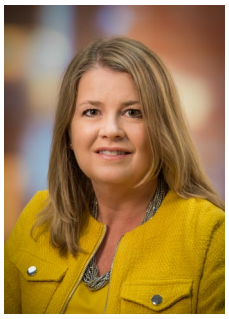
JALMTalk

Demand for Interpretation of a Urine Drug Testing Panel Reflects the Changing Landscape of Clinical Needs; Opportunities for the Laboratory to Provide Added Clinical Value



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Guest: Dr. Gwen McMillin. Dr. McMillin is a Professor of clinical pathology at the University of Utah, and she serves as a Medical Director of Clinical Toxicology, Pharmacogenomics and Mass Spectrometry at ARUP Laboratories in Salt Lake City.

Randye Kaye: Hello and welcome to this edition of JALM Talk, from *The Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

Urine drug testing is widely used in both clinical and non-clinical settings. The landscape of drug testing has largely shifted over recent years due to increasing trends and the illicit use of opioids, as well as the prescription of controlled substances for pain management and for the treatment of substance use disorders. Traditional immunoassay screening methods of drug testing often use high cutoff concentrations, and they do not detect several commonly used drugs. Further, inherent complexities in drug metabolism make drug testing results difficult to interpret.

An original article in the September 2020 JALM Special Collection, Value of Laboratory Testing and the Value Proposition, describes the increased demand of a targeted drug panel designed to detect a larger list of drugs and metabolites at more sensitive concentrations than traditional screens. The panel was offered with the option of a laboratory interpretation, which assessed whether the patient's results were consistent with prescribed medications. The senior author of the article is Dr. Gwen McMillin. Dr. McMillin is a Professor of Clinical Pathology at the University of Utah, and she serves as a Medical Director of Clinical Toxicology, Pharmacogenomics, and Mass Spectrometry at ARUP Laboratories in Salt Lake City. Welcome Dr. McMillin. Can you describe what circumstances led to your laboratory offering a targeted drug panel with patient-specific interpretive comments? Why do you think it's important for a laboratory to offer interpretive services for urine drug testing?

Gwen McMillin: Okay, so I'll take both those questions a little bit separately. I started working in the clinical lab space about 25 years ago. And at that time, urine drug testing was essentially all based on the traditional screen with reflex approach which was modeled primarily after SAMHSA (Substance Abuse and

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Mental Health Services Administration) or NIDA (National Institute on Drug Abuse) type testing. Then we started seeing a huge uptake in demand for urine drug testing from apparently new clients. And so I wanted to ask why and took opportunities to speak with providers as much as I could to understand the clinical need, and found that most of these physicians were actually trying to fit existing urine drug testing tools into a new application which was adherence testing, primarily for chronic pain management patients at that time. And so, I spent a lot of time trying to understand the clinical need which meant the different coverage of drugs, the traditional approach, was not adequate. Physicians were seeing a lot of false negatives and they found that the cost was too high because each one of those confirmation tests would add up. So long story short, we decided that we could save time and money and address the drugs of interest, while also designing the test to reduce likelihood of false negatives if we just went straight to a targeted panel. So that's why we came up with the targeted panel. We couldn't include everything, but we focused on controlled substances and drugs that really were being commonly prescribed in this clinical population.

The second question you're asking about, why offer interpretive services? I actually resisted for several years against providing interpretive services because I figured it was in the best interest of everyone if I could just provide educational materials and training to empower the providers to do their own interpretation, because they know the patient best. And my backgrounds in pharmacology, so I know that looking at just urine drug testing results doesn't tell you a whole lot. But I subsequently came to appreciate that urine drug testing is a small component of what the physician does to provide patient care. And that it really wasn't fair to assume that they had either time or interest in learning pharmacology and doing the interpretation. I also realized that test design and output from my lab might be a lot different than that generated by other labs and that single providers tend to use multiple labs to manage their patients because if nothing else, patients have different insurance coverages that are going to be useful for different laboratories. On top of that, we know that patterns of result may mean more than one thing so I did surrender after a few years to the fact that we needed to provide interpretation, and that was really the responsibility of the lab to take ownership of those results. So, what we did, and what I think makes sense, is to partner with the provider. So they provide us a list of expected medications and then we tell them whether the lab results jibe with those, whether they're consistent with that list or not.

Randye Kaye: All right. Thank you. Now your study retrospectively assessed the most common interpretive comments reported

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from your laboratory. What were some of these common interpretive comments, and why?

Gwen McMillin: Well, so once I surrendered myself to the fact that I had to provide interpretation, I wanted to do it well. And so I wanted to provide more than what was typical at the time. At that time, most labs were providing a comment about whether sample is dilute, and then would also provide a comment whether results were consistent or inconsistent with the medication list. And that's fine and that meets the needs most of the time, but there are many circumstances wherein results could be misinterpreted. And so, we came up with some extra comments, some of which are in that paper. I can give you maybe three examples. One, representing pharmaceutical impurities. It's actually fairly common that will see a small amount of hydrocodone in the presence of a large amount of oxycodone. And we know based on what the pharmacopoeia tells us that that could be a pharmaceutical impurity rather than suggesting the patient was using both drugs. And that's pretty huge because a patient could be denied care if the provider thought he or she was double dipping and getting drugs from multiple places.

