Laura Lai Moochie: I do mostly cancer epidemiology. With a nutrition focus some frosty but more of a color rectal and like gas for intestinal cancers, although it won't be giving the prostate cancer lecture this year. Pauline Picky and Hi, everyone and Michelle kind of delve into a little bit some of the core concepts before that. There's 2 ways to access. The first is you can go open up a web browser and type in POLL. e.backslash, and then my name, Laura Laimuchi, 9, 6. If you want to use your cell phone, you can text the number 37607. So that will get you kind of activated. In the United States, about 40% of cancer diagnoses are thought to be preventable. If you could eliminate all the cancer risk factors, could you actually pre prevent? So is it 7, 2540, or 90? 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. The course will focus on what we think are causal factors in the ideology of cancer. We'll also talk about cancers for which we actually don't know as much about in terms of the epidemiology and areas for for potential growth. So excellent, fantastic. I'll I'll start with the course of Jack's, and then you can. The course will focus on the descriptive epidemiology of cancer. 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 global focus. For for your group project, you're gonna get an opportunity to work with some of the primary data sources. The focus is really learning to understand the literature from a big picture perspective like how to interpret the study. We interpret studies individually, but also in the context of other like studies like. so, oh, yeah. so so the lectures like W, it's kind of broken up in 2 ways. 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 of fame. The classes include presentations by the course instructors, and we have a lot of great guest lectures. We'll have some interactive learning during the classes which we'll get into later. You have assigned course reading readings. II think it would enhance the lecture. We know that not everybody does. Next week we'll 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. But just to give you an overview, that laurel, I does a a great job giving sort of the basic concepts of cancer. This year we have an extra day of work this year. So we have a scatter like some cancer, and then infectious diseases. 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's people really freaked out but 20 so bad. 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. It 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. You'll work in small groups and we'll find out later how how those are. You'll kind of self select and so it'll be focusing on a descriptive epidemiology of a specific cancer. There are the cancers for this year, so it's blad, so you only so you'll be in one of these cancers. There will be like a group presentation. which will do on those 2 days in February. So as a group like there's like 4 or 5 in a group you all come up. So each gives, you know, a little component and that, and that will be 20% of your grade. And then the also part of the grade is another. The assignment is to write a mock letter to the editor, editor and then also, we're gonna have an in person discussion altogether on this paper. The first will be the in class discussion, which will take place on February twenty-seventh. We'll take about 45 to 15 min in total. You'll also write a very short 500 word letter to the editor in response to this article. You can work on your own, or if you want to work with a total of 3 authors altogether, including yourself. That will count for 15. And then the final quiz. it's all there. You can basically schedule anytime from 9 in the morning on March seventh. All the way through Saturday, March ninth. You can use class notes, presentations any related merit materials. It really should be your own work before, like the last week, will usually have like a a session like a ta session. In this particular class, we don't want tools such as chat Gbt, or growerly, 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 things come up and you do need to miss a class or take part in zoom, please just let us know in advance. 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. Cancer is a diverse family of diseases, and it can arise in almost every cell of the body. The word cancer comes from the Greek word carcinoma for for crab. 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. 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 is that? What is it? Cancer epidemiology is about understanding the causes and opportunities for prevented cancer. Even within a single cancer, like breast cancer, colorectal cancer? We can even think of subsets of those those cancers that again, have their own unique factors, based either on molecular characteristics of the tumors or clinical features. Study design web. 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? I think that was a great, a great list. Yep, perfect. In 1761, Dr. John Hill wrote a pamphlet cautioning against the moderate use of snuff. Alexander Pope and his essay on man 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. The first real epidemiology study was in 1912 looking at a case control study of tobacco and lung cancer. 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 had a very high prevalence of of tobacco use. The National Cancer Institute was established in 1,937. 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. Demetrius Chicopoulos was really one of the first. 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. What factors might underlie this association? Once you turn to your neighbor for a minute or 2. Talk about what you know. exposure to human papilloma virus, either 16 or 18 is a necessary, although not sufficient cause of cervical cancer. There'll be a great discussion about reproductive factors, including a pregnancy. That is the explanation for higher than expected risk of breast cancer. Yes, they're like social like. They're environment. 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. and that's where we discovered it was actually human. Pap smears were introduced back in the 1940s as a way to detect presence of either cervical cancer or colorectal cancer. There's a pre, the established, pre malignant lesion. That with a high risk of going on to cancer. So you can. detect the the pre malignancy lesion and take it out and prevent cancer from her happening. The first strong link between occupation and a cancer was made in 1775. Percival Pot was studying 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. The cause of squirrel cancers was initially thought to have a venereal cause so sexually transmitted. Cause wasn't identified until another 60 years later. So it was actually benzo. A pyre in the suit was leading to this excess risk of scroll cancers. It took, despite this observation, to implement changes in occupational setting. About 30% of cancer incidence is due to inherited genetic causes. It took 100 years after the first observation, to get preventive measures in place in the occupational setting. So, we again, we'll talk about cancer during each of the specific cancers as an inherited disease. Family history is 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 mean that it's a genetic cause or not? Does it have to? So why or why not? What's your thinking when you're hearing family history. Family members may be eating the same food together, so they're exposed to the same diet. 