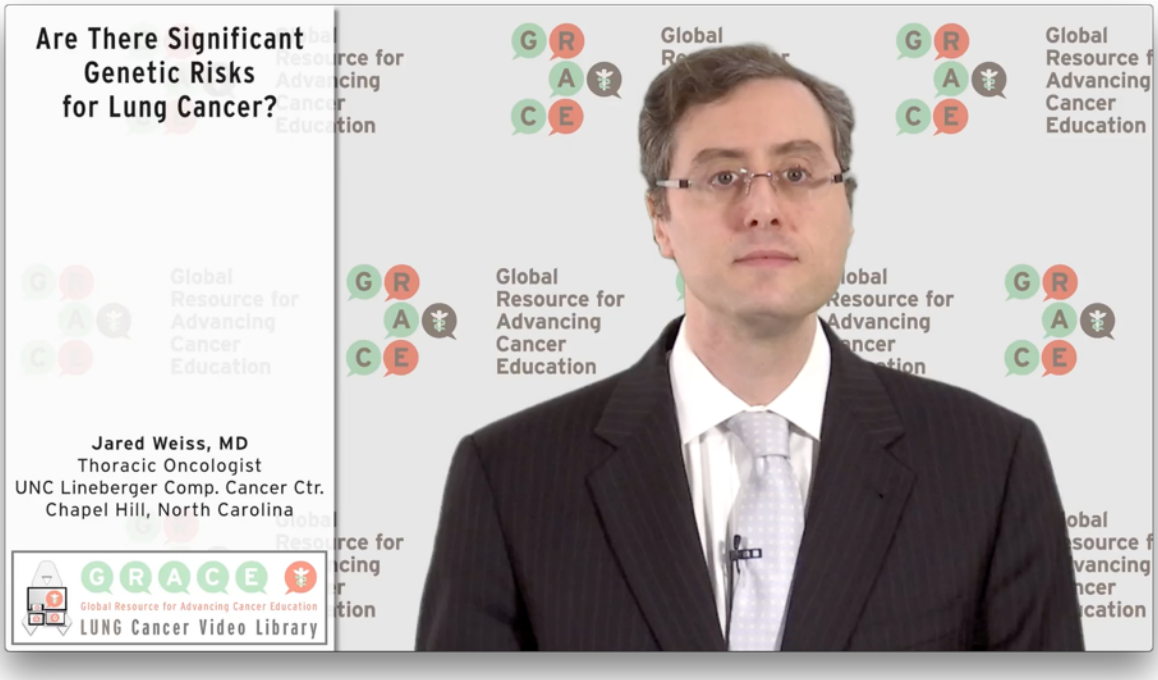
Global Resource for Advancing Cancer Education

