Optimizing the Quality of Colorectal Cancer Screening Worldwide

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Abstract

Screening, followed by colonoscopic polypectomy (or surgery for malignant lesions), prevents incident colorectal cancer and mortality. However, there are variations in effective application of nearly every aspect of the screening process. Screening is a multistep process, and failure in any of single step could result in unnecessary morbidity and mortality. Awareness of variations in operator- and system-dependent performance has led to detailed, comprehensive recommendations in the United States and Europe on how colonoscopy screening should be performed and measured. Likewise, guidance has been provided on quality assurance for non-primary colonoscopy-based screening programs, including strategies to maximize adherence. Quality improvement is now a validated science, and there is clear evidence that higher quality prevents incident cancer and cancer death. Quality must be addressed at the levels of the system, provider, and individuals, to maximize the benefits of screening for any population. We review the important aspects of measuring and improving the quality of colorectal cancer screening.

Keywords: colonoscopy; fecal immunochemical test; Colorectal cancer; colorectal polyp

Evidence-based quality assurance guidelines that cover the entire screening process and provide a list of key performance indicators and standards have been published by the European Union (EU) commission.[1] Comprehensive documents that addressed colonoscopy quality were issued by the United States (US) Multi Society Task Force (MSTF) [2], by a special task force on quality [3, 4], and recently by the European Society for Gastrointestinal Endoscopy (ESGE). [5] Quality indicators for fecal immunochemical test (FIT) performance and follow up were also issued.[6] A detailed evaluation of colonoscopy quality parameters is not feasible; we propose priorities for quality measurement in colorectal cancer (CRC) prevention and discuss proven methods to optimize these quality indicators.

Several tests are available for CRC screening, but the most common options are FIT, colonoscopy, and sigmoidoscopy. Figure 1 lists proposed priority CRC screening quality measures for a healthcare delivery system. These measures relate to CRC screening adherence, colonoscopy (the primary screening method and preferred test for diagnostic analysis and post-polypectomy surveillance), and FIT. We discuss measures to evaluate CRC screening quality and methods to optimize these quality indicators.

Maximizing Adherence to Screening and Diagnostic Colonoscopy Evaluations

Screening programs have reduced CRC incidence, mortality, and surgery at the population level,[7-9] but screening rates remain low in several countries. Screening rates are consistently low, independent of ethnicity and educational level, among the uninsured, individuals of low socioeconomic status, and individuals with limited access to primary care.[10-13] Non-adherence to recommended protocols is an important attributable factor of CRC burden[13] and the social gradient in screening uptake might increase disparities in mortality[14]. EU guidelines proposed acceptable and desirable adherence rates to CRC screening at greater than 45% and greater than 65%, respectively, and compliance with colonoscopy referral among persons undergoing

screening with a positive result from a primary screening test at above 90%.[1] The National CRC Round Table[15] proposed a 80% adherence target for primary screening and the US Multi-Society Task Force on CRC US set a target of 80% compliance with colonoscopy referral in patients with a positive result from a FIT [6].

CRC awareness

Awareness of cancer, as well as of screening modalities, is an important factor in the decision to participate in CRC screening, in that it affects beliefs, attitudes, and motivation.[16] Addressing structural barriers at the health system and organization level might be required to increase participation rates, once awareness has been raised. Analyses of barriers to screening[16] found a link between awareness and health system factors, such as public education and primary care physician efforts, and indicated that although individual knowledge and perceptions drive intentions to participate, issues related to practice organization are important to translate intention into action.[17]

Therefore, the health system, and the context within which it is embedded, affects provider delivery and patient use of screening [18, 19] and compliance with cancer screening recommendations requires multifaceted interactions among patients, providers, and health organizations. Interventions that target multiple levels of care and consider factors outside the individual control of clinicians and integrate different strategies could be the most effective approach to increase uptake of CRC screening.

System-level interventions

Evidence for higher uptake rates and reduced coverage disparities regardless of socio-economic status indicates that population-based organized programs, delivered at the national

level or by healthcare systems, can integrate interventions that address health system and individual-level barriers and help establish an organizational framework that gives each eligible subject a chance to participate.[20] Organized programs produce higher rates of uptake, screening, and follow-up assessment than opportunistic screening. In the US, an organized program based on FIT screening achieved 83% adherence in a large healthcare system, [20] whereas national measures of screening, which largely reflect the opportunistic setting in the US, have been stagnant in recent years at approximately 60%.[21]

Higher screening rates and reduced coverage disparities by socioeconomic status have been reported in the EU, in areas where organized programs had been introduced, compared with areas where only opportunistic screening was available.[20] System-level measures adopted within organized programs are establishing a suitable context to maximize the effects of interventions, targeting provider- and individual-related factors by reducing external barriers to the implementation of their decision to engage in screening.

Financial barriers

The type of insurance coverage and the cost of the test affect rates of screening and subjects' preferences for specific tests. The introduction of free programs (funded by national or regional governments) and mandatory insurance coverage or elimination of cost sharing for screening and assessment tests, have increased the use of screening. Eliminating these economic barriers resulted in substantial increase (ranging from 7% to 50%, depending on background rates of use) in population coverage, in particular among the low-income, least-educated subjects [22-25].

