

NACB Laboratory Medicine Practice Guidelines Evidence-Based Practice for POCT

Occult Blood Testing

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Occult Blood Testing

- Fecal occult blood
 - Screening for colorectal neoplasia
 - Upper gastrointestinal lesions
 - Preferred methodology
- Gastric occult blood



Question One: Does annual or biennial guaiac-based fecal occult blood testing in an average risk asymptomatic population over 50 years old reduce mortality from colorectal cancer compared to no FOBT screening?



Recommendation One:

- We strongly recommend that clinicians routinely provide guaiac-based FOBT for asymptomatic individuals older than 50 years at least biennially to reduce mortality from colorectal cancer (CRC).
- Grade of Evidence: I – randomized controlled trials and case-control studies



CRC Mortality

- CRC is the second leading cause of cancer death in the United States with a lifetime incidence of about 6%, which justifies mass screening.
- Screening can change prognosis and outcome in patients with early disease.
- FOBT detects blood loss in stool arising from colorectal neoplasms.



Minnesota Colon Cancer Control Study

- Enrolled 46,551 volunteers aged 50-80 years randomized to annual FOBT, biennial FOBT or control.
- Dietary restrictions were in place. The hemoccult II method with rehydration was employed.
- 33% reduction in mortality in the annual group after 13 years
- 21% reduction in mortality in the biennial group after 18 years



Nottingham, United Kingdom

- 152,850 people aged 45-74 who lived in Nottingham between 1981 and 1991 were randomly assigned to biennial FOBT or no screening
- No dietary restrictions were in place and the hemocult II specimens were not rehydrated
- A 15% reduction in CRC mortality was found in the screened group with a median follow up of 7.8 years



Funen, Denmark

- 140,000 people aged 45-75 who lived in Funen were allocated to biennial FOBT or no screening
- The hemocult II assay was employed with dietary restrictions but without rehydration
- Biennial screening for 10 years decreased CRC mortality by 18%



Comparison of Three RCTs

- Minnesota:
 - Annual - 33% reduction at 13 years
 - Biennial – 21% reduction at 18 years
- UK:
 - Biennial - 15% reduction at 7.8 years
- Denmark:
 - Biennial – 18% reduction at 10 years
- Study population
- Dietary requirements
- Preparation of samples
- Frequency of testing
- Length of follow up



Other Studies on CRC Mortality

- Burgundy, France – CRC mortality 33% lower in population with at least one FOBT
- O’Leary et al – Reduction in CRC deaths with colonoscopy (31%), annual FOBT (29%), flex sig (21%), biennial FOBT (19%)
- Case control studies – 25-80% lower mortality from CRC from annual or biennial FOBT
- Sweden and China – no reduction in mortality



FOBT and Sigmoidoscopy

- Rasmussen et al - FOBT biennially for 16 years detected more CRC than a single sigmoidoscopy.
- Lieberman et al – FOBT detected 5% of CRC that were not seen by flex sig
- Winawer et al – FOBT and flex sig have higher survival than flex sig alone



Central Laboratory versus POCT

- Specimens obtained at home or in association with digital rectal examination.
- POCT cannot be recommended as a preferred method based on medical outcomes.
- POCT more convenient, but results may not reach medical record (35% physician office tests lost).



Question Two: Does annual or biennial guaiac-based fecal occult blood testing in an asymptomatic population over 50 years old significantly decrease the incidence of colorectal cancer?



Recommendation Two:

- We cannot currently recommend for or against the use of guaiac-based fecal occult blood testing to reduce the incidence of colorectal cancer.
- Grade of Evidence: I – randomized control trials and case control studies



Incidence of CRC

- Some experts have postulated that screening for CRC with FOBT will decrease the incidence of cancer by removing precursor lesions.
- However, small benign adenomatous polyps are less likely to bleed and may not be detected by screening.