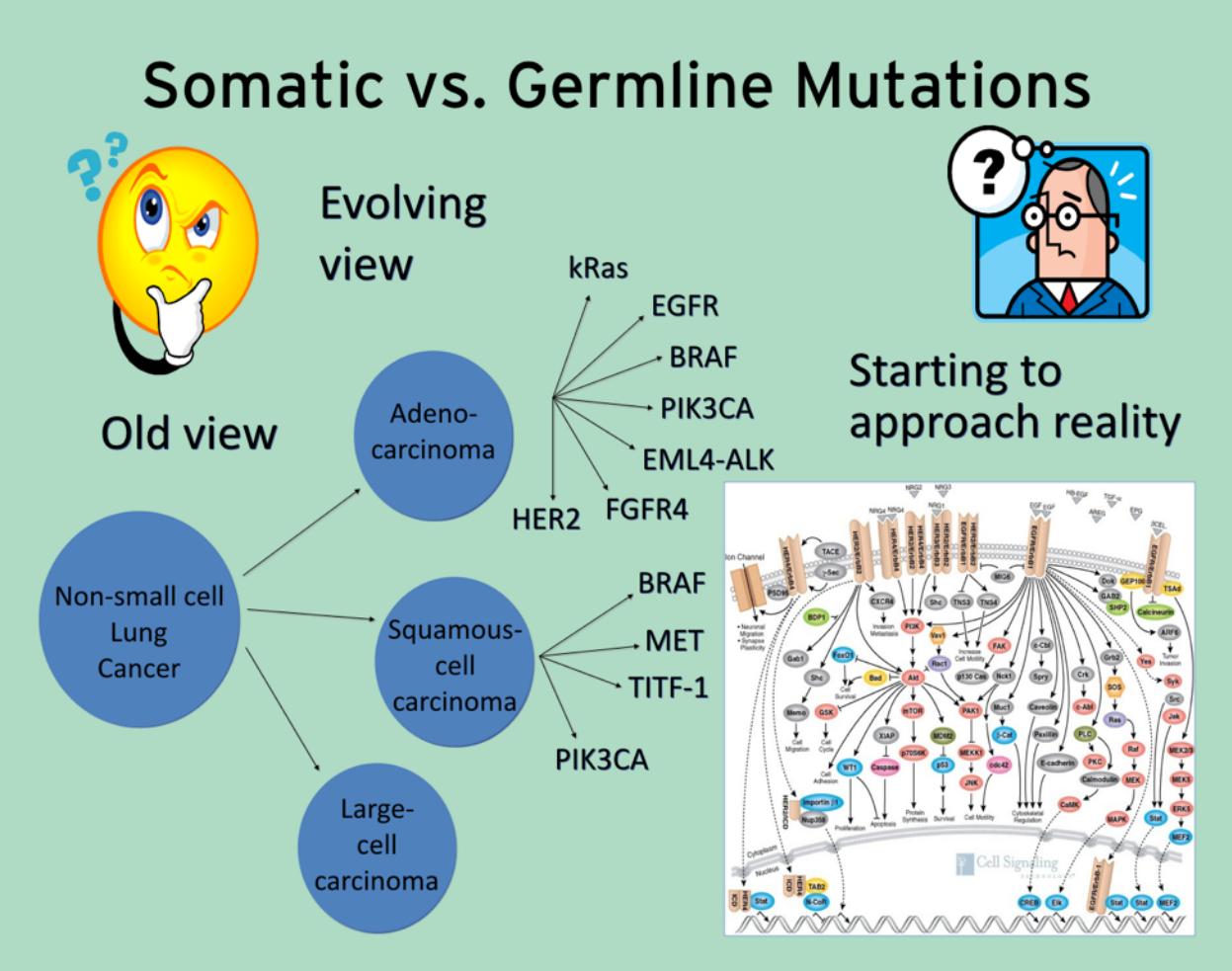
LUNG Cancer Video Library

Are There Significant Genetic Risks for Lung Cancer?



TRANSCRIPT & FIGURES

It is my privilege to speak to you today about genetics and lung cancer, a topic that I think gets some confusion at times that I'd like to clear up. As we develop targeted therapies for lung cancer, in addition to making extra work for our medical students to learn this, we get to a very complex view of genetics.



These are the genetics that are in the cells in the lung; every cell in the body has, in its center, a nucleus, and that nucleus contains DNA. This DNA is the instructions to the cell for how to do all of the work that the cell does. You might imagine an analogy to a computer – imagine that all computers were

sold with every software program you might ever use, and then just certain computers activated certain programs, so if you're an analyst maybe Microsoft Excel is activated, if you're an artist maybe Adobe Photoshop is activated — that's kind of what the cells in our body do. They all have genetics, they all have DNA, but certain programs are activated.

The key distinction that I want to talk about is the difference between the DNA in the cells in the lung, and the DNA in your reproductive cells that you can hand on to your children. So when we talk about the genetics of targeted therapy, when we talk about EGFR, ALK, ROS1, all these wonderful genetic changes that are leading to more effective, less toxic targeted therapies for our patients, we're talking about the genetics in the cell in the lung. We're talking about the genetics that went bad to transform that once-healthy, useful lung cell, into a cell that instead does all the mischief that is lung cancer.