Active invitations

Mailing personal invitation letters, at the recommended intervals, to all eligible subjects, or sending electronic invitations, is a widely adopted, highly effective, organizational measure to engage the target population. This approach is associated with screening uptake, irrespective of the test adopted (Figure 2).[26] Cost-effectiveness is generally lower for client-directed interventions, such as face to face counseling, telephone reminders, or navigators, than for strategies that involve mail or electronic invitations or alerts. Lower cost-effectiveness reduces the sustainability and feasibility of those interventions in the context of large population-based programs.[27, 28] However, direct invitation by primary care physician (PCP) is still a valid option, especially in settings with inadequate information technology infrastructure or limited use of mail or electronic reminders. The combined FIT and multi target stool DNA test is less cost effective than annual FIT, but use of a telephone based navigation system resulted in 71% test completion in a Medicare population.[29]

Type of screening test

Multiple tests have been validated for CRC screening. These differ in effectiveness, acceptability, safety, and cost profile. Dislike of specific tests appears to be a barrier to CRC screening, so choice of the screening method provides an additional system-level factor that affects uptake. Introduction of the FIT was associated with an absolute increase in participation (increases ranging from 5% to 16%) in population-based programs [27], compared with the guaiac fecal occult blood test, likely related to the simpler testing procedure. Participation tends to be lower for invasive, endoscopic evaluations (absolute decrease in participation in a single round ranging from 2% to 30% for the FIT vs computed tomography colonography [CTC] and from 5% to 36% for FIT vs colonoscopy).[27,30] Colonoscopy and sigmoidoscopy have the advantage that they bring a patient into compliance for long time

(more than 10—15 years when no neoplasia is detected), whereas adherence to repeated guaiac fecal occult blood tests or FITs decrease rapidly.[31]

There are also sex differences in uptake of FIT vs endoscopy. Women have higher rates of participation when invited for a FIT (absolute difference between women vs men ranges from 2% to 10%), whereas men have higher rates of response to invitations for endoscopy (absolute difference for men vs women ranges from 2% to 5%). Screening uptake did not increase when individuals were offered a choice of tests, compared with an invitation for a specific test.[27]

Individuals

High-quality evidence indicates that adoption of strategies to facilitate access to a recommended test,[27] or reinforcement of motivation of subjects to attend,[32] can increase subjects' response to an invitation and affect individual-related barriers (Figure 2). Although studies assessing the specific contribution to screening uptake after distribution of information leaflets, in addition to an invitation letter, had inconsistent results[33], the provision of educational material supports efforts aimed to promote informed participation. [34, 35] Leaflets can also provide information that is tailored to address barriers experienced by specific sub-groups.

Information material, designed to overcome language, literacy, or cultural barriers and developed based on theoretical models of behavioral change, mailed together with the invitation letter, as well as increased reminders, can increase overall uptake [36, 37] at a low cost. The observed absolute increase in uptake varied, ranging from 1% to 20%. In the study reporting the lowest effect, the intervention showed, however, a stronger effect in most

deprived groups, indicating that it might reduce the socioeconomic gradient in screening participation.[36]

Primary care physicians

Reports of PCPs demonstrated that provider's involvement can improve compliance to primary screening invitations and recommendations for diagnostic evaluation[38, 39], particularly for less-educated, or older people, who are less likely to use written information material.[40] Changes in practice organization that aim to reduce the effects of commonly reported barriers related to lack of time and resources for preventive care are effective measures to maximize the effects of providers' efforts (Figure 2).

Educational interventions that aim to foster knowledge of program effectiveness, of the accuracy of the adopted method, and of the recommended screening procedures,[41] as well as those that provide regular feedback about individual PCPs' screening rates and their relative performance,[42] can reinforce providers' commitment to promotion of screening. Increasingly, practitioners are evaluated by their success in reaching adherence targets in the opportunistic setting, using available data from electronic medical records.

Diagnostic colonoscopy after a positive result from a screening test

Although adherence to primary screening is an important determinant of the magnitude of the health effects of screening at the population level, the expected reduction of CRC burden can be only achieved if subjects with abnormal findings receive timely and appropriate follow up and treatment, if needed. However, although targets of at least 80% have been proposed, many persons who have positive results from screening tests (ranging from 8% to 34%, according to several reports) do not undergo the recommended assessment.[13] Timeliness of

the follow-up examination is also important; 1 study showed that delays of greater than 10 months for colonoscopies (compared with 8–30 days) were associated with a 2-fold increase in advanced stage cancer.[43]

The lack of an established organizational infrastructure allowing for monitoring compliance with the recommended assessments, as well as difficulties in sharing data between clinical and screening services, have been reported as specific barriers to effective follow up of persons with positive results from screening.[44] Economic (cost of the test and/or co-payment), organizational (limited endoscopic resources), and cultural (fear of the test and of cancer, fatalistic attitude) barriers, already documented for primary screening[44] contribute to limit the response to colonoscopy referral following a positive results from screening tests.

System-level interventions, including elimination of financial barriers for further investigations, and implementation of an active recall and fail-safe system, ensuring systematic assessment of all non-responders, were associated with an increase in the proportion of screen-positive individuals who received timely follow up.[45] Providing tailored written information material, offering access to telephone or face to face counselling, addressing fears related to abnormal findings, patient-level navigation, and provider reminders increased compliance with colonoscopy referral, maintaining a high cost-effectiveness ratio also within organized programs.[45]

Optimizing Colonoscopy Quality

Colonoscopy is recommended as a primary screening method and it is a preferred diagnostic method for persons with positive results from other methods, as well as for surveillance following polypectomy. For this reason, quality of colonoscopy is crucial to achieve the

expected benefit of screening, independent of the strategy adopted for primary screening. Therefore, it is important to discuss each key performance indicator of colonoscopy in detail.

How to optimize bowel preparation for colonoscopy?

The effects of inadequate bowel preparations on colonoscopy resources and costs are substantial [46]. In addition, bowel preparation interacts with detection targets. Inadequate preparation therefore impairs detection and creates inefficiency [47, 48]. In the US, the MSTF recommended that at least 85% of outpatient colonoscopies achieve adequate preparation [49], and the ESGE recommended 90% [50]. Adequate preparation is best defined using clinical grading scales such as the Boston Bowel Preparation Scale, in which a score of 2 or more in each of 3 colonic segments is considered adequate[51]. Excellent and good preparations are also widely accepted as adequate [49]; the MSTF states that a preparation that allowed detection of lesions larger than 5 mm is considered adequate [49]. In scoring rates of adequate preparation, the recommended colonoscopy follow-up interval must meet prevailing surveillance or screening recommendations to be scored in compliance [49].

