Colleen Michelle, who are going to give a presentation about survival in cancer, both methodologic as well, some substantive work. And then, after that. 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. Do you know how to do it on a PC prostate cancer survival. 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? Is it B. Death from other cancers? See Alzheimer's disease and or d cardiovascular disease? Letter to the editor is due on Thursday at midnight. You are welcome to work on your own or up through groups of 3. You can just submit it as a group of 2 or 3. Just make sure everyone's name is on it very clearly. And what person was submitted, we only need one copy. The text of the letter yeah. The header could be separate. And I did it from my laptop. Oh, it just didn't let me share. You couldn't see the slides. Well, yeah. sorry. Someone created a separate desktop on this. And so we don't know how to close it on here. We'll provide an overview of the burden of burden of cancer survivorship in the Us. Discuss a proposed research framework for working with studies of cancer Survivorship. 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. The definition of a cancer survivor is used by the American Cancer Society as well as other institutions like the Nci. Areas of concern in this research space is very wide in scope, but might include things such as the effects of certain treatments, comorbidities, and mortality. 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. This can be attributed to a number of different things, including screening and diagnosis and potential over diagnosis as well as treatment advances. 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. Over 2 thirds of cancer survivors are over the age of 65 in the Us. 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. The majority of cancer survivors in the Us. are breast cancer, prostate melanoma and polar rectal cancers. 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. In the Us. just over 600,000 individuals are metastatic cancer survivors specifically, and this figure itself has also projected to increase. There might be greater options for extending survival 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. Cancer survivors are at an increased risk for reoccurrence of primary cancer. The cancer survivorship care quality framework was created in collaboration with Bergmann Woman's Hospital, Harvard Medical School and Ci experts, policymakers, advocacy groups and cancer survivors. This framework serves as a foundation to define 5 domains of cancer Survivorship care as well as general needs. There's a need for surveillance for subsequent cancers, such as through repeated physical laboratory tests and imaging. 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. Cancer survivors are at risk for physical effects of cancer as well as treatment. So this requires assessment of symptoms, conditions via medical history and physical examination. Some of the side effects that can come with this, for example, with chemotherapy, include nausea, fatigue, constipation, diarrhea, hair loss. Psychological effects include anxiety, depression, cognitive changes, fear of reoccurrence. Social effects include financial toxicity, loss of work, productivity, return to school change in insurance status. Next, we have health promotion. Just because someone has a cancer diagnosis, this does not mean that they will change their health behaviors. 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. Cancer care for cancer survivors is complex. And in the Us. We have a very complex health system. We know another piece of that, not just association, but also the part of physiology. So, of course, some of these outcome measures are not necessarily distinct for the spatial population. Tcg. 30, which is a validated questionnaire for health, related quality of life among cancer survivors, and is applicable in over 100 languages. So outcomes include physical, mental, emotional, social functioning, healthcare utilizations, specifically like emergency care, hospitalizations, critical care. 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. 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. A competing event is something that inhibits our ability to observe the event of interest. If someone died of cardiovascular disease that would be a competing event. To handle this, there are a number of different modeling frameworks and decision to make as someone who's designing this study. You can learn about that in Biosat 223. There is probably a month's worth of lecture on that. There are a bunch of different ways that a mortal time bias can come up in our studies. It's really a nature of the determination of an individual's treatment status or their exposure status. This is a really complex issue, and if you want to learn more about it, you can take bias at B 203. The ideal way to make sure that you don't have a mortal time bias is to emulate a target trial. If you're in lab right now, and F 207 will talk about that extensively. We'll talk about this Michelle and if you want to learn more about mobile time by his colleague is linked this paper. The next bias that we would raise is lead time bias. Bias are particularly relevant in studies of cancer screening. So the lead time is the time between which a cancer is detected by screening versus the time it would have been detected by symptomatic presentation and going to the doctor and diagnosed. The patient would have died at the same period of time. 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 moving on to length bias. 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. And again, this can overestimate the effectiveness of screening. And the last issue we wanted to raise was on prevalent users. Research can improve clinical care, quality of life and understanding of adverse effects of treatment. 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. There are a ton of different ways that we can measure a health related quality ofLife for cancer survivors. Nci office of cancer survivorship posted this on their twitter yesterday. We're looking at research to understand and address survivorship needs of individuals living with advanced cancer. 