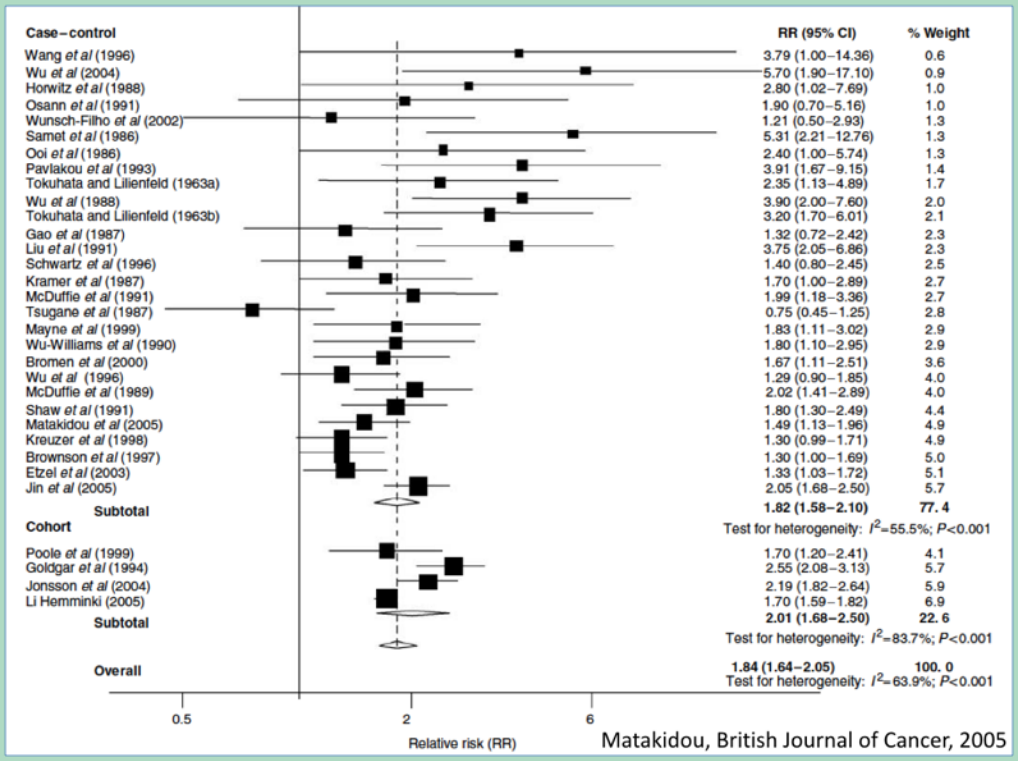
That's one kind of genetics. Those kind of genetics you cannot pass on to your children — the cells in the lung, no matter how much they change, there is no risk to children.

In contrast, people worry about heritable genetics when we talk about cancer. These are the cells in your ovaries or in your testes if you're male, and these are the genes, only these genes, that you receive from your parents and can pass on to your children.

So these are my daughters: at left this is Betty, and I know she has a little more hair than her smiling sister Dina there, but I'll tell you they are actually identical twins. They have the same DNA. When my wife and I made them, I donated a sperm, she donated an egg, those came together. We got those genes from our parents, we shared them to make these beautiful twins, but if later in life, before or after I have them, if I develop mutations in my lung, no matter where they come from — from bad luck, from smoking, from asbestos, from whatever they should come from, I cannot pass those on to my children. That is a different kind of genetics.