Over the last decade, the quality of bowel preparation for colonoscopy has greatly improved. Development and widespread implementation of validated bowel preparation scales increased our understanding of variations in quality, set performance standards, and stimulated improvements.[51-53] A true paradigm shift came from delivering the entire dose the day before colonoscopy to split-dose or same-day regimens. This single change increased the rate of adequate bowel preparation from 63% to 85%.[54] There is an inverse correlation between the degree of colon cleanliness and time between the last dose of bowel preparation and the start of colonoscopy.[55] It is now recommended that the last portion of the bowel purgative be ingested 2-5 hours before colonoscopy.[56]

Another milestone was our increased understanding of the importance of oral and written instructions for bowel preparation. Enhanced instructions, consisting of visual aids, social media apps, telephone/short message service (SMS), and smartphone applications, were all proven to optimize bowel preparation[57]. These are now recommended as an adjunct to standard instructions.[56] New low-volume bowel preparations might increase tolerability without compromising the efficacy of cleansing.[56] Although bowel preparation is considered a barrier to CRC screening, lowering the dose of purgative does not seem sufficient to increase colonoscopy adherence rates.[58]

How to optimize rates of cecal intubation?

Cecal intubation is defined as the instrument tip passing the ileocecal valve and reaching fully into cecal caput, allowing detailed inspection of the mucosa between the ileocecal valve and appendiceal orifice. The cecal intubation rate (CIR) is a priority measurement—low CIR is associated with interval CRC (iCRC) [59]. Recommended targets include more than 90% for all colonoscopies and more than 95% for screening colonoscopies [4, 5]. Programs should audit the quality of documentation, including naming and photography of cecal landmarks—most importantly the appendiceal orifice [4].

Competence in cecal intubation is usually achieved in the process of colonoscopy training since it is a key measure of skills acquisition.[60] Nevertheless, in routine clinical practice, it is common for CIRs of individual endoscopists or practices to fall below the recommended standards.[61-63] The first step in the process to optimize CIR is to measure and provide feedback on performance.[64, 65] Quarterly report cards were shown to improve CIRs among experienced endoscopists.[66] Other specific improvement interventions include optimization of

bowel preparation,[64] provision of sedation,[67, 68] use of adjuvant magnetic endoscopic imaging[69], and additional training using novel competency assessment tools.[70, 71] An unresolved issue is whether continuous long-term measurement of CIR for colonoscopists who repeatedly demonstrate performance well above thresholds is productive—CIRs of individual colonoscopists are typically stable or increase over time.

How to optimize lesion detection?

The adenoma detection rate (ADR) was proposed as a quality indicator for colonoscopy in 2002 by the MSTF. It is generally defined as the percentage of patients undergoing first-time primary screening colonoscopy who are 50 years or older and have 1 or more conventional adenomas detected [3, 4]. The original definition did not restrict measurement to screening [2], though recommended targets were based on screening studies. Recent studies have raised questions about the screening restriction, because screening ADR is intermediate between surveillance ADR (higher) and diagnostic examinations (which are lower, except for those performed for positive fecal blood tests) [72, 73]. Recommendations for ADR include minimum acceptable thresholds, which were recently increased for primary screening in the US to 30% in men and 20% in women, [4] or 25% in mixed population, by the ESGE[52] . Targets for individuals with a positive result from a FIT should be 15%–20% higher than for a primary screening population; these were recommended to be 45% for men and 35% for women by the MSTF[6] . Adjustments based on patient population features such as better general health, obesity, cigarette smoking, etc, are unnecessary [74].

The ADR target is not recommended to include sessile serrated lesions (SSLs, also called sessile serrated polyps and sessile serrated adenomas). The rationale is the well-documented interobserver variation between pathologists in differentiation of SSLs from hyperplastic

polyps (HPs). In a recent clinical trial, ADR included both conventional adenomas and SSL [75], but all lesions detected were reviewed by central expert pathologists. A separate detection target for SSLs has generated some interest, and could be implemented at the institutional level [76, 77]. One solution to the problem of differentiating SSLs from HPs is to create a SSL plus HP target. However, this target requires confining the measurement to proximal colon to avoid incentivizing removal of diminutive HPs from the rectosigmoid. Intra- and inter-observer variations among colonoscopists in identifying landmarks such as the splenic flexure and sigmoid descending colon junction make prospective accurate application of a target confined to the proximal colon unreliable. In general, the correlation between detection of conventional adenomas and various serrated detection targets has been high [77-83]. Given the challenges of a separate serrated detection target, this correlation indicates that a continued focus on ADR in quality programs is reasonable.

Although ADR is not an ideal quality parameter, it has been widely validated by studies reporting its association with iCRC[84] and fatal iCRC.[85] Alternative proposed measures, such as iCRC rates, adenoma and advanced adenoma miss rates, advanced adenoma detection rate, adenomas per colonoscopy, and polyp detection rate all have deficiencies, including issues such as lack of feasibility, requirement for tandem studies, a tendency to measure pathologist performance rather than endoscopist performance, or susceptibility to gaming when used prospectively.

The benchmark of adenomas per colonoscopy (APC) [86] provides greater separation among endoscopists than the ADR[87, 88] and avoids the theoretical concern about 1 and done (in which an endoscopist detects 1 adenoma and then performs a suboptimal examination of the remaining colon).[89] Generally, ADR and APC correlate [87, 88]. In the long term, converting

from ADR to APC appears to be advantageous, because APC measures the quality of colonoscopy over the complete examination, provided that APC is validated as a predictor of iCRC. Implementation of APC should be accompanied by agreement on handling procedures for multiple small and diminutive adenomas in the same colon section—placing them in separate containers for pathology examination would increase costs. Photography of multiple lesions to document the number of lesions, accompanied by the current practice of placing lesions of the same predicted histologic type and from the same segment of the colon in 1 bottle, is could reduce the pathology costs with APC[90]. Regardless of using photography to assist in documentation of APC, routine photography of advanced lesions, including photographs before and after resection, is widely considered best documentation practice.