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. As of 27 since 2,017, cancer survivorship brands have been funded by the Nci. So, as you can see, that number is increasing, and hopefully continues to increase in their patriotism. So we can think about how and when clinicians can actively measure quality of life metrics, for example. We can look at optimization of tools and collecting patient outcomes and processing measures to prevent provider burden. And lastly, we can think about how we can implement full cancer survivor care quality framework in the clinical setting. So our research and what we do in this betting also impacts the policies that are implemented in the United States. Research we conduct 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. 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. 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. Do you have an idea for lead time? I have a nice example. Over diagnosis, too, of anxiety and then unnecessary potential treatment. 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 over diagnosis. So I think the thought was that we'll give people like little time to just discuss we'll come up discussion. We'll come together, maybe at 30'clock for for discussion. Put some questions there. So does anybody want to? Just let's. it's always easy to begin, like what was the stated significance of the article. And then I think I had a question about Oh, yeah, do you think the the assumptions that made were reasonable? Why or more, why not so? CNN's John Sutter asks if screening is actually saving lives. Sutter: Is it competing on all the other life? Is it just really good causes? He asks: How many lives do we actually save? Sutter says some people may get safe, but there are downsides. The paper says multi-cancer screening and alcohol mortality could be used to determine whether screening is saving lives. The paper also distinguishes between cancer-specific mortality and all cause mortality. The authors say that to propose looking at multi- cancer screening andalcohol mortality, to get at whether screenings are saving lives, is reductive. Even for pretty common cancers, seems kind of small. I mean. 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? The Colonel says he doesn't think the screening is saving some lives. But is that offset by the I don't get breakfast. The cones are the same height. So it's like among all people that die, which percent would be due to death. But after 30 years of follow up, you're saying 70% of the people would have died. There were. around 70 deaths in the screening trial. And, like, let's say, around 100 in the control arm. But like there. the total numbers of deaths were almost identical. So you know you have minus 30 debt. So 30 30% reduction sounds impressive. But then, when you looked at the numbers now, you know. The study found a 30% reduction in prostate and no other death. That's out of 1,730. So it's impossible to chance. I think that if you're trying to do a trial to show a reduction in total mortality, even if the trial was successful. The number is going to be too small for the total number. Leonard: Main problem with all at least putting everything in one basket and trying to decide that. I mean, he concluded. That's how how does 5 year over survival is not the accurate circuit marker. But one of the main things that I do from this table that he placed is that we want to show that we can lower the number. The difference of dying cancer is really really small compared to countless of other reasons, whether it's like a disease or even an accident. So also, that's why you would need such a big number of patients with cancer to actually test that. So it doesn't mean that because there's a really small number. And you're definitely gonna have enough power. 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. It's just like, as I said, like, everybody's gonna die. "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," he says. "The whole point was to save lives that were like from the cancer, and not just more generally" Stratification makes sense to capture the cancer-specific mentality through measure. 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. Mortality is really a measurement that we look at. If procedures are in places you know. What's interesting to think about with. these multi-cancer detection assays. Many of them don't even aren't specific to it's elevated. So then what you have to do afterwards? And then you find it biopsy. Cancer is not the biggest death based on their beta. So maybe we should be allocating most of the money to all of the releases. I think cancer is still a major cause of death. A lot of people will have to undergo further testing. And in the end we see it from a public health perspective. Surgical treatment of more aggressive cancers tend to be riskier, more expensive, required ice. There could be unintended with the screening of essentially tackling cancers at lower stages, where surgical management is a lot less risky, less expensive versus only identifying the cancers when they're metastatic and very aggressive. The U.S. 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. confusing recommendation of like talk to your doctor and make informed decisions. So you can already see what's happening when screening rates are going down. Cancer is not going to have a big impact on mortality. There are lots of subtle things like quality of life, how people react to different things. 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. I'm trying to understand is, what about perfect detection, or as cancer state? Is it possible? Right? And so would you argue that just what it is? If you die of something else or the cancer can be enough. Is it more like a question of individual versus population level benefits? I mean, I think age is another important aspect. Some people think, boy, maybe I'll die at 92 instead of 94. They kind of think of it like everyone is getting the same small effect. But there is a 20% chance that you'll die 10 years earlier. To me that seems actually more compelling than saying, like 2 years, adding one or 2 years to everybody in the whole population. You can't tell on an individual basis. 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. Early detection for most people can extend the number of volume life years. 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. There is no study. Daily basis discussion with the patient is based on patient, personal, patient expectation and lots of care. 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. 17. 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. We'll be back next week for a look at some of the other things we've been working on in the past few weeks.