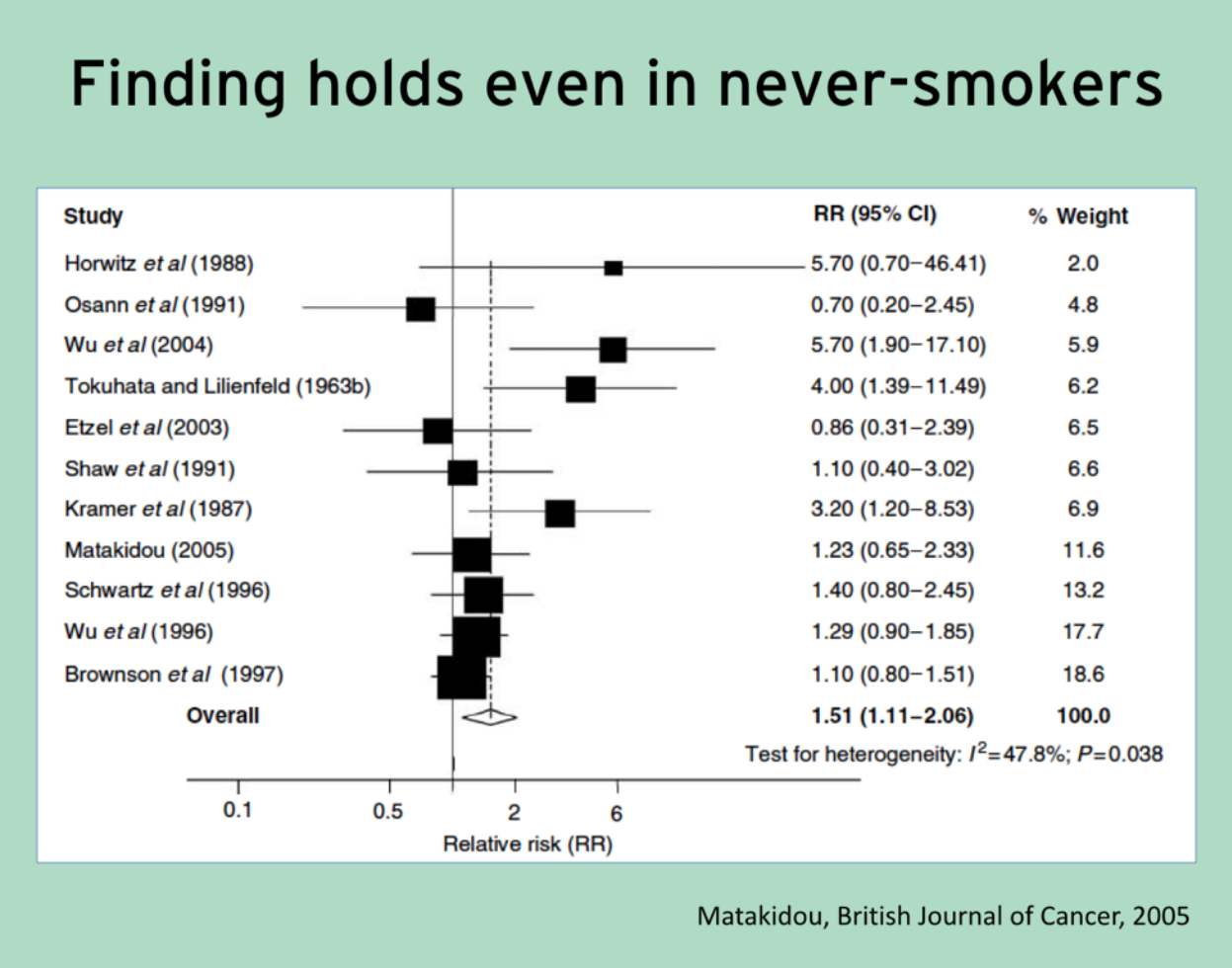
That's probably the most important thing I have to share with you, but one of the most common questions I get in my clinic is, "well, are there any heritable factors to lung cancer?" That's what we'll spend the rest of our time talking about.

