**Jeanette McCarthy Returns to Discuss the Value of Pharmacogenetics in Clinical Practice**

Dr. Jeanette McCarthy, MPH, PhD, Precision Medicine Advisors | June 20, 2019*Welcome to* [*The Precision Medicine Podcast*](https://www.interventioninsights.com/precisionmedicinepodcast)*, where experts come to discuss the problems oncologists, reference labs, and payers face as precision medicine grows, and consider solutions for advancing the quality of patient-centered cancer care.*

Jerome Madison: Thank you for joining us on another episode of the Precision Medicine Podcast. I'm Jerome Madison, Vice President of Provider Relations at Trapelo. We welcome back Jeanette McCarthy, the genome educator. Co-founder of Precision Medicine Advisors. Jeanette, thank you for coming back on the show.

Jeanette M.: Thanks, Jerome, it's great to be back.

Jerome Madison: We had this idea to do an episode about pharmacogenetics in clinical practice, because we've gotten a lot of feedback either on LinkedIn or just in the conversation in the industry about the lack of the ability of clinicians to either interpret or know when to use these tests. So, we asked Janette to come back on to give us some basics about this area of the industry.

Jerome Madison: I guess I'll ask a very basic question, what is pharmacogenetics? There's some who use the term pharmacogenomics. Is it genetics, is it genomics? Can you explain and give us some level ground on that?

Jeanette M.: Yeah, no problem. Pharmacogenetics or pharmacogenomics, and I'll explain the difference in a second, is really using information about a person's genetic makeup to help inform treatment decisions. The term “genetic” generally refers to when we look at a single gene and “genomics” is typically used when we're looking across the entire genome. By extension pharmacogenetics would be looking at a single gene, pharmacogenomics looking at all of the genes in your genome.

Jeanette M.: But in reality, people use these terms interchangeably, and we're really probably always talking about pharmacogenetics because we don't have any tests that are comprehensive. In other words, taking into account all of your genes at once. It's usually just one gene at a time, but I think it became very in vogue to use “omics” on every term at one point. So, people moved from pharmacogenetics to pharmacogenomics, but you could use it.

Jerome Madison: It almost sounds like an SEO opportunity.

Jeanette M.: Yeah, exactly.

Jerome Madison: Some of the reasons that had been cited have been the inability to keep up with data. Either, the clinicians, no matter if they are a primary care women's health or even in the area of cancer, the inability to match a gene with a potential drug interaction or therapeutic that targets it. Knowing which labs to order the testing from or from knowing when to order. There's large panels, there's broad based panels. What are you hearing from clinicians as some of the issues that they're having that is causing unreadiness with using these tools?

Jeanette M.: Well, there are a number of issues, and this is not specific to pharmacogenomics. It really spans all of the genetic testing that's out there now. One of the major concerns is cost, and the fact that many of these tests are not covered by insurance. That's a big issue. If you look at the insurance companies, they're unwilling to cover these tests because there's a lack of evidence of what we call clinical utility. Clinical utility is really this concept that if you have this genetic test and it's good, how is that changing medical practice and importantly for the insurance companies, is it improving health and is it cost effective?

Jeanette M.: Now, for many of these tests, there is clinical utility. It's just the evidence is not out there. There aren't these published, prospective studies that actually demonstrate it. Cost is a big barrier. Again, underlying that is this maybe lack of evidence of clinical utility. But there are other, more practical aspects as well that are really preventing the uptake of pharmacogenomics. One is lack of awareness. A lot of physicians don't know that pharmacogenomic tests are available for specific drugs and what they can actually do.

Jeanette M.: You also have a lot of healthcare providers who lack confidence in their own knowledge and skills of genomics and in particular skills with how to access information about pharmacogenomic tests, what patients are candidates, things like that…which test do you choose? Then, I think, one of the other issues that we're seeing come up is how do you integrate something like pharmacogenomic testing into an existing clinical workflow?

Jeanette M.: There's a big push right now by a lot of companies to offer clinical decision support. How do we make this easier for physicians to know when they prescribe a drug that there's a test available? Or, if somebody's already had testing done, an alert would come up showing that they should be offered a different drug or maybe a different dose of the drug? Those are probably the biggest barriers out there right now.

