* Kresge 502 Cart: Welcome to the epidemiology of cancer. My name is Laura Lai Moochie. I actually don't know how long I've been teaching this class, I should know, I think Ed just told me. Well, he's been teaching it, and but it's been incredible to be part of his team.

0:50

* Kresge 502 Cart: oh, yes, it's this is the 30 first year.

1:09

* Kresge 502 Cart: So but don't worry. We haven't

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* Kresge 502 Cart: many younger people. I do a lot of work in

1:16

* Kresge 502 Cart: Hi Margaret's molecular epidemiology. You'll hear me talk a little bit about prostate cancer, which is a cancer. I do a lot of work on and Ed, yeah, also cancer epidemiologists. I was. I took this discourse and

1:32

* Kresge 502 Cart: 1986,

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* Kresge 502 Cart: and I do mostly cancer epidemiology. With a nutrition focus some frosty but

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* Kresge 502 Cart: more of a color rectal and like gas for intestinal cancers, although it won't be giving the prostate cancer lecture this year. That's yeah. Right. We actually have 2 amazing teaching fellows here. I'm gonna let introduce themselves. So Pauline

2:02

* Kresge 502 Cart: Picky

2:34

* Kresge 502 Cart: and Hi, everyone and Michelle

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* Kresge 502 Cart: kind of delve into a little bit some of the core concepts before that. I always like to start our classes with

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* Kresge 502 Cart: a quiz. And so have people use poll everywhere before. If you haven't. There's 2 ways to access. The first is you can go open up a web browser and type in POLL. [e.com](http://e.com/) backslash, and then my name, Laura Laimuchi, 9, 6. The other way you can do it is if you want. If you want to use your cell phone, you can text the number 37607. And in the.

3:11

* Kresge 502 Cart: you know message, you, you type more alignment G, 9, 6, 6. So that will get you kind of activated. So is everybody on pull everywhere.

3:38

* Kresge 502 Cart: Should I? Does anybody not need a little bit more time?

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* Kresge 502 Cart: Perfect cause? Then I'll go. I'll switch over to the poll everywhere, so we can sort of ask questions.

3:55

* Kresge 502 Cart: And this is not part of the graded assignment. So there's a don't. So don't worry about this. I think it's it's just nice to sort of see where the class is at every every day. So alright. So I'm gonna go over to the

4:07

* Kresge 502 Cart: How do? How do you switch over? Sorry escape. I did a so there we go, perfect

4:21

* Kresge 502 Cart: alright. And

4:28

* Kresge 502 Cart: it was. It was just up a second ago.

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* Kresge 502 Cart: Where is it? Oh, here it is.

4:38

* Kresge 502 Cart: But people have already

4:42

* Kresge 502 Cart: started voting. Okay? Great. So the question, yes, but sorry.

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* Kresge 502 Cart: No, no. Yep. So the question is, you know, each year in the United States, actually, now, it's closer to 2 million people will be diagnosed with some form of cancer. So the question that we're asking you is, what proportion of those cancer diagnoses in the United States do you think are preventable? Meaning, you know what? What

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* Kresge 502 Cart: portion? If you could eliminate all the cancer risk factors, could you actually pre prevent? So is it 7, 2540, or 90? So you can enter what you think is the right answer, and, as you can see, as answers are coming in, and sort of kind of going up and down. So let's give it 5 more seconds.

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* Kresge 502 Cart: 5, 4,

5:36

* Kresge 502 Cart: 3, 2,

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* Kresge 502 Cart: one perfect. So I guess we don't need to really teach this class, because, most of you got the right answer. So in the United States, about 40% of cancer diagnoses are thought to be preventable.

5:42

* Kresge 502 Cart: So we know a lot about how to prevent cancer. So one big challenge. And one thing we'll be talking about here is if we know these risk factors and we'll talk about what the risk factors are or opportunities for prevention. How do we translate that? Why can't we translate or implement those changes in the population? We'll also talk about cancers for which we actually don't know as much about in terms of the epidemiology and areas there for for potential growth. So excellent, fantastic.

5:55

* Kresge 502 Cart: Okay, so we're going to go into the course overview. I already did introductions of all of us.

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* Kresge 502 Cart: I'll I'll start with the course of Jack's, and then you can. Or yeah, once you alright, you would think that we hadn't taught this class before that we're so so there's there's several objectives of of this course. And I think, as I mentioned, we're gonna we're gonna spend a lot of time delving into what are some of the major categories of of what we think are causal factors in the ideology of cancer. And also like what are some

6:32

* Kresge 502 Cart: really interesting hypotheses about? Why cancer occurs. We'll spend some time, both in class in each of the lectures, as well as one of your assignments, is going to be focused more on the descriptive epidemiology of cancer and looking not only in the Us, we really try to have a global focus. Third. And I guess this is really across the lectures, is looking at. What are the populations of people

7:02

* Kresge 502 Cart: for which Ca, a specific cancer may have a higher incidence, a higher mortality. We're gonna weave into the course and today and today and some. And on Thursday spend some time talking about some of the core methodological issues and cancer epidemiology, study, design analysis and bias and then, as I mentioned, for for your group project, you're gonna get an opportunity to work with some of the primary data sources

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* to look at the descriptive epidemiology of cancer.

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* Kresge 502 Cart: Sure, yeah.

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* Kresge 502 Cart: the I think you all have a syllabus. So basically.

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* Kresge 502 Cart: the the course. Like, you know, we're trying to give an overview of concepts like methods and and issues like we, we won't get

8:05

* Kresge 502 Cart: into very like, you know, like statistical methods like this is more of a broad picture

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* Kresge 502 Cart: view of of cancer. And get into a lot of like the descriptive epidemiology. but you know, the focus is really learning to understand the literature from a big picture perspective like how to interpret

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* Kresge 502 Cart: the study. You know, we interpret studies individually, but also in the context of other like

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* Kresge 502 Cart: studies like. so, oh, yeah.

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* Kresge 502 Cart: so so the lectures like W, it's kind of broken up in 2 ways, conceptually like we have some lectures that'll focus on exposures like tobacco obesity infections

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* Kresge 502 Cart: radiation. We, we don't have a lot. Specifically. We used to have a lecture on radiation which is actually interesting topic, even though it doesn't really cause a lot of cancers. But there are a lot of that interesting ways that helps understand how

9:05

* Kresge 502 Cart: how cancers occur, like, you know, like mutations, things like that. But we, we will talk about a little bit for some of the cancers, but we don't have a specific lecture, and then genetics and and then diet also, I I'll I'll be talking about like obesity diet, and can also include physical activity there.

9:22

* Kresge 502 Cart: And then some lectures will be mostly focused on the disease like specifically breast prostate colon liver and pancreatic cancers. And then in in their class assignments, we'll talk about other cancers that that won't have the big lectures, but well, you know, they'll each get at least 15 min of

9:44

* Kresge 502 Cart: of fame for for into some individual cancers. And of course, you know, like what? When we're talking about the exposures, we'll be talking about specific cancers. But that's just the way the lectures will be focused more.

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* Kresge 502 Cart: When, when like, we're talking about tobacco, a lot of it will be on one cancer. So you'll get a lot of one cancer. But we'll also talk about other

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* Kresge 502 Cart: alcohol smoking related alcohol is another thing that you'll you'll get some exposure to alcohol. I mean, I don't mean physical exposure.

