* That are looking for other people are suffocial cancer and ovarian cancer. Both of which are fascinating cancers.

1:01

* I mean, all of the cancers that we listed are really interesting in terms of the epidemiology.

1:08

* So, no, no, I saw ajial in the variant. Yeah. Okay. I'm sorry.

1:10

* I think there's about 5 students who haven't yet signed up yet. Yep, and on canvas, you should be able to see your group full lock after today after we put people in a, you didn't sign up death.

1:23

* And then there is a function on canvas where you should be able to just message my group that you're in, usually on campus.

1:40

* Oh, and then this is a last in a reminder next Tuesday, February sixth, your first assignment is huge.

1:48

* Yes. Any questions being before we start the trivia? Okay, great. So our question today is, you know, oftentimes when we do, you know, oftentimes when we do, studies, particularly when we're trying to get an early life exposures, you don't have, studies, particularly when we're trying to get at early life

2:00

* exposures, you don't have direct measures. And so we're often trying to use proxies to get at those exposures.

2:21

* So there's been some hypotheses in the literature around the role of sex halo, things like estrogen and androgens.

2:27

* So this question is in cancer epidemiology studies, which of the following have been used as proxies for greater exposure to androgens like testosterone in utero.

2:35

* Is it a exposure to DES during pregnancy. B, is it male pattern baldness? C is it the ratio of your second finger to your fourth picker or D is a higher birth weight.

2:48

* So which of these? Do you think is a proxy for greater exposure to androgen such as testosterone during, while you're a neuter.

3:00

* So not for the mom, but the actual. The infant and looking at future cancer risk. So how do we?

3:09

* Not the touch. Sorry. Oh, touch panel required. Oh, I don't know.

3:26

* I don't see it here.

3:34

* Hmm. If you turn around, I don't know if you can capture the one that's just behind you or just go to the website and pull up, Laurel, L, 900, and, 66.

3:37

* So yeah, because I don't see it right here.

3:46

* It's a little required. Sure.

3:53

* Hmm.

4:02

* Okay.

4:06

* Okay. See if I do it. All right, we'll give it just 10 more seconds to respond, Ted, 8 7.

4:11

* 6, 5. 4 3 to

4:42

* Okay, let's see. And then, go to responses. Great, so, so interesting, levels of responses.

4:56

* So, looks like the majority of students thought that exposure to DES during pregnancy and this was given to present many decades ago to prevent complications during pregnancy.

5:07

* Also, there were some answers for the other ones as well. Actually, interesting DES exposure has been linked to more rare cancers in the offspring, including vaginal cancers.

5:20

* There's also a suggestion of an increase in breast cancer, but it's actually attributed to higher exposure to estrogens rather than testosterone anderds.

5:27

* Actually, interestingly, the correct answer is the second to fourth digit. You need this. Yeah, if it's really interesting, I'm not exactly sure why it is.

5:42

* But, that ratio is determined fairly early in life and it's very strongly determined by the amount of, and, very early during pregnancy.

5:51

* And so it's interesting you see a lot of variability between men and women and also across the world you'll see a lot of variability.

6:05

* So my ratio, I mean I don't know if this is HIPAA or not? You're second before, meaning I had much lower exposure to androgens and higher exposure to estrogen.

6:15

* So it's an interesting ticket. My birthday, surprisingly actually is associated with lower levels of testosterone that thought to be higher levels of estrogen during pregnancy.

6:22

* OK. Why don't I know how to do this? Oh, sorry. Yeah.

6:34

* Okay. Okay.

7:25

* Okay. Okay. Got a call, Mike. So first question, speak loudly.

7:32

* I can't hear. Okay, so yeah, so we talked the Tuesday, right? So I covered the first 2 like, background, a wide diet, okay, so, yeah, so we talked, Tuesday, right?

7:44

* So I covered the first 2, like, I covered the first 2, like, background, so, yeah, so we talked, Tuesday, right?

8:04

* So I covered the first 2, like, background, a wide diet, maybe important for cancer, and then we discussed a bit about observational randomized trials.

8:12

* So, I'm going to finish these last 2 topics and then get into, like body weight and physical activity.

8:19

* So I'm not going to give, like this is more to help you like assess dietary nutritional studies throughout the course, like for specific topics, you like assess dietary, nutritional studies throughout the course, like for specific topics, you'll get more specific knowledge of the nutrition cancer association, particularly for example in colon cancer, where there's a lot of dietary association.

8:23

* So I won't get into a lot of specifics, but be kind of broad. So a big question, different ways to measure diet in large studies.

8:40

* Now, the best way to to measure diet in small studies like if they're doing a study like without a hundred people or something like that, you can have dietary records where people are instructed and they measure.

9:01

* Whatever they eat, they record everything. Sometimes they even have like a scale. And they're supposed to be very dedicated.

9:16

* And of course you can't do this for a year, but you can do it like for a week or something in multiple weeks.

9:23

* I'll talk a little bit about that. Then most of the data are food frequency questionnaires.

9:26

* For better or worse you know they get criticized sometimes but that's where almost all of the available data are 24 h recalls are sometimes used.

9:36

* Now, bial markers are not you know, there are few biomarkers that tell you exactly what somebody is eating, but they're like indirect.

9:43

* So for example, if you eat lots of fruits and vegetables, your blood beta carotene levels will be highs.

9:57

* We talked a little bit about beta carotene last time. And then I just, you know, they're like maybe this is more for the future, like O Mix.

10:04

* Things like metabolomics where you measure lots of metabolites and again these don't really tell you exactly what someone is eating, but they might be useful in indicating what the effects of diet.

10:13

* And then there are things like iPhone apps, like, you know, you take a photo of your mail and then it somehow, it's measured.

10:26

* You know, those could be useful but they're not perfect like for example they won't distinguish between a diet coke and sugar sweetened beverage, which would be something very important, like to miss the misclassified, just because visually you can't tell the part.

10:30

* There any questions or?

10:51

* Okay, now. It's also like, you may recall, The last time we talked about, you know, different ways to conceptualize diet.

10:55

* It's not like a simple exposure. Like, you know, number of cigarettes per day. Their complexities with tobacco too, but it's a fairly, you know, one dimensional, how many cigarettes you smoke a day.

11:07

* Diet, you can look at it in a lot of different ways. And the later I'll talk about like an energy balance just like if you're eating too much more than you're spending.

11:21

* And there's no really good dietary assessment to that. I mean you would have to have like almost a perfect measure of caloric intake.

11:29

* And almost a perfect measure of energy expenditure. So the balance in minus out and neither one of those are really that feasible in epidemiologic studies that you can do studies like a small metabolic war type of studies but they're not feasible.

11:43

* In fact, given in small metabolic ward studies, there's a fair amount of measurement error.

12:05

* And you know, like if someone Like, you know, you have to measure. Things almost perfectly to get energy balance.

12:06

* So like if you, 100 calorie a day difference over like many years. What will increase your body weight, maybe a few kilograms.

12:17

* So you need always a perfect measure, which is really not feasible. Now for some of these aspects of diet other than energy balance, like FFQ, 50 questionnaires are currently the best, being the best ways for micronutrients, the best ways.

12:23

* For micronutrients, you have biomarkers, like you can measure blood beta carotene, which again doesn't tell you exactly how much.

12:47

* Person beta carotene they consume because it also is affected by absorption and breakdown in the blood.

12:54

* You know, there are lots of factors, but it gives you a pretty good indicator like on average people who eat more.

13:02

* Beta carotene will have higher blood levels. So they can be useful. They're more objective markers.

13:09

* And I also mentioned RCTs because you can actually feasibly do RCTs for this.

