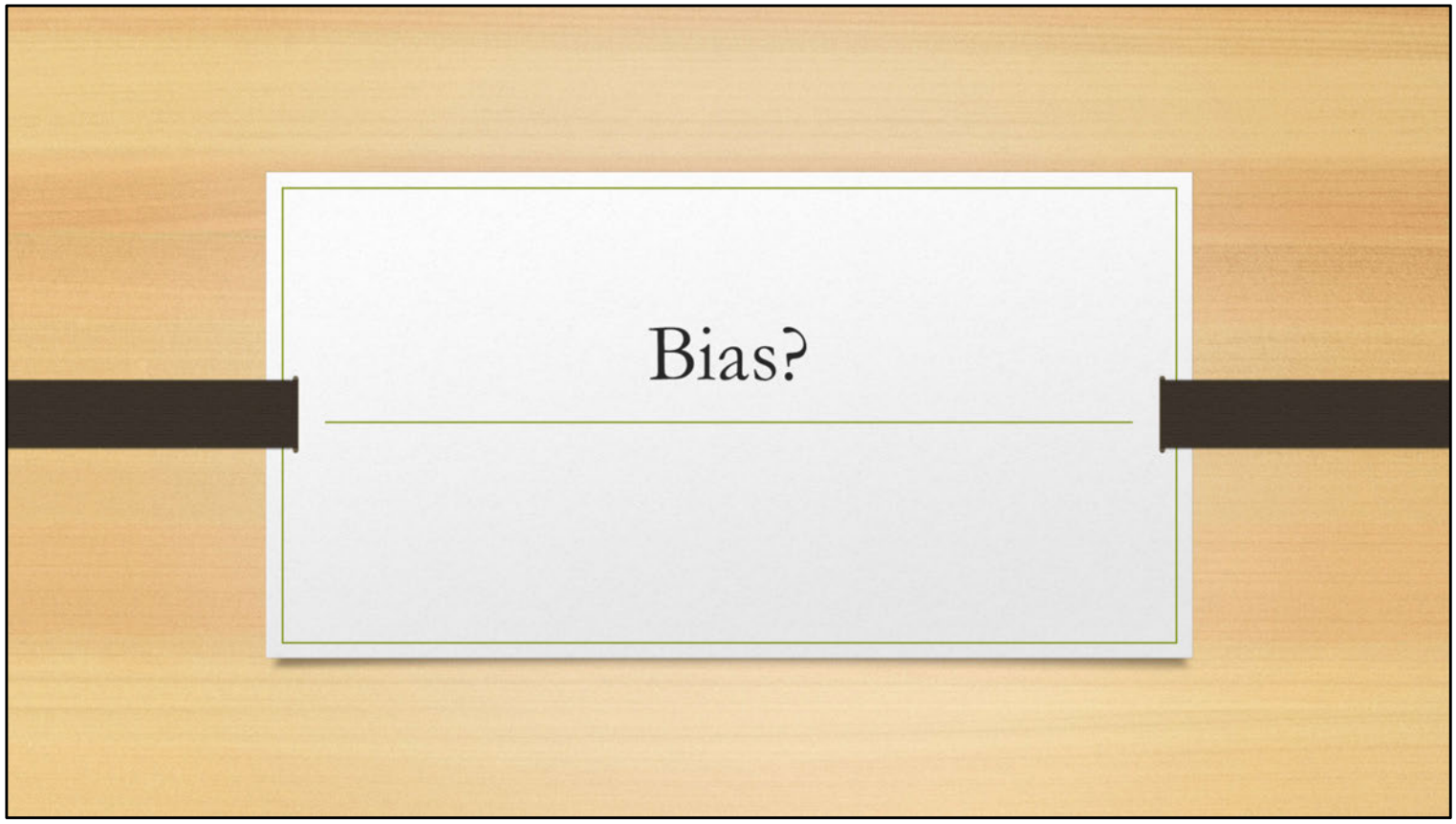
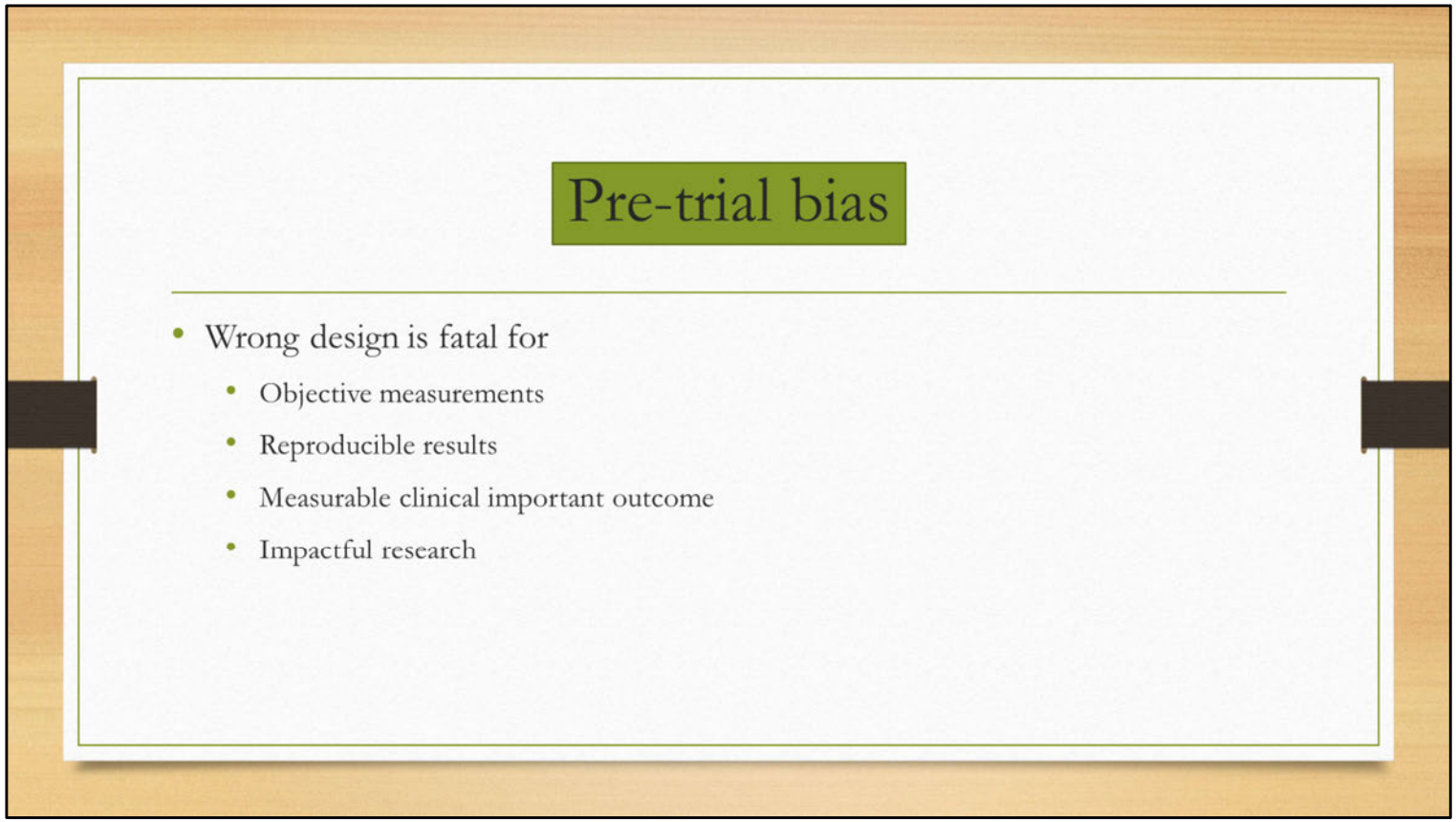
