's interesting to think about with. This is sometimes the first test is not invasive, but then what you have to do afterwards can be

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* Kresge 502 Cart: invasive can cause harm, can cause stress. So it's interesting. These multi-cancer detection assays. Many of them don't even aren't specific to it's elevated. You might have cancer. Do you have lung? Do you have blood, or do you have hidden? So then what you have to do afterwards? And then you find it biopsy. So there's these follow-up things that you need to do.

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* Kresge 502 Cart: Can. They are expensive, even though they're not expensive on an individual assay. If you have millions and millions of people

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* Kresge 502 Cart: pretty substantial, false positives, false negatives. So that's not the problem. Let's say 90%.

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* Kresge 502 Cart: It's

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* Kresge 502 Cart: and through true positive, like 90%. So we have 10% of all positive. These people are going to be biopsy because most of the people don't have cancer.

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* Kresge 502 Cart: And even from economic perspective, if they are trying to save some money. I think that this measure would actually cost more expenditure on the long run.

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* Kresge 502 Cart: because where people will have health positives. A lot of people will have to undergo further testing. And in the end we see it from a public health perspective. Cancer is not the biggest death based on their beta.

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* Kresge 502 Cart: So maybe we should be allocating most of the money to all of the releases.

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* Kresge 502 Cart: Yeah, it's interesting. I think cancer is still a major cause of death. But what they're saying is the proportion that's prevented by screening doesn't seem like a little bit screening is expensive to see if the screening is true.

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* Kresge 502 Cart: At least surgical treatment of more aggressive cancers tend to be riskier, more expensive, required ice, so there could be unintended with the screening of essentially tackling cancers at lower stages, where surgical management is a lot less risky, less expensive

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* Kresge 502 Cart: versus only identifying the cancers when they're metastatic and very aggressive, and suddenly requiring very expensive IC care or very risky procedures. They quoted 40%

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* Kresge 502 Cart: mortality after surgery is not cancer-related, but it tends to be riskier with higher stage cancer diagnosis.

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* And actually, just to that conventional horse I've just moved in. Then I'm sorry

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* Kresge 502 Cart: there's sort of this natural experiment, and I know we haven't done prostate cancer yet. But you know the the Us. Preventive Service Task Force, which is one of the groups that makes decisions or recommendations about screening came out strongly against prostate cancer screening in around 2,012 and then updated it to a more.

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* Kresge 502 Cart: You know, confusing recommendation of like talk to your doctor and make informed decisions. And so what you can see, these are are data from American Cancer Society, showing the up strong uptick across all racial groups in the incidence of cancers now being diagnosed, either locally advanced or metastatic. Already a diagnosis. So you can already see what's happening when screening rates are going down getting this up tick

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* Kresge 502 Cart: to your point. Exactly.

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* Kresge 502 Cart: Okay.

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* Kresge 502 Cart: yeah. The it I mean, I was. I don't know if this is a valid.

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* Kresge 502 Cart: Yeah, I was thinking in terms of like the the screening itself can cause like, strive if you get a screen detected cancer that eventually wouldn't cause death. You know, you're adding, like stress, unnecessary stress to the that person's life. Ii mean another aspect to that is like, let's say, you know, like, like 50 years ago.

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* Kresge 502 Cart: 40 years ago, you know, if you got cancer, it's like, it's almost okay, you know, right, burn your will. Whereas, like now, even though it's more like.

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* Kresge 502 Cart: you know, maybe maybe some cancer like there's lead time bias like that. But at least, if you have a diagnosis of cancer in most cases. Now, you know, maybe pancreatic. There's some exceptions definitely, but it's not like you have like 6 months to live. And that's it, you know. So II think you know it's I don't know if that's a good point you still like.

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* Kresge 502 Cart: It's better not to know or to just wait till the cancer is very advanced and you're diagnosed rather than being diagnosed 5 years earlier like that. So if it's not going to have a big impact on mortality. But I don't know. There are lots of

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* Kresge 502 Cart: subtle things like quality of life, how people react to different things. So. okay, are there any other. I guess we have 5 min left.

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* Kresge 502 Cart: I mean.

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* Kresge 502 Cart: So in general, like, what do you think like

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* Kresge 502 Cart: of their I mean, I mean, I did you

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* Kresge 502 Cart: think that they have a good point or a valid point in general? Or.

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* Kresge 502 Cart: yeah, something that I'm trying to understand is, what about perfect detection, or as cancer state. Is it possible?

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* Kresge 502 Cart: Right? And so would you argue that just what it is? If you die of something else or the cancer can be enough.

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* Kresge 502 Cart: Is it more like a question of individual versus population level benefits?

