Effective Health Care

Fecal DNA Testing to Screen for Colorectal Cancer Nomination Summary Document

Results of Topic Selection Process & Next Steps

- Fecal DNA testing to screen for colorectal cancer is not feasible for a full systematic review due to the limited data available at this time; however, it will be considered for a potential technical brief by the Effective Health Care (EHC) Program.
  - To see a description of a technical brief, please go to http://effectivehealthcare.ahrq.gov/index.cfm/what-is-the-effective-health-care-program1/.
  - If this topic is developed into a technical brief, key questions will be drafted and posted on the AHRQ Web site. To sign up for notification when this and other EHC Program topics are posted, please go to http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/.

Topic Description

Nominator: Government agency

Nomination Summary: The nominator questions whether fecal DNA testing can aid in screening for or surveillance of colorectal cancer.

Staff-Generated PICO
Population: Asymptomatic (for colorectal cancer) patients age 50 or older eligible for colorectal cancer screening
Intervention: Fecal DNA testing
Comparator: Other fecal screening tests: guaiac fecal occult blood testing (FOBT), high sensitivity guaiac FOBT testing (Hemoccult Sensa), fecal immunochemical tests (FITs)
Outcome: Increased detection of colorectal cancer, improved survival, reduction in colorectal cancer morbidity and mortality, false-positive rates leading to unnecessary procedures, false-negative rates resulting in a delay of diagnosis and treatment

Key Questions from Nominator:

1. Does the use of fecal DNA screening, in a clinical setting or marketed directly to consumers, for colorectal cancer (CRC) lead to improved health outcomes in the general population ≥50 yrs old, or is it useful in medical decision making? (*overarching question*)
2. What is known about the *analytic validity* of the test(s) used to identify methylated Vimentin gene from fecal DNA samples in cancerous and pre-cancerous lesions, including the analytic sensitivity and specificity, reproducibility, assay robustness (e.g., failure rates, resistance to changes in variables such as sample quality), and other factors?

3. What is the *clinical validity* of fecal DNA screening for CRC, including clinical sensitivity and specificity and positive and negative predictive values, false positives and negatives, and ability to discriminate (area under the Receiver Operating Characteristic curve) in identifying pre-cancerous and cancer tissue?
   a) How well does fecal DNA screening alone identify the presence or absence of pre-cancerous lesions?
   b) How well does fecal DNA screening alone identify the presence or absence of cancerous lesions?
   c) How well does this testing perform in combination with other tests (e.g., does it find the same lesions as fecal occult blood tests (FOBT), or would the detection rate (sens/spec) of FOBT and DNA on the same specimen be higher (better) than either test alone?
   d) How do other genetic and environmental factors (e.g., race/ethnicity, family history, age, smoking, diet, exercise level, other conditions) affect the clinical validity of this test?
4. Does the use of fecal DNA testing lead to improved health outcomes with or in addition to use of standard colorectal cancer screening, diagnosis and management practices? (*clinical utility*)
   a) Does fecal DNA screening influence decisions on whether to proceed to colonoscopy?
   b) Are treatment or management decisions for either pre-cancerous or cancerous lesions influenced by fecal DNA screening?
   c) In what ways could the use of fecal DNA screening impact clinical outcomes (e.g., morbidity / mortality)?
   d) What is known about the cost-effectiveness of using fecal DNA screening to guide future clinical management decisions?
   e) How do other genetic and environmental factors (e.g., race/ethnicity, family history, age, smoking, diet, exercise level, other conditions) affect outcomes from detection and clinical management?
5. What are the potential harms of testing and subsequent diagnostic and management options associated with fecal DNA screening for CRC diagnosis and management decisions?
   a) Errors in test assay leading to inaccurate results.
   b) Potential for clinically significant CRC to be missed in individuals presumed to be at “low risk” based on fecal DNA screening (false-negatives).
   c) Potential for unnecessary and costly screening and management of individuals presumed to be at “high risk” of clinically significant CRC as a result of fecal DNA screening (false positives or over-diagnosis).
   d) Potential for morbidity related to altered screening/management (e.g., colonoscopy, sigmoidoscopy) on the basis of fecal DNA screening.
   e) Potential for social, economic, or psychological harm associated with use of fecal DNA screening for CRC diagnosis and management.
   f) Are there differences in performance between fecal DNA testing marketed directly to the public and testing in a clinical setting?

Considerations

- The topic meets EHC Program appropriateness and importance criteria. (For more information, see http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/.)

- Among all cancer, CRC ranks third in incidence and second in cause of cancer death for both men and women. Some projections state that CRC mortality in the US will begin to rise given the aging population. It has been suggested that one potential measure to counteract this potential rise in mortality may be the identification and implementation of more effective and user-friendly screening options. Fecal DNA testing may offer a non-invasive, home-based technique for CRC screening.

- There is insufficient evidence to complete a systematic review that would give any insight into the current state of fecal DNA testing because there is very little data addressing the marker measured in the only currently commercially available fecal DNA test, Colosure. However, a technical brief may be considered to address some of the issues related to regulation and methodology surrounding this topic. There are methodological questions regarding the point at which previous evidence is no longer applicable to a new test that has gone through iterations of technological or marker changes.