13:16

* And then things like carcinogens and contaminants. I think a good example, carcinogen is that there's something this is something Laura Live, studies called the chromeide.

13:23

* Which you get like if you like let's say toast or You cook. Brad, I think it's mainly st and there.

13:35

* They're putative carcinogens and like, and so you can measure them like in red blood cells because they buy to red blood cells.

13:46

* A little bit like he, I think, heema Global, A. OneC concept like for glucose measuring diabetics.

13:54

* So they're getting good studies done by Lori and others that, for example, shown reassuringly that they're not at least associated with cancer risk, which is good for me because 2 big sources are like toast and coffee, which that would kill my breakfast.

14:01

* Probably most of you have seen, food frequency questionnaire, I just show one here.

14:29

* I think this is front of one of our cohorts. And so there's an item like, I think the current one has about 140 items.

14:37

* And, you know, so for example, skim or low fat milk, 8 ounce glass and there's 9 categories.

14:46

* And your report like over the past year, so this is your consumption. Sometimes people say, well, this is your consumption.

14:51

* Sometimes people say, well, how could you remember over the past year. Sometimes people say, well, how could you remember over the past year.

15:05

* Sometimes people say, well, how could you remember over the past year? But actually, the longer-term memory is sometimes even better than short-term memory, sometimes even better than short-term memory is sometimes even better than short-term memory is sometimes even better than short term memory is sometimes even better than short term because because you might have a sense of like, oh yeah, I have like the longer term memories, sometimes even better than short

15:06

* term because you might have a sense of like, oh, yeah, I have like chicken pretty consistently 2 times a week.

15:20

* You know, that's I guess we did have the last night yet, but I just happened. But I did like last Friday. I don't know what it meant.

15:25

* So the long-term memories, and actually that's what you really want for for cancer studies because remember we want long-term dietary.

15:29

* And take. An important question is the accuracy of how accurate are these. I'm sorry that thing.

15:45

* So, how do you assess it? Like, so how do you assess it? Like, actually, Dr.

15:49

* Willett, who's in department, and nutrition here. Who is my advisor.

16:10

* Like, led some of the studies and, you know, he did a lot to show that nutrition can be assessed in epilogic studies.

16:17

* And one of the first studies, and now they've been multiple studies like this, is this is like in a nurse's health study and what they did is they sent the questionnaires like, it's 100,000 women.

16:29

* So FFQs, but then they wanted to know how good the data was. So, and a sample of 173 participants that happened to be in Boston just for feasibility, assuming participants from Boston, their representative.

16:45

* The whole country in terms of so And these women, they did, they tuck it, they did a food frequency questionnaire, say June, the nineteenth, 80 and the second one in June, 1,981, then did 4 one week diet records.

17:01

* And remember, diet records are considered the gold standard. So, you know, the 4 weeks is a pretty, you know, that gives you a pretty good long-term estimate.

17:21

* What a person would be consuming, like, over a year or so on average. And then like you average them.

17:34

* These are the correlations between some of the items. So a perfect correlation would be 1.0.

17:41

* On average, you know, It's, the average about point 6 4.

17:52

* And so it's not like They're not perfect and of course the diet records aren't really perfect either so there could be some measurement error in guide directly.

17:56

* So it's a good concept to keep in mind. Like sometimes when people say like let's say you're assessing something, sometimes when people say, let's say you're assessing something compared to a goal standard.

18:12

* The goal standard sometimes is not perfect and that's particularly true in some of those studies with energy balance.

18:23

* There's actually a lot of measurement error in the lab of getting like the exact energy of expenditure for example and then like you correlate your surrogate with that and your surrogate may not you know the correlation may be over than you expect but some of that could be error from your gold standard.

18:29

* But in any case, These are, you know, these are the kind of correlations to keep in mind that when you're looking at diet and cancer, like most of the studies have correlations and it varies by You know, nutrient, some are better than others in Lodocanas that here are pretty close.

18:51

* Like protein is a little bit lower. Than the others. And the reason for that, is actually what correlations, your range of consumption, it also.

19:11

* Contribute to your correlation coefficient. So protein is more restricted in the population. You don't have people having like 90% of the calories from a protein or 5%.

19:27

* They're all like, 90% of the calories from a protein or 5%. They're all like around, you know, like 15 to 20% that range.

19:39

* So if you have a restricted rate, you have a lower correlation. So in a sense it's not so much that the absolute measure is worse than the others.

19:43

* It's actually that you have less variation. Population. I should know this answer, but depending on the time of the year, the season of the year, was there any variability or these estimates kind of consistent?

19:52

* By season. I'm just thinking you might eat more fresh foods and vegetables in the summer. Yeah, it's a good question.

20:10

* I don't know if that's been looked at specifically, but the way the questionnaire is worded, it's been looked at specifically, but the way the questionnaire is worded, what you're supposed to do is integrate in your mind like the year so like so for example like if you eat a lot of peaches in the summer but not in other months like that.

20:14

* You know. You're supposed to take that into account. So, which is could be a little bit difficult.

20:38

* So that probably does add noise. And but it would be interesting to see like for example people who responded in the summer versus people responded in the winter.

20:46

* Like, you might get a bias where people respond this summer reporting more fruits or like let's say peaches or something like that.

20:56

* Yes. Good question. Does anybody have any thoughts on that? So, yeah, I mean, that's a good rule of thumb.

21:07

* Yeah, I mean, that's that's a good rule of thumb I mean if there's no I mean that's a good rule of thumb I mean if there is no I mean like point for me like point 2 is definitely too low.

21:26

* I mean, there is no, I mean, like, point for me, like point 2 is definitely too low.

21:36

* It's very low. Point 8 would be. You'll be very happy if you get that in theology for tradition.

21:38

* Personally, I'd say like below point 5 would be problematic. The other thing to keep in mind is one of the advantages of the nurses.

21:50

* And health professional studies, which is pretty unique, is that there are multiple measures like every 4 years. So participants fill out a questionnaire.

22:00

* So some of reports have like 8 or 9 questionnaires over their life. So that kind of, you tend to get Probably better information like more people because you average over a long time a lot of studies have one questionnaire for somebody's lifetime so like age 50 they start to study they fill out their questionnaire and then they could be followed for 30 years.

22:08

* And so, you know, in top of the measurement error from the questionnaire itself, Then, you know, does the error from having one year or assessment followed for 30 years?

22:38

* But I'd say about like, you know, point 5 is the rule of thumb. I like to see like I get happy when it's about, 0 point 5 is the rule of thumb.

22:48

* I like to see, I get happy when it's like, 0 point 7. But point 6 is, is sort of acceptable.

22:59

* There are also, like, Molin, and every department like she and Donna Spiegelman who was here have done a lot of like formal measurement error correct.

23:00

* So you have the data from the validation study. Which you can kind of use to, adjust your findings in your studies because of the measurement error.

23:20

* So things that have a lot of measurement error. Like you kind of take that into account. Like, so for example, if you see.

23:32

* Like let's say a relative risk of 1.5. But you know how much measurement error there was in that estimate that could bump it out to like 2.0.

23:40

* So conceptually you say, well, if we had a perfect measure. We see even a much stronger relative list than one.

23:49

* People sometimes don't like that, but that's, you know, one way that it's dealt with.

24:01

* Another way, sorry, the slides a little, complicated, but, Yes, so let's see.

24:09

* You You have like, what this show, let's just focus on foli here. There are different biomarkers here.

24:16

* So this is another validation study that was done more recently in the men's validation study. This is like the health professional study.

24:27

* So what they did is they had like different measurements on these men about 626 men a single That's a 24 h recall, 24.

24:39

* A 4 24 h calls. An FFQ for food for can see questionnaire.

24:51

* And then this one is average, so they're 2 for averages. And then a single and.

