Why Low Cholesterol & ApoB Levels Are Critical for Longevity | Dr. Peter Attia & Dr. Andrew Huberman

Would you agree that smoking is causally related to lung cancer Yes So just to be clear Andrew you do not think that it's just an association that smokers get more lung cancer No I do not In other words you believe that smoking causes lung cancer then yes I mean there are a number of mechanistic steps in between I mean if somebody was really want to get uh to you know drill into the logic they could say OK it's not actually the smoking it's a you know some uh uh disruption of the endothelial cell lining that you know smoking triggers that that triggers that So and I agree with you By the way I think the data are very very relieved to hear So but but I'm going someplace very important here because if there's one topic that doesn't get enough attention in medicine it's causality and uh causality is an obsession of mine Like most of the day on some level I sit around thinking about causality And I think the hardest part about studying medicine with respect to human beings is how difficult it is to infer causality for most things that we do So if you believe that smoking is causally related to lung cancer then smoking cessation reduces the probability of lung cancer That is a that is a logical equivalency There can be no debate about that What if I said to you Andrew this is going to be our new philosophy around smoking cessation You're you're I'm gonna anoint you the czar of smoking cessation So um if people pick up smoking no problem we're gonna let the smoke but we're going to assess their risk for lung cancer Using a model that predicts when their 10 year risk of lung cancer gets above a certain level We're gonna recommend that they stop smoking So we're gonna look at their age their sex their family history some biomarkers that might help us we're gonna even do scans of their lungs And once we think they cross a threshold where their risk of lung cancer is high enough let's just say it's 25% Boom you make them stop You tell them it's time to stop Is that a logical approach to treating smoking and lung cancer Or would be better to say given that we know cigarettes are causally related to this How about you never start smoking And the minute you do we pull the cigarette out of your mouth and explain to you that you're doing something that is causally related Of course it would be the latter not the former It would be idiotic to suggest that we endorse smoking until you cross a certain threshold Well this now becomes the germane question There is no ambiguity that A ob is causally related to

atherosclerosis You know how how how can I tell you that I can tell you that looking at all of the clinical trial literature all of the epidemic epidemiologic literature and perhaps even most importantly the Mendelian randomization all of these things tell us because by Mendelian randomization meaning genetic mutants humans out there that make very little ABO B or access So we have a whole So you can say if you make very little you aren't gonna die as uh quickly in your life as if you make too much So Mendelian randomization is such an elegant tool where you basically let genes do the randomization And as you said there is a gradation of LDL concentration or a OB concentration that occurs from insanely low to insanely high And this is a wildly polygenic polymorphic set of conditions And we can look at the outcomes of those people based on the random sorting of those genes And there's no ambiguity LDL is causally related LDL cholesterol or a ob causally related to atherosclerosis Well if that's true and I haven't seen a credible argument that it's not there are people who argue that it's not by the way but they just don't have credibility in their arguments then you have to say that what we're doing in medicine today is very backwards because what we're doing in medicine today is the following We're saying I'm I'm coming at this in a long way But your question is so important that I want to answer it this way We're answering your question today as follows We're saying Andrew let's do a 10 year risk calculation of your risk of mace Mace stands for major adverse cardiac event It is the metric we use in medicine So a major adverse cardiac event is a heart attack stroke you know or death basically resulting from these things So and we have calculators that are pretty good at predicting your 10 year event risk They'll look at your cholesterol levels your blood pressure they'll ask if you smoke they'll ask some family history questions and they'll spit out a number Now we should do yours after the fact Um And I don't know if we did it for a person who's is you know you're in your mid forties like it would probably spit out less than 5% risk for a major adverse cardiac event in the next 10 years In fact the models don't even work if age is below 40 So the first time I went to do one of these tests when I was in my mid thirties it I couldn't do it like the the the algorithm breaks So it's sort of like uh you know just doesn't work So the i the implication there is if you're uh and if your mace risk is less than 5% the thinking is you do not need to treat LDL or a OB I argue that that makes absolutely no sense It's just as idiotic as the analogy I used around smoking If a risk is causal and it is modifiable it should be modified regardless of the risk tail in duration So then the question becomes to what level and again the

earlier you start the less aggressive you need to be the less damage that's there already So for example we do CT angiograms on our patients If the CT angiogram shows no evidence of calcification no evidence of soft plaque That means grossly their coronary arteries are still normal histologically they're probably not because nobody probably makes it to our age with histologically perfect coronary arteries You know we might be satisfied with a person's a ob being at the fifth percentile of the population which would be about 60 mg per deciliter But if we have any other factors meaning we're starting later in life you know or a person already has gross evidence of disease calcification soft plaque family history is significant Any other risk factors are present I mean we'll we'll treat a ob to 30 to 40 mg per deciliter which is you know probably the first percentile And if somebody's sitting up in the say low one thirties um where where does that Uh what kind of flag does that raise For you And I realize it's highly contextual age et cetera No no it's a huge red flag again Um just because something is causal doesn't mean it's you're you're guaranteed to get it There are smokers who don't get lung cancer So you know there's gonna be somebody listening to this who says my my grandmother is 95 years old She's as her cholesterol is sky high and she's alive and well and I will say absolutely There are a lot of people walking around that way just as there are a lot of smokers walking around who don't get lung cancer Um You can't you can't impute these things on an individual basis You basically have to ask the question Um How do I make the best judgment about an individual from heterogeneous population data And based on what are causal and non causal inferences around risk