Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/clinicians-roundtable/liquid-biopsy-for-colorectal-cancer-screening-benefits-and-barriers/33196/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Liquid Biopsy for Colorectal Cancer Screening: Benefits and Barriers

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:
Despite the proven benefits of colorectal cancer screening, participation rates in the United States remain low, with only about 65 percent of eligible patients staying up to date. As interest in less invasive screening grows, liquid biopsy tests are gaining attention for their potential to improve access and adherence. But how do they compare to established methods, and what should we keep in mind as they emerge?

Welcome to *Clinician's Roundtable* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss liquid biopsy tests for colorectal cancer screening is Dr. Brennan Spiegel. Not only is he a Professor of Medicine in Public Health at Cedar Sinai in Los Angeles, but he's also the Director of Health Services Research there. Dr. Spiegel, thanks for being here today.

Dr. Spiegel:
Thanks for having me.

Dr. Turck:
So, Dr. Spiegel, let's start with the broader picture. How would you describe the current state of colorectal cancer screening uptake in the United States and what factors do you think are influencing participation rates right now?

Dr. Spiegel:
Well, this is a key question. We've made progress over the years for sure, but screening uptake in the United States is still far from where it needs to be, especially in certain communities, like underserved communities, for example. So, right now, I'd say around one in every three eligible adults is not up to date on screening. So that's really a huge gap. It's one we've been trying to close for years. At one point, we thought we would get to 80 percent by 2018. That was the goal. It's 2025 and we're just a click over 60 percent right now. It's really not just about access to care; it's also about the test burden itself. There are also psychological barriers we need to think about, and in some cases, even mistrust in the system itself, something my team has studied over the years.

Now, obviously, we have colonoscopy and I'm a gastroenterologist, so I'm all for it, but not everyone loves it. It's invasive. It could be time consuming and sometimes logistically complicated for certain individuals. Then, on the other hand, we have other approaches to testing: FIT and stool DNA testing. And even among people who have insurance and access to care, adherence can be shaky to all of these different forms of cancer screening. So it's really not just a resource issue, it's also a human and a behavioral issue.

And finally, I just want to acknowledge that COVID obviously disrupted everything. It disrupted routine care. It also widened these gaps. And while recent policy changes have occurred—like lowering the recommended screening age to 45—and these are a step in the right direction, it hasn't solved all the fundamental issues. We still haven't made screening easy or appealing enough, I'd say, for large groups of our population.

Dr. Turck:
Now, there's been a lot of attention on blood-based screening tests for colorectal cancers. So, when you look at the emerging data, what stands out to you most about their potential role in clinical practice?

Dr. Spiegel:
This is a big opportunity and an exciting one. And I think this is a really interesting conversation we're having because it's so timely and affects so many primary care doctors, gastroenterologists, and frankly, all of us who are getting old enough to need colon cancer screening. And really, what stands out to me about this discussion is the potential to finally reach those people who simply aren't getting screened at all—not that this is the best way to get screened, but it is a way to get screened. So no matter how good colonoscopy is or stool-based tests are—and clinically they could be very good—they don't work if people don't use them.

So blood-based tests offer a different entry point than these other tests. They are noninvasive. They don't require any prep. They could be done during a routine blood draw, like when somebody is going in for their CBC or chem panel. And so that's a major psychological and logistical shift. There are millions of adults who just say “no thanks” to every existing option, and for them, a blood test could be the first “yes” that we get from them, and that would be more of a behavioral nudge.

So, that said, we really need to be careful not to over-sell this. The promise is in access, not necessarily accuracy, at least not yet. It's all about, to me, positioning these blood-based screening tests as not the best test, but one that some people are finally willing to use to enter that process of getting tested.

Dr. Turck:
And what can you tell us about the overall accuracy of these blood-based screening tests?

Dr. Spiegel:
Well, so far we have early but very important data. There was the ECLIPSE trial. That study showed that a blood-based test can detect colon cancer with about an 83 percent sensitivity—if my memory serves me correctly—and a 90 percent specificity. Now, on the surface, those are good numbers, especially for a blood test, and they do meet the minimum threshold that Medicare coverage requires, so that’s a big deal. But those are pretty low thresholds. Those thresholds are, I think, a 74 percent sensitivity and 90 percent specificity. So it barely hit the specificity, and it beat the sensitivity mark.

But the real issue here with this test—the Achilles heel in a way—is detecting advanced adenomas, because long before we have cancer, we have adenomatous polyps and advanced adenomas. And these are precancerous lesions. And the idea of colonoscopic screening is to not just detect cancer but to prevent cancer. And that means we're finding these early adenomas and more advanced adenomas. But the problem is, in the ECLIPSE study, the advanced adenoma sensitivity was 13 percent. So that's pretty low, right? That means the test, sure, is good at identifying established cancer, but not at preventing it—unto itself, of course.

So from a GI perspective, that's a concern. Because if you're missing the precancerous stage, you're not changing the natural history of the disease in a way that we can do, certainly, with colonoscopy. And FIT, every year, has a higher accumulative ability to detect advanced adenomas than the liquid biopsy every 3 years.

So, we're waiting on more data. I think there's the PREEMPT study coming. But what we know today is that liquid biopsy is more of a detection tool than a prevention tool, and that's an important distinction.