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* Kresge 502 Cart: So a in the class format. The classes include presentations by the course instructors, and we have a lot of great guest lectures. And but even though it's a lecture format we actually like and and

10:43

* Kresge 502 Cart: you know, prefer a lot of interaction. So over the years, I've tried to have more time for for people to have discussion. I don't often do a great job in that, but but we'll try to have more, you know. Feel free any time to to raise your hand if the points not clear, or if you wanna make a point so and then also. We'll have some interactive learning

11:00

* Kresge 502 Cart: during the classes which we'll get into later. You have assigned course reading readings. That. You know, it's great

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* Kresge 502 Cart: to to do in advance. II think it would enhance the lecture.

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* Kresge 502 Cart: I live in the real world. We know that not everybody does. All the readings before class. II didn't always do it so have to admit, but but it's it's good if you can. So

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* Kresge 502 Cart: yeah. So so office hours. we'll we'll have a couple of specific off our office hours, that is, are set up around the Descriptive Epidemiology project. We're gonna talk about that in a second and then also before the final quiz. But also you're so welcome. If you wanna meet with us at any time. Just reach out to set up an appointment with either colleen

11:56

* Kresge 502 Cart: Michelle, Ed, or myself, and I think generally we're available immediately after the class until about 4, 4 30. So that's a great time to set some time up to me.

12:20

* Kresge 502 Cart: Yeah, this is the what

12:32

* Kresge 502 Cart: the lectures.

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* Kresge 502 Cart: So the we'll start like the first to lectures. I won't go through every one of these. But just to give you an overview, that laurel, I does a a great job giving sort of the basic concepts of cancer. Epi on some of the descriptive epi and the methods and then next week we'll

12:39

* Kresge 502 Cart: del start delving into the specific topic. So I'll do mostly next week the diet, cancer, obesity, physical activity. And then as you can, you know I will. I won't read all of this. So we have

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* Kresge 502 Cart: a scatter like some cancer, and then infectious diseases. So, and then the in class presentations are, February 20 and the twenty-second. And we'll get into that.

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* Kresge 502 Cart: What? Specifically that means.

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* Kresge 502 Cart: We'll have a class discussion of a paper in February twenty-seventh

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* Kresge 502 Cart: oh, we have February 20 ninth this year. So we have an extra day of work this year. And then, like the final quiz, which always gets people a little anxious. But it's it's only 20% of your grade. So it used to be like 80. So it's people really freaked out but 20 so bad. So and that's on the last day you don't actually have to come, you can do it at all.

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* Kresge 502 Cart: so we'll we'll give you the details

14:07

* Kresge 502 Cart: so so we have, a few different assignments, and and we tried to make them as sort of things that you could take into the real world with you. So one of one of these assignments, which I think we've gotten great feedback on is doing sort of a mock journal critique. So it's learning how being a peer reviewer for a medical journal. So we'll give you some guidelines on our approach of how to look through

14:12

* Kresge 502 Cart: an article and provide, you know, constructed both positive and suggestive feedback. For the authors. It's meant to be short. And again. We'll go into a little bit more detail, probably on Thursday about this specific assignment, which is due on February 6. And it's actually a really interesting paper. So some of you might have heard of an initiative that the Us. National Institute of Health has started a a new group

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* Kresge 502 Cart: cohort study called the all of Us research program. And so this particular article looks at the association between air quality and the risk of cancer using all of us study so you're so welcome each to discuss the article come up with. Maybe some of the points themselves, but we want each of you to write up the assignment independently.

15:02

* Kresge 502 Cart: Yes, sure. So the the other assignment.

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* Kresge 502 Cart: which is 35% of your grade is actually actually has like 2 parts, and this is You'll work in small groups and we'll find out later how

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* Kresge 502 Cart: how those are. You'll kind of self select and so it'll be focusing on a descriptive epidemiology of a specific cancer. So you give like a background of you know that it's it's pretty basic descriptive of epidemiology, incidence, you know, differences by like race things like that. And then also, you you pick

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* Kresge 502 Cart: you select the risk factor for that cancer? And you could, you know, you'll discuss with one of us like, what works factor should you pick? And so there's flexibility in that, and then so you'll

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* Kresge 502 Cart: listed. There are the cancers for this year, so it's blad, so you only so you'll be in one of these cancers, will be a 1 one of the groups. So bladder and the metro ovarian.

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* Kresge 502 Cart: sophocus, kidney glioma like brain melanoma, gastric and testicular cancer. So we're actually doing all of those. Yeah. So and then there's 2 graded components one is the individual where you can read it. So so you'll write up, you know, to short 2 to 3 pages, double space

16:34

* Kresge 502 Cart: and then that's worth the 15% of your grade. And then there will be like a group presentation. which will do on those 2 days in February you have to 20 and 20 s. So as a group like there's like 4 or 5 in a group you all come up. And you know, you, you decide how you gonna break up the presentation. So each gives, you know, a little component and that, and that will be 20% of your grade.

17:00

* Kresge 502 Cart: And then the also part of the grade is

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* Kresge 502 Cart: another. Anybody can ask questions for each presentation. But there's a group that

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* Kresge 502 Cart: is so. For example, like, let's say, the endometrial group is presenting. And then, like the kidney group

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* Kresge 502 Cart: leads to questions. So so.

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* Kresge 502 Cart: yeah, yeah, and actually, so, just so would to sign up for the cancers. You can start thinking already. Now which cancer would be most you're interested in exploring. We'll set it up in in canvas as a way to organ. And so when do you think we should launch that? Okay, okay, perfect.

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* Kresge 502 Cart: So the

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* Kresge 502 Cart: great. So so one of the other assignments again, and thinking about like some real practical things that you can take away from this class is learning. How do you write a letter to the editor? So oftentimes you'll read a public health or medical journal article that's really interesting. And you'd like to respond in a way to either

18:17

* Kresge 502 Cart: highlight. One or 2 specific issues that the paper raise, maybe think about where you might wanna take the paper in a different direction. And so this is going to be a mock letter to the editor, editor and then also, we're gonna have an in person discussion altogether on this paper. So again, this this assignment actually has 2 parts the first will be the in class discussion, which will take place on February twenty-seventh. We'll take about

18:37

* Kresge 502 Cart: I think. Probably 45 to 15 min in total. First, we'll have you in this classroom, break up into small groups together with your neighbors, and just kind of talk through some of the issues. Secondly, we'll all come together with the 4 of us, and really kind of go through. And it's a really interesting paper by Gilbert Welch, who's based on women's hospital and Doctor Day thinking about

19:02

* Kresge 502 Cart: you know, how does cancer screening save lives? So it's a really interesting perspective, perhaps a little controversial, but we'll have a really, I think this is a nice paper also to bring in the concept of of screening into cancer epidemiology. So we'll have the discussion. And some people may not feel as comfortable raising points in class. So we also have. We'll have

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* on of a canvas board, not looking for people to make comments there as well, and then secondly, you'll actually write a very short 500 word letter to the editor in response to this article, and you can work on your own, or if you want to work with a total of 3 authors altogether, including yourself. You can do that as well. That will count for 15.

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* Kresge 502 Cart: And then the final quiz.

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* Kresge 502 Cart: it's all there. Yeah, yes. So you'll have 90 min, and usually we, we try to make it that 90 min should be more than enough but sometimes people say that, but usually it is so and so so you're so you can do it at home or any place. And then I guess it's set up that like once you start.

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* Kresge 502 Cart: you have 90 min. And then II don't know how this tech stuff works. But

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* Kresge 502 Cart: that's it. Yeah, yeah. So you can basically schedule anytime from 9 in the morning on March seventh. All the way through Saturday, March ninth. Yeah, it's 90, continued continuous minutes. True fall short answers multiple choice. You can use class notes, presentations any related merit materials, but it really should be your own work

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* Kresge 502 Cart: before, like the last week, will usually have like a a session like a ta session that you're welcome to? Questions.

