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Assessing Efficacy and Cost of Blood-Based Tests for Colorectal Cancer

Announcer:
You're listening to *Clinician's Roundtable* on ReachMD, and this episode is sponsored by Exact Sciences. Here's your host, Dr. Charles Turck.

Dr. Turck:
This is *Clinician's Roundtable* on ReachMD, and I'm Dr. Charles Turck. Here with me today is Dr. Samuel Muench, who's a board-certified and fellowship-trained gastroenterologist at Capital Digestive Care in Washington, DC. Together, we'll be discussing a recent modeling study for colorectal cancer screening that compared blood-based screening tests to established tools like fecal immunochemical testing, or FIT, and colonoscopy. Dr. Muench, welcome to the program.

Dr. Muench:
Hi Dr. Turck, thank you again for having me. And thanks to you and your team. I'm happy to be here. I'm happy to provide my insights and thoughts on how we can improve screening.

Dr. Turck:
Well, to start us off, would you let us know how many eligible individuals remain unscreened for colorectal cancer?

Dr. Muench:
There is quite a number across the United States. Our main threshold—this was set nationally—is, I think, about 80 percent. It actually varies considerably between states and within states, as well as between urban and rural communities, and even within urban communities.

Across the board, we're screening about 59 percent of eligible individuals across the United States. Really quite a gap between that and our national chart set at 80 percent. And again, if you look at a map—and this has been published and is very well known—the coastal areas tend to be better screened. The metropolitan areas tend to be better screened. We have a huge swath of the interior of the country that is not up to the level of screening that we're seeing in major metropolitan areas, in an area that's really ripe for additional screening mechanisms.

Dr. Turck:
Now, what do you think are the main reasons behind this? And how might blood-based tests fit into the screening landscape?

Dr. Muench:
That's a great question. So blood-based screening tests are sort of on the horizon of screening strategies for this. Really, if we take a step back, we're looking at one of the standards of screening, which is colonoscopy, and that's been around for decades and entered into the USPSTF guidelines, along with a few other screening mechanisms. Some are endoscopic, some are radiologic, and some are non-invasive colon cancer screening tests.

But there is the advent of these non-invasive screening tests. One of the more common ones is CT colonography, or virtual colonoscopy, and that has been around for some time. We still use this to a much lesser extent, I would say. But we have the advent of stool-based colon cancer screening tests, both with the earlier generation of FIT testing and FOBT testing. And then we have the newer generation of testing, which has been clinically used now for the last decade or so, with multi-target stool DNA testing looking at a number of biomarkers—11 to 12 biomarkers that are present in stool—and shedding stool is a non-invasive screening method with

really considerable sensitivity and specificity, which are really our concern for any screening test, including colonoscopy.

The patients in your office are there, you physically have them present. Let's do a blood test. Let's do a PSA for occult prostate cancer screening, another one for bile duct screening, another one for AFP for liver cancer screening. So why not have a blood-based marker for colon cancer screening? That is where I think most of the efforts are concentrated and, again, would be an incredible resource to have in screening people and actually closing this gap between the 59 percent and the 80 percent.

Dr. Turck:
Now, the study we'll be discussing today modeled a couple of different screening tools; looking at the results, what stood out to you about how blood-based tests compared to traditional options?

Dr. Muench:
So let's take a step back. Blood-based testing has been on the horizon for some time, in an era where primary care providers are already tasked with screening so many things, from blood pressure, to multiple conditions like cardiovascular risk, to all the various cancers that we're currently screening for, and a blood-based screening method would make sense.

The barriers to screen that traditionally limit access to such as access to a gastroenterologist, transportation to or from procedures, ability to tolerate anesthesia, or desire to do the procedure. And for some people, be it they have kids, be it they're a single parent, be it they have work, it's actually a pretty hard thing to find time to do in the middle of the day.

So again, while blood-based testing has shown some promise in detecting mostly later stages of colorectal cancer, the shortfall has been in the reduced efficacy in the earlier stages, particularly stage I cancers. And the best screen test is the one that finds the earliest cancer. So we want to find these early cancers. We want to find the cancer that we're going to be able to intervene on and that we're going to be able to resect, treat, and completely remove, such that our cure rate is as high as is possible. And this test is really one that is still somewhat in its infancy, but it does show promise, again in these later stages, and hopefully at some point in these earlier stages of colon cancer.

The second part of this is that—and this is due to a physiological theoretical limit—the detection of not just cancer, but these pre-cancerous lesions or advanced pre-cancerous lesions, such as advanced adenomas or sessile serrated adenomas, really is going to be limited. We're not shedding enough material or cells to be detected in blood, and this has to be taken into account when electing to offer this screening method to our patient as part of any other risk-benefit discussion.

Dr. Turck:
Now, another component the study highlighted was participation rates. So how important is uptake when we think about the potential of a new screening test?

Dr. Muench:
So when any medical test enters clinical use, including the multi-target stool DNA testing, there are multiple aspects that need to be considered, like ease of ordering, availability, insurance coverage, cost effectiveness, knowledge of the reliability of said test, and just general awareness of the test itself. Screening, fortunately, has been largely centralized within the United States Preventative Services Task Force, or USPSTF, as I alluded to, and this allows for a concise guideline to reference. And as we've seen with multi-target stool DNA or stool-based colon cancer screening, awareness and knowledge of a test exists on a curve. And simply just takes time.

