

## EDITORIAL

# Optimizing the Quality of the Colorectal Cancer Screening Continuum: A Call to Action

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Worldwide, colorectal cancer (CRC) is the third most common cancer among men and second most common cancer among women (1). Screening can reduce CRC incidence and mortality (2) and has led to both opportunistic and organized efforts to promote uptake worldwide. While colonoscopy is the most commonly performed screening test in the United States, internationally, noninvasive tests such as the fecal immunochemical test (FIT) are commonly implemented. Further, noninvasive screening and alternatives less invasive than colonoscopy are increasingly being made available in the United States. Indeed, as part of the latest US Preventive Services Task Force Guidelines, screening for individuals age 50 to 75 years was given a “Grade A” recommendation, with potential options of colonoscopy every 10 years, FIT annually, guaiac fecal occult blood testing annually, FIT–DNA every one to three years, computed tomographic colonography every five years, and sigmoidoscopy every five years (or every 10 years with annual FIT) (2). Having multiple options may increase screening rates, based on research showing that noninvasive tests may be more acceptable to some (3–5), as well as practical considerations, such as ability to offer screening outside locations where colonoscopy is performed. Nonetheless, realizing full potential of any alternative other than colonoscopy requires repeat screening for individuals with normal tests and high-quality complete diagnostic follow-up colonoscopy for individuals with abnormal results (6).

High-quality complete diagnostic follow-up for individuals with abnormal results is of particular concern because by virtue of having an abnormal test result these individuals are at increased risk for prevalent CRC and significant polyps requiring resection. For example, between one in 10 and one in 30 individuals with an abnormal FIT have CRC, and between one in three and one in seven individuals have advanced neoplasia (CRC or advanced adenoma) (7,8,17). Failure to complete diagnostic colonoscopy and detect all lesions results in missed opportunities for early detection and prevention. Prior work has shown that

complete diagnostic colonoscopy follow-up rates after abnormal guaiac FOBT and FIT may be as low as 22% (9–12). Further, a recent modeling study has suggested that delay in follow-up results in higher CRC stage at presentation, incidence, and mortality; the relative reduction in life-years gained associated with screening was estimated to be 10% lower for diagnostic colonoscopy within two weeks vs 12 months after a positive FIT (13).

In this issue of the Journal, Lee and colleagues emphasize the consequences of failure to follow-up by demonstrating, for the first time, that failure to complete high-quality follow-up leads to increased CRC mortality (14). They utilized data from a national screening program that invited residents age 50 to 69 years to biennial FIT screening, specifically focusing on 59 389 individuals who had an abnormal FIT result over a five-year period. CRC incidence and mortality were compared for individuals exposed ( $n = 41\,995/59\,389$ , 70.7%) vs unexposed (10 778/59 389, 18.2%) to diagnostic colonoscopy. Further, results were evaluated taking into account baseline hemoglobin concentration measured by FIT, as well as colonoscopy quality.

Several key findings are of note. First, risk for CRC mortality increased 1.6-fold for individuals unexposed to colonoscopy. Second, a quality of colonoscopy metric—exam complete to the cecum—was critically important. On multivariable analyses, risk for CRC death increased 2.31-fold for individuals unexposed to colonoscopy vs exposed to colonoscopy complete to cecum and increased 1.65-fold for individuals exposed to incomplete colonoscopy vs exposed to colonoscopy complete to cecum. Further, a statistically significant reduction of risk for proximal, in addition to distal, CRC mortality was seen only among individuals exposed to colonoscopy complete to cecum. Third, risk for CRC mortality among individuals unexposed vs exposed to colonoscopy varied by hemoglobin concentration of the abnormal FIT, such that increasing concentration was associated with increasing mortality.

**Table 1.** A call to action: Recommended priorities for improving complete diagnostic follow-up after abnormal colorectal cancer screening tests

Research	Fund multilevel (ie, health system, provider, patient) research on: Barriers to completing diagnostic follow-up after abnormal colorectal cancer screening tests. Solutions for completing diagnostic follow-up after abnormal colorectal cancer screening tests. Implementation processes for completing diagnostic follow-up after abnormal colorectal cancer screening tests.
Policy	In the United States, eliminate cost sharing for diagnostic colonoscopy after an abnormal screening test. In the United States, a quality metric measuring rate of diagnostic colonoscopy could be implemented nationally. (ie, the Healthcare Effectiveness Data and Information Set, the Universal Data Set for Federally Qualified Community Health Centers). Worldwide, make rate of complete diagnostic follow-up a quality metric.
Practice	Redouble efforts to ensure high-quality colonoscopy, especially among participants of organized colorectal cancer screening programs. Monitor and address low follow-up rates.

Strengths of the study include use of a large sample size and multiple strategies to adjust for potential confounders and lead time bias. Limitations include potential for residual confounding by unmeasured factors, no information on reasons for follow-up failures, and low cecal intubation rates among individuals exposed to colonoscopy (79.3%). The suboptimal rate of cecal intubation raises questions about the training of colonoscopists involved with the program and might explain in part why CRC incidence continued to rise among individuals who were exposed to colonoscopy compared with those unexposed, even taking into account screen-detected (prevalent) cancers.