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* Kresge 502 Cart: Good.

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* Kresge 502 Cart: Yeah. Question. It sets up to 105. What? Oh, no, this is because this is wrong. This slide is wrong, but not that. Yup. I apologize. It's only 20. We did make changes. I apologize, but very, very thank you for keeping an eye on that. Yeah.

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* Kresge 502 Cart: but on the syllabus it should be correct. Yep.

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* Kresge 502 Cart: see if we haven't noticed that you could have got 5.

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* Kresge 502 Cart: Okay, so generative. AI, so

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* Kresge 502 Cart: so in this particular class, we don't want tools such as chat Gbt, or growerly,

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* Kresge 502 Cart: and using text that's produced by this as part of this course, the assignments really should be written by you in your own words, that reflect your thoughts, and the your understanding of of the content. If you if you feel like you, wanna use it these kind of tools to check grammar spelling that is acceptable. But if you are going to be using it, you should let us know it should be appropriately cited, as it's as you should, otherwise it would be considered

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* Kresge 502 Cart: plagiarism, and we understand that this is a rapidly evolving field in different classes are using generative AI in different ways. But this is the approach that we're gonna be taking for this class.

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* Kresge 502 Cart: So any any questions about the assignments? Or oh, I should say also regarding

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* Kresge 502 Cart: the use of zoom again, we understand that. And there's extenuating circumstances. People may not be able to be in class. We really do hope, though. I think this class is successful because people are here discussing breakout sessions. So. But if things come up and you do need to miss a class or take part in zoom, please just let us know in advance. But any questions about the assignments, or

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* Kresge 502 Cart: what's that?

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* Kresge 502 Cart: Anything else to add?

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* Kresge 502 Cart: Pencil?

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* Kresge 502 Cart: Okay, great, excellent. Well, we'll get started with

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* Kresge 502 Cart: sort of the first part of of the actual lecture, talking about cancer coughs up. So first in terms of what the goals of the lecture today. I think there's so many interesting landmark discoveries that we've made in cancer epidemiology and how

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* Kresge 502 Cart: one those were discovered. And then how long it might take before those initial observations get translated into saying, yes, this is a causal factor. Thinking about that. History, I think, is really interesting. We'll give a really brief overview of the pathology and biology of cancer. And for people who feel like they want to read up more. We have some recommended readings and a book. Chapter. So we'll be talking also

23:49

* about some of the key molecular and genetic features, although I think actually, most of that is probably going to be on Thursday, and then also in Thursday, will be going into more of the actual methodologic concepts and cancer epidemiology. So what is what is cancer. So the the word cancer comes from the Greek word carcinoma for for crab. And this is based on the fact that

24:14

* Kresge 502 Cart: sometimes breast cancer lesions. Can be seen on the surface of the skin and the the appendages going out look like they're reading like a like a crab. It really is a diverse family of diseases, and it can arise in almost every cell of the body.

24:35

* Kresge 502 Cart: They can be a solid tumor or in non solid leukemia.

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* Kresge 502 Cart: and while it kind of rise in almost every cell type, there's considerable variability in the incidence, prevalence, and mortality of these cancers, and and one really striking example, I think, is, is the prostate which is

25:00

* Kresge 502 Cart: again, you'll you'll you'll hear about this in a lecture. But prostate is the most commonly diagnosed cancer in in men or people with prostate in a hundred countries around the world. In including of the United States, however, the structures adjacent to the prostate the seminal vessels. You almost never see a primary cancer rising there. So why.

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* Kresge 502 Cart: no, you have this. You have the prostate. It just shakes kind of like a walnut

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* Kresge 502 Cart: like this. And then you have these adjacent to the seminal vesicles. So you know, the lifetime risk in the us is about one in 8. Yeah, you almost never have a cancer that's primarily here. So why is that? What is it? What's leading to that variability. In addition to unique ideology, there's unique opportunities for prevention, prognosis and treatment. And one of the things that we'll get into for some of the malignancies is that even within a single cancer, like breast cancer, colorectal cancer? We can even think of subsets of those

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* those cancers that again, have their own unique factors, based either on molecular characteristics of the tumors or clinical features of the tumors.

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* Kresge 502 Cart: So let's see what, when you signed up for this course.

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* Kresge 502 Cart: what? What were you thinking that cancer epidemiology is?

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* Kresge 502 Cart: What did you think we would be doing this class? So what for? What is cancer? Epidemiology to you?

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* Kresge 502 Cart: Yes, I thought,

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* Kresge 502 Cart: I'll learn more about it. How the cancer is focusing the

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* Kresge 502 Cart: what are the new ways and treatments that

27:00

* and edit?

27:04

* Kresge 502 Cart: What are the different types of cancers. How? What are the risk? Factors that are involved?

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* Kresge 502 Cart: Learn more about different types of studies?

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* Kresge 502 Cart: Yeah. So I think you've had. You've hit on so many great points. So really think about patterns of cancer occurring in different populations, how we might identify the causes and opportunities for prevented. We might not talk as much about treatments specifically, although in some cases, you know, I think some of our lectures and and some of our individuals we talk about like clinically, what is cancer? Look like when it's presented? And what are the treatments for it?

27:14

* Kresge 502 Cart: And then there was something else that you mentioned. Study design web. Exactly. So, thinking about the methods that we use. You know, there's there's you. You all have taken, probably epidemiology intro to to an epidemiology course. Well, thinking about really, specifically, what is it about cancer that might be unique or ways to think about some of these biases confounding study design specific for cancer epidemiology. What about anybody else? Have anything outside of those things that they were thinking of?

27:43

* Kresge 502 Cart: I think that was a great, a great list.

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* Kresge 502 Cart: Yep, perfect.

28:16

* Kresge 502 Cart: So there's there's a great review article called Landmarks in the history of cancer epidemiology. That I pulled from as well as a a book chapter called the Textbook of Cancer Epidemiology, I think. Did we put the book chapter in the Harvard campus? You can. You can take a look at it as well. Alexander Pope and his essay on man

28:19

* Kresge 502 Cart: said, the proper study of mankind is man. I, you know, as an epidemiologist, I think we're very interested in understanding what are the causes of cancer in the population? Of people rather than in mice or other creatures.

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* Kresge 502 Cart: So just some historical perspective. So the use of tobacco. Actually, it was already in 1761 that Dr. John Hill wrote a pamphlet cautioning against the moderate use of snuff. And this is really he. He wrote this article or this pamphlet, really just a few decades after tobacco became popular in London, and before it was combustible, the first, it was actually an oral type of

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* Kresge 502 Cart: tobacco, called snuff and

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* Kresge 502 Cart: What he observed was that in individuals who are regularly using this smokeless tobacco product. There were all sorts of oral lesions and oral cancers that were occurring. This population, so was already back in 1761 that this he made this kind of connection between use of tobacco and risk of cancer. But it actually wasn't until really many centuries later. That it became

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* Kresge 502 Cart: really established that tobacco was a major cause of different cancers. And we'll go into what those cancers are when we talk about the tobacco and cancer lecture. But it was actually the first real epidemiology study was in 1912 looking at a case control study of tobacco and lung cancer. And then

30:01

* Kresge 502 Cart: It was in the 1950 s. That the first prospective cohort says so again, we'll talk on Thursday a little bit. What's the difference between a case control cohort study for cancer epidemiology? But it was in 1950 s. That the epidemiology really solidified one of the big cohort studies was a a cohort of physicians from the Uk which which actually had a very high prevalence of of

30:19

* Kresge 502 Cart: tobacco use showing up and as a cause of lung cancer. But before then there's a lot of pushback from people. Say it's not tobacco. There must be other factors that these people are doing that would cause cancer. And just give you a context. The Us. Congress establish the National Cancer Institute in 1,937.