25:05

* 2 weeks of diet records. So, so they have all these measures and then they have a bayer mark.

25:13

* So full aid is measured in the blood. And again, you know, as I mentioned, your dietary foliage should be correlated with your blood flow, but it won't be like 1.0 because you know, you people absorb falling differently and gets broken down.

25:17

* But, you know, there should be a correlation if you have high flow. So, so these are the correlations like so for an average 7 day diet.

25:36

* Correct. So this is, you can think of this as a gold standard. The correlation, you know, it's about point 7 here.

25:49

* And then the second one is single seventh day diet director. So, so this actually, this is nice because it sort of gives you a sense of like if you have 1 7 day diet directed it's actually not much worse than having to.

25:59

* You know, correlation is a little bit lower. The higher the correlation, to zoom like the better the higher the correlation to zoom like the better the measurement but it's not like the better the measurement but it's not like a big increment.

26:16

* But it's not like a big increment. But it's not like a big increment.

26:26

* And this is the, food frequency process, 2 food flips. So this is like showing that at least for falling food fields.

26:27

* So this is like showing that at least for falling food frequency questionnaire is really not much worse than a food frequency questionnaire is really not much worse than a one day diet record, or one week directed.

26:36

* And, you know, not that much

26:47

* 2 weeks of diet records which you know would be like there actually isn't any large study that has 2 weeks of diet records, epidemiologic studies.

26:50

* Like some people have argued that while you can't believe in full frequency questionnaires, you know.

27:02

* You should do studies that like a multiple week diet directors. And yeah, that might be better, but it's not, you know, at least for some things it's not much better.

27:08

* Now what's interesting is you see a bigger difference. For sodium where the diet records are better.

27:18

* Than the food frequency question for Sodium. And the reason for that is that, sodium varies a lot in foods like, you know, things like folate or, you know, protein, potassium, someone eats like, you know, serving a red meat.

27:25

* Those items should actually be pretty consistent. Like, you know, particularly something like potassium. You know, it'll be pretty much the same in all kinds of meats.

27:45

* But sodium depends on processed foods and some add a lot of sodium. Some, you know, add much less.

27:55

* So. So like you do like the FFQ does miss some of the specificity. In some cases, but for some broad items like potassium or foli, it actually does pretty well.

28:03

* Okay, so, yeah, sorry. That we would want to use a full frequency questionnaire as close to a diagram.

28:19

* Yes, it's much, much, much less expensive. Yeah, yeah. Food frequency questionnaire, food frequency questionnaire, is, like, you know, It's almost like pennies.

28:29

* I mean, when the study started like in 1,980, I know this sounds kind of like low, low tech now, but one of the big, improvements was like optical scanners like you fill in the little bubbles.

28:43

* He's gonna help us with our touch panel required, sorry. Hope it's worth.

29:02

* Okay. Oh, wow, what did you do? The room was just in video conference mode, which our users, so likely the people for you.

29:15

* That was fast. I was worried it's gonna be like 40 min. I was worried it's going to be like 40 min.

29:30

* So for example, I'm sorry, your question, yeah, the frequency question. Yeah, they're like the diet record, like so for example, and the food for, yeah, instead of optical scanners, you know, which.

29:45

* Basically, it's like you fill in the little bubbles like that. I mean, this is like, 1980.

29:56

* Wow, we can send this out to 100,000 people. That made the study very feasible to do in large numbers, even though it was all done by the mail.

30:00

* Use like the internet like that. But like diet records, you need training from a dietician. So it would be like, mag, like even 170, women that studies, that that part of the study was very expensive.

30:10

* Appear to the like 100,000. For you. So it's exactly it's it's just costs and feasibility.

30:27

* Well I mean that that and also participants like, you know, should take you, you know, I don't know, like, 20 min, maybe like half hour if you're very careful.

30:37

* Diet records have been matching like every meal you're bringing a little scale like so yeah there's a also the participant though And then it's also like once.

30:50

* Like the FFQ like you make assumptions like this item has like this much potassium with the diet records is a lot more variability in the foods that are accessible, which is an advantage in a way, but then you have to have a dietician look through all the items like somebody's eating something and they typical like that.

31:09

* So there's a trade-off, you know, but I think like this kind of study, it gives you an idea like, well, is it worth like?

31:31

* Yeah, it would be great to do, even like 4 one week diet records during the study.

31:42

* Or like why not like one year diet, right? It's people every day they record their data.

31:48

* But there's always a trade-off. So how much worse is the FFQ?

31:55

* The FFQ is definitely, you know, not as good, but it's, you know, for a lot of nutrients, it's not much worse.

32:00

* Okay. I'm just going to quickly go, and again, we'll see examples in in the specific cancer as we discuss like the nutrition cancer associations.

32:11

* But I just wanted to give a very broad overview about assessment of evidence and this actually, you know, I mean, this is not much different from what you have, you know, hopefully you're getting this in your courses like in epidemiology like how to interpret evidence broadly from lots of studies.

32:23

* And I just used the WCRF the ICR, that are, you know, they have a, their, their existence is, is to assess nutrition and the cancer.

32:43

* And so I was on like their panel for about 10 years. So the way they assess the data, so they look at all the way they assess the data so they look at all the like just about any question like you know coffee and colon cancer you know sodium and breast cancer, anything that there's data out there.

32:50

* And so they do like meta-analyses, things like that. So they, so the conclusion, so based on the methodologic, you know, rigor consistency across studies and, you know, bigger consistency across studies and I underlying prospective data.

33:22

* I'll talk a little bit about that because there's a lot of case control studies and I underlying prospective data.

33:40

* I'll talk a little bit about that because there's a lot of case control studies too. There's also experts in the group that help and integrate epidemiologic findings with the like mechanistic data, animal studies, biologic plausibility.

33:43

* And then like the, at the end of the days that these experts sit around and come up with convincing probable or limited data or evidence.

33:58

* I'm not sure if this will be keep going in the future, but they had like 3 big reports.

34:14

* I was just involved in the last one. About every 10 years because things change all the time, you know, so now, talk about this briefly, but Laurel, I already mentioned.

34:20

* Like case control studies and cohort studies. And, she mentioned that study that indicated there was recall bias.

34:35

* I'd already showed this slide last week. Just Just to remind you that in 1990, there was evidence from case control studies pretty consistently that saturated fat and take was evidence from case control studies pretty consistently that saturated fat and tank is associated with a higher risk of dress cancer.

34:39

* And then, in, The. These are like.

35:06

* From a told analysis of cohort studies. I was published the 1,996 New England Journal of Medicine.

35:15

* This is like from, this included the nurse's health study but also other studies. And you can see very, very now a finding for fat and percent energy for fat.

35:25

* Going from a pretty wide range of less than 20% greater than 45%. So the fat composition of the diet from prospective studies were very different from the case control studies which tended to show an association.

35:38

* And now that they're even like, I think this number is probably like 10 times larger.

35:56

* There's like, it's completely flat. And you know, and at some level, even like with 50,000 cases let's say you know even if there is like 50,000 cases let's say even if there is like measurement error even if the correlation is like point 5 like what you know fat and take measured versus real fatigue, should probably see something, a hint of something, 50,000, like you see

36:01

* nothing. So the cohort study is pretty. Consistently show no association with the fat. And why do you think is the main reason for the difference?

36:24

* I mean, there are several differences between these 2 designs and I assisted later through each one of them.

36:40

* These studies, what was the main? Yeah, I think there's 2 potential, well, some people have argued and I think this was a reasonable, well, some people have argued, and I think this was a reasonable argument like maybe 20 years ago, but I don't think it is anymore, that like some of the cohort studies had one measure.

