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Advances in Colorectal Cancer Detection: Exploring the Role of Blood-Based Tests

Dr. Buch:
This is *GI Insights* on ReachMD. I'm Dr. Peter Buch, and today I'm joined by Dr. Aasma Shaukat to discuss a review titled "AGA Clinical Practice Update on Current Role of Blood Tests for Colorectal Cancer: Commentary," which was published in *Clinical Gastroenterology and Hepatology* in August 2025. In addition to being a coauthor of the review, Dr. Shaukat is the Robert M. and Mary H. Glickman Professor of Medicine and a Professor of Population Health at NYU Grossman School of Medicine. She also serves as the Director of Outcomes Research in the Division of Gastroenterology and Hepatology at NYU Langone Health.

Dr. Shaukat, welcome back to the program.

Dr. Shaukat:
Thank you so much. Always a pleasure to speak with you.

Dr. Buch:
Dr. Shaukat, to start us off, what can you tell us about the Shield test and the test by Freenome, which is not yet FDA approved?

Dr. Shaukat:
This is an exciting time in colon cancer screening. Not only do we have an option of newer stool tests, but there are two new blood tests that are either recently approved or in the process of getting their final approvals. The first test, as you mentioned, is called Shield—by Guardant—and it's a blood test that both the FDA and Medicare approved last year for average-risk screening in the US. And the test is being commercialized as we speak. And the second test is by Freenome. It's called Simple Screen. And the test is in its final stages of FDA approvals. And after that, then, I'm sure it will be seeking Medicare approval as well. So this very much changes our clinical landscape, and for the first time, we now have potential blood tests to offer to our patients who are average risk and due for colon cancer screening.

Dr. Buch:
Thank you. Just as a way of getting some insight, is there any significant difference between the Shield test and the test that will be available by Freenome?

Dr. Shaukat:
So with the two tests, it's important to remember that they haven't been tested against each other, so we don't have any direct evidence—which we call comparative effectiveness studies—of the two tests head-to-head. They have both been studied in independent populations—large US studies. The Shield test was done in over 22,000 individuals, and the clinical validation was 9,000 individuals. The Freenome test included 50,000 individuals across the US and the validation cohort was comprised of a smaller number, but they were done in average-risk US populations. And, independently, the performance of the two tests is surprisingly very similar—very similar in terms of sensitivity for colorectal cancer detection and its specificity. And both tests have a lower-than-expected detection rate for these advanced adenomas, the precursor lesions that we worry about and are really looking forward to or eager to detect in a colon cancer test. So I would say they perform very similarly, but again, no direct comparisons.

Dr. Buch:
Thank you for that. And what should we know about the updated multi-target stool DNA test called Cologuard Plus?

Dr. Shaukat:

Yes. So not only do we have two new blood tests, we also have two new stool tests that also completed their population-based clinical validation studies, and both underwent both FDA and Medicare approvals. One of them is Cologuard Plus, and this is a newer version of the Cologuard test which has a slightly different marker panel for detection of abnormal signals for colon cancer in the stool. And the pivotal study—called BLUE-C—that was recently completed demonstrated that the test has a higher specificity than the older Cologuard version in detecting colorectal cancer, but the sensitivity and the detection rate for advanced adenomas is about the same as the previous Cologuard version. But what this could mean for practice is fewer false positives, because the specificity of this test is a little higher than the previous version, so, again, an exciting development. And I believe in the next year or two, the older test will get phased out and be replaced with this newer test.

The second test is by Geneoscopy, and this test is, again, based on a pivotal study that validated the test. It's a multitarget stool RNA test. And again, it's called CRC-PREVENT, and it looks for these aberrant signatures in messenger RNAs in the stool. Again, very similar stool test; it requires a collection, and then performance shows good sensitivity and specificity for colon cancer detection and similar sensitivity for these advanced adenomas as the Cologuard Plus. So I think our field is just growing wider with the addition of these stool and blood-based tests.

Dr. Buch:
So just as a follow-up to that and for clarification for our audience, the standard Cologuard had about, from my understanding, a 15 percent false positive rate. What's the false positive rate for the Cologuard Plus?

Dr. Shaukat:
It's nine to 10 percent, so it's definitely improved.

Dr. Buch:
Thank you. And, Dr. Shaukat, thinking about the future, what are your thoughts on multicancer detection tests?

Dr. Shaukat:
Yeah. So as if these single cancer detection tests weren't confusing enough, the new wave that's coming—and is in some ways already here—are multicancer early detection and MCED tests. And essentially, the idea is that these tests are blood-based tests that can detect an abnormal or mutated methylated DNA in our peripheral blood, and then, based on the methylation profile, they can map the signal coming from a certain organ. So not only can it detect that there's aberrant DNA in the peripheral circulation, but it could be coming from which organ: colon, breast, lung, ovarian, and so the list.