A second example of an important comment is one that was intended to alert the provider that no expected metabolites were detected. So metabolites are breakdown products of the drugs and are really important to include in a urine drug test because many drugs are eliminated as metabolites and also because a metabolite essentially proves that the drug was ingested and processed by the body. Also, sometimes metabolites are pharmacologically active so it's really important to know that those are there. There are two primary reasons that metabolites would not be detected. First, is that the person can't metabolize the drug and obviously that's important clinically to know if there is a drug interaction or perhaps a pharmacogenetics explanation for why a person can't metabolize, or a liver condition, or so forth. A second reason would be that the person is adding drug directly to the urine to mimic compliance, and of course, that's really important too because that is deceptive. So that comment has been very well received.

And then the third example I will provide is about the drugs detected below the cutoff. So, I think this is really valuable because providers don't realize that cutoffs are not perfect. They're not magical. And urine samples just represent a snapshot in time. Taken together, they may not provide the most appropriate information. And many times, we in the lab know that the quality of the data below the cutoff is still great. It meets other acceptance criteria. So if I see a result that is below the cutoff and matches the provider's expectation, I think it's important to share that information.

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A common example we encounter is, my patient's on low dose buprenorphine and I swear he or she is compliant, but the urine drug test came back negative. So, as I mentioned from my pharmacology background, I know patients are really complicated. We don't really know what the drug concentration is supposed to be in the urine for a particular dose in a particular time of collection relative of the last dose. Oftentimes, in these patients we'll look below the cutoff and voila, there it is. So, the providers are then assured that the patient is probably compliant.

Randye Kaye: Wow, very interesting. Let's talk about another example. One of the interpretive comments described in the article actually involves the possible impurity of THC in a CBD product. So, can you explain how your lab would handle positive test results for THC when a patient claims to be using CBD oil?

Gwen McMillin: Yeah, so we do append a comment. I'll give you a little bit of history. As the CBD product started to pop up everywhere around the nation, we really did start to see quite a few medication lists for patients that included CBD oil. We also started getting numerous calls from providers who said they confronted patients about a positive THC result, and they claimed it's because of the CBD. And so, we did two things. First, we looked at whether CBD would cause a false positive in our THC test and it didn't, which was reassuring because that would have been really embarrassing actually if our THC test was positive because of CBD. Second, we pulled a bunch of residual urines from cases where this was the scenario, where THC was positive and then the medication list claimed CBD, and what we saw was a huge range of concentrations, which means that either one, the CBD product that the patient is taking actually contains THC, which I think is possible as many of those products are not regulated; or the second possibility is that the patient is actually taking THC.

So, they might be taking CBD but they're also taking a THC containing product. Anyway, we're not in the business of testing those products, nor could we possibly do that for all products so we just depend this comment that essentially alerts the provider to those two possibilities and hopefully stimulates a conversation between the patient and provider.

Randye Kaye: Great. Thank you. You know, we often think about the non-specificity of drug assays leading to false positive results, but your article also describes questions from providers about potential false negative results. What are some of the causes for these false negative results and what consequences could it have for a patient?

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Gwen McMillin: Yeah, so that is the major issue. And that was one of the things I discovered when I very first started looking into this field. False negatives can have serious implications for the patient because if the provider doesn't think the patient is taking the medication, they may deny access to those medications or may actually kick him out of the program entirely. And we've actually had some desperate calls from patients that have been kicked out of programs, which is very disheartening when they're actually limitations with testing. So, when we talk about false negatives, what we're really talking about is unexpected negatives, which in my opinion need to be investigated to understand why the result was negative before taking action against the patient. And so you could have a true false negative because the cutoff is too high, the urine is too dilute, or there is some sort of analytical interference that prevents detection or resolution of the drug. But unexpected negatives can also occur because of reasons outside the scope of the lab such that the patient didn't take the drug or perhaps the drug had already been eliminated when they provided their urine sample. Actually, we've seen some pretty common scenarios with amphetamine preparations like Adderall where a patient is likely to take the drug first thing in the morning to help him focus during the day, and then they may go into the provider and give them a urine sample at the end of the day when you would expect the drug to be eliminated. So, of course, we're not going to find it. We see the same thing with sleep drugs like zolpidem. So you would expect a patient to take that at night before they go to bed and then they go into the physician's office sometime the next day to provide a urine and again, it's already eliminated. So, we're not going to find it.

Randye Kaye: Right, so timing, timing, timing, and other factors as well. So, let's talk about other labs who may want to offer interpretive services for drug testing. Do you have any recommendations, and under what circumstances should the labs consider changing the content or design of their drug testing assays?

Gwen McMillin: Yeah, you know, drug testing is a work in progress. I think sometimes the administrators think that the test should be locked down and good forever. And that's just not the case because drug patterns change so frequently. But my recommendation for labs that want to start offering interpretive services is to know your population. Urine drug testing, you know, while we've spoken primarily about the pain management population, it is used widely for other applications, like monitoring substance use disorder patients or testing pregnant women, and we know that drugs and drug use patterns vary by geography and also by population. So, know your population, know the drugs of interest, know what your provider's biggest concerns are,

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and then try to align your testing and your interpretive comments with their needs. So, it's all about customization and you got to keep on top of that. I'm always wanting to talk to physicians and constantly learning about new things. So, I encourage labs to be very dynamic.

Randye Kaye: Great advice. Thank you so much for your time today. Thanks for joining us.

Gwen McMillin: Thanks for having me.

Randye Kaye: That was Dr. Gwen McMillin from the University of Utah describing the JALM article "Demand for Interpretation of a Urine Drug Testing Panel Reflects the Changing Landscape of Clinical Needs; Opportunities for the Laboratory to Provide Added Clinical Value." Thanks for tuning in to this episode of "JALM Talk." See you next time and don't forget to submit something for us to talk about.

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