Jerome Madison: If we're talking about getting to a place where this is, I guess, routine in our clinical workup, what does good look like? How can we get to a point of being unfamiliar…maybe not robust evidence of clinical utility…to making this routine as a part of our clinical workup?

Jeanette M.: Well, a lot of things have to happen. Number one, we need to do a better job educating health care providers. By health care providers, I mean not just physicians obviously, but some people think that perhaps pharmacists are the gatekeepers here, and they're the ones who should be ordering pharmacogenomic tests. Education is probably one of the biggest things. You also really need to get that evidence of cost effectiveness out there.

Jeanette M.: I know there are several groups who are working on studies to demonstrate cost effectiveness of pharmacogenomic tests. But if we step back a second and look at cost and cost effectiveness, the price of pharmacogenomic testing has really come down, so that it's actually cost-effective at current price points for many of these tests. You can get a large panel of genes, different pharmacogenomics tests in one test, about 300 or so drugs are covered in that test. This can be obtained for relatively low cost, less than $300.

Jeanette M.: Cost is becoming less of an issue. You're seeing some patients willing to pay out of pocket for these costs. That's one thing that's happening in this space.

Jerome Madison: This is another one I didn't have written down, but I think it's interesting. Last week at the Precision Medicine Leaders’ Summit, there was Kelly Coddle, and she was from St. Jude's Children's Research Center. She talked about the market that is available for pharmacogenetic testing.

Jerome Madison: Now, they've implemented this type of testing as standard at St. Jude Children's, but she also talked about the other end of the spectrum in America where there's upwards of 65 million retired patients in the population here in the United States where they may be taking up to 20 prescriptions a year. She mentioned about just the market dynamics that makes considering pharmacogenetic testing massive. Can you speak more to the market dynamics that you see out there and what we can expect for the demand to grow in the future?

Jeanette M.: Well, when you think about the market for pharmacogenomics, some people referred to pharmacogenomics as precision medicine for everyone. Because just about everyone has variants in their genome that impact their response to drugs. But then you have to ask, of course, who's taking the drugs? If you have a young population, young people tend to not be taking many drugs, but as you get older, obviously, you're taking drugs and you have this issue of polypharmacy too—people taking many drugs at once.

Jeanette M.: I do see that the market for these tests is probably going to be an older population that has chronic diseases, taking multiple drugs. But having said that, one way to deliver pharmacogenomic testing is to do it preemptively. This idea that when you're young, or at any time in your life before you're prescribed drugs, that you undergo pharmacogenomic testing for a large panel of genes. You have this information now in your medical records so that when the time comes for you to take a drug, whether it be a Statin to lower your cholesterol or even some pain medications, you have that information about your pharmacogenomic profile, and you can utilize it at any time during your life.

Jeanette M.: Really, even though the older population may benefit from this information the most at this point, the market is really everybody.

Jerome Madison: Yeah. The availability of the testing, I think you can speak more to that. To that point, the FDA has stepped in to regulate at least one of the direct-to-consumer pharmacogenetic tests on the market. This ruffled quite a few ... Let me say that again. Speaking about accessibility of testing, there's a number of labs on the market that do this testing, and maybe you can speak to that a little bit. But I know you mentioned the FDA stepped in to regulate at least one of these direct-to-consumer pharmacogenetic tests. It ruffled quite a few feathers in the industry. How are these tests currently regulated and how might this FDA oversight, I guess if we can say, change the expectations of how regulation is going to be in the future?

Jeanette M.: Well, pharmacogenomic tests and indeed most genetic tests out there today are very loosely regulated. Let me step back a second and talk about, first of all, how do you evaluate a genetic test? You pretty much look at three things. The first is the test's analytical validity. In other words, how well does the assay actually detect the variance that it says it's detecting? The second thing is clinical validity. How well does this variant predict the, in this case, response to the drug? And then thirdly is the clinical utility, which we've touched on already.