There are multiple MCEDs in development. Two are pretty much more advanced in their development. One of them is already launched as a lab-developed test, or what we call the LDT, which means that it's not been evaluated by the FDA, and it's not covered by insurance, so it is an out of pocket. The test is called Galleri, by Grail. And so essentially, this test will tell an individual if there's any cancer signal, and what the cancer signal origin might be. So that specific testing could be done to narrow down the source of the cancer. And these tests cover different panels of cancers that they can detect, but all of them have pretty much the common ones in there that you can expect: colon, lung, ovarian, breast, and pancreas. Some have even prostate and liver cancer signals. So these tests could be potentially game-changers. However, there's a lot that we don't know or understand about the use of these tests, and there are several thorny issues that are yet to be uncovered. And suffice to say, there's multiple studies ongoing to understand the application of these tests, which cancers they should actually be looking for, and how best to then follow them up. So I think there's a lot we have to learn before we get excited about it and offer them to our patients.

Dr. Buch:
So not quite ready for primetime.

Dr. Shaukat:
Absolutely.

Dr. Buch:
Thank you. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Aasma Shaukat about blood tests for colorectal cancer.

So, Dr. Shaukat, what do prediction models tell us about annual fecal immunochemical testing, also known as FIT, triennial multitarget stool DNA testing, which is Cologuard, and colonoscopy every three years compared with triennial Shield testing?

Dr. Shaukat:
Yeah, so actually, none of the guidelines have considered the triennial blood test yet because, up until the last guidelines were issued, we just didn't have a blood test and didn't know its performance. So we know that annual FIT, or fecal immunochemical test, one to

three-year Cologuard, or a colonoscopy every 10 years perform pretty similarly in terms of life years gained, colon cancer prevented, and colon cancer deaths prevented in prior modeling studies. And based on that, those three tests are predominantly what we use in the US and are guideline approved as well as Medicare, and all insurances pretty much cover the two stool tests that we have and the colonoscopy.

So now we're all looking at modeling studies and incorporating these new blood tests into the comparison and seeing how they fare. So far, what the modeling studies are showing is that the blood tests, at their current performance, are inferior to the performance of colonoscopy or FIT done every year. And that's because their detection rate or ability to detect advanced adenomas is so much lower that having to do them triennially—or every three years—just doesn't prevent the same number of colon cancers or colon cancer deaths as the other strategies do. So at the moment our position is to encourage patients to get either a stool test or a colonoscopy as colon cancer screening modalities. For individuals unwilling or unable to do those tests, those patients could be offered a blood test currently, because it's better than no screening in modeling studies. But it's certainly inferior to colonoscopy, annual FIT, or Cologuard every three years.

Dr. Buch:
Thank you, and that's so very important for our audience to be aware of. So how should we be reframing our discussions on colonoscopy screening with our patients?

Dr. Shaukat:
So in the US, colonoscopy is the predominant screening strategy, and we think that it will remain so in the near foreseeable future. Colonoscopy allows a high-quality exam where we can not only detect colon cancers, but also resect polyps of every size and, thus, prevent colon cancer in the long term. So it has the highest preventive potential, and it's a one-and-done test, while these other stool or blood-based tests require a follow-up colonoscopy if they're abnormal. And still, colonoscopy allows patient choice to be valued, and then if the colonoscopy is negative—meaning nothing worrisome is found—then a 10-year interval is possible, which, again, is really appealing to both physicians and patients. So in that regard, colonoscopy will stay the predominant screening strategy, for the near foreseeable future.

So what may change that in the future is if a blood or a stool test is disruptive enough—meaning that its detection of advanced adenomas is extremely high—and that we have a system to follow up with colonoscopy for anybody with a positive test. And we're not there yet, so I think in the near foreseeable future, screening colonoscopy remains the predominant screening modality, and certainly a test we should encourage our patients to undergo.

Dr. Buch:
So we're in the last few minutes of our conversation, Dr. Shaukat. Do you have any additional thoughts you'd like to share with our audience?

Dr. Shaukat:
For patients, it's really important to discuss with your providers what tests are potentially available or might become available, but to use either colonoscopy or a stool test at the moment to undergo screening, because, again, any screening is better than no screening. So we definitely want people to be up to date on their screening. And for providers and healthcare systems, it's a confusing landscape, and it's not important or necessary to offer every single test under the sky. Basically, look at the patient population, look at the resources, and figure out what the best combination might be for your particular patient population and health system with the goal of maximizing screening—meaning having high adherence rates and everybody that's screen eligible in your population undergoing screening. And that might look different for different healthcare systems, so it's important to definitely offer choice, but not necessary to have everything under the sky and get overwhelmed.

Dr. Buch:
Dr. Shaukat, we always learn so much from you. Thanks for this very informative presentation on blood-based testing for colorectal cancer.

Dr. Shaukat:
Thank you so much for having me. Always a pleasure.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit *GI Insights* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening, and looking forward to learning with you again very soon.