Clinical Chemistry

Newer Fecal Tests: Opportunities for Professionals in Laboratory Medicine

Bob Barrett: This is the podcast from *'Clinical Chemistry.'* I'm Bob Barrett. In a recent podcast, we spoke with Dr. Liselotte Kok of the Netherlands regarding her paper published in the June 2012 issue of *'Clinical Chemistry'* on the diagnostic accuracy of point-of-care test for fecal calprotectin and occult blood in primary care, and assessing what they term organic bowel disease.

Joining us now to provide his commentary on that study is Professor Callum Fraser from The Scottish Centre for Research into Cancer Prevention & Screening in Dundee who observed some interesting ways the research group could apply their techniques to clinical practice.

Professor Fraser, why do you think that the paper by Kok and colleagues warranted an editorial and why did you choose the intriguing title *'Opportunities for Professionals in Laboratory Medicine'*?

Dr. Callum Fraser: The study from the Netherlands is really important because all endoscopy including visualization of the colorectal by colonoscopy is a very, very scarce resource in many countries. Indeed, in some, the colonoscopy maybe limited to people with comprehensive health insurance. And as a result of these considerations there has been much interest in using fecal tests to decide who will truly benefit from colonoscopy.

And this is particularly important because the symptoms reported by patients who have colorectal diseases overlap considerably making it very difficult for physicians and primary care in particular to decide who should be referred for colonoscopy.

So the study from the Netherlands reported on the diagnostic accuracy of point-of-care test in primary care for two relatively new tests, fecal calprotectin and fecal occult blood. And it's important to recognize that the fecal occult blood test that they use was in fact a qualitative immunochemical test for hemoglobin. And my colleagues and I would prefer to use the abbreviation FIT or fit as we call the test, because guaiac based fecal occult blood test, the traditional occult blood test and FIT are very, very different. And FIT are rapidly superseding these traditional guaiac FOBTs in a variety of clinical settings.

And one of the reasons that I chose the title *'Opportunities for Professionals in Laboratory*

Medicine' was that I believe such professionals do have major roles in trying to ensure that the best available laboratory tests are used in all sorts of clinical settings. And therefore, I encourage professionals in laboratory medicine to try to ensure that all current uses of fecal occult bloods test in laboratories, clinics, wards, primary care, wherever they are appropriate that these older tests are eliminated and that these are replaced with a more efficient and effective FIT test.

Bob Barrett: Now doctor, it was noted that STARD guidelines were followed in this?

Dr. Callum Fraser: Yes, these guidelines on how to describe adequately the results of studies on the diagnostic accuracy of tests, have been around for some years, they were generated mainly by professionals in laboratory medicine. Unfortunately, our clinical colleagues often do not follow these in publications, in spite of most good quality journals emphasizing the benefits of following these guidelines.

If the guidelines are not followed, this results in being quite difficult to judge the evidence that's been collected and published. And I think that professionals in laboratory medicine should participate with our clinical colleagues and studies done on diagnostic accuracy and made sure that these very, very well-proven and rational guidelines are followed.

Bob Barrett: Doctor, calprotectin and FIT are relatively new tests, why should they be of interest of the Laboratory Medicine community now?

Dr. Callum Fraser: The work from the Netherlands builds on previous studies of fecal calprotectin in particular, it has been amply demonstrated to be useful in the differential diagnosis of lower abdominal symptoms, particularly to distinguish irritable bowel syndrome from inflammatory bowel disease and these tests, the calprotectin tests are potentially very useful in clinical management of inflammatory bowel disease in particular. It's I think very interesting that not all laboratory tests are used to ruin disease, they are not diagnostic investigations to find disease.

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Certain times the available evidence supports the view that the finding of a negative test is useful, and in this case, a negative Calprotectin or a little

Calprotectin concentration in a low-risk patient supports discharge of that patient without further investigative exploration such as colonoscopy.

Much less work has been reported on use of either of the traditional guaiac fecal occult blood test or the better in your FIT in assessment of symptomatic individuals. In fact, most guidelines suggest that these tests have no value, however a recent excellent meta-analysis in the British Medical Journal showed good diagnostic performance for colorectal cancer, but suggested that real evidence from primary care is lacking.

And I support that view, the view expressed in that article that high-quality studies are needed, and I think that professionals in laboratory medicine could play pivotal roles in the planning and execution of these very necessary studies.