36:43

* And then they had the long term follow-up like 2030 years. So, so some people who were like pro stat hypothesis.

37:09

* They argue like, well, the cohort studies have more measurement error because because they have a lock follow, whereas the case control studies.

37:18

* Ask about recent diet. And maybe recent diet is more important. Now that would be a, you know, at least a plausible argument.

37:26

* But there's a, like you can look at the subset of cohort studies that have like 5 years of follow up, short enough follow ups like so it would be similar to case control studies and they're pretty null too.

37:36

* The other thing is that like Like some would argue, well, the methodology in the case control studies is better, like the dye assessment is better.

37:50

* But that's not really true. I mean, they use similar, it's not like the case control studies have a perfect measure.

38:00

* So there's a similar measurement error. The 2, you know, plausible reasons are recall bias, the 2, you know, plausible reasons are recall bias, and selection bias.

38:03

* In fact, I'll, this is, These are. We actually did this about 5 years ago we just looked at summary of adherence to healthy dietary patterns and risk of cancer.

38:20

* I'll explain a little bit what we mean by healthy dietary patterns, but just ignore that for now.

38:39

* But, so, so these are, summary of the literature at the time and you can see for a lot of cancers.

38:44

* There's for case control studies you see except for prostate you see an inverse association so good diet lower risk and for prospect of studies.

38:52

* Not much there, you know, a little bit for colon cancer, colorectal, that is a significant, but it's much weaker.

39:06

* It's like, 0 point 8 9 versus point 4 8. And this is looking at like high versus low one tile like that for brass, you know, a little bit.

39:09

* So, you know, if you look at the case control studies, you conclude, while a healthy diet dramatically reduces your risk for, you know, most cancers except prostate.

39:24

* Whereas the cohort studies show, and you know, it's not that promising, a little bit there for Colin and Brest, you know, so like I think one of the biggest issues in in recent I guess I would say decades now.

39:28

* Is that in case control studies, like what people do like to get the cases are relatively easy to identify.

39:51

* And then you have to get controls. And controls like they were done by like random digit dialing because you want to get, so for example if you're doing a case control study in Boston so you have all of the you know colon cancer is in Boston or identified then you want like a random sample of the Boston population.

40:03

* So what they would do is they would get like like if anybody had a phone their brand that you can randomly get call okay so you can think like first of all not everybody has phones and then not everybody answers.

40:27

* And then the people who answer are going to be. Likely bias to people with a good diet. Like if you have, you know, if you know even subconsciously that you have this crappy diet, I don't, I don't think I want to do this study, but if you, you know, really health conscious and you're like, go, you live at Whole Foods like that.

40:45

* You might like, you know, oh yeah, I'll participate in this study. So you can actually show like response rates could be 30, 40%.

41:04

* So I think there's a lot of participate in this study. So you can actually show like response rates could be 30, 40%.

41:15

* So I think there's a lot of, so I actually think the selection bias is probably even more important than the recall bias.

41:20

* So, but it is quite amazing how many, it's actually a little hard for me to explain why case control studies like so often get a protective or if they're looking at something, bad, like, you know, perceived to be bad, they have a positive association.

41:21

* But it's pretty consistent as the prospect of studies are pretty, So I guess conservatively will go with the prospect of studies.

41:37

* There's still some people who will argue the case control studies get the right answer. Okay, so this just, you know, this isn't an important, like you don't have to memorize this or anything, but this just shows that how the WCRF.

41:48

* You know how you know they make recommendations and and the criteria basically the hills you've probably got Bradford Hill criteria like you know.

42:14

* Like all of these with. Would contribute to something being like strong evidence. There are not many things that actually get strong convincing evidence, but there are some items that we'll see that get like probable evidence.

42:26

* And they would still be considered probable, still pretty strong evidence, which that they could actually make recommendations. But, just as a point.

42:44

* They first review the science. Come up with this list. And then the recommendations are made later because like recommendations might be, you know, like for example, like what if there's something that seems pretty consistent that's good for cancer but that's let's say bad for cardiovascular disease so you don't you don't want to just make recommendations based on the findings.

42:57

* The For now, this is just a summary of. The findings and a lot of these. Will be talked about later in the course, but this is a list of what the WCR FX here came up with as related to cancer with strong evidence like probable or convincing and at this, now, like, the second in a few minutes, I'll talk about energy balance, which seems to be

43:25

* the most important. And I'm also excluding alcohol, which is part of diet in a way, but that's a different topic.

44:00

* But, this is the percent of cancers that are attributed to all the potentially and you can see that they add up to about 5% so so in other words if people did well in all of these, lower sugar sweetened barriages, lower red meat for example.

44:12

* They, you would prevent about 5% of the total cancer. Now, Interestingly, this is dominated by colon cancer.

44:36

* So almost like for all at least. From what we know from what they list as probable or convincing evidence.

44:47

* Most of the prevention from diet would be for colon cancer. So out of the 5% like I think you would have like 80% of these would be colon cancer.

44:51

* Which is interesting. So, so there is a, you know, it's not like not nothing, but it's not like traumatic.

45:10

* But remember that this is independent. So this is like just selecting specific items and trying to elect them to cancer.

45:14

* Now, I think in the future and actually WCRF, I'm actually working on a project with them.

45:30

* They're a lot more interested in dietary patterns. They're a lot more interested in dietary patterns.

45:31

* They're a lot more interested in dietary patterns now. Dietary pattern rather than looking at a single item.

45:39

* It's just a definition from the US guide theory guidelines. Dactory patterns are a combination of foods and beverages that constitute an individual's complete dietary intake over time.

45:46

* This may be a description of a customer way of eating or a description of a combination of foods recommended for consumption.

46:00

* There are some advantages, from looking at a dietary pattern than just the specific item like I'm just going to focus on red meat.

46:09

* But, you know, I just make a list here of argument why conceptually it's better to look at it.

46:21

* So for example, the whole looking at the whole diet with, you know, like any single item might have a small effect, but if you look at, any single item might have a small effect, but if you look at, 20 small effects, they might add up to something substantial.

46:30

* It's also, you know, in some ways it reduces like the confounding and just as an example.

46:46

* So when you look at a dietary pattern, like let's say for example, you're looking at the effects of a vegan diet.

46:56

* You're not like necessarily saying that they're like like anything specific like, oh, it's the carrots that that's important.

47:05

* In fact, it may also be that like a vegan diet by, you know, definition excludes animal products.

47:14

* So if you see like a vegan diet is beneficial. You just say, okay, we see a vegan diet is beneficial.

47:20

* But it's not like you have to make a statement like, oh, like red meat is bad or cheese is bad or like red meat is bad or cheese is bad or carrots are good you're just talking about the whole guy. It's bad or, carrots are good. You're just talking about the whole diet.

47:23

* It's a more general statement. It's a more general statement. It's probably more conservative than trying to find a whole diet. It's a more general statement.

47:42

* It's probably more conservative than trying to find a single factor. It's probably more conservative than trying to find a single factor.

47:45

* And it's potentially more conservative than trying to find a single factor. And it's potentially more beneficial.

47:48

* There are different ways, so what do you mean by dietary pattern? I'm gonna talk a little bit late, I'll mention.

47:52

* I hypothesis oriented, but most of them are based on scores on prior knowledge. So this is just to give you an example.

47:59

* There is something called alternative healthy eating index scoring. I mean, this is probably more give for cardiovascular disease, but, Like you get points like basically there are like good things, presumably good things like vegetables and fruits, whole grains, where you get like points by eating more, then you get negative points by eating or drinking sugar sweetened beverages or like processed meats.

48:09

* trans fad, which you know is not an issue now, a sodium like so it's basically kind of a score but it's based on the consensus of what's good in one's bad.