30:43

* Kresge 502 Cart: So again, first report in 1761, and then it was 1964 before the Us. Surgeon General first came out with its report on smoking and cancer, and then warning labels appeared on cigarettes in the United States in 1965. So another about 25 years later and one of the the former chairs of epidemiology. Here at the Harvard School of Public Health. Demetrius Chicopoulos was really one of the first.

31:01

* Kresge 502 Cart: I think there were 2 parallel articles that came out looking at secondhand smoke so passive exposure to tobacco smoke as a risk factor for lung cancer, and just like it, with primary smoking and lung cancer. There was a lot of push back on that. And again, we'll we'll talk about that now, but now it's it's pretty well established that exposure to secondhand smoking is a risk factor for lung cancer.

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* Kresge 502 Cart: So another historical perspective. So in the eighteenth century there was an Italian doctor, Ramazini, who made the following observation, in a population of nuns they seem to be immune from developing cervical cancer, but had a higher than expected risk of breast cancer.

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* Kresge 502 Cart: What factors might underlie this association? Once you turn to your neighbor for a minute or 2.

32:10

* Kresge 502 Cart: Talk about what you know. What is this? Up observation? What might be done? A link what? Why, none seem to have a much like a basically immune developing cervical cancer, but a higher than expected risk breast cancer, talk with each other, and we'll come back together in a minute.

32:17

* Kresge 502 Cart: Alright. So maybe we will come back together.

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* Kresge 502 Cart: So I'd love to hear people the the thoughts from your discussion. So

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* Kresge 502 Cart: what were something that you talked? We talked a little bit about what might be the common underlying factor. And you're thinking about non potentially not engaging sexual activity which would be protective factor against sort of cancer. But I remember reading somewhere, and I could be totally wrong that pregnancy is actually associated with a lower risk. So it would be beneficial in one way. But detrimental. Yeah, that's exactly right. So

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* Kresge 502 Cart: for in terms of cervical cancer, exposure to human papilloma virus, either 16 or 18 is a necessary, although not sufficient

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* Kresge 502 Cart: cause of cervical cancer. And we'll, you know. So we just because we have it, doesn't have the infection doesn't get cervical cancer but then, on the flip side. There'll be a great discussion about reproductive factors, including a pregnancy. That is the explanation for higher than expected risk of breast cancer. So that's exactly yep. Any other conversations like or points that you want us to raise up about that?

35:38

* Kresge 502 Cart: Yes, they're like social like. They're environment.

36:03

* Kresge 502 Cart: Oh, that's interesting, right? So we could there also. Right? So I age better. P is an important factor for breast cancer. So the younger age of underp is assisted with an increase to breast cancer. So could there be something in their environment that at least makes that link with breast cancer. So that would be interesting to think about as well.

36:11

* Kresge 502 Cart: Great

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* Kresge 502 Cart: so another historical perspective. And and maybe I give those

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* Kresge 502 Cart: punchline here away. But Harold Zarhausen was a virologist, who had originally hypothesized back in 90 s. 74, that cervical cancer might have a a viral ideology. He initially, he didn't. He thought it was related to herpes virus, too. But what he did was then to look at under the microscope. Cervical cancer specimens.

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* and that's where we discovered it was actually human. Papillomavirus, or Hpv. 16 and 18, ultimately received the Nobel Prize in 2,008

37:06

* Kresge 502 Cart: cool

37:16

* Kresge 502 Cart: right? And so just even it was interesting, though, even though they didn't know the exact cause of cervical cancer pap, smears were actually introduced back in the 1940 S, as a way to really detect presence of either

37:18

* Kresge 502 Cart: cervical cancer earlier than it would otherwise before symptoms, or even with with cervical cancer as well as colorectal cancer. There's a pre, the established, pre malignant lesion. That with a high risk of going on to cancer. So you can. Actually, instead of detecting the cancer itself, you can detect the the pre malignant lesion and take it out and prevent

37:34

* cancer from her happening. So it's a really interesting, an important model for early detection of cancer.

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* Kresge 502 Cart: Yeah. So, and then, just in terms of a timeline so the discovery of Hpv. DNA and cancer cervical cancer specimens made in 1983, and then, about 20 years later, a vaccine against Hpv was approved for the prevention of cervical cancer. Unfortunately, despite the fact that the vaccine is quite effective and preventing

38:05

* Kresge 502 Cart: Hpv infection. It's not broadly available to all parts of the world you still have, and we'll talk about in the descriptive epidemiology and looking at cervical cancer around the world, you have some countries with very high incidence and mortality. From cervical cancer, despite the fact that there's prevention and vaccination. So again, thinking, this is in an interesting model where you know a lot about how to prevent the cancer.

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* Kresge 502 Cart: But we haven't been able to implement those prevention strategies equally around the world. And even in the United States across different populations.

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* Kresge 502 Cart: So in terms of occupational exposures, I think really one of the first strong links between occupation and a cancer was made in 1775. Percival Pot was studying

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* Kresge 502 Cart: children who work chimneys sweep so they would go in down the chimneys and clean with a brush. And there's an excess risk of a cancer that otherwise is quite rare, which is cancer of the scrotum. And you know, this is language that was taken from his observations on this, and he said, You know I've never had seen squirrel cancers under the age of puberty.

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* Kresge 502 Cart: which is what one reason that initially thought to have a a venereal cause so sexually transmitted. Infectious cause. He talks a lot about the brutality of working as a chimney sweep, where they had very young children who are small enough to fit down the chimneys. And they were exposed to these. You know, the he actually wasn't exactly sure what they were being exposed to, but made this observation that it was because they were working as a chimney sweep

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* Kresge 502 Cart: that they had this excess risk of scuttle cancers. So but 100 years later I it took, despite this observation, to implement changes in occupational setting to prevent exposure to you know the suit, but really wasn't identified even until another 60 years later. That what the causal agent

40:14

* Kresge 502 Cart: so it was. So it was actually benzo. A pyre in the suit was leading to this excess risk of scroll cancers. So again, you know, it's interesting with with with smoking and lung cancer. Some people pushed up against that hypothesis being true because one smoking wasn't specific to lung cancer, increase the risk of other cancers, but also they said, Well, what is it? What is it

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* Kresge 502 Cart: carcinogen so you don't know with the carcinogen, so you can't say it's a causally associated with the cancer. So it was interesting here to see how long it really took to translate these findings. These observations into identifying the causal agent, and even took 100 years after the first observation, to get preventive measures in place in the occupational setting.

41:04

* Kresge 502 Cart: So, we again, we'll talk about cancer during each of the specific cancers as an inherited disease. So if you looked at

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* Kresge 502 Cart: the risk of any type of cancers, about 30% of cancer incidence is due to inherited genetic causes. And that's evidence that comes from family based studies and twin studies as well.

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* Kresge 502 Cart: so the the one of the first descriptions of family history of cancer was a was done by Paul Broca, who described this very detailed family history from 1,866, where there were this family had a number of breast cancer cases as well as other cancer cases

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* Kresge 502 Cart: occurring and showing. So the the first matriarch of the family was Mrs. D. And the

42:17

* Kresge 502 Cart: dark spot here is breast cancer, and then there are other cancers as well, looks like there was liver cancer in some of the members as well as other malignancy. So it was really an interesting one of the first ways of tracking that people who have a family history with a sibling, a parent who has cancer or at increased risk of cancer themselves. So does having a family history.