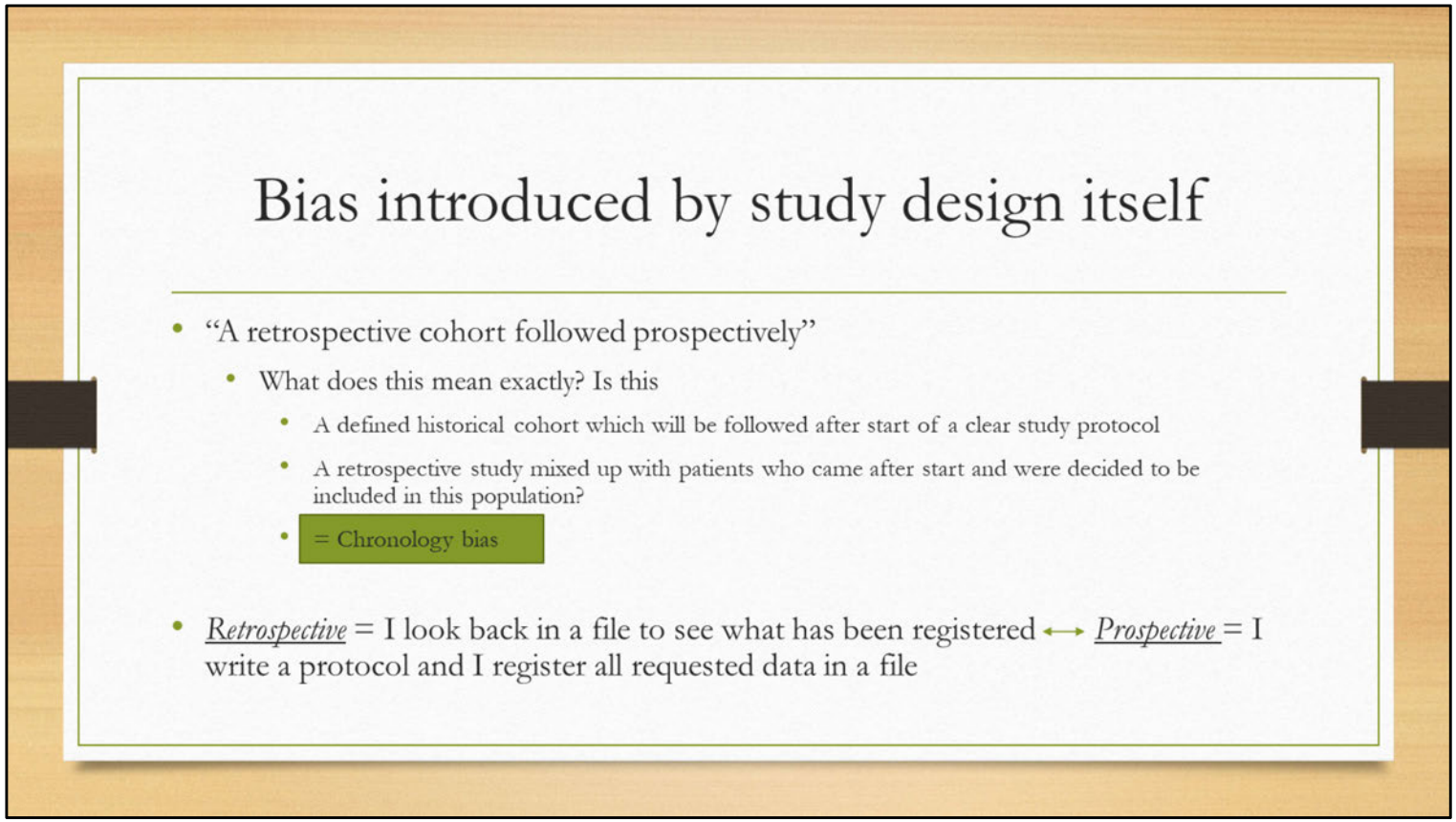