48:43

* Which could change over time.

48:56

* And, we actually did a validation study. Shouldn't say I mean I wasn't directly involved in this but the and 2 weeks of diet records and FFT frequency. They're pretty good correlation.

48:59

* So for frequency questionnaire does pretty good at. Picking up a dietary pattern, which to me intuitively kind of makes sense because, you know, like someone might argue like, well, how could a full frequency question here be tell you the precise amount of beta carotene someone's eating or something.

49:10

* That's a little bit harder to get, but if you're talking about a whole dietary pattern, people tend, you know, there's some people tend to eat a lot of healthy foods and some people less so.

49:31

* And so I think you, you know, does at least to me intuitively, I think it makes sense that you are likely to pick up, you have good information, diet.

49:49

* So, so you're getting like good general information. Of course, you're losing some specificity over what I specific item might be.

50:00

* The interesting thing is like we're doing this summary for the world's cancer research fund, summarizing dietary patterns and summarizing dietary patterns in colorectal cancer research fund summarizing dietary patterns in colorectal cancer research fund, summarizing dietary patterns in colorectal cancer.

50:09

* Where this is an official, I mean, we do, in, in, I can tell you even though I shouldn't you know it's not like published yet or anything but some of the dietary patterns do seem robustly associated with total answer.

50:18

* But what's interesting is you see there's like a lot of dietary patterns. And so it becomes like, you know, what is the advantage of dietary patterns?

50:37

* Is like you're integrating information, dietary patterns is like you're integrating information, but I'm almost thinking now it's becoming like you're integrating information but I'm almost thinking now it's becoming like there's too many.

50:46

* But I'm almost thinking now it's becoming like there are too many. Some of them you might be like, they're too many.

50:54

* Some of them you might be afraid of like the dashed diet, some of them you might be like, you've heard of like the.

50:56

* So some of them you might be like, you've heard of like the dash diet, the, healthy eating index, the, Mediterranean diet should be somewhere.

51:01

* Yeah, it's the first one, Mediterranean. And then there's some, like, you know, there's Danish dietary guidelines.

51:02

* So anyway, I'll talk a little bit about more about those later, but I want to spend, you know, make sure I have some time to get into obesity.

51:08

* But I just want to spend, you know, make sure I have some time to get into obesity.

51:23

* So this is just a quick summary of what I've talked about so far, I have some time to get into obesity.

51:26

* So this is just a quick summary of what I've talked about so far, including last week. So our randomized trials would be ideal, but.

51:29

* There is limited utility for most questions for nutrition and cancer. Case control studies seem to be prom to recall selection bias, making cohorts the most feasible.

51:34

* That's the most feasible. And you know correlations we discussed about roughly about point 5 to point 7 for most things.

51:47

* There's some things that maybe are not measured well. Established factors outside of energy balance contribution are red process needs fibre whole grains, dairy, calcium, fruits, vegetables.

51:56

* They contribute to about 5% of total cancer and about 40% of colon cancer. And so the next part.

52:09

* Is going to be obesity and fiscal activity, which we'll see is probably more important.

52:16

* Now, you know, how is adiposity measured? So does anybody like mention a way that we measure or received?

52:28

* You can look at the next slide, don't she? Wait, yeah, that's a good way.

52:37

* Oh, oh yeah. Yeah, the bio impedance that they shoot some like electricity and then like if you have more fad I think like you have the bio impedance that they shoot some like electricity.

52:48

* And then like if you have more fad I think like you have the conduction is lower. Salesforce.

53:05

* Oh, like calipers like those. Yeah, yeah, that's right. That would be right.

53:16

* That's right. Any others? Right here. Oh, sorry.

53:17

* Yeah. Yeah, BBBB is always like controversial, but yeah, but I mean it does like, it's actually not as bad as people think at least for some cases we'll see. Right. And then there's, yeah, I have to have a list here.

53:29

* So I think it's actually not as bad as people think, at least for some cases we'll see actually not as bad as people think, at least for some cases, we'll see. Right, and then there's, yeah, I have to have a list here.

53:47

* So most of if someone gained like, you know, 20 pounds like from age 30 to 50 I must they suddenly became like a body builder that's mostly fat you know well it's not I mean it's actually even when you came wait you also do gain like some muscle but it's it's predominantly like fat.

53:57

* So that's kind of an indirect way. And then, I'm gonna talk a bit about visceral, and a little bit about her patic fat, which is, you know, like you can't get that visceral and a little bit of autopatic fat, which is, you can't get that from what a simple measure you need.

54:21

* The scanning like CT scans or depths.

54:36

* Now, this is the punchline for just using BMI, which is not perfect, but you know, it's a crude measure of fat.

54:41

* They're 13 cancers that have been established as causally related to be a higher BMI.

54:49

* And now i think lower live mentioned which will get talked in the breast cancer that breast cancer is a little bit like, you know, early life BMI is actually associated to.

55:03

* Protective effectiveness cancer. So high B and I, but in post metopausal women like weight gain, for example, it's definitely a risk factor.

55:18

* And you can see that there's a variation in like the magnitude like 4, and so these are for 5 kg meter squared increment based on a container.

55:27

* So for at the metro and for Admiral Carson on the soft is a pretty strong association.

55:35

* And but for others it's, you know, a liver are pretty strong. Some are pretty weak.

55:45

* So like, you know, like for a veryvarian cancer, BMI, I mean excess body weight, you know, if you had to give like a percent like, you know, it might account for about 5, maybe 10% of where in Kansas.

55:51

* So it's not like the smoking in lung cancer, but it is a contributing factor. But when you look at like that it's dirty cancers, they do add up.

56:08

* So if you're looking at total cancer, it's actually pretty, it's not trivial.

56:13

* The other important thing is I'm sure, you know, everybody's aware of that.

56:24

* Increasing . in in younger population, young adults, and for a Monday obesity related cancers.

56:30

* So I, here I have 12, okay, 13, but guess. You know, I, I won't get into a little detail, but let's say they have 12 here.

56:45

* 9, among young adults like young onset, colon cancer. You have, like 9 out of the 12 are increasing.

56:53

* In association with increasing adiposity. Of course, this does not prove that it's the adipocity that's increasing the risk, but it is, It is consistent.

57:02

* It's kind of what you would forget. Yeah, young onset calling kids. It's by definition.

57:24

* So can't any cancer like before the age 50 like there's been a lot in the news recently about colorectal cancer like that so This is one cancer that I cannot get.

57:33

* But, so this is a worldwide that this is how many cancers are attributable to excess body weight.

57:40

* And you can see from men the big ones are liver colorectal kidney. For women it's breast and a metral colorectal in fact for in terms of cancers of cherry bolt.

58:01

* Obesity is much higher in women than in men, almost like twofold. And that's predominantly because the end of mutual cancer and breast cancer.

58:17

* Yes. Oh, it's coming up. It might even be in a probably 2 slides or so.

58:29

* So, and just just to point out that, there, there are differences by grace and ethnicity and adult obesity and now it's interesting that in Asian, this is using BMI as the standard BMI.

58:45

* You know, like above like 30 which would be the But for the agents like the standard should probably be lower because of the different body composition, which of whichel talked about a little bit.

59:09

* But anyway, there are some racial differences in obesity that probably contribute. It's not like maybe the big dominant factor, but it does contribute to some of the differences in cancer rates.

59:25

* For like potentially breast cancer. Yes. This is the mechanisms now. Okay.

59:37

* So. So I, I think they're. Broadly, there are lots of research, you know, people delving deeply into mechanisms.

59:42

* But broadly, I think there are 3 major mechanisms. And, Let's see.