Relative Risk with a Family Member with Lung CA

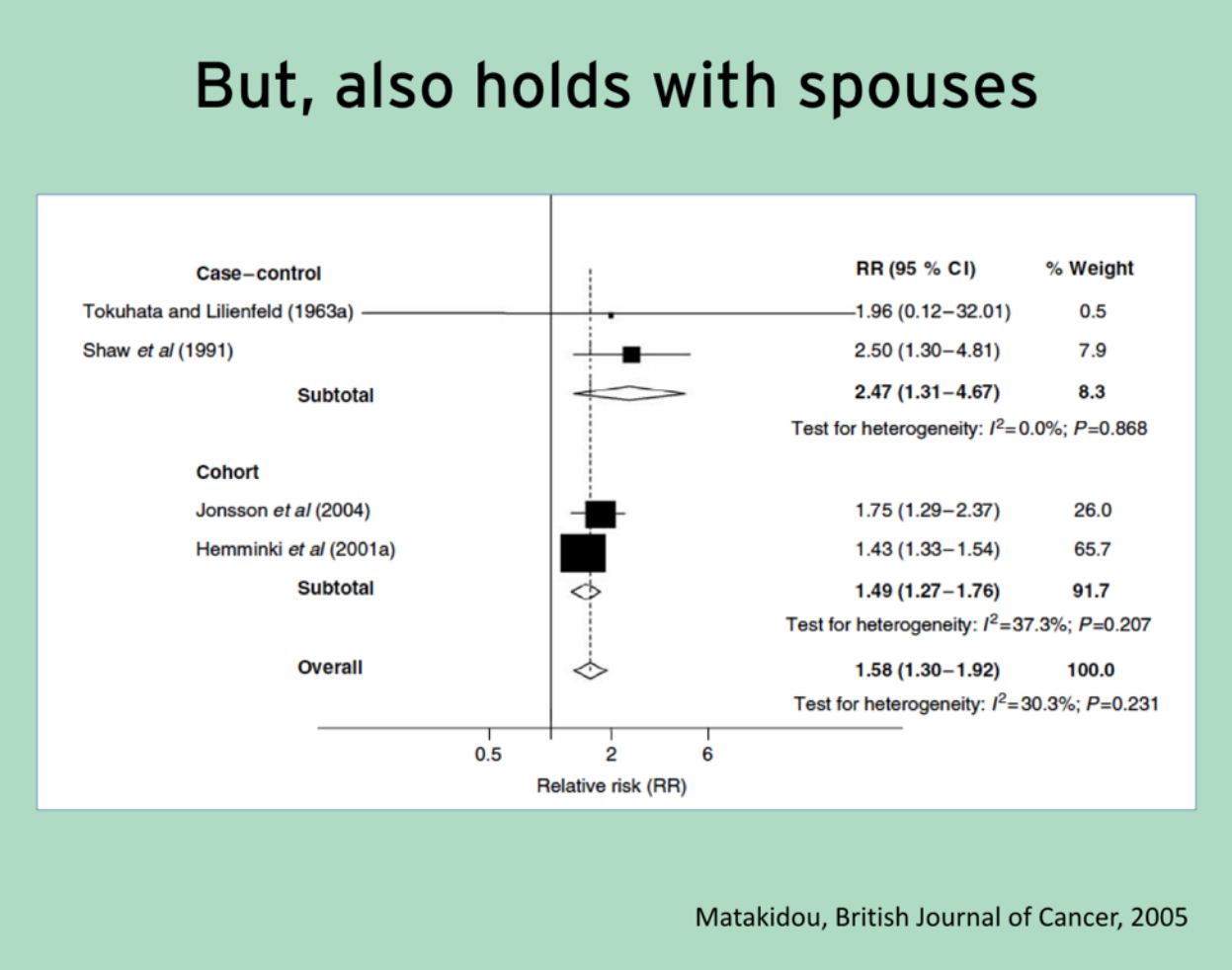


This is in the realm of epidemiology or big studies of large numbers of people. I'm showing you here the relative risk of getting lung cancer if you have a family member with it. It's roughly double, so there is some kind of family association here. You might say, "well, is this all smoking," that you're

smoking, you're around people who are smoking, and if you look at never-smokers, this effect basically still holds.