Bias seems obvious and a lot of people know the terms selection bias and recall bias. There is however a lot more bias that can enter a study without always being very obvious. Let's look at it more detailed.



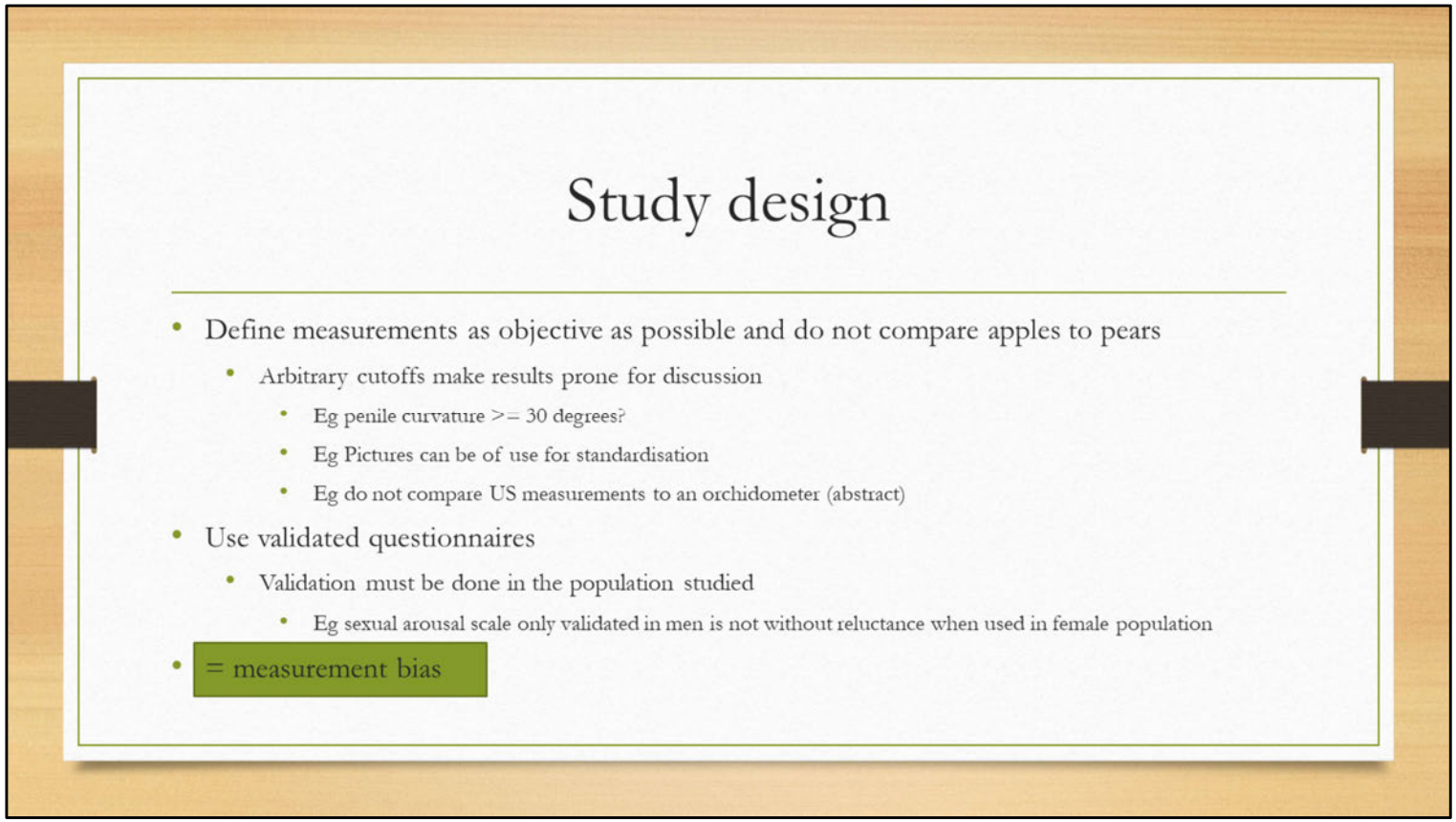
In fact, everything starts with a study design. And everything depends on a well thought set up of your study. A wrong design is fatal for everything: objective measurements if performed, reproducible study results, a clinically important outcome and so, shortly said, if you want to perform research that is impactful, you have to know everything about bias before even setting up a protocol.