59:54

* Yeah, okay, so this slide. Shows, I'll talk a little bit more about this, what I mean by cancer triad, but because diet and physical activity impact on obesity and obesity affects all of these estrogen levels.

1:00:01

* In pulse metopausal women and in men most of the estrogens are made in adipose tissue.

1:00:26

* So the more adipose tissue have. It's just, it's basically a converging of like anrogen to best proteins.

1:00:33

* You know pre menopausal women obviously it's different it's the oak area and the post menopausal women, like if you do just even a cross-sectional study.

1:00:40

* Body weight, BMI, and estrogen level. There's a linear association. So an estrogen which you'll hear about in future, like I guess there's electron breast cancer, a group that will be looking at at the mutual community.

1:00:52

* And, I don't know what specific topic you'll, but when you talk about the topic, you'll, you know, but when you talk about individual cancer, you have to at least mention, obesity, cause that's like.

1:01:10

* That's almost like smoking and blood cancer. I mean, obesity is very important. Now, and then I'm gonna talk, most of my talk will be about this middle part here, but just.

1:01:21

* By local inflammation like gallbladder cancer is related to obesity, most likely that the main reason is that obesity causes gallstones and the main risk factor for gallbladder cancer, which is rare in the US, is golf.

1:01:33

* So you have got stumps for many decades. If they cause a queue. Sentence, then the gallbladder gets removed and then you don't get involved a lot of cancer but if the stones are there asymptomatically for years.

1:01:50

* That that could cause God blood cancer. And then, I don't know, carcinoma with the oesophagus, and that's, Jail can't just another one of your topics so so acid reflux so obesity, particularly in men because it's central because it causes like the acid from the stomach to go into the lower part of the esophagus.

1:02:02

* And, and so the suffrageal, the 2 types of main types of suffix, this cancer.

1:02:30

* One is, add, no squams, which is in the upper part of the esophagus, which is due almost entirely to smoking and alcohol, you know, poor diet quality, probably continues, but smoking alcohol, the lower part, adamo carcinoma is probably continues, but smoking alcohol, the lower part, adeno carcinoma is just the part where you get the reflux.

1:02:36

* One or 2 cm right at the bottom. So the chronic They're rotation due to the acid.

1:02:56

* Now, I'm going to talk a lot about insulin and inflammation which which are related and I think these are the multiple cancers which I'll talk about.

1:03:06

* So just remember like chestrogen for these cancers, we'll talk about that later. And then these very specific mechanisms localize information for gallbladder esophagus.

1:03:20

* So like insulin, I mean most people think insulin diabetes, right? That has something to do with diabetes.

1:03:26

* What does it have to do with cancer? It's, actually insulin is a growth factor and, cod like it's, it's, if your insulin level, this is my simplistic way of thinking about it.

1:03:35

* If you if you're not eating a lot you know energy restriction. Your insulin novels will be low, right?

1:03:55

* And that's indirectly signal to the body. But you're not eating a lot.

1:04:04

* So why should you be having a lot of cellular activity, particularly in the gastrointestinal system.

1:04:11

* Log insulin reduces soft full of fluorine. And, and there's, I mean, I'll talk more about the epidemiologic studies.

1:04:19

* There's even like, Like, Gillian randomization, which I. People familiar with that, 1 billion.

1:04:27

* I Like, it's basically using genetic variants to test the causal hypothesis.

1:04:42

* So for example, people that have genetic variant that makes their insulin levels a way higher than average.

1:04:51

* Those variants are consistently associated with what some of these cancers, particularly colorectal cancer. So that kind of gives pretty good causal evidence.

1:04:59

* The problem like if you're studying something like insulin from epidemiology, you can measure insulin, see if it increases risk, which is fine.

1:05:04

* And it does, studies consistent, you know, show their high levels of insulin.

1:05:18

* But, you know, Islam is going to be related to a lot of things. Basically, if having too much quality waiting for since long, but I don't increase like 100 other things long, but I don't increase like a hundred other things.

1:05:24

* So it's hard to PIN it just to insulin, but I don't increase like 100 other things. So it's hard to PIN it just to insulin.

1:05:36

* This actually, Mendelian randomization studies to suggest that it's actually the insulin level that's the causal risk factor, which kind of makes sense.

1:05:39

* And I won't get into a lot of, you know, this stuff. Which I don't have a great understanding.

1:05:45

* You know, this stuff, which I don't have a great understanding either, but there's like people from a laboratory perspective.

1:05:48

* There's good evidence that insulin stimulate receptors. These are insulin and IGF one receptors that are important for metabolic signaling.

1:05:59

* So, so there there's lots of mechanistic data that supports the effect of insulin. So.

1:06:12

* Yeah, so, anyway, just quickly go back here. So I'll like. Just to keep to remind you that so we're focusing on on insulin and you know like insulin like growth factor is related to insulin.

1:06:21

* It's also a growth factor, but let's just. To make it simple, focus on insulin, which is, like a marker for cancer risk.

1:06:36

* Okay, and well, I'll get back a little bit to insulin, but I think it's important to understand.

1:06:45

* Festival, which is remember DMI has been used because it's very convenient to use in lots of studies but visceral fat and liver fat, Might be more directly relevant.

1:06:53

* The visceral fat is the fat that's internal like around your organs like the mainly digestive organs and the kidneys.

1:07:13

* In What in the previous life I used to. That was a pathology resident. I would do lots of autopsies.

1:07:22

* And it's amazing like when you look, you know, do autopsy and like some people have a lot of fat around it work and it's makes it like sometimes I've found it hard if you can find the case because there's so much fat.

1:07:29

* And the top is a correlated with body overall body fat, but it's not, you know, entirely.

1:07:46

* I can be some people that relatively slim. Looking that had a lot of visceral fat.

1:07:48

* And this slide gives you a sense of that. Where? This is, I think it's a CT scan.

1:08:00

* And that's why. It's hard to measure this real fat, like you can't do it like just like a questionnaire or something you need the more sophisticated measures.

1:08:10

* So what this shows, okay, this is a section, this is the umbolicus, just to give you a sense of where it's being measured.

1:08:21

* And, and these are 2 in this is just an example. I'm sure they pick kind of extremes, but I think it makes their point pretty well.

1:08:30

* So 2 individuals, the same. Body fat percentage. Age sex in the BMI of 24.

1:08:34

* And the white like is, ventures fat. That's the density to do with the CT scan.

1:08:47

* So these individuals have the same percent. So these individuals have the same percent body fat. I mean, it's not even, I mean, it's not even, I mean, big same BMI, but you know But this person has about 4 times the visceral fastest person.

1:08:56

* So.

1:09:18

* If you had to guess like one.

1:09:21

* Thank you.

1:09:25

* Is a marathon runner. One is a couch potato. Which one do you think this is?

1:09:27

* Yes, so people even like the same waste or comfort. The web circumference isn't a bad.

1:09:37

* So people even like the same wastes or comfort. What circumference isn't a bad

1:09:39

* When you look at the whole population, there's definitely a good correlation between waistcoat and visceral fat.

1:09:47

* But especially at the lower end. You do guess a lot of people that actually have high missile fat.

1:09:55

* This slide actually gives you.

1:10:03

* Which is looking at like BMI, but this is a very wide range of BMI. It has a pretty good correlation with visceral fat.

1:10:06

* So when you look at, people would have BMI of 35.

1:10:15

* Our tent, it won't be low.

1:10:22

* But you know when you get around like you know and even in the normal range You see

1:10:27

* People have almost 0 missile that people that have levels comparable to BMIs of 30. So so it's just a lot of overlap particularly in the lower end.

1:10:34

* So, and I'll explain why this is important. these are factors that increase glycerol fat, you know, beyond, obviously people would hire B and Ns will tend to have more visceral fat as we just saw.