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* Kresge 502 Cart: Yeah, I mean, I think age is another

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* important aspect. And for

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* Kresge 502 Cart: for some screening tests. Like prostate and colorectal. I'm not sure about breast. There's a cut point where you usually don't recommend doing screening

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* Kresge 502 Cart: for prostate Psa. Was it beyond age. 75 or 80.

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* Kresge 502 Cart: something like that. So, yeah, I mean, you are like.

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* Kresge 502 Cart: like a lot of these statistics are population based. We're talking first and years. But

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* Kresge 502 Cart: if you look at it from an individual perspective, it can be quite different. So sometimes, one way, statistics were there.

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* Kresge 502 Cart: But sometimes you'll read a statistic like, Oh, if you exercise, you'll gain on average

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* Kresge 502 Cart: 2 years of life. And the way psychologically, some people think, boy, Ok, maybe I'll die at 92 instead of 94, maybe I'd prefer to die in 92 than 94. They kind of think of it like everyone is getting the same small effect. But if you think about it as

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* Kresge 502 Cart: well, like another way to think of it is like 2 out of 10 people will die 10 years prematurely

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* Kresge 502 Cart: like, are you willing to take that risk? Ok, maybe you don't exercise, and maybe it won't perturb you like that. But there is a 20% chance that you'll die 10 years earlier. To me that seems actually more

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* Kresge 502 Cart: compelling than saying, like 2 years, adding one or 2 years to everybody in the whole population. So person years is useful for statistics.

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* Kresge 502 Cart: I don't think it's useful to a way to think about risk

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* from an individual perspective, how you would make a decision. Yeah.

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* Kresge 502 Cart: no? Sorry. Yeah. I was struggling with the same thing. But I had a question also about over diagnosis.

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* Kresge 502 Cart: I should start looking at like how that's

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* Kresge 502 Cart: determined that something would not eventually go on to cost mortality. That's kind of another similar as individual versus population. You can't tell on an individual basis.

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* Kresge 502 Cart: If it's over diagnosed, you can just tell on the population because you have a lot more cancers diagnosed by a screening test. But reduction on mortality was, let's say, modest, pretty low. So from that population perspective, you know that.

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* Kresge 502 Cart: Yeah, if you knew those people that weren't going to die anyway. Yeah. But that's like a valid point is from an individual perspective. Unless you have better ways of looking at the histology and telling

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* Kresge 502 Cart: which cancers are really important. It's like Laura, like talked about, you know, pseudo cancers. But that's basically what that means is, histologically, they look like a cancer, you know just by looking at the features, say, yeah, this looks like all has all the definitions from cancer. But

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* Kresge 502 Cart: it's possible that if you knew exactly the mutations, and that some of them were very, very unlikely to progress. That would be kind of like a Holy Grail, you know, if you not just told a person to have cancer. But oh, this cancer is won't progress. If you knew that, then say, don't have cancer, but

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* Kresge 502 Cart: we're not there yet.

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* Kresge 502 Cart: Yes. Do you think that early detection for most people can extend the number of volume life years? Or does early detection sometimes just spend the amount of time that someone's going to be experiencing treatment

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* Kresge 502 Cart: their light years

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* regardless of screen.

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* Kresge 502 Cart: Yeah, II mean, I think that's that's sort of the question like we don't know, like, on an individual basis, like for some people, it may actually be benefiting other people.

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* Kresge 502 Cart: They would die at the same day.

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* Kresge 502 Cart: Or is it just like all of that time, you can detect it so early. You're going to be undergoing treatment, and that's decreasing quality of life, or all of those remaining 10 years.

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* Kresge 502 Cart: III don't know. I mean it. Probably I mean, it's a great question. It probably depends on answer.

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* Kresge 502 Cart: I don't know. Some more clinical people might have better answer. But

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* Kresge 502 Cart: yes.

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* Kresge 502 Cart: So basically, what would have to happen is even as a person, let's say.

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* Kresge 502 Cart: died at the same, you know, but you know that same day, but the early detection they were treated, and it avoided some of the therapies that they would have gotten

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* Kresge 502 Cart: had. They were diagnosed with more of a man's gauge.

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* Kresge 502 Cart: but they are still theoretically dying the same day, so maybe they're still getting some.

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* Kresge 502 Cart: It's not like they do perfectly fine, and then just guide. One day they probably still have a lot more fish, but they could be avoiding.

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* Okay.

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* Kresge 502 Cart: 17. Daily basis discussion with the patient is based on patient, personal,

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* Kresge 502 Cart: patient expectation and lots of care. I mean, there is no study. That's exactly what

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* Kresge 502 Cart: symbolize it with that.

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* Thank you. I think we're over. Thank you. I think we covered most of the important facts.

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* Kresge 502 Cart: Any any final comments or

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* Kresge 502 Cart: great thanks, everybody. We'll see you on Thursday for the prostate cancer lecture. And then just a reminder you're doing office hours today at right now and in room.