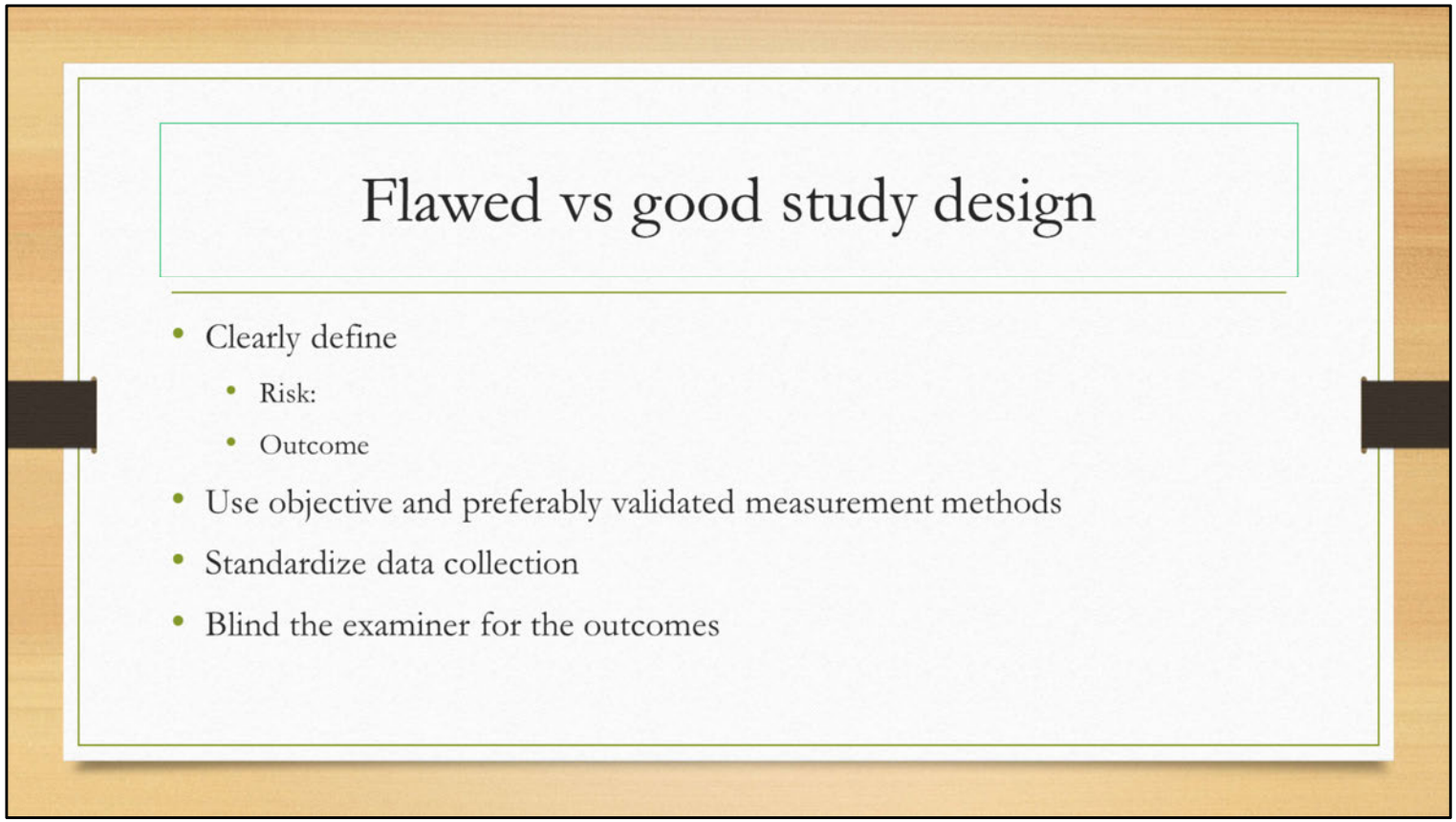
Every study design has its shortcomings. Randomized controlled studies are considered to have the least bias in themselves. Think however about the risk factors of the patients who were considered to be included in the study. If these are female patients after their reproducing age, how about comparing them with women in childbearing age, who are thus susceptible to all risks of being pregnant, or with different levels of hormonal influences throughout the month?

While reviewing, I regularly find the study-design which is called: a retrospective cohort followed prospectively. What is this: a historical cohort with people who are followed prospectively with a study protocol, or a retrospective study were you added or will add some future patients whom were decided to be included because of too few patients in the study yet? The latter is bias, it is called chronology bias. To be clear: a retrospective prospective cohort study does NOT exist.

