

Voices of VA Research Podcast Episode 24.

MICHAEL RICHMAN: Dr. Vassy, welcome to "Voices of VA Research." It's great to have you on.

JASON VASSY: Well, thanks so much for the opportunity.

RICHMAN: There are a series of medications in the statin family. Do they all cause myopathy, or is there one that stands out as causing muscle pain more than the others?

VASSY: Many of the statins can cause myopathy of varying degrees of severity from just mild aches and pains to really life-threatening muscle damage. Simvastatin or ZOCOR, in particular, has been known to be associated with these effects, although atorvastatin, or LIPITOR, can certainly also cause these same kind of symptoms, too.

RICHMAN: What is the name of the gene that you're testing, and why is it relevant to the myopathy caused by simvastatin or atorvastatin?

VASSY: The gene is technically called SLCO1B1, and most doctors and patients don't need to necessarily remember that gene name, but it was the gene that was discovered by a large association study to more commonly have a variation in patients who experience simvastatin-associated muscle symptoms. We now think that using that information in clinical care might help doctors and patients avoid those muscle symptoms in patients that are more genetically predisposed to have them.

RICHMAN: So those are the findings in the test that will determine if someone is at high risk for statin myopathy?

VASSY: Exactly. That's right.

RICHMAN: In terms of demographics, who is at greatest risk for muscle discomfort caused by statin drugs?

VASSY: So, yeah, separate from genetics, we already know there are just some regular clinical risk factors for statin myopathy. The older you are, the more likely you might be to have that myopathy. There are certain drug-drug interactions such as amlodipine, which is a common blood pressure medication, that if interacts with statin can increase your risk of simvastatin myopathy, and there are numerous other drug-drug interactions that can cause that. Other conditions such as thyroid disease or other conditions that might already predispose someone to muscle damage can also increase their risk of having statin-associated muscle damage.

RICHMAN: I understand that your study is one of the first randomized control trials involving pharmacogenetics. Why is that the case, and what types of studies have been used instead?

VASSY: Ever since the first blueprint of the human genome was sequenced about 15 years ago, there's been a lot of excitement about bringing this new genetic information into clinical care, and so a lot of researchers or even healthcare systems are rushing to deliver this information to patients and to doctors. In doing that, they haven't necessarily used randomized controlled studies such as the one that we're conducting here at the VA. Instead, they are just giving the information to doctors and patients on the promise that this actually will help improve patient care and patient outcomes, and that certainly may be, but we know from other fields of science and biomedical research that carefully controlled studies are important to determine the effect of new information or new tests, and it's important to have a control group that doesn't get the information to see what would happen if very similar people didn't have, in this case, this SLCO1B1 gene test.

This allows us to have an unbiased comparison between the patients that get the test and the patients that don't to see if the test really does make a difference in their medical care.

RICHMAN: Along the lines of what you're describing about methodology of the trial, I was wondering if you could go a little more in depth. How many patients will you have? What type of comparison will you be doing, and how will you be acquiring your results?

VASSY: So another important feature of this study called the I-PICC is that we are integrating it right into primary care here across VA Boston, so this kind of real-world evidence for or against the use of this test in clinical care. So we are nesting research right into patient care. We've completed enrollment this summer of 408 patients here across VA Boston, and patients are randomized essentially with a flip of a coin to either get this genetic test done right at the baseline of the study or at the end of the study, 12 months later, and that allows us to compare the two groups of patients and what happens in their medical care over the year of the study during which we observe them. The VA has a phenomenal resource in its electronic health record data, so we're able to at the end of the study use patients' EHR data to look at the clinical outcomes and the clinical care they received over the course of those 12 months, and those are the outcomes of our study. So were more patients or were fewer patients in one arm compared to the other started on statin medications? Was there a greater number of statin side effects in one group of patients compared to the other? Did their changes in cholesterol if they were started on a statin medication differ by the end of the study? All of these are important processes and outcomes in managing patients' cardiovascular disease risk, and so we'll be able to just pull those outcomes right from electronic medical record data, which is one of the real strengths of the VA as both a patient care environment and a research environment.

RICHMAN: What do you expect to learn from this study? What do you expect the conclusion to be?

VASSY: Well, we are still gathering the data on the outcome, so we don't yet know will this information have made a difference in the care of these 408 patients or really the 204 that they've got the test from the baseline or not, but what we hope is that positive or negative this information will be useful to primary care providers at the VA, policymakers at the VA to make decisions about whether it's worth incorporating this test more broadly into patient care across the VA. It's also kind of a proof of principle study in a way because there are dozens of other similar pharmacogenetics tests besides SLCO1B1 that have been identified to determine a patient's risk of benefitting from a certain kind of medication or having an adverse event to a different kind of medication, so even though what we're learning in the I-PICC study is very specific to simvastatin and the class--the statin class of medications, some of these concepts of whether doctors and patients use this information to improve medical care will be generalizable to the dozens of other pharmacogenetic associations that exist, too, and that others are proposing might be used in patient care. So we don't have final outcomes yet, but I'm hopeful that the I-PICC study will be able to inform the VA and other healthcare systems into whether pharmacogenetic information can be used effectively to improve patient outcomes.

RICHMAN: Do you yourself think that a genetic testing program will someday be implemented in the VA system, and if so, what will it take?

VASSY: Yes, I do. I think it will take--in some shape or form, genetics and genomics is going to increasingly be incorporated into healthcare, and that's a very active area of research right now. There are several barriers to incorporating genetics and genomics more broadly into medical care, and not all--these barriers not unique to the VA. These are unique to healthcare systems and the way medicine is practiced in 2018. Providers, especially primary care providers, are busy, and genomics is not necessarily something they learned in medical school and don't have a lot of familiarity with some of these concepts. The electronic health record systems that they use to take care of patients are not fully equipped to incorporate genetic and genomic information in meaningful ways because there are lots of peculiarities about the way genomic data are different from just regular lab tests and medical care. So there's some infrastructure that needs to be built up there. There's some provider education that needs to be incorporated, and there's not yet a sufficient stimulus to make these things happen because we don't yet have studies demonstrating that patients experience better outcomes when this information is used in their care. Once that happens--and the I-PICC study hopefully will be one of those studies that contribute to that evidence--then healthcare systems, including the VA, will have greater incentive to try to overcome the barriers to putting this into medical care. A lot of people have tried to predict how soon this is going to happen. I'm not gonna begin to try to venture a prediction. Will we see a genomic revolution in 5 years, 10 years, 15 years? It's hard to say. There are a lot of barriers to overcome, but each step towards overcoming each barrier is an important step in that direction.

RICHMAN: Well, sounds like so many things in medicine, we're just gonna have to wait over time to see how this evolved.

VASSY: That's right. Yes. Improvements in medical care come in increments. Genomics has sought to maybe be a just big disruptive technology, and I think in many ways it is. Medical care and healthcare is difficult to disrupt. There are lots of moving pieces and interlocking gears that turn slowly to have big change, but every little step is important.

RICHMAN: Dr. Vassy, your genetic research on statin drugs sounds like it has the potential to open new doors in medicine. Thank you for coming on "Voices of VA Research."

VASSY: Absolutely. Thanks so much for the opportunity, and thanks for your interest.