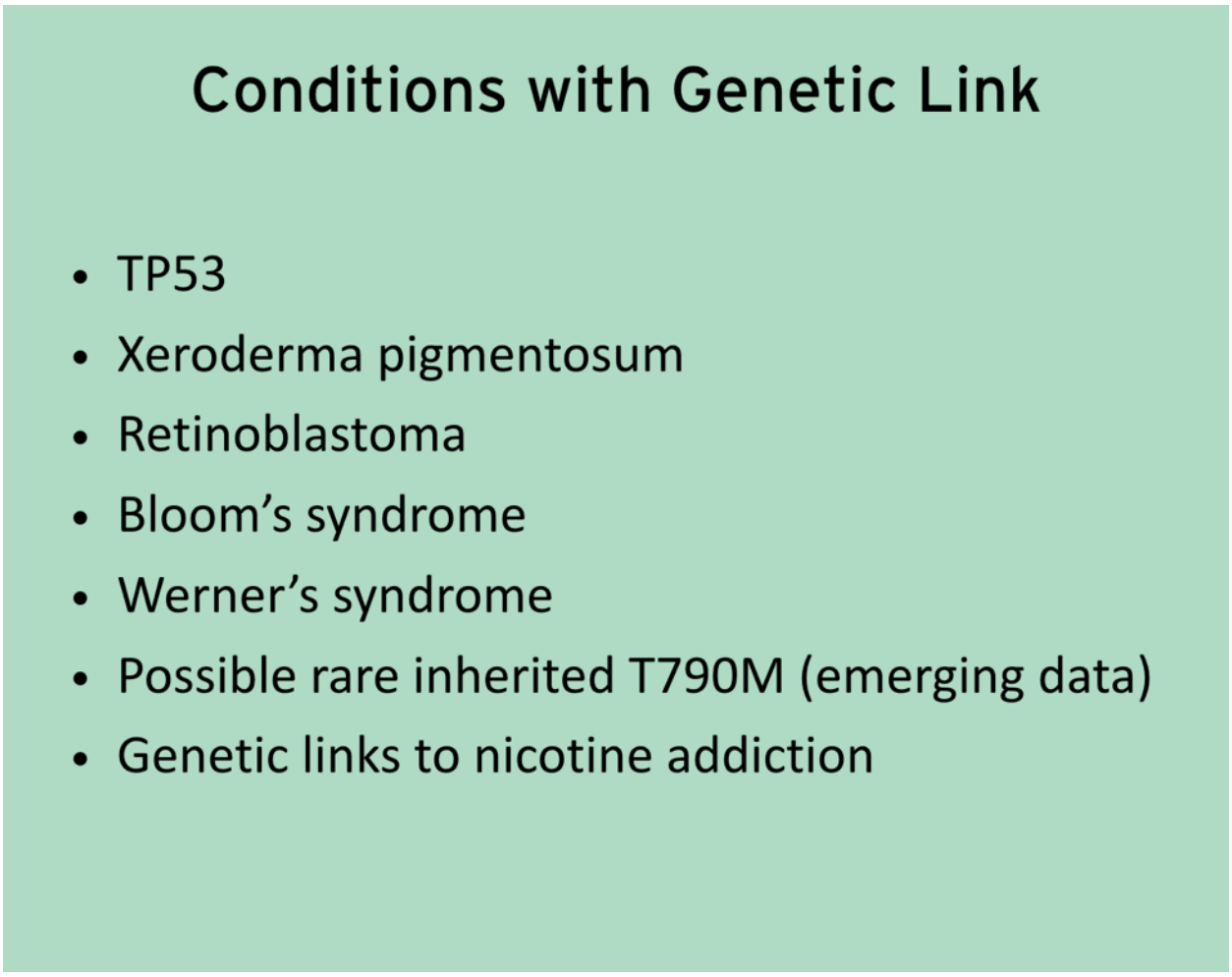


There's a greater risk in the family of developing lung cancer even if nobody smokes. So you might say, "okay, is there a heritable genetic factor to be talked about?"



The problem is if you look at spouses, the same effect holds, and most of us aren't too related to our spouses so it's hard to argue that there's genetics going on there. So it's probably some of each.

In general, lung cancer is one of the cancers least associated with the kind of heritable genetics that can be received from your parents or passed to your children.



There are a few specific syndromes that do have an association – TP53, xeroderma pigmentosum, retinoblastoma, Bloom's syndrome, Werner's syndrome, there's some new data about a very rare but heritable T790m mutation, and there's some cool data out there about genetic links to nicotine addiction – that there may be a heritable component to why some people taste that first cigarette and say, "this isn't so good, not for me," and other people start craving the next one.

So to summarize, the genetics you pass on to your children are not the same as the genetics we're talking about when we talk about molecular mutations

leading to targeted therapy, and the link with those heritable mutations is extremely, extremely weak in lung cancer. If you have lung cancer, it's unlikely that your children have a greater risk. The only thing I really have to say about that is that if your children smoke, make them stop.

I thank you.

GRACE.expert/GCVL