Increases in ADR have been associated with reduced risk of iCRC and fatal iCRC.[91, 65] Therefore minimum thresholds should activate remediation when not reached [4]. Colonoscopists with ADRs above recommended thresholds should also strive to improve their ADR,[92] since CRC protection increases with ADRs above minimum thresholds. Although the target thresholds are unknown, colonoscopists could be reasonably recommended to aspire to ADRs of 40%–50% in primary screening[92]—the risk of iCRC continued to decrease to these levels of ADR.[85] Remediation of low detectors requires multifaceted change of endoscopists behavior and examination technique, which can be coupled with improved imaging technology.[93-95] Audit and performance-enhancing feedback seem have the greatest effect in improving ADR,[91, 96, 97] although not all programs have proven successful.[98] The optimal frequency and method of providing feedback are unknown. A major focus should be put on examination technique, which could be deconstructed into 4 main components: looking behind all folds, cleaning residual stool, providing adequate bowel distension and withdrawing slow enough.[99]

Effective interventions to improve fold examination include double inspection of the right colon (either forward viewing or in retroflex)[100] and use of mucosal exposure devices (Endocuff, Endorings, or G-Eye balloon). Of all mucosal exposure devices, the Endocuff is the most comprehensively studied and has the best evidence of efficacy.[101, 102] Better cleaning of residual stool can be achieved by optimized cleansing regimens described earlier in this article or use of water exchange method.[103] Successful bowel distension can be achieved by dynamic position changes during withdrawal.[104] Application of effective examination techniques will consistently result in longer withdrawal times. Withdrawal time was originally recommended to average 6–10 minutes in normal colonoscopies, and then altered to 6 or more minutes.[105] Detection of adenomas[92] and probably also serrated lesions[106] is optimized at a mean withdrawal time of 9 minutes. Short withdrawal times are a surrogate of poor examination technique, and indicate need for technique remediation for endoscopists with low ADRs. However, a policy of adequate withdrawal time as the primary quality indicator was unsuccessful.[107]

Of the multiple imaging modalities developed to improve ADR, relatively few were proven effective in clinical practice. High-definition white-light imaging increased absolute ADR by 3.5% compared with standard definition endoscopy.[108] However, it might require more than 1 change in instrument generation to increase ADR in practice.[109, 110] Conventional chromoendoscopy increased ADRs by 6-7% compared with standard or high-definition white-light colonoscopy, although chromoendoscopy adds 4–10 minutes to the procedure time and is considered too cumbersome to implement in clinical practice.[111] A change from topical to a per oral multimatrix structure methylene blue formulation was recently reported to increase ADR by 8.5%.[112] Electronic chromoendoscopy was generally considered ineffective,[113] but a

recent meta-analysis showed that brighter-illumination narrow-band imaging increased ADRs, particularly when bowel preparation was excellent.[114] Similarly, Fujinon has developed 2 forms of brighter-illumination electronic chromoendoscopy, called blue-light imaging and linked-color imaging; each increased ADRs in initial studies.[115]

Optimizing rates of polyp resection

Ineffective resection of precancerous lesions might contribute to iCRC.[116] Rates of complete resection of lesions 5–20 mm varied 3-fold, [117] along with assessments of polypectomy competency. [118] Two scales have been validated for measuring resection skill.[119, 120] The Direct Observation of Polypectomy Skills applies to small lesions and endoscopic mucosal resection.[119] The Cold Snare Polypectomy Assessment Tool is used specifically for cold snaring[120] and is easily applied to routine colonoscopies. Detailed recommendations on optimal resection technique were made by the ESGE.[52, 121]

Lack of formal national guidelines and training courses in colorectal polypectomy or endoscopic mucosal resection are likely key reasons for high variability in competence and complete resection rates among endoscopists.[118, 122] There is considerable variation and incompetency in polyp assessment, including its size[123] and morphology[124] as well as accuracy in positioning snare over the lesion and grasping an appropriate amount of tissue.[118] Use of structured competency scales (such as the Direct Observation of Polypectomy Skills or Cold Snare Polypectomy Assessment Tool) might improve polypectomy training.[125] Lecture-based training for gastroenterology fellows seems insufficient to increase polypectomy competence.[126] Importantly, feedback and training in polypectomy performance, coupled with educational videos, improve polypectomy skills, especially for diminutive polyps.[127] For polyps larger than 3 mm, emphasis on appropriate resection technique using a snare instead of

biopsy forceps is crucial.[52, 128] For larger lesions, priorities should include training with ex vivo models,[129] appropriate number of procedures,[130] and focus on en bloc resection of all pedunculated and non-pedunculated polyps up to 20 mm.[116] The EU guidelines for quality assurance mandate that all endoscopists performing screening colonoscopies should be level 3 competent in polypectomy, which includes removal of all pedunculated polyps and virtually all nonpedunculated polyps up to 20 mm.[131]

How can we optimize post-polypectomy surveillance?

Colonoscopy is overused in low-risk patients [132] and underused in high-risk patients.[133] Recommendations for screening and surveillance intervals should be monitored for consistency with published recommendations.[134, 135] Adherence to post-polypectomy surveillance is low, with more than 50% of patients undergoing surveillance either too early or too late.[136] The key to optimizing surveillance is to ensure that correct recommendations are given by gastroenterologists, surgeons, or family physicians, because these are the most important predictors of patient adherence.[137, 138] Another solution is to integrate surveillance interval into electronic medical record system (to set reminders), so other provides can follow patients and refer them at proper intervals.[139]

How Can We Optimize Screening Sigmoidoscopy?

There is evidence that single sigmoidoscopy screens can reduce CRC incidence and mortality. However, data do not show an additional benefit of subsequent rounds of screening.[140] There are many parallels in developing and monitoring quality assurance in sigmoidoscopy programs to colonoscopy-based programs. Just like colonoscopy, there is high-quality evidence for wide variations in sigmoidoscopy performance[141, 142], which translate into differences in cancer prevention[143]. Important quality metrics for sigmoidoscopy include prep

quality, depth of insertion, and polyp detection. Recent studies reported the association of withdrawal times of at least 3.25 minutes and scope advancement to the splenic flexure with increased adenoma detection[144]. Guidance regarding quality performance in sigmoidoscopy have been provided by some organizations[145, 146].