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. Brennan Spiegel about the role of liquid biopsies in colorectal cancer screening.

So, Dr. Spiegel, high-level view: let's look at the overall potential of liquid biopsies. What key factors determine their effectiveness as a screening tool?

Dr. Spiegel:
I think there are a few critical levers that will determine how effective a blood-based test can be. So the first to me is, as I've said, sensitivity in both colorectal cancer detection and advanced adenomas. I can't really state that enough. That's a key point. Most of the mortality benefit in colorectal cancer screening comes, as I said, not from finding the cancer after it’s formed, but from finding precancerous lesions before they've progressed. So if a test can't reliably detect those lesions, its impact is fundamentally limited.

Now the second factor for me is the screening interval and adherence. Those are key issues. So a test that's 80 percent sensitive but only done every 3 years is very different from a test with the same performance done every year—by the way, at a considerably lower cost. Now, cost doesn't have to do with effectiveness, other than if people are not able or willing to get the test; then it affects effectiveness.

So this is why FIT—despite being a low-tech test—performs relatively well. It's an annual test, it's cheap, and it accumulates benefit over time. And this is what the American Gastroenterological Association has said in their expert roundtable health economic modelings.

Then finally, there's cost, as I've already said. And there's follow-up. These tests don't exist in a vacuum. If a blood test comes back positive, then patients still need a high-quality colonoscopy. It's not like you're done. This is just the beginning of the road if the test comes back positive. And that raises real-world issues, like will the system follow through? We need to make sure every time somebody goes in for a CBC and chem panel, happens to get a liquid biopsy, and it comes back positive, that now we have a process where we bring them to colonoscopy, or else that was just wasted potential and money. So the effectiveness isn't just about the test, it's about how well it's integrated into a system that ensures adequate follow-through.

Dr. Turck:
And looking a little bit more at potential barriers, what factors might limit the broader adoption of liquid biopsy tests in colorectal cancer screening?

Dr. Spiegel:
There's some headwinds, for sure. I already touched on one of them, and I'll just talk about that again briefly, and that's cost. So for the blood-based tests, we're still trying to find the price point. They're not cheap. In the health economic modeling that the American Gastro Association did, they just said, let's assume that they're 500 dollars. Right now, they're more than that. But even if they were to bring down the price to 500 dollars, which is way higher than FIT, it's still quite expensive, and from a health economic standpoint, there are concerns about whether that's the best use of funds.

I've already said, the other big headwind is the follow-up logistics. So I don't want to repeat myself too much, but again, a positive blood test is not the end of the story. It's just the beginning, so we have to make sure that we have navigators, reminders, and support systems in place to get patients. And there's going to be a lot of them if we're routinely doing blood-based testing as a part of everyday care for cancer. There's going to be a lot of false positive and true positive tests, and that means we have to be ready for that. And we have to have enough gastroenterologists who have enough bandwidth to be able to bring in an avalanche of people. And, by the way, most of those people are going to have a normal colonoscopy. But we have to be prepared for all of that.

And then I'll just say there's always the risk of creating new disparities. So these tests are marketed as more accessible, which they are, but if insurers don't cover them fully, or if follow-up care isn't equitably available, then we could end up reinforcing the same gaps that we're trying to solve.

Dr. Turck:
And before we wrap up our program, Dr. Spiegel, what should clinicians watch for in the next few years as liquid biopsy continues to evolve both in clinical data and real-world use?

Dr. Spiegel:
I think that we need to be watching on two fronts. There's the science front, where we examine with new data sensitivity, specificity, predictive value, and all that, but also the system side, which is what I've been emphasizing. There's the science and there's the systems, and often we forget about the systems and we focus on the science. So on the science side, we need to understand with upcoming studies whether future blood-based tests can improve their sensitivity for advanced adenomas. I mean, that's really going to be critical for me. Now if we can ideally hit 40 or 50 percent hit rates for advanced adenomas, that would start to close the gap with stool-based tests. And in terms of triennial testing, which is the recommendation now, that may not be enough. It may not be enough time on task, we can call it, to catch the lesions early and change outcomes meaningfully.

And then, on the system side, it's about real world integration. So, how are these tests going to be offered? How are they going to be communicated around? How are they going to be reimbursed? What is the follow-up going to look like? Are they actually going to reach unscreened populations that we're targeting, or are they just going to be a convenience upgrade for already engaged patients who are already seeing the doctor? Will the healthcare system ensure that a positive test leads to a timely colonoscopy or are people going to fall through the cracks, like they have in many cases?

So really, in other words, the test itself is only part of the story. The real impact is going to come down to how well we operationalize this test. And clinicians should stay engaged but also critical of the evidence. I think we really owe it to our patients and to closing this gap to offer what works to our patients, not necessarily what's new. But that said, it's a very exciting time. I'm watching with a lot of interest, and I think this is a very important advance in our field.

Dr. Turck:
Some compelling comments for us to consider as we come to the end of today's program. And I want to thank my guest, Dr. Brennan Spiegel, for joining me to share these key considerations for the use of liquid biopsies in colorectal cancer screening.

Dr. Spiegel, was great having it on the program.

Dr. Spiegel:
Thanks for having me.

Announcer:
This episode of *Clinician's Roundtable* was sponsored by Exact Sciences. To access this and other episodes in our series, visit *Clinician's Roundtable* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!