



COLONPREV Trial of FIT vs Colonoscopy



Timothy Yen, MD

Assistant Professor of Medicine, Division of Gastroenterology, Loma Linda University School of Medicine, Loma Linda, CA

Timothy Yen, MD
Associate Editor

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This summary reviews Castells A, Quintero E, Bujanda L, et al. COLONPREV study investigators. Effect of invitation to colonoscopy versus faecal immunochemical test screening on colorectal cancer mortality (COLONPREV): a pragmatic, randomised, controlled, non-inferiority trial. *Lancet*. 2025 Apr 12;405(10486):1231-1239.

Correspondence to Timothy Yen, MD, Associate Editor. Email: EBGI@gi.org

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STRUCTURED ABSTRACT

Question: Is an invitation to colorectal cancer (CRC) screening using fecal immunochemical test (FIT) non-inferior to colonoscopy?

Design: Pragmatic randomized controlled non-inferiority trial of biennial FIT compared to 1-time colonoscopy.

Setting: Fifteen tertiary hospitals in Spain.

Patients: Eligible participants were aged between 50-69 year old persons at average risk for CRC with no recent screening (FIT within 2 years, sigmoidoscopy/colonoscopy within 5 years). Excluded personal history of CRC/adenoma/irritable bowel disease, family history of CRC, severe comorbidity, or prior colectomy.

Intervention: Invitation letter to schedule either 1-time colonoscopy or biennial

FIT with educational material, with reminder letters at 3 and 6 months if no response. Crossover was allowed.

Outcomes: Primary outcome was CRC-related mortality at 15 years. Secondary outcomes included incident CRC rate at 10 or 15 years, major adverse events, yield for pre-cancerous polyps, cost-effectiveness, covariate factors for participation.

Data Analysis: The primary analysis assessed intention to screen (original assigned group) population, while the secondary analysis included a per-protocol analysis (only those who completed originally assigned screening test). Risks calculated with risk ratios (RRs) and odds ratios (ORs). Inverse probability weighting for age, gender, and institution for as-screened and per-protocol analysis (a form of propensity score weighting in causal inference).

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Results: Overall, 26,322 eligible persons were invited to colonoscopy, and 26,719 eligible persons were invited for FIT. Among those invited to colonoscopy, 31.8% completed some sort of screening, while 39.9% completed some sort of screening in the FIT group (RR 0.79 [95% CI 0.77-0.82]). Among those who completed FIT, 53.0% participated in > 80% of offered tests.

In the intention to treat population, CRC mortality was 0.22% for colonoscopy and 0.24% for FIT (RR 0.92 [95% CI 0.64-1.32]). CRC rate at 10 years was 1.13% for colonoscopy versus 1.22% for FIT (RR 0.92 [95% CI 0.79-1.08]). Advanced colorectal polyps were found in 3.2% and 2.4% of colonoscopy and FIT groups, respectively (RR 1.39 [95% CI 1.25-1.54]). Major complications rate was 0.3% (no significant between group difference). Among 15,818 who completed their invited test in the per-protocol population, there was a significantly lower incident CRC rate of 0.85% vs 1.28% (RR 0.67 [95% CI 0.47-0.95]) and CRC-related mortality of 0.02% vs 0.11% (RR 0.17 [95% CI 0.02-0.64]) in colonoscopy versus FIT.

COMMENTARY

Why Is This Important?

Prior to this study, there was no substantial randomized controlled trial (RCT) data comparing the “real-world” use of the 2 most common screening modalities. Although colonoscopy is commonly considered the “gold-standard”, it is costly, has a higher risk than non-invasive tests, and inherently has a lower participation rate than FIT due to its need for substantial healthcare resources and patient participation with bowel preparation etc.¹ Similar to the NordICC pragmatic RCT,² this was a study assessing the uptake of invitation to screening, rather than a study aimed at assessing efficacy of screening modalities. While the NordICC study compared colonoscopy to no-invitation, COLONPREV compared invitation to FIT against an invitation to colonoscopy.

Key Study Findings

COLONPREV found that an invitation to FIT was no different in preventing death from CRC (or CRC diagnoses) than an invitation to colonoscopy. This affirms the use of FIT-based organized screening programs in select healthcare networks/institutions around the United States, particularly when participation and/or cost is a major concern.

Caution

The authors clearly point out that

participation was 32% for colonoscopy invitations and 40% for FIT invitations, which is quite a bit lower than the 80% screening goal of the National Colorectal Cancer Roundtable.³ This may be related to the fact that invitees were randomized to colonoscopy/FIT before offering consent for screening, in contrast to including only persons that agreed to participate in screening for the study. This also highlights the importance of quality improvement in an organized screening program, such that those leading the program can monitor the impact of outreach efforts (such as patient navigation, etc.) in reaching a desired screening uptake goal. Also, the FIT test was calibrated to different hemoglobin concentrations during the first versus subsequent rounds of screening. This is known to impact the yield of FIT, and is commonly done in other countries based on screening resources and population prevalence, but is not as commonly done in the United States.⁴

Finally, the per-protocol analysis favoring colonoscopy over FIT are encouraging but must be interpreted with caution, as those willing to respond to a colonoscopy invitation in a country where colonoscopy is not as commonplace as the United State are likely different from other participants for a variety of reasons that cannot be controlled.

My Practice

Most of my practice, liked much of the United States, is in an opportunistic screening setting in which CRC screening is done through shared decision-making between the patient and provider. In this instance, this pragmatic RCT does not change my discussion with each patient that whether colonoscopy is truly the “gold-standard” for CRC prevention is still an open question yet to be answered. That being said, I do spend some of my clinical time at a safety-net and federally qualified health center, in which an organized CRC screening approach using FIT is a very reasonable tactic operationally for patient care.

For Future Research

The CONFIRM and SCREESCO studies are underway in the United States and Sweden, respectively, which will hopefully answer the question of how much FIT reduces CRC-related mortality and incident CRC rate compared to colonoscopy.^{5, 6} CONFIRM in particular will more likely represent practice patterns in the US, where uptake of screening is generally high, including colonoscopy which is the test of choice for many people.

Conflict of Interest

No conflicts of interest.

Abbreviations

CRC, colorectal cancer; FIT, fecal immunochemical test; OR, odds ratios; RCT, randomized controlled trials; RR, risk ratios.

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