Conflicting Conclusions

	Incidence CRC in FOBT	Years of follow-up
Minnesota	Decreased	13 and 18
United Kingdom	Increased	7.8
Denmark	No change	10
France	No change	11
Sweden	Decreased or no change	2 and 7

Question Three: Which fecal occult blood testing method, chemical-based, heme-porphyrin assay or immunological, is the most accurate (sensitivity, specificity, positive predictive value) in an outpatient setting for the detection of CRC in asymptomatic individuals over 50 years old?



Recommendation Three:

- We cannot currently recommend an ideal fecal occult blood method for the detection of colorectal cancer based on the current methodology or available literature.
- Grade of Evidence: II – prospective comparative trials, descriptive studies and opinion



Fecal Occult Blood Methods

- Guaiac-based methods – detect pseudoperoxidase activity in hemoglobin
- Immunological methods – reverse passive hemagglutination and detect intact hemoglobin and globin
- Heme-porphyrin methods – detect hemoglobin breakdown product, porphyrin



Method Comparison in Screened Patients

- 8104 asymptomatic patients scheduled for routine physicals had both guaiac and immunological methods.
- HOS had highest sensitivity (79.4%) for the detection of CRC and HO had highest specificity (97.7%)

Comparison of Methods

	Sensitivity	Specificity	PPV
HO (n=9)	37.1-90.0%	94.1-99.0%	3.7-21.0%
HOS (n=5)	50-85.3%	86.7-95.5%	2.5-14.0%
HSel (n=3)	68.8-86.0%	92.0-98.0%	3.8-50.0%
HO+HSel	65.6%	97.3%	9.0%

**Question Four: Is highly sensitive
guaiac-based FOBT useful in
symptomatic patients to
differentiate bleeding due to upper
GI lesions (including
gastroesophageal cancer) from
bleeding due to lower GI lesions?**



Recommendation Four:

- We cannot currently recommend FOBT to differentiate upper from lower sources of gastrointestinal bleeding.
- Grade of Evidence: II – case control and cohort studies



Bleeding from GI Lesions

- FOBT was designed to detect lower gastrointestinal sources of bleeding by monitoring intact hemoglobin.
- Blood from the upper GI tract may undergo degradation by intestinal enzymes leading to false negative results.
- More sensitive methods can detect bleeding from upper GI sources, but no evidence suggests that the source can be determined.



Source of GI Bleeding

- Nakama et al – Immunological FOBT is insensitive for gastric cancer and upper GI disease
- Rockey et al – guaiac-based FOBT detects both upper and lower GI lesions
- Harewood et al and Ahlquist et al – Suggest heme-porphyrin method more sensitive for upper GI bleeding
- Rockey et al – Combination of guaiac-based and immunological may differentiate source



Question Five: Can gastroccult testing of gastric fluid from a nasogastric tube be used to detect gastrointestinal bleeding in high-risk intensive care unit patients receiving antacid prophylaxis?



Recommendation Five:

- We cannot currently recommend for or against the use of gastroccult to detect gastric bleeding in intensive care unit patients receiving antacid prophylaxis.
- Grade of Evidence: III – small study, clinical evidence



Gastroccult Tests

- FOBT should not be used to measure occult blood in gastric fluid because of interferences from low pH, certain medications and metal ions.
- The presence of occult blood in gastric fluid can be useful to detect stress ulcer syndrome, so specific gastroccult tests are utilized.

Bleeding in ICU Patients

- A small study with 41 patients showed that 13/14 patients with positive gastroccult tests had a source of upper GI bleeding as seen by upper endoscopy.
- However, patients with negative gastroccult tests did not undergo upper endoscopy.

Clinical Utility of Occult Blood

- FOBT reduces mortality from CRC and should be performed.
- No definitive guidelines for preferred methodologies, FOBT in upper gastrointestinal lesions or gastroccult testing can be made.



Future Directions

- FOBT decreases mortality, but does it affect the incidence of CRC?
- Role of occult blood in management of CRC
- Role of occult blood in inpatients
- Use of occult blood on non-GI specimens



Future Directions

- Preferred methodology for FOBT including cost analysis
- POCT versus central laboratory
- Utility of FOBT in upper gastrointestinal lesions
- Utility of Gastrocult
- DNA based fecal occult blood testing



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