How Can We Optimize the FIT?

There are important considerations for implementing high-quality FIT-based programs. For example, decisions must be made about the type of FIT (such as qualitative vs quantitative) to be used and the frequency with which it will be applied. Separately, decisions must be made about which FIT brand to use—if a quantitative platform is used, the numeric definition of a positive result must be established. Fortunately, there have been many articles published on these topics. Several large-scale national programs and clinical trials have produced findings that can be used in considering development of high-quality FIT based programs (see Table 1).

Optimizing patient preparation for the FIT

Adherence increases the success of any CRC screening program, so programs should aim to simplify regular completion of FIT. A significant advantage of the FIT, compared with the guaiac fecal occult blood test, is that the FIT directly measures hemoglobin in stool, and results are not affected by diet [147]. So, to maximize adherence, no dietary changes should be recommended before stool collection. Similarly, simplifying recommendations about medications (such as aspirin and non-steroidal anti-inflammatory drugs [NSAID]) is also important. Hemoglobin degrades during gastrointestinal transit, so drugs that cause upper gastrointestinal tract bleeding should not greatly affect FIT results. Two recent meta-analyses found that NSAIDs and anticoagulants have little to no effect on test characteristics[148, 149] and

support US multi-society task force recommendations not to stop taking NSAIDS before a FIT[6]. Direct-acting oral anticoagulants might reduce the positive predictive value of FIT to a significantly greater degree than conventional anticoagulants[150], but further studies are needed.

Optimizing choice of FIT and application

There are qualitative and quantitative FITs. Qualitative tests have a visual indicator that indicates when there is hemoglobin in the sample, above a pre-set level. Quantitative tests rely on immunoturbidimetric methods and automated readings, in which the cut-off value for a positive result can be set by the operator[151]. Quantitative tests have a number of advantages over qualitative tests; large national programs and clinical trials therefore often use the quantitative tests. There is evidence for significant variation in performance of qualitative tests[152], and quantitative tests allow better matching of definitions of positive results to colonoscopy resources. For example, a screen program in The Netherlands changed a positive cut-off value from 15 to 47 ug Hb/g feces to improve positive predictive value and decrease colonoscopy burden[153]. However, in countries where colonoscopy resources are less limited, quantitative tests can facilitate application of the test to increase sensitivity. In fact, in an analysis of 16 studies, a FIT threshold of 10 ugHB/g identified patients with colorectal cancer with 91% sensitivity and 90% sensitivity.[154]

It is also important to determine how many FIT samples (1, 2, or 3) will be tested. Lower number of samples per cycle increase adherence. For example, in randomized controlled trials that compared results of FITs to 3-card conventional fecal occult blood tests, participation was more than 20% higher in the FIT group [155]. In a recent population-based study over 4 rounds that directly compared 1 FIT vs 2 FITs (on a biennial schedule), there was no

significant increase in diagnostic yield or decrease in interval CRC between the groups. Colonoscopy demand was higher in the 2-FIT group and the authors concluded that the 1-sample FIT was the preferred approach.[156]

A separate issue is whether to perform FITs on an annual or biennial basis. Although annual screening, most population-based programs outside the US and 2 other trials of FIT vs colonoscopy used biennial testing (see Table 1).[157]Tradeoffs between the approaches include increased participant burden with more frequent application and delays in diagnosis of important lesions (such as advanced adenoma) with less frequent application. Differences in important outcomes including the overall number of positive results and detection of advanced neoplasia were not large, and programs have latitude in choosing the optimal approach within a population.[158]

Optimizing FIT distribution and quality control

Recent studies[159-161] confirmed findings from earlier studies[162-164] that positive results of FIT testing decrease in warmer months and might affect lesion detection. Programs are not currently considering season in FIT distribution, but do emphasize the importance of returning samples quickly. Improved FIT buffers are being developed, to prevent sample degradation.[165] Quality control within the laboratory, including standardized result reporting, is required for program success.[166, 167] Although the details are outside the scope of this review, a quality control program in The Netherlands investigated how changing collection devices, reagents, and laboratories affects positive results [168]. FIT-based screening programs should track the percentage of kits received that cannot be processed; in the US, this value is recommended to be below 5%.[6] Quality improvement efforts have been effective in reducing rates of laboratory-rejected samples.[169] For example, placing red stickers on the FIT to

remind users of the need for rapid return increased rates of sample processing at the laboratory.

New Screening Strategies Under Evaluation

CTC is recommended for patients with positive results from a screening test who have contraindications to colonoscopy. The role of CTC as primary screening test is still under evaluation. Guidance for CTC quality has been published.[170, 171] Although the details of those recommendations are beyond the scope of this review, some general statements can be made. High-quality colonic preparation, often with fecal tagging and adequate insufflation, is important for adequate test performance.

With regard to imaging, use of multi-detector scanners is key, along with efforts to minimize radiation exposure. Although recommendations about primary mode of reading are generally not specific (such as starting with either the 2-dimensional or 3-dimensional rendering), it is clear that software should provide multiple display formats. Reporting should be standardized—the CT Colonography Reporting and Data System [170] is generally used for this purpose. Finally, it is important to use a data registry to track performance. The ability to regularly audit patient safety and outcome for use CTC is key, and performance indicators have been described.[171, 172]

Multi-target DNA test

MT-DNA test is available for only routine screening in the US. The Food and Drug Administration approved this proprietary device (Cologuard; Exact Sciences, Madison WI) in 2014 and the Center For Medicare and Medicaid Services provided payment coverage at a frequency of every 3 years.[173] After an order is placed, the company directs the subsequent

distribution, receipt, processing, and results notification. Details regarding the laboratory methods and analytic use of the results have been described.[174] In brief, institutions or programs using this device would rely on the Exact Sciences laboratory for all quality control.