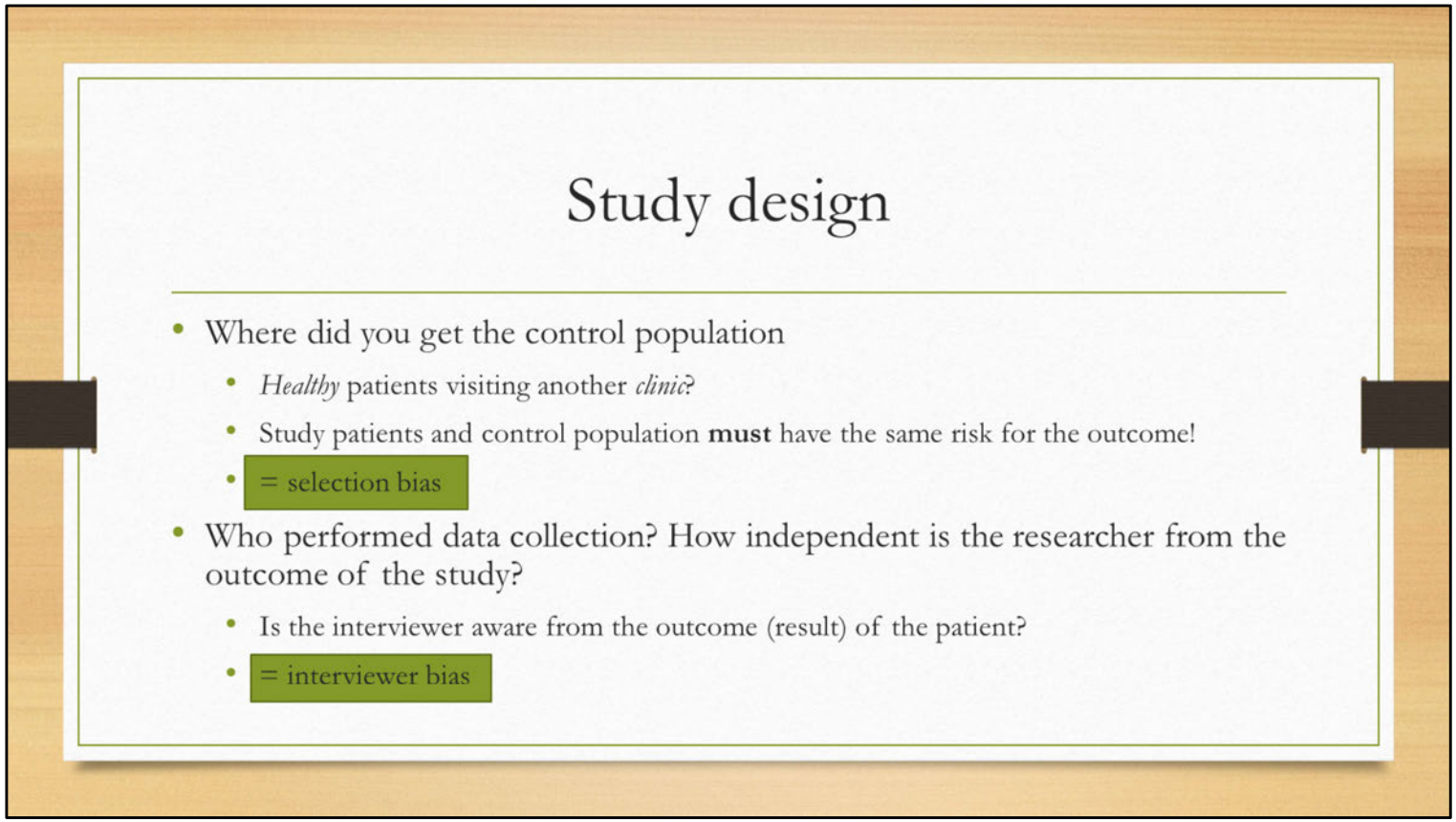
Be aware about the words retrospective and prospective: retrospective means that you look back to what has been registered, so the study protocol was written after the patients were treated. Pitfall of that design is that there might be a lot of missing data. Prospective means that you follow up on patients after having written a study protocol... So the patients are included AFTER the study protocol was written.



While writing a study design, it is very important that every measure or factor is well defined. You can't compare something that is measured in millilitres to something that is measured in metres, since the scaling of both instruments was different and since rounding of numbers is different when rounding before or after a comma.
Vague descriptions do not help if different people do the measurements. For example: do we all agree on a curvature when said that it is more or less than 30 degrees?
Questionnaires that are validated in men, might not be valid in females... Or that are valid in healthy people, might not be valid in sick people, and so on...
All this is called measurement bias