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* Kresge 502 Cart: Mean that it's a genetic cause

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* Kresge 502 Cart: or not? Does it have to? So why or why not?

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* Kresge 502 Cart: What's your thinking when you're hearing family history. What? What might be the reason that your family history is.

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* Clara.

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* Kresge 502 Cart: In what way would you say this might be.

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* Kresge 502 Cart: yeah. So I,

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* Kresge 502 Cart: yeah, yeah, exactly. Right. So so the family members may be eating the same food together, so they're exposed to the same diet. Or maybe there's one person smoking the house, so they're all exposed to passive smoking. Or maybe they're just as likely to get screens like if one of them has cancer than the other. So there's there's sort of this shared environmental factor, that part is family history. And then, of course, there is that genetic component

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* Kresge 502 Cart: as well. So we'll talk about this a little bit more detail. On Thursday.

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* Kresge 502 Cart: So another I think really interesting historical perspective. As as Ed was saying that understanding the impact of radiation on the development of cancer has really helped to understand a number of different factors about mutations that occurring about latency. So there was a really interesting study. And there's actually a movie that was made about this about the it was called the Radium Girls.

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* Kresge 502 Cart: So in 1915 to 1929, which was soon after radiation was really first discovered. they would use a form of radium radium, 2 26 to paint the dials of watches so that they would glow in the dark. So

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* Kresge 502 Cart: with us women were recruited to paint these watch styles, and in fact, I think one of the first watch factories was in Waltham, Massachusetts, so familiar, I think that's right. And so they would basically

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* Kresge 502 Cart: So they had a very fine point on the paintbrush, and so they would be painting the numbers on the dial, and then they would point

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* Kresge 502 Cart: the pink brush meeting that would, they would lift the tip of the paint brush to make it really skinny, you know, if you're trying to

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* Kresge 502 Cart: put thread into a needle, you have to kind of get it really small, so they would do the same thing with the paintbrush. And essentially they were ingesting all of this radiation. Well, soon after they saw an excess incidence of fractures of the bone and then ultimately bone cancers. And it was through this perspective that they made the link between one of the links between radiation and cancer.

45:03

* Kresge 502 Cart: So do you think I can play this video? II forgot to see if we could do this

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* Kresge 502 Cart: if I click on this bullet. Okay, perfect. So Robert Weinberg, there's a there's a recommended meeting in the

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* Kresge 502 Cart: on the Harvard campus page

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* Kresge 502 Cart: which was written by Robert Weinberg. About is Hannah and Weiberg about the. And we'll talk about what these are the sort of the the defining features of cancer he's a he's a biologist physician. But I thought it was really this beautiful piece about importance of cancer prevention. So we thought we would play that here.

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* Kresge 502 Cart: So. And one thing we've talked about in prior classes was, what did what did you think about his comment that if we all live long enough

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* Kresge 502 Cart: we'd ultimately all develop cancer. What do you think about that statement?

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* Kresge 502 Cart: Scared? Scary. Yeah. Yeah.

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* Kresge 502 Cart: It's it's interesting. There, there's, you know, in in again, if we look in the United States. About one in 2 people will develop. Then 1, 2 people identify as men are will develop cancer and women's one and 3

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* Kresge 502 Cart: So there's certain people who seem to be immune from cancer. So I'm not. It's interesting to think what Michelle and colleen what you're

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* Kresge 502 Cart: thoughts are. Ed, what your thoughts are about like. Do you think really, that everybody would develop cancer if we lived to 100 2,130 years, or do you think we really are? There are some people who are really immune, or is it really prevention, death from other causes? Right? If you know, if you didn't die of a heart heart attack, or getting hit by a bus would again would be all live to be

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* Kresge 502 Cart: able to develop cancer. Like, put their eyes down.

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* Kresge 502 Cart: cancers that are not lethal prostate cancer.

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* Kresge 502 Cart: Like Van Biden.

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* Kresge 502 Cart: probably 50%. Yeah, card

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* Kresge 502 Cart: chances are, let's

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* Kresge 502 Cart: that's interesting. Yeah.

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* Kresge 502 Cart: yeah. So what? What that is referring to is a series of what we call autopsy studies. So these are looking at the tissues of people who die of many different causes other than cancer to see if you can see evidence of cancer. And so it goes to this idea of sort of what we call almost like pseudo cancer. Truly cancer, right? It has all the features of what you say is cancer. But it didn't come

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* Kresge 502 Cart: to light anytime while the person was alive. So they died with the cancer, not from the cancer. So that that's an interesting point. Yes, yeah.

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* Kresge 502 Cart: II actually, really. And I think, really, it's really matters how you define cancer. I mean.

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* Kresge 502 Cart: there are certain kinds of cancers, or maybe called by some 3 malignant status. I mean.

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* Kresge 502 Cart: I'm a so in our world, we have all kind of stays that we just discovered in the last couple of years that

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* Kresge 502 Cart: we have the vast majority of older patients have mutations in their DNA and and

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* Kresge 502 Cart: these are with them in a very high risk for certain types of cancers. But I mean. So eventually, almost all of the I would say, for 80,

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* Kresge 502 Cart: almost all, all the people over a have certain kinds of these mutations. Whether or not it is frank cancer. It's debatable

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* Kresge 502 Cart: on the type of how you define cancer. Yeah, that's a great point.

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* Kresge 502 Cart: really great. But any other thoughts on that.

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* Kresge 502 Cart: Okay.

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* Kresge 502 Cart: okay. So I'm gonna go. And just to just to give you kind of a kind of so we can get some common terminology down. And again. So Dr. Weinberg and Hannah wrote this wonderful article in cell. Talking about some of the key fee hallmarks of cancer.

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* Kresge 502 Cart: So what is a tumor versus what is cancer? So tumor is really sort of a non dis nonspecific description of any sort of lump or spelling of tissue and a tumor can be both benign or cancerous. And so if you compare these 4 features the tumor invasiveness, the rate of growth.

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* Kresge 502 Cart: whether the cells look like the original cell of origin. So, for example, if it's a prostate cell, does it still look like prostate? Or does it look

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* Kresge 502 Cart: like poorly differentiated or d differentiates. It doesn't look like that anymore. Kind of metastasize. And then, if you compare benign tumors and malignant tumors, malignant tumors. I think the one feature that all tumors that are cancer have is that they're invasive and benign tumors are often sort of encapsulated in themselves, and they're not invasive into the adjacent tissue.

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* Kresge 502 Cart: This is not all. But the rest of the other features are not always true. Again, talking about prostate cancer. Prostate cancer that is invasive can actually grow very, very slowly some. Not all do. And similarly, breast. Maybe thyroid cancer in some cases can grow very, very slowly so, but more often than not malignant tumors will grow rapidly versus benign tumors, which have very slow, or even are not really growing at all.

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* Kresge 502 Cart: So again, in terms of the differenti differentiation, how much does it look like the tissue of origin? Malignant humans are often poorly differentiated, or even d differentiated versus well differentiated. And this is again, this is just looking under the microscope. The pathologist looks at the tissue and says, Does this look like the original tissue of origin or not, and then from metastasis, which means that the cancer leaves

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* Kresge 502 Cart: it's a regional organ and goes to a different part of the body. And I'll I'll talk about that in a moment. So it does. Malignant tumors don't always metastasize, but they often or can metastasize, whereas benign tumor will never metastasize. So can you think of an example, though. So you can see, these features of malignant tumors or cancer are are really much more aggressive, they often can cause death.

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* Kresge 502 Cart: Can a benign tumor ever cause death? Can you think of an example? If it does?

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* Kresge 502 Cart: Yes.

