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Tamara S. Syrek Jensen, J.D.
Acting Director, Coverage and Analysis Group
Centers for Medicare & Medicaid Services
Mail Stop C1-09-06
7500 Security Boulevard
Baltimore, MD 21244

By Online Submission

Re: Proposed Decision Memo for Screening for Colorectal Cancer – Stool DNA Testing (CAG-00440N)

Dear Ms. Syrek Jensen:

The American College of Radiology (ACR), representing more than 35,000 diagnostic radiologists, radiation oncologists, nuclear medicine physicians and medical physicists, appreciates the opportunity to comment on the recent proposed approval of coverage of Cologuard stool DNA test by the Centers for Medicare and Medicaid Services (CMS). We believe that the stool DNA test provides another option in the armamentarium for colorectal cancer (CRC) screening. By encouraging unscreened individuals off the sidelines who may be reluctant to undergo optical colonoscopy, this decision will have a positive impact against this deadly cancer. At the same time, this precedent-setting approval should serve as the new evidence standard for Medicare coverage of colorectal cancer screening tests– including CT colonography (CTC). Initiating coverage of CTC would further improve adherence rates and help to reserve the most invasive and expensive procedure – optical colonoscopy – for those patients who are most likely to require therapy.

Although detection of cancer is obviously an important task, it should be noted that the greatest societal benefit from CRC screening is actually the prevention of cancer through detection of precursor advanced adenomas, as emphasized by the American Cancer Society screening guidelines.\(^1\) Large (≥10 mm) adenomas, which are at increased risk for developing into cancer, represent the target of highest yield in terms of both clinical efficacy and cost effectiveness. In a typical average-risk screening population, 1 in 20 individuals will harbor a large adenoma, whereas only 1 in 500 will have an invasive cancer.
While Cologuard may successfully detect up to 92% of CRC, the sensitivity for large advanced adenomas is only 42%, falling well short in this critical area of cancer prevention. In comparison, CTC is 96% sensitive for cancer detection, but also has a sensitivity of 90% or greater for large adenomas, providing for robust cancer prevention over at least a 5-year time horizon. In fact, CTC detection of advanced adenomas and cancer matches or exceeds that of the more invasive and expensive OC procedure in actual practice.

Specificity and positive predictive value (PPV) data are often overlooked in favor of sensitivity when considering the performance of CRC screening tests, but these may have enormous implication in terms of cost-effectiveness, resource utilization, and patient anxiety. Assuming a typical cancer prevalence of 0.2%, the 87% specificity of Cologuard for cancer detection would translate into a PPV of less than 2%. In comparison, the PPV of CTC for large polyps is well over 90% and is even higher for cancer. To put this into perspective, for a screening population of 10,000 adults, Cologuard would on average detect 18 cancers, miss 2 cancers, and generate about 1,300 false-positive results (i.e., no cancer). The ramifications of a false-positive “genetic” test (which will outnumber true-positive cancer detection over 70 to 1) are currently uncertain in terms of the need for additional testing with associated costs. Additionally, due to false positives and no knowledge about the location of a potential tumor, patients will still need a more specific test available to make the diagnosis. CTC should be one of those tools.

Although the Cologuard stool DNA test showed nearly twice the sensitivity of fecal immunochemical test (FIT) for advanced adenoma detection (42% vs 24%), the CTC sensitivity of 90% or greater is double that of Cologuard and nearly quadruple that of FIT. In addition, Cologuard showed a lower sensitivity for cancer detection in women (83%), as well as lower sensitivity for advanced adenoma detection in women (39% vs. 45%). There is no evidence that CTC has lower performance in women compared with men.

Beyond clinical performance, CTC is more cost-effective than stool DNA and currently recommended to be performed at a 5 year interval compared with every 3 years for stool DNA. Unlike all other CRC screening tests, CTC also provides for extracolonic screening, particularly for abdominal aortic aneurysms (AAA), osteoporosis, and cancers outside the colon. In terms of the low-dose radiation exposure associated with CTC, the health effects in adults are either too small to measure or are non-existent. The benefit to risk ratio comparing the potential lives saved using screening CTC to the potential deaths caused by fatal cancers induced due to the low radiation from the test demonstrated a large benefit to risk ratio in favor of screening CTC.

Of note, on September 9, 2013, the Office of the Commissioner of the U.S. Food and Drug Administration (FDA) convened a joint meeting of the Gastroenterology-Urology Devices Panel and the Radiological Devices Panel to discuss current evidence.
on the risks and benefits of computed tomography colonography (CTC) for the screening of asymptomatic patients for colorectal cancer (CRC). Members of the FDA panel unanimously agreed that, given the risks and benefits identified, CTC should be made available as an option for CRC screening of asymptomatic patients.

In summary, it is encouraging to see that CMS has begun to expand the available Medicare screening options by proposing to include the Cologuard stool DNA test for coverage, despite its current “I” rating from USPSTF. Given the superior performance profile of CTC over stool DNA, including the important benefit of cancer prevention, we anticipate that CMS will agree with the recent FDA conclusion and that it should soon cover CTC as a safe and effective minimally-invasive option as well to further benefit the Medicare population.

Sincerely,

[Signature]

Judy Yee, MD, FACR
Chair, ACR Colon Cancer Committee

References

21. [http://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm366949](http://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm366949).