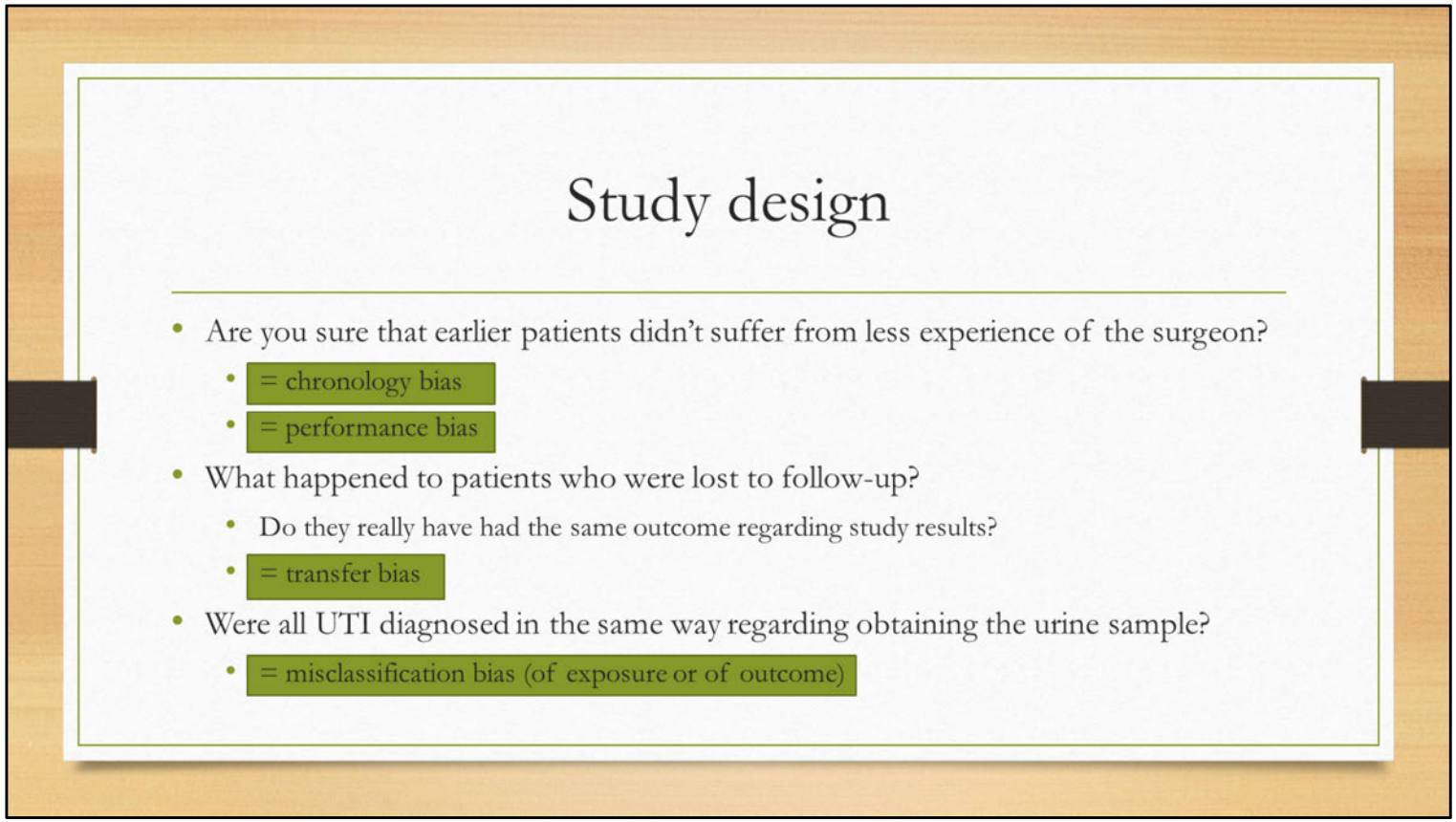


So, to summarize: for a good study design, define clearly the risk factors and outcome you are measuring. Use objective and preferable validated measurement methods, try to standardize blinded data collection... And yet, one is not done since during and after the study other bias can come in.



Selection bias and interviewer bias seem clear items. But what about healthy patients visiting another clinic? What are healthy people looking for while visiting a clinic? How healthy are there? It is not always easy, but while comparing groups, the patients of both groups should have the same risk factors for everything, so live expectancy, diseases, but thing also about obesity, sports performances... It is almost impossible to find a control group that is perfect to the study group – if you can't find them you have to be aware of the bias it might introduce in the results and you have to report on them.

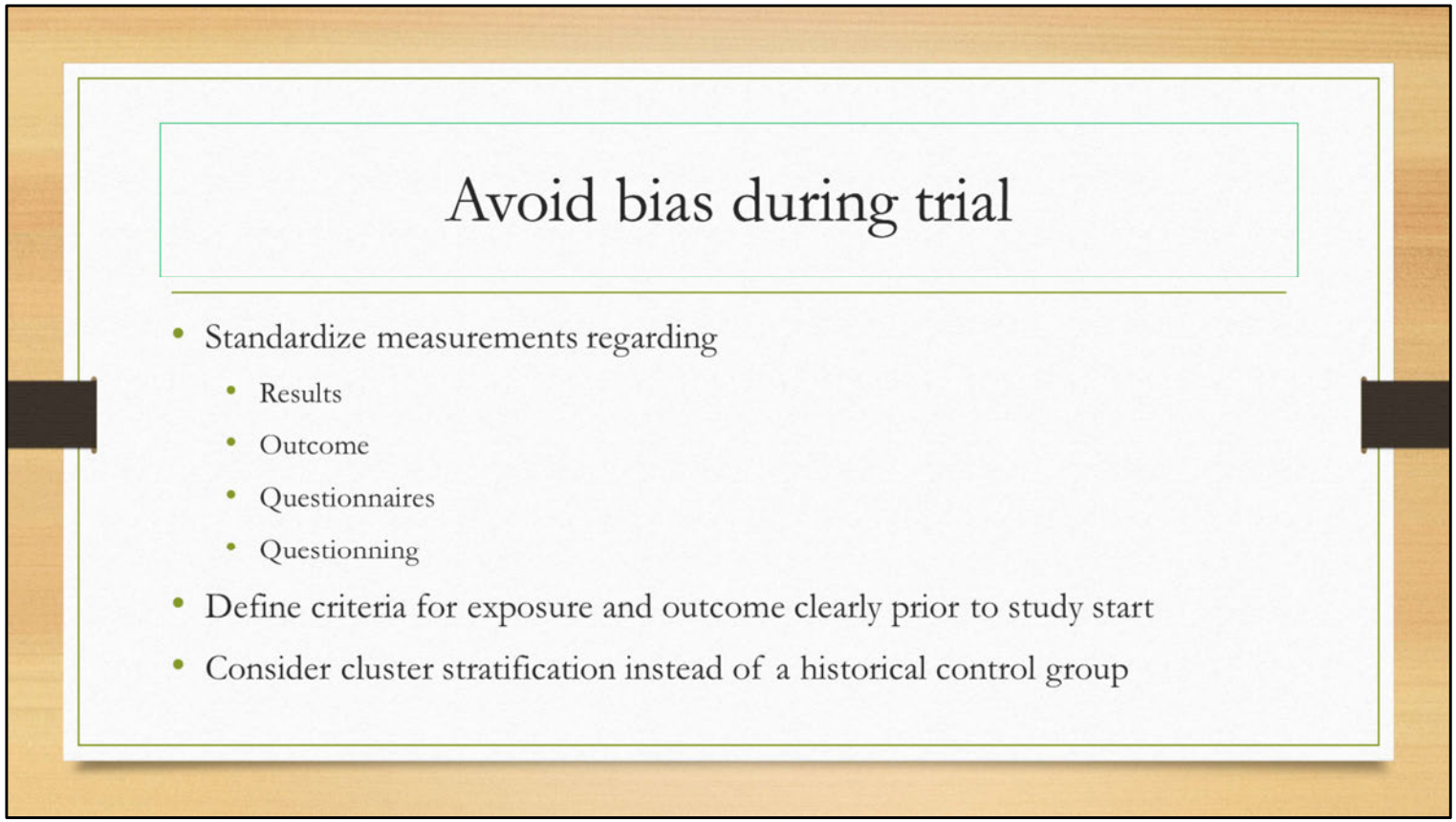
Interviewer bias can have different faces: an interviewer has to be blinded. Blinding must go as far as possible, and what has to be blinded depends on the issues the interviewer has to search for. Think about police-men: if they are convinced that the thief sits before them, they will ask every question possible to guide the thief into guilt. This is not allowed in law cases... But neither is it in studies!