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* Kresge 502 Cart: so again, there's there's a number of hallmark features of of cancer. Essentially, it's it's doing a lot of different biologic pathways to allow it to keep growing to avoid signals that are telling it to either stop growing or undergrow cell death it needs as it grows it needs its own blood supply called angiogenesis to both

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* Kresge 502 Cart: get additional nutrients, but also take away waste and also some of the hallmarks of cancer involve being more invasive. And then ultimately, if you have a cancer growing in the breast tissue that then can metastasize it has to be able to set up in a different environment and be able to grow and proliferate as well.

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* Kresge 502 Cart: So again, these II don't think these are things that you not need to memorize, but I just wanna kind of show you. Kind of one is the growth between the normal tissue into invasive cancer. And then some terminology that talks about specific classifications of of of cancer. So first, we have 3 different

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* Kresge 502 Cart: descriptors of sort of either normal tissue or pre malignant tissue. So hyperplasia is just simply refer to the fact that you have an increasing growth of the number of normal cells in a tissue. But the normal. The cells look pretty normal. Otherwise they're growing. So you get growth. So you have hyperplasia. But these are unlikely to form cancer. They don't show any evidence

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* Kresge 502 Cart: of the stat disease, I think one, and again sorry to use so many examples of the prostate, but one of the conditions that affects a lot of older people with with prostate is a benign, prostatic hyperplasia and which is a benign enlargement of the prostate.

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* Kresge 502 Cart: The next one, though, is dysplasia. So in contrast to hyperplasia, you can start to see

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* Kresge 502 Cart: pre malignant changes of these tissues and the specifically of of epithelial cells, and if you look under the microscope, they're not invading right? They don't have the the features that the cancer has there. There. They might even still be slow growing, but they're starting to look atypical, and there's many cancers for which you have dysplasia as an evidence. And again, in some ways the hope for the early detection is not only that you detect

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* Kresge 502 Cart: cancer earlier, but that there are these pre malignant conditions, and the goal would be to actually identify those before cancer occurs, because then you could sort of remove them, treat them before the cancer progresses, and then carcinoma inside 2 are malignant cells that have all the features, otherwise of cancer, except for the invasiveness components. So that's carcinoma inside. 2

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* Kresge 502 Cart: and so just in terms of you know, once cancer occurs yes.

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* first of all, and said to

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* Kresge 502 Cart: in in insight, I think inside you right in. It's the it's sort of like

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* Kresge 502 Cart: so like I think breast cancer in side 2 is probably breast carcinoma in side 2. It's it's sort of like

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* Kresge 502 Cart: it's located still in the breast tissue. It just hasn't invaded into the adjacent organ. So inside to

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* Kresge 502 Cart: not activated

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* Kresge 502 Cart: activated just hasn't like just hasn't invaded into any adjacent organ. So it's probably still encapsulated to some extent.

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* Kresge 502 Cart: Oh, sorry. Yeah. Oh, I'm just wondering. Lower stage, it's not considered cancer. And we actually, there's some debate about this. We've actually, we've had some really interesting discussion. Love to hear your perspective on this. But you know, is it truly cancer? If it doesn't have that invasive

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* Kresge 502 Cart: feature? So I do. You have a thought about? If it's cancer type of cancer. So cervical cancer? Yes, no. Inside of means that there is a buzzer. Learn that cancer. So did not

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* Kresge 502 Cart: go across it and and and and invade it beyond that. That's what those good. That's the system about that. So

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* Kresge 502 Cart: the implication is different and and service, and and every type of sensor. So. as as you said, these are different type of diseases, so I can't really refer to. All of them is one. But

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* Kresge 502 Cart: inside, to usually means less in place. That's how I didn't didn't spread.

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* Kresge 502 Cart: Yeah, but it. But it's still it hasn't. Actually, you know, I think, that the distinction, if you, if you believe that you have to have these features to call it cancer like, even with Cervix, the insight to it still has not invaded into the adjacent tissue. So that but it's still the risk that it will is high, right? So it's really concerning you still wanna remove it? Is it cancer? Per se?

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* Kresge 502 Cart: It's important to like,

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* Kresge 502 Cart: II think this is correct. Cancer inside to

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* Kresge 502 Cart: is like

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* Kresge 502 Cart: what would happen had breast cancer.

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* Kresge 502 Cart: 2 of all those people

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* Kresge 502 Cart: there, there would be a risk. Answer. And relatively well, I mean, it's not

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* Kresge 502 Cart: over many years.

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* Kresge 502 Cart: 5%.

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* Kresge 502 Cart: And like for for color record.

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* Kresge 502 Cart: there is a actually indistinguishable from what we would call

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* Kresge 502 Cart: added, Oh, my, that's a precursor with high displacement. So if you, if you look just at the cells.

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* Kresge 502 Cart: looks pretty bad with some cancer, but it hasn't faded yet.

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* Kresge 502 Cart: But if you leave those regions again.

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* Kresge 502 Cart: like maybe into 5,

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* Kresge 502 Cart: you're great, slightly.

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* Kresge 502 Cart: Chad, or 20%.

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* Kresge 502 Cart: Yeah? Well, depending on the type of poly, right? There's different risk of cancer occurring, depending on the type of poly

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* Kresge 502 Cart: right? Right? Right?

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* Kresge 502 Cart: And actually, so, and trained actually as a pathologist before studying epidemiology. Just to few years. Yeah.

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* Kresge 502 Cart: so again, just to give you a lay of the land in terms of some of the like. Once cancer is occurring, the way that it gets described is based on where the tissue originated from. So

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* Kresge 502 Cart: sarcoma is a malignant tumor that is, arises from mesenchymal tissues, and it's usually defined by the tissue of origin, so a malignant tumor arising in bone would be referred to as an Osircoma carcinoma is malignant tissue that occurs in epithelial organs, and it's defined by

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* Kresge 502 Cart: the type of origin of the epithelial tissue. So again, for static carcinoma, and particularly if if it's occurring in these glandular structures, this is a lot of detail. But again, you're gonna hear these words. I just want to give you a sense of where they come from. When they are occurring specifically in the glandular structures of the epithelial tissue that's referred to as add no carcinoma. But instead of it's on the superficial epithelial cells.

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* Kresge 502 Cart: it's going to sell a personoma malignant tumors occurring in lymph nodes is lymphoma or from circling blood cells or bone marrows leukemia, and then finally, malignant tumors that derive from melanos sites is melanoma, so just can get the origin.

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* Kresge 502 Cart: And so this is really been interesting to think about how we might integrate. And all of this is is histology. So it's it's things that the pathologists is looking at under the microscope. And

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* Kresge 502 Cart: describing. So here's an example of lung cancer histology. So the vast majority of lung cancer is carcinoma meaning it's originating from epithelial tissues. But then you can break down the carcinoma into those that are small cell

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* Kresge 502 Cart: and versus non small cell lung cancer. And then within that non small cell lung cancer, you have 3 different bins 40 or so are abnormal carcinoma. 30 are squamous cell. And again, that just refers to the actual

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* Kresge 502 Cart: part of the epithelial tissue that's rising from, and then more rare, these large cell lung cancers. And so this is a figure looking at the association between the number of cigarettes smoked per day. And the relative risk of lung cancer that's in red is this squamous cell cancer? Green is small cell lung cancer and blue is, add no carcinoma. So when you look at this figure.

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* Kresge 502 Cart: what what does this figure

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* Kresge 502 Cart: say to you

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* Kresge 502 Cart: in terms of anything you could talk about? The overall association of of smoking and lung cancer. You could talk about the relative risk in terms of the different subtypes of cancer or not. No differences. What? What does this sound. Tell you.