1:10:45

* But at the lower end, particularly, it's a lack of exercise, sedentary lifestyle, probably diet, smoking actually.

1:11:00

* That being male aging is a very strong association between aging and visceral fat. In this city.

1:11:15

* For the same BMI, given the low VMI, the Asian population will tend to have higher higher visceral fat, which is why in some Asian countries like their high rates of diabetes, even though if you look at the overall BMI, they're not that, and then, you know, probably stress, I mean, there's a hypothesis having to deal with.

1:11:24

* Like cortisol in chronic stress. I mean, that could well be true.

1:11:52

* Okay.

1:11:58

* The whole literature. So there are all these factors that contribute to this.

1:11:59

* Yeah. And There's very little data that examine directly visceral fat and cancer risk.

1:12:04

* Actually I know.

1:12:13

* Some students working on that. You care about your bank. But some studies have examined visceral

1:12:16

* Positives just by CT scan so kind of like they you know things like this where they can directly measure people going in for colonoscopy and then seeing whether they have an adenoma which is a cancer.

1:12:29

* So, and this study shows.

1:12:43

* Linear association.

1:12:46

* Would add a normal risk even within the normal rank of BMI. So actually we did.

1:12:49

* With this show, this is the, you know, odds ratio, and this is a visceral fat area.

1:12:54

* And so you can see a nice linear association. And what I put here is like this is the normal range of nearby.

1:13:01

* Interestingly, most of these studies We're done in either Japan or South Korea. And most people had a DMI less than 25, so we considered that normal, right?

1:13:10

* But even within the normal range, it'd be a viceral fat is associated with cancer. You can see like people have.

1:13:22

* Levels like very low. I mean Don't worry about like what the units mean, but you have people that levels around 30 to

1:13:31

* Like, 160 or like 200. Big range of small fat and even within the normal range.

1:13:40

* You have about like, What's the fivefold difference in this year of that?

1:13:50

* I'll just. Quickly discuss discuss this. When people say how much cancer is attributable to excess body weight.

1:13:57

* Like you look at the whole population, but what you find actually is Okay, non smokers, the association is much stronger.

1:14:14

* So if you look at in the nurses in health professional study, like amongst smokers you can say.

1:14:26

* Okay, a high body mass index. Or weight gain. Like, among smokers, it only you know, contributed to 3 or 4% the cancers, but a non-smoke, it's almost 20%.

1:14:33

* Does anybody have any? Potential explanation. So the observation is that body mass index and weight gain seem to be much stronger risk factors for cancer when you look at non smokers than in smokers.

1:14:50

* Any thoughts why that might be?

1:15:09

* Okay. They're, they're, sorry, they, someone have. Yeah, that's definitely one of the contributing factors.

1:15:17

* So like smokers have You know, they're getting lots of cancers, cancers like from the smoking like.

1:15:38

* So one cancer which is probably not related to might have a small relationship to VMI, but it's typically not.

1:15:48

* So it kind of dilutes the effect. So that's part of it. Yes.

1:15:49

* Okay. And what's up? Yeah, yeah, that's actually right. I mean, It's, well, yeah, I mean, dislike I think kind of shows that.

1:16:03

* So basically, what this shows is that smoking. Actually increases visceral fat. But actually has For subcutaneous fat, which is most of the fat in your body, it has, little effect, maybe even slightly inverse.

1:16:16

* And it decreases lean body mass. So smoking is often associated with lower BMI. But actually increases visceral fat.

1:16:41

* So you actually like you know, I mean one way to think of it is that and smokers like .

1:16:53

* Not a good indicator of adiposity. Like, let's say it not smokers, BMI isn't perfect, and not smokers, BMI isn't perfect, and non-smokers BMI isn't perfect, it's not bad because it's going to be correlated with visceral fat.

1:17:02

* But in smoke, it's completely different. So I think BMI just is a bad measure in smokers I think BMI just is a bad measure in smokers of visceral fat.

1:17:11

* Okay, I'm sorry, I remember my hearing isn't too good. Yeah, right. With smoking, like some people use smoking to keep their body weight low.

1:17:22

* And then like when they stopped smoking. Like they they start gaining weight and you know smoking also reduce it like actually like my brother-in-law was big smoker and then he stopped smoking and he said I can't believe how food actually has taste. So, it's still probably better to stop.

1:17:37

* But yeah, so, it's still probably better to stop. But yeah, so, it's still probably better to stop.

1:18:05

* But yeah, so, there's lots going on with smoking. This just kind of summarizes that.

1:18:07

* You can look at that maybe, but basically, you know, I, so I actually think that .

1:18:09

* Looking at the whole population, including smokers, kind of underestimates the impact of obesity on cancer.

1:18:20

* So, so like if you, look at most estimates, which includes the whole population, like typical estimates that people come up with is 5 to 7% of cancer.

1:18:26

* Are related to smoke out of excess body weight but if you look at non-smokers probably get it more realistic estimate which is almost 20%.

1:18:40

* That's pretty bad. I have to talk quickly about physical activity. So, but.

1:18:51

* The nice thing about physical activity is that I think if you understand obesity, visceral fat and cancer, you, you understand, 80% of physical activity in cancer.

1:19:00

* These are just the guidelines. Now. The WCRF A ICR, to date only have 3 cancers.

1:19:14

* That date attribute, to lack the frisbee activity or their physical activity contributes a colon, post-menopausal breast, and end of nature.

1:19:25

* It's a it's a little bit outdated to be honest and then the other organizations list more including abreast.

1:19:32

* Something else here. And the metro esophagus kidney bladder and stomach.

1:19:44

* Again, kind of interestingly, in 2,016 there was a study, where they pulled 12 large cohort studies.

1:19:51

* So this is like, they looked at 26 types of cancer, about 1.5 million adults.

1:20:01

* This is looking at high versus low activity. You see a lot. Associated with. With.

1:20:08

* At least an association, let's not say it's causal at this point, but physical activity is more possibly associated with a lot of cancers.

1:20:15

* Now, there's 2 cancers, cross state and melanoma, where physical activity has a positive association.

1:20:24

* So being more active, people reported being more active of a virus. Does anybody have a suggestion why there's an association with prostate cancer?

1:20:31

* It's assuming that it's not causal. Yes. Yeah, that's probably very likely the recent from Melano.

1:20:35

* So it's not, you know, so I guess the message is not to not be physically active because of melano.

1:20:54

* So I guess the message is not to not be physically active because of melanoma, but to not be physically active because of melanoma, but maybe put on sunscreen, you know, take care of, you know, so, so yeah, if you're physically active outdoors, it'd be interesting to studies separate by the whether they exercise in a chair or outdoors.

1:21:03

* Got, I don't know if that's been done. How about prostate cancer? Anybody like why physical activity being more physically?

1:21:21

* I guess this would be easier after the Just guys. But that's a good thought. I think that was a hypothesis.

1:21:30

* I think, yeah, that's conceivable. I think, yeah, that's conceivable.

1:21:41

* Even though the You know, I'm not sure if that's true, but it could be true.

1:21:50

* At least it depend on type of physical activity. Probably like resistance training, I think does increase testosterone.

1:21:56

* I think like running, if anything, reduces. But it's probably to do with screening.

1:22:05

* Physically active people are more likely to get PSA tests. They'd be more likely to be diagnosed across it.

1:22:08

* If anything, they have a lower rate of prostate cancer mortality. Physically active. But you're more likely to be diagnosed with these.

1:22:18

* So. Okay, so yeah, so summarizing that slide so that there was 17 cancer types of physical activity associated.

1:22:28

* And then we talked about the positive ones. So let's look at the inverse. So, 17 cancer types.