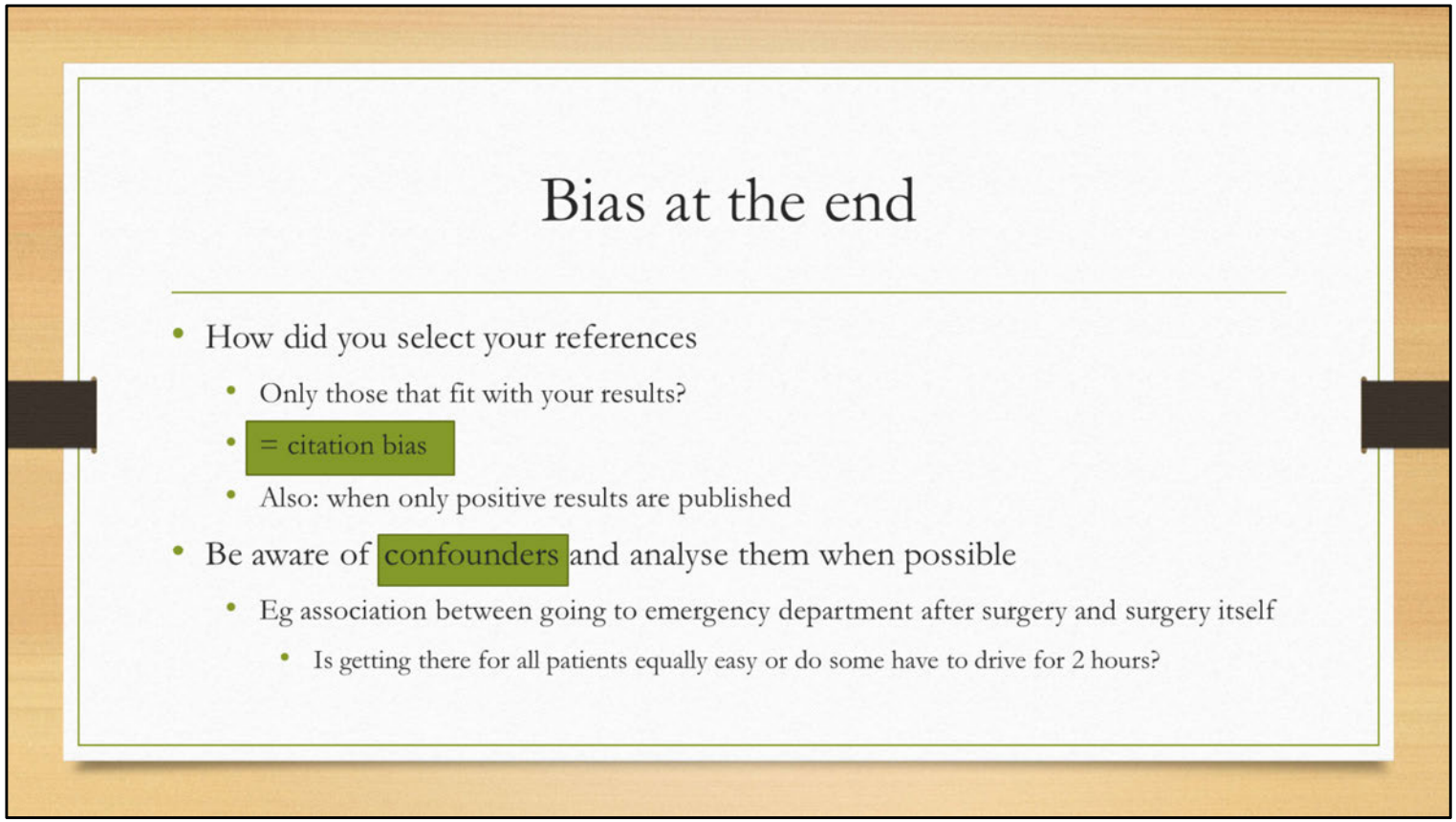
Another issue is contained in the sentence: " we compared the study group to a historical control group". Did the historical control group suffer from the same risk factors than the study group, example given was the experience of the surgeon equal? Otherwise we might have an issue with performance bias. Or with chronology bias: did the patients of the study group have to wait longer before having access to treatment?

What happened to the patients who were lost to follow up? Were they lost because they were cured, whereas the patients coming back were not? Or did the patients lost to follow up have an issue with having had a treatment that didn't help, and did they go to another doctor?