Dr. Turck:
For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Samuel Muench about the pros and cons of available screening options for colorectal cancer.

Now, Dr. Muench, you touched on this before, but the study also evaluated the detection of advanced pre-cancerous lesions, or APLs; to what extent should we consider APLs when evaluating test performance?

Dr. Muench:
That's a great question. And for many of these non-invasive colorectal cancer screening tests, APLs have not been the focus of the study. The study is primarily a colon cancer screening test. These remain a secondary outcome, and they are important markers of not just test performance, but actually, how we can prevent colon cancers to begin with. And colonoscopy will likely remain the standard in terms of screening, because it's not only a direct examination of the colon itself, but it's coupled with the therapeutic advantage of advanced polyp or lesion resection. It's largely considered not just screening but preventative in terms of colon cancer, because you're removing a lesion that could theoretically then turn into cancer. So this polyp or advanced polyp detection with multi-target stool DNA, this has improved from the initial iteration of the tests to actually the subsequent generation of the tests, which are soon to enter clinical practice. But even this still lags behind colonoscopy in terms of advanced polyp or advanced lesion detection.

Taking this a step further, the blood-based tests really have demonstrated an even larger drop: we're thinking about 40 to 50 percent in the case of multi-target stool DNA testing in terms of detecting these advanced lesions, in the case of these blood-based tests. And there's a variety out there, where the sensitivity drops to 20 percent or even lower in some of these tests. This has to be considered. This has to be discussed with our patients, not only for informed consent, so that he or she can understand the limitations of this non-invasive test, but the adherence, not only to that one test itself, but screening intervals over his or her lifetime. It's not just a one-time screening test. This is a lifelong screening program.

Dr. Turck:
Now, if we shift gears a bit and come back to the idea of cost effectiveness, what role do you see cost playing in how and where blood-based tests might be used?

Dr. Muench:
So cost, again, is a discussion in every aspect of our healthcare system, from pharmaceuticals to procedures to surgeries to really any corner. And there's no secret that we have the most expensive healthcare system in the world, with the highest populations of any developed country in the world. And it's no secret that colonoscopy and the related anesthesia is very expensive, and that non-invasive testing will largely remain less costly. However, this does not translate into increased cost efficiency. In some cases, that may be the case. In other cases, it may not be the case.

The current model of this FIT or multi-target stool DNA testing results in a positive result that is then followed by diagnostic colonoscopy, and has shown that we actually can, in a very cost effective manner, screen more people that otherwise may not have access to colonoscopy or may not be able to afford the co-pay of a colonoscopy, which has largely been reduced by the Affordable Care Act. But for this additional step, one could argue, doesn't this increase cost if they have to see a gastroenterologist? This is then balanced by the overall increased rate of screening, and hopefully the reduced demand and already prolonged wait times for colonoscopy in various areas, and hopefully the reduction in colon cancer cases, such that the cost benefit will be seen, but over a longer period of time.

The cost to the patient will remain a barrier. But this, again, was largely addressed by the Affordable Care Act, and this made screening included with every health plan, regardless of the plan terms. Screening the uninsured population will always remain a challenge, but this is a population, again, right for a non-invasive testing.

And whenever we look at a screening test, we look at something called an efficiency frontier, and we look at the number of colonoscopies as sort of an X axis needed to generate or improve a life year gained. What we've seen primarily is that colonoscopy is considered an efficient test. FIT testing is no longer considered an efficient test. It's considered near efficient, but not an efficient test. And what we've seen with multi-target stool DNA testing is that it actually achieves this efficiency, and is the only non-invasive screening test to achieve that status, alongside colonoscopy.

Dr. Turck:
And finally, Dr. Muench, let's look ahead for just a moment. What would you like to see, whether in research, policy, or anything else, to better define the role of blood-based tests in colorectal cancer screening?

Dr. Muench:
I think the more research we have, the more knowledge we gain and the more we can improve this test. And hopefully even within the theoretical limitations of the test, we can improve the performance of the test. That being said, again, there is a theoretical limitation in early colon cancers and the detection of these advanced pre-cancerous lesions, and we need circulating tumor fragments to be in a large enough concentration to be detected by our machines and our equipment.

Enhancement of the early colon cancer stages must also improve before we really give and allow blood-based screening to enter into clinical use and certainly a more widespread basis, especially before it enters our certain repertoire of colon cancer screening, along with the advanced precancerous detection properties it has. But as with other screening methods, I suspect that this testing will just take time. I expect it to be covered, as is colonoscopy and multi-target stool DNA testing, by both government and commercially insured patients. But awareness of this as a screening option—and we've seen this with multi-target stool DNA testing—is just going to take time. It takes time to teach providers. It takes time for all of us, gastroenterologists included, to learn how to order this and how to act on it. How do we screen our patients? Do we do it yearly? Every 3 years? This is something that takes a considerable amount of effort and time, but I do think this is one of the main mechanisms that we have to really bridge the gap, again, between that 59 percent national screening rate to 80 percent, which is our real target.

Dr. Turck:
Well, with those final insights in mind, I want to thank my guest, Dr. Samuel Muench, for joining me to discuss where blood-based screening tests might fit into the broader landscape of colorectal cancer screening. Dr. Muench, it was great having you on the program.

Dr. Muench:
Thank you for having me. Take care.

Announcer:
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