Future Directions

CRC screening reduces cancer-specific mortality and incidence. The effectiveness of cancer screening, however, relies not only on the efficacy of screening test but also on the process of screening delivery, which includes adherence, quality of screening, and analysis of results. This complicated process requires monitoring and optimization of several steps. Screening programs create a perfect framework for comparative effectiveness research, in which screening optimization strategies can be tested. This framework includes joint database management systems, resources already allocated to potential interventions, and large numbers of potential participants.[175, 176] Several aspects of CRC screening quality, such as rates of colonoscopy completion or adenoma detection, or adequacy of bowel cleansing, have been addressed. Others, such as variable and insufficient rates of adherence to screening, rates of complete endoscopic resection, and adequate post-polypectomy surveillance, are important quality issues to be tackled in the near future.

References

1. von Karsa L, Patnick J, Segnan N, et al. European guidelines for quality assurance in colorectal cancer screening and diagnosis: overview and introduction to the full supplement publication. Endoscopy 2013;45:51-9.
2. Rex DK, Bond JH, Winawer S, et al. Quality in the technical performance of colonoscopy and the continuous quality improvement process for colonoscopy: recommendations of the U.S. Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol 2002;97:1296-308.
3. Rex DK, Petrini JL, Baron TH, et al. Quality indicators for colonoscopy. Am J Gastroenterol 2006;101:873-85.
4. Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. Gastrointest Endosc 2015;81:31-53.
5. Kaminski MF, Thomas-Gibson S, Bugajski M, et al. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) quality improvement initiative. United European Gastroenterol J 2017;5:309-334.
6. Robertson DJ, Lee JK, Boland CR, et al. Recommendations on Fecal Immunochemical Testing to Screen for Colorectal Neoplasia: A Consensus Statement by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2017;152:1217-1237.e3.
7. Libby G, Brewster DH, McClements PL, et al. The impact of population-based faecal occult blood test screening on colorectal cancer mortality: a matched cohort study. Br J Cancer 2012;107:255-9.
8. Zorzi M, Fedeli U, Schievano E, et al. Impact on colorectal cancer mortality of screening programmes based on the faecal immunochemical test. Gut 2015;64:784-90.
9. Fedeli U, Zorzi M, Urso ED, et al. Impact of fecal immunochemical test-based screening programs on proximal and distal colorectal cancer surgery rates: A natural multiple-baseline experiment. Cancer 2015;121:3982-9.
10. White A, Thompson TD, White MC, et al. Cancer Screening Test Use - United States, 2015. MMWR Morb Mortal Wkly Rep 2017;66:201-206.
11. May FP, Yano EM, Provenzale D, et al. The Association Between Primary Source of Healthcare Coverage and Colorectal Cancer Screening Among US Veterans. Dig Dis Sci 2017;62:1923-1932.
12. Gellad ZF, Provenzale D. Colorectal cancer: national and international perspective on the burden of disease and public health impact. Gastroenterology 2010;138:2177-90.
13. Doubeni CA, Fedewa SA, Levin TR, et al. Modifiable Failures in the Colorectal Cancer Screening Process and Their Association With Risk of Death. Gastroenterology 2019;156:63-74.e6.
14. Breen N, Lewis DR, Gibson JT, et al. Assessing disparities in colorectal cancer mortality by socioeconomic status using new tools: health disparities calculator and socioeconomic quintiles. Cancer Causes Control 2017;28:117-125.
15. Meester RG, Doubeni CA, Zauber AG, et al. Public health impact of achieving 80% colorectal cancer screening rates in the United States by 2018. Cancer 2015;121:2281-5.
16. Honein-AbouHaidar GN, Kastner M, Vuong V, et al. Systematic Review and Meta-study Synthesis of Qualitative Studies Evaluating Facilitators and Barriers to Participation in Colorectal Cancer Screening. Cancer Epidemiol Biomarkers Prev 2016;25:907-17.

17. McLachlan SA, Clements A, Austoker J. Patients' experiences and reported barriers to colonoscopy in the screening context--a systematic review of the literature. Patient Educ Couns 2012;86:137-46.
18. Anhang Price R, Zapka J, Edwards H, et al. Organizational factors and the cancer screening process. J Natl Cancer Inst Monogr 2010;2010:38-57.
19. Turnbull E, Priaulx J, van Ravesteyn NT, et al. A health systems approach to identifying barriers to breast cancer screening programmes. Methodology and application in six European countries. Health Policy 2018;122:1198-1205.
20. Levin TR, Corley DA, Jensen CD, et al. Effects of Organized Colorectal Cancer Screening on Cancer Incidence and Mortality in a Large Community-Based Population. Gastroenterology 2018;155:1383-1391 e5.
21. Sabatino SA, White MC, Thompson TD, et al. Cancer screening test use - United States, 2013. MMWR Morb Mortal Wkly Rep 2015;64:464-8.
22. Fedewa SA, Goodman M, Flanders WD, et al. Elimination of cost-sharing and receipt of screening for colorectal and breast cancer. Cancer 2015;121:3272-80.
23. Eisinger F, Cals L, Calazel-Benque A, et al. Impact of organised programs on colorectal cancer screening. BMC Cancer 2008;8:104.
24. Carrozzi G, Sampaolo L, Bolognesi L, et al. Cancer screening uptake: association with individual characteristics, geographic distribution, and time trends in Italy. Epidemiol Prev 2015;39:9-18.
25. de Moor JS, Cohen RA, Shapiro JA, et al. Colorectal cancer screening in the United States: Trends from 2008 to 2015 and variation by health insurance coverage. Prev Med 2018;112:199-206.
26. Camilloni L, Ferroni E, Cendales BJ, et al. Methods to increase participation in organised screening programs: a systematic review. BMC Public Health 2013;13:464.
27. Senore C, Inadomi J, Segnan N, et al. Optimising colorectal cancer screening acceptance: a review. Gut 2015;64:1158-77.
28. Jager M, Demb J, Asghar A, et al. Mailed Outreach Is Superior to Usual Care Alone for Colorectal Cancer Screening in the USA: A Systematic Review and Meta-analysis. Dig Dis Sci 2019;64:2489-2496.
29. Swartz R, Weiser E, Parks P, et al. Colorectal cancer screening: compliance with multi-target stool DNA testing among Medicare beneficiaries. Digestive Disease Week 2019. San Diego, CA, 2019.
30. Sali L, Mascalchi M, Falchini M, et al. Reduced and Full-Preparation CT Colonography, Fecal Immunochemical Test, and Colonoscopy for Population Screening of Colorectal Cancer: A Randomized Trial. J Natl Cancer Inst 2016;108.
31. Liang PS, Wheat CL, Abhat A, et al. Adherence to Competing Strategies for Colorectal Cancer Screening Over 3 Years. Am J Gastroenterol 2016;111:105-14.
32. Raine R, Duffy SW, Wardle J, et al. Impact of general practice endorsement on the social gradient in uptake in bowel cancer screening. Br J Cancer 2016;114:321-6.
33. Hewitson P, Ward AM, Heneghan C, et al. Primary care endorsement letter and a patient leaflet to improve participation in colorectal cancer screening: results of a factorial randomised trial. Br J Cancer 2011;105:475-80.
34. Edwards AG, Evans R, Dundon J, et al. Personalised risk communication for informed decision making about taking screening tests. Cochrane Database Syst Rev 2006:Cd001865.
35. Hart AR, Barone TL, Gay SP, et al. The effect on compliance of a health education leaflet in colorectal cancer screening in general practice in central England. J Epidemiol Community Health 1997;51:187-91.