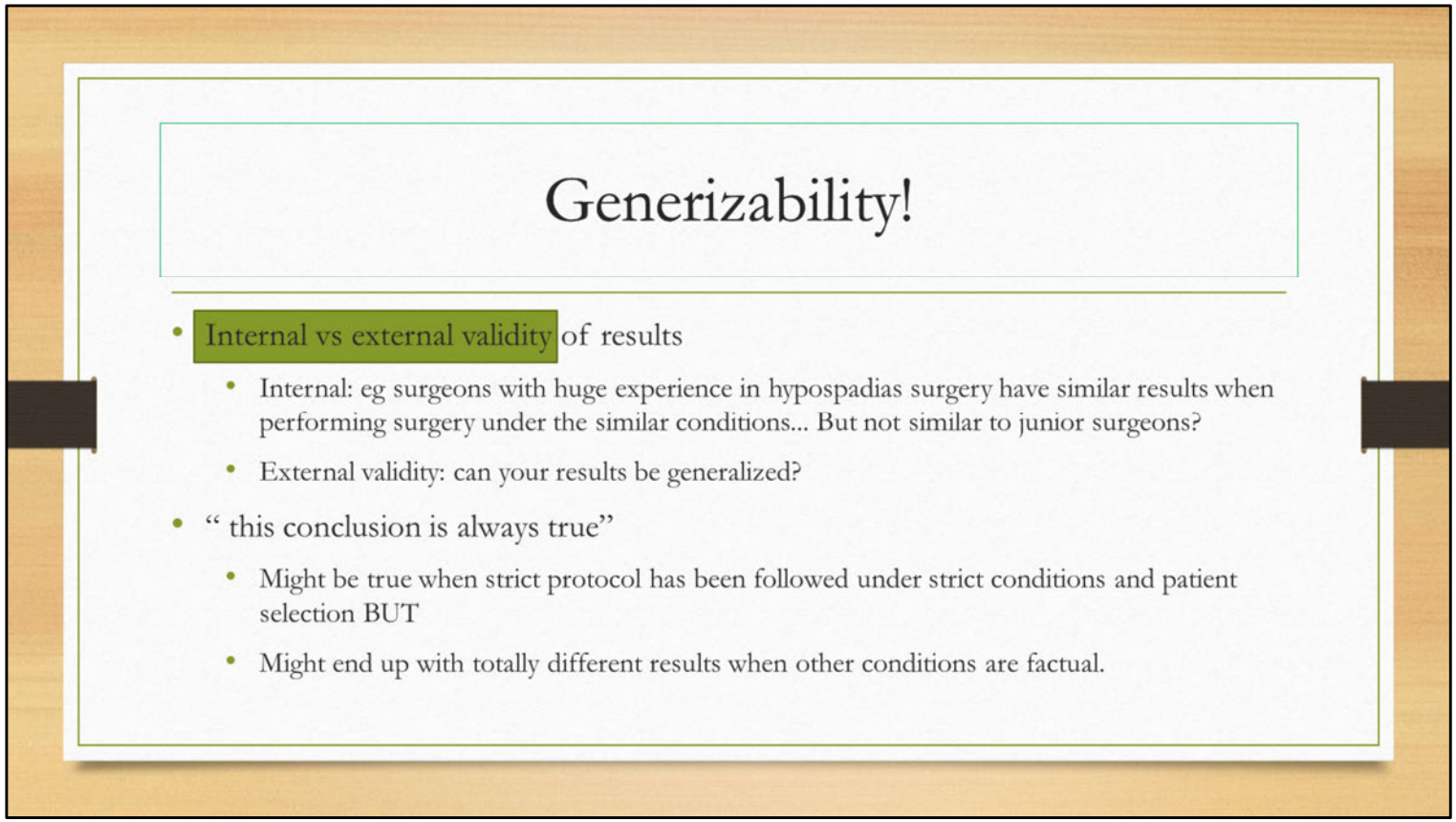
Last, but not least, misclassification bias can frustrate any result. Think about different levels of exposure, for example to smoke, but also about different ways how a disease was diagnosed. A good example is the collection of urine samples: if they were collected by a collecting bag, the number of diagnoses of UTI might have been much higher than if patients had only a diagnosis of UTI when a sample was considered positive only after having collected the urine by a single catheterisation. When thinking about study groups and both methods of urine collection were allowed, children having had 3 or more UTI in the past diagnosed with positive bagged samples only might have been misclassified!



So, to summarize, during a study trial you have to continue to think about bias. Think about standardisation of whatever you can standardize, define every outcome, primary and secondary, and try to think about other study designs introducing less bias if possible.



And even when done, one is not free of the introduction of bias while analysing the results. First of all, try to consider all available literature on the topic, and not only the literature that fits to your outcome. This means that you should search for evidence in the literature that fits to your hypothesis rather than to your results. And while doing statistics, try to think about confounders. The definition of a confounder is: a confounder is a factor that influences the disease and the outcome in a similar way. The classic example is the link between a cigarette and lung cancer. One might think that smoking is the link... But it is not only smoking, it is also the products that are in the burning of the cigarette, in the air... Some of these factors can be measured and some can not. Those who can be measured have to be measured, and statistics can calculate if a factor acts as a confounder... But this is why we never speak about a causality: a cause is a confounder for which no other confounder, known or unknown, can be found that explains the result. One cannot measure the unknown... So one can speak about a confounder but not about a cause.



And than, after a perfect study protocol, a perfect adherence to the protocol, a perfect analysis of the study... You are not done. Not every result is generalizable to every other situation. The fist question you have to as yourself is whether you would find the same results if you would repeat the same study under strictly the same conditions. If the chance for that is high, you have high internal validity. You can only speak about high external validity if the chance of finding the same results is still the same when you change any of the conditions of the patients or the risk factors or whatever other condition you can have. The latter is almost never true... So no study is truly always fully generalizable.
That said... There are a lot of good studies and we know an awful lot of the world around us, so as long as we are aware of the risks, we can continue to cross streets.