Jeanette M.: In terms of FDA regulation, it's really just that first piece, that analytical validity, which is regulated for all of these, what we call laboratory developed tests, the pharmacogenomic tests. What that looks like is laboratories who perform these tests need to comply with clear regulation, and that ensures that the laboratory is just doing a good job doing all of its checks and balances, proper controls to ensure good quality analysis.

Jeanette M.: But this big piece of clinical validity, in other words, how well does this gene actually predict the drug response? That is not currently regulated. Now, the FDA has jurisdiction over all of these genetic tests, has the ability to regulate these tests. But so far it’s really used its discretion and not enforced that regulation except in a few cases. One of the cases where it will catch the FDA's attention is if you're doing a direct-to-consumer test, and this could be pharmacogenomics or other genetic testing. In these cases, the FDA really needs to make sure that if it's a test that's being marketed and sold directly to consumers and no physician is involved that the test has to be delivered in such a way that consumers really get this information. There are very few examples.

Jeanette M.: In terms of companies out there now being regulated by the FDA, the only one that has actually gone through and received FDA approval for pharmacogenomic tests is 23andMe. Now, that's a direct-to-consumer genetic test. However, this test is not supposed to actually be used for clinical practice. There was a case that came up recently, a company called Inova Genomics who was also offering a pharmacogenomic test directly to consumers. The FDA came in and basically told them that you need to comply with FDA regulations, you need to be regulated by the FDA.

Jeanette M.: This was, I guess a red flag for the whole industry because number one, it's a direct-to-consumer test. Certainly, you have to make sure that patients understand this information. But the thing that ruffled people's feathers in the industry was that the FDA was claiming that these tests were not clinically valid, when in fact by all of the standards that we use—by we, I mean those in the industry—the tests they were offering were clinically valid.

Jeanette M.: It was seeing that they were maybe overstepping their bounds a little bit or not interpreting that data correctly. Now, what implications does this have for the rest of the testing industry? It's not clear. We know that the FDA is considering new regulation, new legislation for regulating laboratory developed tests, which could affect not just direct-to-consumer companies, but some of the major testing labs as well.

Jerome Madison: Yeah. You touched on it briefly just a second ago, but I want to jump back into this. One, how does this information benefit patients? I guess for clinicians who get these patients, who come and demand these tests or have these results, how often are they going—they, meaning the patient—going to receive actionable data that may have changed treatment or affect a physician's treatment decisions?

Jeanette M.: You use a pharmacogenomic test because it can help reduce the side-effects or improve the efficacy of drugs. We know that there are some drugs that have serious adverse events associated with them. Things like Steven's Johnson syndrome and other life-threatening side effects. For some drugs there are actually very good pharmacogenomic tests which can tell you which of your patients are at increased risk of these adverse events. For these patients, you would probably want to avoid giving them that drug and instead choose an alternative therapy.

Jeanette M.: There are other pharmacogenomic tests which can also increase the side effects of these drugs in patients, but also reduce the efficacy. For these tests, the results will tell a patient whether they might have to be on a different dose of the drug, because their metabolism of the drug is slower or faster than the average person.

Jeanette M.: Again, in these cases, you can reduce side effects but also improve the efficacy of these drugs. These are the real benefits of pharmacogenomic testing. Now, you ask, for how many patients out there are these tests relevant? That answer is pretty much everybody because as I mentioned earlier, just about everybody has variants in their genome that impact their response to drugs. If you look at the five or six most commonly used drugs for which there are pharmacogenomic tests available, just about everyone has an actionable variant.

Jerome Madison: I think it's no secret that I go to quite a few conferences, a lot in the oncology space. But as precision medicine grows, we know that precision medicine is more than just cancer care. It has spread to a number of other autoimmune diseases. The common refrain to treating physicians, Jeanette, is how do we make sense of all of this? They need a resource, they need education on what to do with these different types of tests, the interpretation, the genes. Precision Medicine Advisors, you created your company to meet this need. What does Precision Medicine Advisors offer to clinicians and is it just for clinicians or lay people or other healthcare providers?