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 this shared environmental factor, that part is family history. And then, of course, there is that genetic component as well. Women were recruited to paint the dials of watches so that they would glow in the dark. They would use a form of radium radium, 2 26, to do the work. Soon after they saw an excess incidence of fractures of the bone and then ultimately bone cancers. It was through this perspective that they made the link between radiation and cancer. Hannah and Weiberg: What do you think about Robert Weinberg's comment that if we all live long enough we'd ultimately all develop cancer? Hannah: Scared? Scary. Hannah: It's interesting. There's, you know, in in again, if we look in the United States. About one in 2 people will develop. Do you think 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 didn't die of a heart heart attack, or getting hit by a bus would again would be all live to be able to develop cancer. In our world, we have all kind of stays that we just discovered in the last couple of years that we have the vast majority of older patients have mutations in their DNA. These are with them in a very high risk for certain types of cancers. So eventually, almost all of the I would say, for 80, almost all, all the people over a have certain kinds of these mutations. Tumor is really sort of a non dis nonspecific description of any sort of lump or spelling of tissue. A tumor can be both benign or cancerous. If you compare these 4 features the tumor invasiveness, the rate of growth. Whether the cells look like the original cell of origin. 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. Malignant humans are often poorly differentiated, or even d differentiated versus well differentiated. So again, in terms of the differenti differentiation, how much does it look like the tissue of origin? Can a benign tumor ever cause death? Can you think of an example? If it does, yes. So it does. Malignant tumors don't always metastasize, but they often or can metastasizing. So you can see, these features of malignant tumors or cancer are are really more aggressive, they often can cause death. Cancer is doing a lot of different biologic pathways to allow it to keep growing. 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 grow and proliferate as well. Hyperplasia is an increasing growth of the number of normal cells in a tissue. But the normal. cells look pretty normal. So you have hyperplasia. But these are unlikely to form cancer. They don't show any evidence of the stat disease. dysplasia, you can start to see pre malignant changes of these tissues. Carcinoma inside 2 are malignant cells that have all the features, otherwise of cancer, except for the invasiveness components. So inside to not activated activated just hasn't like just haven't invaded into any adjacent organ. So it's probably still encapsulated to some extent. Lower stage, it's not considered cancer. Inside of means that there is a buzzer. So the implication is different and and service, and and every type of sensor. But inside, to usually means less in place. That's how I didn't didn't spread. 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? It's important to like, II think this is correct. There's different risk of cancer occurring, depending on the type of poly right? Right? And actually, so, and trained actually as a pathologist before studying epidemiology. 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. The vast majority of lung cancer is carcinoma meaning it's originating from epithelial tissues. 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. it's going to sell a personoma malignant tumors occurring in lymph nodes is lymphoma. 30 are squamous cell. And again, that just refers to the actual part of the epithelial tissue that's rising from, and then more rare, these large cell lung cancers. 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. 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. 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 people talk about some of those things in general, but I think this is just an illustrative example. metastasis is thought to be the highest degree of malignancy. Most cancer deaths occur because they've left the original tissue and have gone to another part of the body. Prostate is primary side of metastasis to the bone, and you can see here other sites. Cancer cells have to get out of that or 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. One is called histologic grade, which is what the pattern of differentiation looks like. As they get less and less looking like the original tissue of origin, th they're thought to be more aggressive terms of prognosis. 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. The staging of cancer, and for many different cancers. We use a system called T and M to define is the cancer still localized to the original tissue of origin. And then finally, metastasis to more distant organs. And you would usually use some sort of imaging to assess whether the cancer is metastasized or not. We're really starting to see with breast cancer and heather lies, and we'll talk about this in some detail. Not all risk factors are the same for cancers that have the estrogen receptor present in the tumors versus those are absent. And then we have some lectures on prostate and and colorectal cancer. 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. Some risk factors may be acting, not by doing damage to DNA, but actually by impacting something called epigenetics. The way DNA works through a different modifications. The DNA you get that's inherited that you get from the parents. And then DNA that can be damaged somatically. So, for example, I think lung cancer and smoking. 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. Who are astronauts that were part of the Us. NASA Space program. One of the twins spent a year in space, while the other twin, who was also an astronaut, was on the ground. I think this effect of biologic aging, right of the environment and epigenetics. 99.6% of our inherited genome is the same across all of us here. But a lot of that changes in gene expression. kind of some of them went away. Some of them didn't. The majority of this variation is actually single nucleotide polymorphism. So it's a single alteration in a base pair. 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. 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 I think I wanted to just kind of highlight these sort of 3 main classes of mutations. one is oncogenes tumor suppressor genes and DNA repair genes. Oncogenes are, you can kind of think of our the gas 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. tumor, tumor repressors. There's a theory about this to hit hypothesis in in cancer. 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. You can have from your parents. We'll talk about some inherited cancer syndromes at our next lecture. With breast cancer, you might get an inherited mutated copy of Brca. One. That on its own isn't sufficient to cause cancer. 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. At the next lecture we're gonna go into more about genetic susceptibility to cancer. Then also some of the more methodology talking about bias confounding. There's actually an article that would be great. Talking about recall bias. In case, control studies of cancer epidemiology. going to have a breakout discussion about that next time.