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* Kresge 502 Cart: when you look at this cigarettes, quote per day. And the rest of

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* Kresge 502 Cart: all types of

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* Kresge 502 Cart: yeah, yeah, absolutely. And you can see it's pretty dramatic right? So compared to people are not smoking. You have a range of about 8 to probably 20 fold increased risk in those people who are smoking 30 or more cigarettes.

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* Kresge 502 Cart: and so does it look like. There might be a difference in terms of the strength of the association

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* Kresge 502 Cart: when we don't have confidence intervals here, so we can't make a statistical comparison. But if you were qualitatively saying, there might be a difference.

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* Kresge 502 Cart: Do you think there is

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* Kresge 502 Cart: maybe a little bit. Yes. Yeah. Yeah.

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* Kresge 502 Cart: Yeah, yeah, definitely. It looks like the strongest association are for cancers that are squamous cell cancers still significantly associate with. Add no carcinoma, but does seem to be not as strong of an association. And so the question is, why right is, you know, what is is it about the carcinogens. Is it based on how tobacco is taken up into the lungs? I think people talk about

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* Kresge 502 Cart: some of those things in general, but I think this is just an illustrative example that the association of risk factors and cancers, we're starting to realize may differ based on things like the histology of of the tumor, and we'll talk about some examples. I think, colorectal cancer. It also may be not only histology of meaning how it looks under the microscope, but also molecular features in the different cancer types.

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* Kresge 502 Cart: Yes.

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* Kresge 502 Cart: I. So

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* Kresge 502 Cart: oh, between small and non-smell. So so there, I think it's basically just the cell of origin. I'm not a lung cancer expert. So I think, but it's basically do.

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* Kresge 502 Cart: It was just a

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* Kresge 502 Cart: the historical one.

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* Kresge 502 Cart: I think it's based on installments.

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* Kresge 502 Cart: small cells. And so

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* Kresge 502 Cart: so

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* Kresge 502 Cart: balancing.

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* Kresge 502 Cart: it's it's

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* Kresge 502 Cart: relate to the type of mutations that are in the sales and also how they present small cell present

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* Kresge 502 Cart: within the central area of the one field, whereas and also we don't really operate how we treat them. So we don't really operate. Small cell

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* Kresge 502 Cart: can serve, whereas in.

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* Kresge 502 Cart: especially when it's not

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* Kresge 502 Cart: the.

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* Kresge 502 Cart: And do you do not do surgery in those because of the or where it's located in the lung

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* Kresge 502 Cart: cause it doesn't help interesting. Yeah, interesting. Yeah. Yeah. So it's interesting to think about all of the things that we like. We're thinking from the cancer epidemiology, lens of risk factors being associated with these different cell types. But they also have impact on prognosis, on treatment decisions, etc. So it's interesting to kind of think about how to integrate these into depending on what you're setting. So

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* Kresge 502 Cart: so metastasis is thought to be really the highest degree of malignancy and most cancer deaths occur because they've left the original

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* Kresge 502 Cart: tissue and have gone to another part of the body and cures really much less likely possible. At this stage. And interestingly, specific cancers seem to metastasize to different parts of the body. So, for example. Again, prostate is primary side of metastasis to the bone, and you can see here other sites, common sites of metastasis.

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* Kresge 502 Cart: So it is interesting to think about that. You know, you have cancer cells, let's say in the testis, in the bladder, in the kidney. They then have to get out of that or

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* Kresge 502 Cart: organ, and get either potentially through the blood systems. They may metastasize one that is, through nerves. One thought is through lymph nodes to other parts of the body, and then they have to be able to survive and then grow in that in that side of metastasis

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* Kresge 502 Cart: and then tumor grade. We talked a little bit about histology. So epithologists makes the diagnosis of cancer by looking under the microscope. And then also we'll try to give a sense of what's called the tumor grade. And there's 2 different main descriptions of grade. One is is called histologic grade, which is what the pattern of differentiation looks like, and you can sort of see

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* Kresge 502 Cart: this is things that are well differentiated, meaning they look more like the tissue of origin, and then, as they get less and less looking like the original tissue of origin, th they're they're thought to be more aggressive terms of prognosis. You may treat these differently, but also from an epidemiology perspective. You may be interested in studying, say, the association between smoking and a cancer

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* Kresge 502 Cart: that's either poorly differentiated. We've all differentiated. Come to the point that we talked about earlier, which is that you may not be interested in setting the risk of cancer overall, but rather the risk of cancers that are going to do harm.

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* Kresge 502 Cart: And then the other grading system that's used in some types of cancers is a based solely on the the shape and size of the nucleus, and that's called a nuclear grade.

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* Kresge 502 Cart: Again, this is again, just to give you kind of a background in cancer itself. And then so the other one of the other factors clinically, that's used. But again, we can think about this from our epidemiology studies is the staging of cancer, and for many different cancers. We use a system called T and M to define is the cancer still localized

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* Kresge 502 Cart: to the original tissue of origin, whether brass, prostate bladder, or has it? Gone beyond the origin? And so you look at sort of the extent of the tumors. It here, you can say, was, it's not detectable other than by screening, or can get larger, and then it can even go to the the borders, are there? Lymph nodes that are involved?

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* Kresge 502 Cart: and that can give you a sense of how aggressive the cancer heads. It's likely for spread. And then finally, metastasis to more distant organs. And you would usually use some sort of the imaging to assess whether the cancer is metastasized or not.

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* Kresge 502 Cart: And then, as I mentioned, for some cancers, we're learning a lot about the molecular subtypes of these cancers. Here's an example with breast cancer. So if a person is diagnosed with breast cancer, they'll get additional kind of

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* Kresge 502 Cart: biomarker workup to see whether they their tumors expressing the estrogen receptor progesterone receptor. If it's positive for her 2 or if it's triple negative. And again, that could be important for how the

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* Kresge 502 Cart: the physician will treat the cancer the likelihood of a bad or better prognosis, but also from an epidemiologic perspective. We're really starting to see with breast cancer and heather lies, and we'll talk about this in some detail that not all risk factors are the same for cancers that have the estrogen receptor present in the tumors versus those are absent. So she'll talk about that. And then we have some lectures on prostate and and colorectal cancer as well. Talking about some of the molecular subtypes.

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* Kresge 502 Cart: Okay? So just again, just to kind of wrap up this very biologic kind of discussion. When we think about how risk factors. Or, first of all, how cancer occurs. And as well as how risk factors may lead to either the prevention of cancer or an increased risk. We can kind of think about this, you know central dogma of going from DNA to Rna

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* Kresge 502 Cart: to protein, and then even to metabolites. And we, you know, Dr. Weinbergen is his

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* Kresge 502 Cart: In the video we played. And also, when you think about cancer, often think about these mutations in the DNA occurring, but not all cancers are occurring through simply through mutations. There can be effects that are not through mutations that are on the Rna level quantity, so how much the gene is turned on or off and then, or it could be to the translation going from Rna

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* Kresge 502 Cart: to protein is the protein expressed in high levels, has it been altered in some way? And so all of these things we can think about cancer the other way in which we can think about an infect on the DNA is actually not through a mutation, but actually through epigenetics. So some risk factors may be acting, not by doing damage to DNA, but actually by impacting

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* Kresge 502 Cart: something called epigenetics, which doesn't change the the DNA,

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* Kresge 502 Cart: you know letters but actually can modify. The way DNA works through a different modifications. So one important thing, just to kind of know, there's a couple of different ways in which genes and our DNA can be altered. The first is that they could be. You could get an altered copy from from your parents, so it can be inherited through the germline.