36. Raine R, Atkin W, von Wagner C, et al. Programme Grants for Applied Research. Testing innovative strategies to reduce the social gradient in the uptake of bowel cancer screening: a programme of four qualitatively enhanced randomised controlled trials. Southampton (UK): NIHR Journals Library
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37. Kerrison RS, McGregor LM, Counsell N, et al. Use of Two Self-referral Reminders and a Theory-Based Leaflet to Increase the Uptake of Flexible Sigmoidoscopy in the English Bowel Scope Screening Program: Results From a Randomized Controlled Trial in London. Ann Behav Med 2018;52:941-951.
38. Grazzini G, Castiglione G, Isu A, et al. Colorectal cancer screening by fecal occult blood testing: results of a population-based experience. Tumori 2000;86:384-8.
39. Seifert B, Zavoral M, Fric P, et al. The role of primary care in colorectal cancer screening: experience from Czech Republic. Neoplasma 2008;55:74-80.
40. Senore C, Armaroli P, Silvani M, et al. Comparing different strategies for colorectal cancer screening in Italy: predictors of patients' participation. Am J Gastroenterol 2010;105:188-98.
41. Woodrow C, Rozmovits L, Hewitson P, et al. Bowel cancer screening in England: a qualitative study of GPs' attitudes and information needs. BMC Fam Pract 2006;7:53.
42. Sabatino SA, Habarta N, Baron RC, et al. Interventions to increase recommendation and delivery of screening for breast, cervical, and colorectal cancers by healthcare providers systematic reviews of provider assessment and feedback and provider incentives. Am J Prev Med 2008;35:S67-74.
43. Corley DA, Jensen CD, Quinn VP, et al. Association Between Time to Colonoscopy After a Positive Fecal Test Result and Risk of Colorectal Cancer and Cancer Stage at Diagnosis. Jama 2017;317:1631-1641.
44. Turnbull E, Priaulx J, de Kok I, et al. Results of a health systems approach to identify barriers to population-based cervical and colorectal cancer screening programmes in six European countries. Health Policy 2018;122:1206-1211.
45. Selby K, Baumgartner C, Levin TR, et al. Interventions to Improve Follow-up of Positive Results on Fecal Blood Tests: A Systematic Review. Ann Intern Med 2017;167:565-575.
46. Rex DK, Imperiale TF, Latinovich DR, et al. Impact of bowel preparation on efficiency and cost of colonoscopy. Am J Gastroenterol 2002;97:1696-700.
47. Froehlich F, Wietlisbach V, Gonvers JJ, et al. Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. Gastrointest Endosc 2005;61:378-84.
48. Radaelli F, Paggi S, Hassan C, et al. Split-dose preparation for colonoscopy increases adenoma detection rate: a randomised controlled trial in an organised screening programme. Gut 2017;66:270-277.

49. Johnson DA, Barkun AN, Cohen LB, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the U.S. multi-society task force on colorectal cancer. Gastrointest Endosc 2014;80:543-62.
50. Hassan C, Bretthauer M, Kaminski MF, et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 2013;45:142-50.
51. Clark BT, Protiva P, Nagar A, et al. Quantification of Adequate Bowel Preparation for Screening or Surveillance Colonoscopy in Men. Gastroenterology 2016;150:396-405; quiz e14-5.
52. Kaminski MF, Thomas-Gibson S, Bugajski M, et al. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy 2017;49:378-397.
53. Calderwood AH, Jacobson BC. Comprehensive validation of the Boston Bowel Preparation Scale. Gastrointest Endosc 2010;72:686-92.
54. Bucci C, Rotondano G, Hassan C, et al. Optimal bowel cleansing for colonoscopy: split the dose! A series of meta-analyses of controlled studies. Gastrointest Endosc 2014;80:566-576.e2.
55. Seo EH, Kim TO, Park MJ, et al. Optimal preparation-to-colonoscopy interval in split-dose PEG bowel preparation determines satisfactory bowel preparation quality: an observational prospective study. Gastrointest Endosc 2012;75:583-90.
56. Hassan C, Bretthauer M, Kaminski MF, et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2013;45:142-55.
57. Guo X, Yang Z, Zhao L, et al. Enhanced instructions improve the quality of bowel preparation for colonoscopy: a meta-analysis of randomized controlled trials. Gastrointest Endosc 2017;85:90-97.e6.
58. Pisera M, Franczyk R, Wieszczy P, et al. The impact of low- versus standard-volume bowel preparation on participation in primary screening colonoscopy: a randomized health services study. Endoscopy 2019;51:227-236.
59. Baxter N, Sutradhar R, Forbes DD, Paszat LF, Saskin R, Rabeneck L. Analysis of administrative data finds endoscopist quality measures asociated with post-colonoscopy colorectal cancer. Gastroenterology 2011;140:65-72.
60. Koch AD, Haringsma J, Schoon EJ, et al. Competence measurement during colonoscopy training: the use of self-assessment of performance measures. Am J Gastroenterol 2012;107:971-5.
61. Bretthauer M, Kaminski MF, Loberg M, et al. Population-Based Colonoscopy Screening for Colorectal Cancer: A Randomized Clinical Trial. JAMA Intern Med 2016;176:894-902.
62. Shah HA, Paszat LF, Saskin R. Factors associated with incomplete colonoscopy: a population-based study. Gastroenterology 2007;132:2297-2303.
63. Hoff G, Bretthauer M, Huppertz-Hauss G, et al. The Norwegian Gastronet project: Continuous quality improvement of colonoscopy in 14 Norwegian centres. Scand J Gastroenterol 2006;41:481-7.
64. Aslinia F, Uradomo L, Steele A. Quality assessment of colonoscopic cecal intubation: an analysis of 6 years of continuous practice at a university hospital. Am J Gastroenterol 2006;101:721-731.
65. Ball JE, Osbourne J, Jowett S, et al. Quality improvement programme to achieve acceptable colonoscopy completion rates: prospective before and after study. Bmj 2004;329:665-7.