Bob Barrett: Well, could the published approach be improved since it's clinically important to detect most colorectal disease, and ideally, never to miss any significant colorectal neoplasia or other serious disease?

Dr. Callum Fraser: That is absolutely correct, and the study published in the '*Clinical Chemistry*' uses qualitative, which are Yes/No or positive/negative point-of-care tests for both Calprotectin and FIT.

Generally, these tests are based upon immunochromatographic test cassettes or test strips, and they do have many advantages, in that they are relatively inexpensive, they are allegedly easy to perform, and usually each has an in-built positive quality control. So they might be considered very suitable for use in primary care, wards, clinics and the like.

However, it's very well-documented that analytical performance and point-of-care settings maybe inferior to that achieved in the laboratory.

However, I think most tellingly these tests have the disadvantage that the cutoff concentration between what is a negative test and what is a positive test are set by the manufacturers of the devices, and they can't be adjusted by the end-user.

So it's really important for readers to recognize that the cutoff concentrations for Calprotectin and FIT test do differ substantially from manufacturer to

manufacturer. And different cutoff concentrations will lead to different clinical performance characteristics.

So while the work published by Kok and her colleagues is excellent, the results may not be exactly transferable over time and geography if other tests are used. And again, selection of tests is really one of the primary rules for professionals in laboratory medicine, and I think that the ways in which the tests are selected, the way they are used right from the very beginning from sample collection through to the end to the reporting of results would be facilitated by involvement of professionals in other field and application of the special expertise in these topics.

Bob Barrett: Doctor, there have been many studies on the use of the FIT in asymptomatic population screening, why do many structured screening programs currently use automated analytical systems that measure fecal hemoglobin concentration?

Dr. Callum Fraser: There are number of existing analytical systems which allow the measurement of fecal hemoglobin, and they have the advantages of most automated systems of higher throughput and enhanced quality, and they eliminate potential visual observer bias.

However, the most telling advantage is that the user can select the cutoff concentration that is used to trigger further investigation, in this case, colonoscopy.

Our recent work has confirmed that fecal hemoglobin concentrations are very dependent on gender and age, and it's possible that different cutoff point concentrations would be appropriate for different groups, just as partitioned reference intervals are used for many analytes -- acid in the clinical laboratory.

Moreover, it's been recently shown that the future risk of colorectal neoplasia becomes higher as the fecal hemoglobin increases, and that has ramifications for decision-making regarding the ideal cutoff concentration to be used.

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Furthermore, there is a growing interest in what are called Risk-Scoring Algorithms for asymptomatic individuals, and for symptomatic patients, and these

risk scores might benefit from the incorporation of a fecal hemoglobin concentration.

And again, professionals in Laboratory Medicine could play important roles in developing clinical applications of calprotectin and hemoglobin concentration measurement because of their undoubted expertise in dealing with all aspects of automated systems.

And this is particularly important I think for colleagues in the US, because currently the FDA has no category concerning quantitative assay of fecal hemoglobin, and this is because I led to believe that there is no evidence based upon American populations, although there is much evidence from Australian and East Asian and European populations, and it might be that if professionals in Laboratory Medicine got interested in these newer fecal tests, then they would be the professionals that could generate the data that would influence the FDA to change their current approach and adopt these newer, better, and really interesting quantitative automated fecal hemoglobin analytical techniques.

Bob Barrett: Well, finally Dr. Fraser, I think it's interesting that you pointed out that the editors of Laboratory Medicine journals recently published an appeal to medical journal editors on the need for a full description of laboratory methods and specimen-handling in clinical study reports.

Dr. Callum Fraser: Yes, it's certainly true that many of the recent publications on newer fecal tests are deficient in this regard. Many of the publications are very interesting, but it is quite difficult to tell what is actually being done, because the descriptions of the methods, the specimen-handling, the imprecision of the analysis and so on are somewhat deficient.

I think that professionals in Laboratory Medicine are the ideal investigators to not only participate in and facilitate their significant research and development required for these newer fecal tests, but they of course could also ensure that the study description and data presentation fulfills the stated requirements by the laboratory medicine journals.

There are many, many opportunities for professionals in Laboratory Medicine, and I really do think that they should be involved in the rapidly expanding field of fecal testing.

Bob Barrett: Dr. Callum Fraser is from the center for Research into Cancer Prevention & Screening in Dundee, Scotland. He has been our guest in this podcast from *'Clinical Chemistry.'*

I'm Bob Barrett, thanks for listening!

Total Duration: 13 Minutes