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* Kresge 502 Cart: You can also get sort of a

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* Kresge 502 Cart: alterations that can lead to what we call somatic damage or changes to to DNA after somebody's born. So, for example, I think lung cancer and smoking. You can think about that. You have sort of normal DNA that you've inherited that can then be damaged somatically. Through the accumulation of exposure to tobacco smoke. So that's a that's a key distinction, though.

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* Kresge 502 Cart: The DNA you get that's inherited that you get from the parents. And then DNA that can be damaged somatically. And that's after you know the initial

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* Kresge 502 Cart: you know your initial formation. This is, I think, a really interesting example of the impact on the environment on DNA, that's not through mutation. So this was a case study of 2 identical twins. So they were monozygotic or identical twins. Who are astronauts that were part of the Us. NASA Space program.

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* Kresge 502 Cart: One of the twins spent a year in space, while the other twin, who was also an astronaut, was on the ground. And they did some detailed biologics on these 2 identical twins and said, Well, do you know the DNA inherited DNA of these 2 individuals was identical?

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* Kresge 502 Cart: Right? Because they're they're monozygotic twins, or their inherited DNA was identical. But after spending a year in space

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* Kresge 502 Cart: they looked at the epigenetics and the impact of the environment on modifications to the DNA and found pretty big differences in the Gene expression of 800 genes that seem to be due to epigenetic modifications. They also showed shortening of the telomeres now, after some time of the. And I

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* Kresge 502 Cart: think Oh, no, I don't remember actually sorry. I'm not gonna say if I had to guess I don't know why I would think this twin was the one who went to space.

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* Kresge 502 Cart: It looks like right a little bit of an effect on aging in a little way, but I could be. No, I'm serious. No, no, it's true. I think this effect of biologic aging, right of the environment and epigenetics. So sorry. But I think I think this was the 21 space. But a lot of that. Actually, those changes in gene expression. kind of some of them went away. Some of them didn't. Some of them kind of stayed

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* Kresge 502 Cart: for a long time after. But you know, I think that epigenetics is something that is

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* Kresge 502 Cart: kind of potentially modifiable, whereas, like a DNA mutation is, unless you can get rid of that mutation through program cell death, or something like that is not modifiable.

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* Kresge 502 Cart: so so just kind of thinking about inherited genetic variation. When we look at the DNA of everybody in this room, 99.6% of our inherited genome is the same across all of us here.

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* Kresge 502 Cart: and so about one in 400 base pairs and the Mo. The majority of this variation is actually single nucleotide polymorphism. So it's a single alteration in a base pair. Lot of those things don't affect

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* Kresge 502 Cart: Rna don't affect protein. Some do. Some of the individual genes are different, and they do contribute, but some of them don't. And then about 10% of the genet genetic variations in the more structural. But a lot of the studies that we've done and trying to understand the genetics susceptibility to cancer have been focused on measuring these single nucleotide polymorphism. So again, about one in 400 base pairs vary

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* Kresge 502 Cart: between all of us, and whether some of those are associated with cancer or not. Associated with cardiovascular disease or other types of diseases is something we can do.

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* Kresge 502 Cart: You know, I'll talk about in a moment. So, as I mentioned already, these these sips may exist, but we don't know what they do. But then you might say, these sips are more common in this disease than in people who don't have that disease. And the question is, why, what are they affecting? Are they changing? Yes.

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* Kresge 502 Cart: yeah, yeah, that's super interesting.

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* Kresge 502 Cart: Thank you.

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* Kresge 502 Cart: so yeah, so

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* Kresge 502 Cart: so anyway. So so we'll we'll we'll talk about this when we start going into some of the discussion have. There's a great course, I think, on genetic epidemiology. If people are interested in getting more depth on some of the underlying genetic causes of disease. So if you're interested in this, but within some of the individual lectures, we'll talk about the role of inherited genetic factors

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* who?

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* Kresge 502 Cart: So I think I wanted to just kind of highlight these sort of 3 main classes of mutations.

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* Kresge 502 Cart: one is oncogenes tumor suppressor genes and DNA repair genes. And I think I think there's a great chapter that's in from the textbook of cancer epidemiology called the Origins of cancer. So people again, who won't want to read more up on the biology of cancer. It could. Guys goes into a lot more detail about this. But oncogenes are, you can kind of think of our the gas

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* Kresge 502 Cart: of of cancer. So kind of when when these genes are mutated, it's like the gas keeps the gas pedals down and tells kit grow, grow, grow, grow, grow, grow, grow, grow.

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* Kresge 502 Cart: tumor, tumor repressors. On the other hand, normally their role is to tell cells not to grow without a gross stimuli being present. And so what happens there when you get a mutation in these tumor suppressors? Basically, the great, the break is broken and so you stepping on the break. But nothing's happening. And so basically, you're

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* Kresge 502 Cart: the the cells are not no longer getting these signals to stop growing, so they keep growing, and then DNA repair. Jeans are those genes that are involved in sort of, you know, as as Dr. Weinberg said, you know you have

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* Kresge 502 Cart: millions upon billions of cell

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* Kresge 502 Cart: cell division happening. And by chance you can get mutations occurring. And so you need mechanism in place, and there's genes that are involved in the repair of of or cells, and either repairing the DNA damage that's occurred, or or telling the cell to undergo cell death. And so what can happen, though, is you can have mutations in these DNA repair genes. So they're not as effective in identifying

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* Kresge 502 Cart: when mutations are occurring and then getting rid of the cells. So these are kind of the 3 main classes. When we think about mutations in DNA, these are the kind of 3 main classes of of the types of genes that are involved in cancer.

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* Kresge 502 Cart: And so I think this is the last idea. And so there, there's a theory about this to hit hypothesis in in cancer. That it takes.

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* Kresge 502 Cart: you know, 2 alterations

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* Kresge 502 Cart: in the chromos like. So you have. You know you have 2 chromosomes so you need to have a mutation in both in order for cancer to occur. Now, if you have it. We'll talk about some inherited cancer syndromes at our next lecture.

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* Kresge 502 Cart: You can have from your parents. Unfortunately, one of your chromosomes has that alteration already, so it could be in an oncogene. It could be in tumor, suppressor, gene, or it could be in a DNA repair gene. So, for example, with breast cancer, you might get an inherited mutated copy of Brca. One, for example, or Brca. 2. That on its own isn't sufficient to cause cancer.

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* Kresge 502 Cart: but it increases the risk of cancer of happening so much because you already have the one strike against you. So you just need that second strike to occur in order for cancer to occur. So again, this PIN on the left kind of shows you you have. Your parental genes. One of them has a mutated copy. Unfortunately, you got that copy. So then you just need that second hit, that second mutagenic hit in order for cancer to occur

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* Kresge 502 Cart: in this example here, with the 2 hit hypothesis you happen to have from your parental genes no mutation there. You really have to get end up getting 2 mutagenic hits in the same cell in order for cancer to occur. So that's the 2 hit hypothesis. So again, this is just sort of an overview of some of the key concepts in

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* Kresge 502 Cart: kind of the path of biology, of cancer. At the next lecture we're gonna go into more about genetic susceptibility to cancer we're gonna talk about. Then also some of the more methodology talking about bias confounding. There's actually an article that would be great. If you can read before the class. Talking about recall bias. In case, control studies of cancer epidemiology.

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* Kresge 502 Cart: going to have a breakout discussion about that next time. So, any any questions, any thoughts?

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* Kresge 502 Cart: okay. Great. Well, excellent. We're really excited to have you all here feel free to email, any of us make sure if if anybody is having any trouble accessing the Harvard canvas page, email, any of us. And we otherwise we'll see you on Thursday.

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* Kresge 502 Cart: Great thanks.