1:22:35

* Well, that's pretty cool. It's a lot. 17 cancers. I wrote, excuse me, I wrote this up some few years ago.

1:22:49

* And, just looking at that paper and I I noted, like if you look at the cancers that are associated with physical activity is inversely associated.

1:22:59

* 17, like most. That they fall into 2 categories. Some most of them would be considered the obesity related cancer so so we're physical activity is protected with obesity as a risk factor.

1:23:07

* And then there's 4 cancers or so where are strongly related to smoking. So physical activity is related to obesity related cancers and tobacco related cancer.

1:23:29

* Now, for tobacco related cancers, did you have, you talk about this, right? No, we will.

1:23:42

* We don't talked about it yet. Right, sorry. some people think it's possible that physical activity is directly protected for lung cancer.

1:23:45

* But. There could also be a bias because like light cancer is strongly related to smoking smokers.

1:24:04

* Can't exercise that much to get one disease, which, you know, smokers who have lung disease like daphragm are actually higher risk for, lung cancer.

1:24:12

* So it's this is I think something that's really hard to tease out. It's just so strongly like, you know, you smoke a lot, you get one disease, you know, it's going to inhibit your exercise.

1:24:23

* You're at high risk for cancer. For lung cancer. So if you're in this study they looked at physical activity which seemed to be protective for lung cancer.

1:24:32

* But the only group there wasn't, well, the occupational activity was not detected for lung cancer and I also endeavor smokers.

1:24:50

* So, so this kind of argues that smoking could be a founder. So that, you know, even though you do measure smoking, it may not be measured that well or perfectly and you get lung disease anyway.

1:24:59

* So. It's possible, you know, it's conceivable there's some causality, but I think it's conceivable there's some causality, but I think it's most likely related to.

1:25:07

* Not causality. So what's most interesting is the cancers that are obesity related. I'm simple minded.

1:25:22

* I said, wow, no, every cancer practically they were physical activity is protected is also a obesity related cancer.

1:25:33

* And its physical activity is protected even if you were just for but I think there's like, is that just a coincidence?

1:25:41

* Just shows like a summary that particularly in the digestive system. Physical act this is a meta-analysis where physical activity.

1:25:54

* Associated with lower risk of almost every cancer in the digestive system. Remember insulin, you know, like.

1:26:04

* Adjustive system. This is just from the, this is just a high versus low.

1:26:16

* If you want, a, Just analysis that we did. In, 2,016 and the health professionals.

1:26:25

* This is a dose response with physical activity. And digestive system cancer. So. This is just based on the recommendations that the current recommendations.

1:26:35

* So you can see if you're handling the maximal recommendations. Which is like, you know, up to 300 min per week of moderate intensity or 150 vigorous.

1:26:47

* You get them also the benefit but you can get more benefit perhaps by going even higher. But anyway,

1:26:57

* That's a dose response. So why is physical activity related to cancer? At least I think this is likely to be the biggest reason.

1:27:09

* There could be other things, but. Just physical activity is very important for visceral fat. It's.

1:27:16

* And you can see this in these like randomized trials and prevention trials. So just slides a little.

1:27:28

* To see everything here. It's a little crooked. This is from a systematic review. This is from a systematic review.

1:27:39

* So what this shows is all the studies that they identified that had looked at exercise training like over typically like a 4 6 month period and body weight and they also measured this little fat directly like that.

1:27:47

* So what what you can see here, and that they also measured this little fact that wrapped away like that.

1:28:05

* So what you can see here, this is the percent of weight change. Body weight change. In the different trials and then this is the percent visceral What you can see is like that this is much sneaper than body percent body change.

1:28:10

* So, so just for example, let's focus on this line. So you can see So the studies that caused the about a 5% weight draw.

1:28:26

* They had about a 20 to 25% drop in this real fat. You can find some studies like this one for example where maybe it had to do with the tendency of exercise.

1:28:38

* We take it almost like very little weight change like to maybe 2%. They hardly sell wages. It saw about a 45%.

1:28:49

* So you can really reduce your visceral fat without having a big impact on your weight change. So, so I think the bottom line is that, and you know, especially if you think of people like.

1:29:05

* Remember like in that lower like people with normal BMI. I think, once a very active, again, tend to have very low visceral fat.

1:29:17

* Once they are inactive, still have pretty highness of fat. So I think physical activity can still be acting.

1:29:29

* True. That's well fat. I'll just, I'll kinda end here.

1:29:36

* I, I don't have to necessarily go through the last part there. That's bonus.

1:29:45

* So that one, you don't have to worry about that, that's bonus. So you don't have to worry about that for tests but I this is just a kind of, you don't have to worry about that for the test.

1:29:50

* But I, this is just, a kind of a take 1 min, kind of a summary slide. That basically this is almost like 30 years of my work that I've been thinking about this that can be summarized on one slide, which is kind of pathetic.

1:29:59

* That if you look at the whole body fat, I mean, and these are like averages. It's mostly your facts subcontaneous fat.

1:30:13

* So let's say it's about 90%. Vicero fat and liver fat.

1:30:26

* Liver fats also probably important for liver cancer. Because it's fatty liver, illiterate damage and liver cancer.

1:30:31

* They're actually a very small proportion of the fat. But they're also the type of fat that's very sensitive to physical activity.

1:30:39

* In value. Subcontaneous fat is much harder to change. I think a lot of people love stuff.

1:30:44

* I just can't, you know, do subcontaneous fat that much by exercise. You probably have to have a big massive reduction in date.

1:30:54

* But vessel of fat you can be affected by physical activity. And these have a big impact on information insulin resistance.

1:31:05

* Which particularly affects digestive system cancels. But other cancers too, probably contributes to breast and and then estrogen is mostly related to subcutaneous fat.

1:31:13

* In fact, there's some of Mendelian randomization studies that suggest visceral fat is not a associated with any material.

1:31:24

* It's the subcontaneous fat, which kind of makes this pretty nice model. This is very comprehensive.

1:31:34

* Like I think if you understand This slide you conceptually understand also. Physical activity and obesity epidemiology.

1:31:43

* Oh, sorry, not 2 min, so. There any questions so

1:32:00

* Does this make things clearer or more confusing?

1:32:12

* I mean the main point here is that like you can have these kind of big impacts. Like, you know, like, let's say visceral fat.

1:32:18

* Let's say a person might have, let's say, 1 kg of this world fat, which is kind of a lot.

1:32:29

* Let's say they exercise a lot and they cut.

1:32:34

* Have to have

1:32:37

* That's a dramatic.

1:32:39

* Pack that will have a big effect on inflammation in science resistance. It may not make a big impact on subcutaneous tissue.

1:32:41

* They may actually even gain some lean mass. So you won't see much of a difference on body weight.

1:32:50

* So. But

1:32:55

* Okay.

1:32:58

* Most of the effect.

1:33:06

* So like the effect of physical activity could still be mediated largely through things like this or or

1:33:22

* Padded catapults. We don't have

1:33:28

* Okay.

1:33:31

* Like the If you look carefully at the epidemiology of physical activity. And cancer, I think you can explain a lot of it. This concept. And there could be other things going on.

1:33:39

* I mean, if people study physical activity, they don't wanna make it too simple specific markers like immune system things like that which you know could be relevant but I really think that this is looking broadly at the literature this kind of, most of what's going on with physical activity.

1:33:56

* There's Maybe.

1:34:18

* At least by population, what people do.

1:34:19

* Is much more

1:34:20

* But resistance would have some of the effects too. We've actually booked that in our data. You see pretty

1:34:21

* The correlations with resistance strengthening and Lord.

1:34:22

* Something like that. So yeah, either one, but mostly I think a class might be waiting. I'd be happy to.