Nonetheless, important conclusions can be drawn from this study. Failure to follow-up through the entire screening continuum results in increased cancer mortality. Quality is critical to ensuring population effectiveness of colon cancer screening. Additionally, by emphasizing increased risk among individuals with higher stool sample hemoglobin concentrations, providers might be able to leverage quantitative FIT results to nudge these individuals to complete diagnostic follow-up.

It is intuitive that failure to complete high-quality colonoscopy after an abnormal FIT will lead to adverse outcomes. And yet, failures often occur with dire consequences, as shown by Lee and colleagues. This work should serve as a catalyst for patients, providers, researchers, and policy-makers to redouble their commitment to ensuring high-quality follow-up, particularly given the growing available list of options for screening other than colonoscopy. Specific to the area of complete diagnostic follow-up, we offer recommendations for research, policy, and practice priorities that should be considered (Table 1). Funding for research on multilevel (ie, health system, provider, patient) barriers, solutions, and related implementation processes (eg, PRISM) should be increased. Policy wise, cost sharing (in the United States) for diagnostic colonoscopy after an abnormal screening test should be eliminated and the rate of complete diagnostic follow-up should be formalized as a quality metric, as suggested by European guidelines for quality assurance in colorectal cancer screening, and the US Multi-Society Task Force on Colorectal Cancer (16). In practice, we should increase efforts to ensure high-quality colonoscopy, as well as monitor and address low follow-up rates. The now-proven substantially increased mortality for failure to follow-up should serve as a call to action to optimize the quality of CRC screening across the screening continuum.

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## References

- American Cancer Society. *Global Cancer Facts & Figures*. 3rd ed. Atlanta, GA: American Cancer Society; 2015.
- Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. *JAMA*. 2016;315(23):2564–2575.
- Inadomi JM, Vijan S, Janz NK, et al. Adherence to colorectal cancer screening: A randomized clinical trial of competing strategies. *Arch Intern Med*. 2012; 172(7):575–582.
- Gupta S, Halm EA, Rockey DC, et al. Comparative effectiveness of fecal immunochemical test outreach, colonoscopy outreach, and usual care for boosting colorectal cancer screening among the underserved: A randomized clinical trial. *JAMA Intern Med*. 2013;173(18):1725–1732.
- Singal AG, Gupta S, Tiro JA, et al. Outreach invitations for FIT and colonoscopy improve colorectal cancer screening rates: A randomized controlled trial in a safety-net health system. *Cancer*. 2016;122(3):456–463.
- Tiro JA, Kaminen A, Levin TR, et al. The colorectal cancer screening process in community settings: A conceptual model for the population-based research optimizing screening through personalized regimens consortium. *Cancer Epidemiol Biomarkers Prev*. 2014;23(7):1147–1158.
- Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening. *N Engl J Med*. 2014;370(14):1287–1297.
- Jensen CD, Corley DA, Quinn VP, et al. Fecal immunochemical test program performance over 4 rounds of annual screening: A retrospective cohort study. *Ann Intern Med*. 2016;164(7):456–463.
- Jimbo M, Myers RE, Meyer B, et al. Reasons patients with a positive fecal occult blood test result do not undergo complete diagnostic evaluation. *Ann Fam Med*. 2009;7(1):11–16.
- Humphrey LL, Shannon J, Partin MR, et al. Improving the follow-up of positive hemoccult screening tests: An electronic intervention. *J Gen Intern Med*. 2011;26(7):691–697.

11. Rao SK, Schilling TF, Sequist TD. Challenges in the management of positive fecal occult blood tests. *J Gen Intern Med.* 2009;24(3):356–360.
12. Chubak J, Garcia MP, Burnett-Hartman AN, et al. Time to colonoscopy after positive fecal blood test in four U.S. health care systems. *Cancer Epidemiol Biomarkers Prev.* 2016;25(2):344–350.
13. Meester RG, Zauber AG, Doubeni CA, et al. Consequences of increasing time to colonoscopy examination after positive result from fecal colorectal cancer screening test. *Clin Gastroenterol Hepatol.* 2016;14(10):1445–1451.
14. Lee Y, Chen SL, Yen AM, et al. Colorectal cancer mortality of colonoscopy noncompliers with gradient fecal hemoglobin concentration. *J Natl Cancer Inst.* 2016;109(5):doi: 10.1093/jnci/djw269.
15. Feldstein AC, Glasgow RE. A practical, robust implementation and sustainability model (PRISM) for integrating research findings into practice. *Jt Comm J Qual Patient Saf.* 2008;34(4):228–243.
16. von Karsa L, Patnick J, Segnan N. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First edition—executive summary. *Endoscopy.* 2012;44(S 03):SE1–SE8.
17. Robertson DJ, Lee JK, Boland CR, Dominitz JA, Giardiello FM, Johnson DA, Kaltenbach T, Lieberman D, Levin TR, Rex DK. Recommendations on Fecal Immunochemical Testing to Screen for Colorectal Neoplasia: A Consensus Statement by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology.* 2016 Oct 18. pii: S0016-5085(16)35025-9. doi: 10.1053/j.gastro.2016.08.053. PubMed PMID: 27769517