Jeanette M.: Well, you're right, education is really a key factor prohibiting the uptake of precision medicine, and there are a lot of good tests out there, but they're not getting into the hands of the people to use them. Healthcare providers, including physicians, pharmacists, nurses, anybody who's in the practice of delivering medicine really needs to be aware of what's going on in this space and how to use these tests.

Jeanette M.: I really turned my attention to this about six, seven years ago and focused on reaching these people and giving them the baseline genomic literacy as well as the skills for implementing these tests into practice. I do this through online courses, I do this through webinars, and I do this through in-person workshops or boot camps. Healthcare providers are a big component for that. They're like the key gatekeepers. But I've also found that many of the companies that are involved in developing these tests or selling these tests, they can also benefit from having some genomic literacy.

Jeanette M.: You'll have some people in these companies who obviously have a very deep understanding of this field, but not everybody does. You have software engineers maybe developing new software tools, or you have engineers working on developing a new sequencing technology. You have people on the sales force going out and selling these products. None of these people may have a background in genetics, genomics. So, providing some basic genomic literacy for them is important because you want within a company for people to speak the same language, have the same baseline understanding. You also want everybody in an organization like this to really understand what are the clinical applications of the products that they're developing?

Jeanette M.: I found myself now more and more going into these companies and providing onboarding experiences and continuing training for their employees just to bring them up to speed and get them on the same page with respect to genomics and precision medicine.

Jerome Madison: I think that's a huge opportunity. I have conversations with those pharmaceutical manufacturers who have developed whole sales forces of people just to go in to talk about biomarkers and not necessarily selling anything. From your perspective, you just talked about it. One of the huge challenges with scaling precision medicine is to create a sales force when they're going in selling these tools to accurately talk about it. What do the pharmaceutical companies and clinical testing labs need to do in order to effectively educate and service their market?

Jeanette M.: Well, as I mentioned, they really need to understand, well first of all have that basic vocabulary, that genomic literacy. They need to understand what DNA is, what are genetic variants, how are genetic associations made in the research setting? They really need to also get in the heads of their potential customers and understand what are their pain points and how might they use these products, how are they going to change medicine? What's on the horizon in terms of newer technologies. Really understanding things like the concerns that physicians have with cost and clinical utility and evidence supporting these tests.

Jeanette M.: Really just getting that basic genomic literacy is really important for these people.

Jerome Madison: Absolutely. So, for those out there who would like to contact you and your organization, where could they find you, what's your website and your social media links so they can connect with you?

Jeanette M.: Well, I have a website, precisionmedicineadvisors.com, where you can see what different types of services that we offer. We also have an education portal called Precision Medicine Academy. This is where you can locate the online courses that I offer. I have several free courses. I also have courses that are clinically focused, research focused, and those covering basic genomic literacy. I'm on LinkedIn and on Twitter I am @Genomeducator. You can follow me there. That's it.

Jerome Madison: Awesome. We'd like to thank Jeanette McCarthy of the Genome Educator for coming on once again and giving us the 101 and the 201 of pharmacogenetics in clinical practice. Thank you for being a guest on the Precision Medicine Podcast.

Jeanette M.: Thanks, Jerome.

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**About Our Guest: Jeanette McCarthy, MPH, PhD**
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Jeanette McCarthy is a UC Berkeley trained genetic epidemiologist and spent the early part of her career in industry at Millennium Pharmaceuticals before transitioning to academia. She currently holds adjunct faculty positions at Duke University and UCSF. Her previous research had focused on the genetic underpinnings of complex diseases, both infectious and chronic. More recently, she has become a leading educator in the field of genomic and precision medicine involved in demystifying genomics for non-technical audiences, including health care providers, patients and other stakeholders. In 2014 she helped launch the first consumer-facing magazine in this field, *Genome*, where she served as editor-in-chief until 2016. She teaches genomic and precision medicine through UCSF and UC Berkeley Extension and online through *Coursera* and through the *Precision Medicine Academy* (precisionmedicineacademy.org). She also designs and delivers custom workshops and courses to international audiences and advises companies on strategic and technical aspects of precision medicine. Jeanette is coauthor of the new book, *Precision Medicine: A Guide to Genomics in Clinical Practice* (2016, McGraw Hill Education).

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