66. Kahi CJ, Ballard D, Shah AS, et al. Impact of a quarterly report card on colonoscopy quality measures. Gastrointest Endosc 2013;77:925-31.
67. Bannert C, Reinhart K, Dunkler D, et al. Sedation in screening colonoscopy: impact on quality indicators and complications. Am J Gastroenterol 2012;107:1837-48.
68. Radaelli F, Meucci G, Sgroi G, et al. Technical performance of colonoscopy: the key role of sedation/analgesia and other quality indicators. Am J Gastroenterol 2008;103:1122-30.
69. Mark-Christensen A, Brandsborg S, Iversen LH. Magnetic endoscopic imaging as an adjuvant to elective colonoscopy: a systematic review and meta-analysis of randomized controlled trials. Endoscopy 2015;47:251-61.
70. Walsh CM, Ling SC, Khanna N, et al. Gastrointestinal Endoscopy Competency Assessment Tool: reliability and validity evidence. Gastrointest Endosc 2015;81:1417-1424.e2.
71. Barton JR, Corbett S, van der Vleuten CP. The validity and reliability of a Direct Observation of Procedural Skills assessment tool: assessing colonoscopic skills of senior endoscopists. Gastrointest Endosc 2012;75:591-7.
72. Rex DK, Ponugoti PL. Calculating the adenoma detection rate in screening colonoscopies only: Is it necessary? Can it be gamed? Endoscopy 2017;49:1069-1074.
73. Anderson JC, Butterly LF, Goodrich M, et al. Differences in detection rates of adenomas and serrated polyps in screening versus surveillance colonoscopies, based on the new hampshire colonoscopy registry. Clin Gastroenterol Hepatol 2013;11:1308-12.
74. Jensen CD, Doubeni CA, Quinn VP, et al. Adjusting for patient demographics has minimal effects on rates of adenoma detection in a large, community-based setting. Clin Gastroenterol Hepatol 2015;13:739-46.
75. Repici A, Wallace MB, East JE, et al. Efficacy of Per-oral Methylene Blue Formulation for Screening Colonoscopy. Gastroenterology 2019.
76. Abdeljawad K, Vemulapalli KC, Kahi CJ, et al. Sessile serrated polyp prevalence determined by a colonoscopist with a high lesion detection rate and an experienced pathologist. Gastrointest Endosc 2014.
77. IJspeert JE, de Wit K, van der Vlugt M, et al. Prevalence, distribution and risk of sessile serrated adenomas/polyps at a center with a high adenoma detection rate and experienced pathologists. Endoscopy 2016;48:740-6.
78. Kahi CJ, Li X, Eckert GJ, et al. High colonoscopic prevalence of proximal colon serrated polyps in average-risk men and women. Gastrointest Endosc 2012;75:515-20.
79. Liang J, Kalady MF, Appau K, et al. Serrated polyp detection rate during screening colonoscopy. Colorectal Dis 2012;14:1323-7.
80. IJspeert JE, van Doorn SC, van der Brug YM, et al. The proximal serrated polyp detection rate is an easy-to-measure proxy for the detection rate of clinically relevant serrated polyps. Gastrointest Endosc 2015;82:870-7.
81. Anderson JC, Butterly LF, Weiss JE, et al. Providing data for serrated polyp detection rate benchmarks: an analysis of the New Hampshire Colonoscopy Registry. Gastrointest Endosc 2017;85:1188-1194.
82. Occhipinti P, Saettone S, Cristina S, et al. Correlation between adenoma and serrated lesion detection rates in an unselected outpatient population. Dig Liver Dis 2015;47:508-11.
83. Kim JH, Choi YJ, Kwon HJ, et al. Simple colonoscopy reporting system checking the detection rate of colon polyps. World J Gastroenterol 2015;21:9380-6.
84. Kaminski MF, Regula J, Kraszewska E, et al. Quality indicators for colonoscopy and the risk of interval cancer. N Engl J Med 2010;362:1795-1803.

85. Corley DA, Jensen CD, Marks AR, et al. Adenoma Detection Rate and Risk of Colorectal Cancer and Death. N Engl J Med 2014;370:1298-1306.
86. Zhao S, Wang S, Pan P, et al. Magnitude, Risk Factors, and Factors Associated With Adenoma Miss Rate of Tandem Colonoscopy: A Systematic Review and Meta-analysis. Gastroenterology 2019;156:1661-1674 e11.
87. Barclay RL, Vicari JJ, Doughty AS, et al. Colonoscopic withdrawal times and adenoma detection during screening colonoscopy. N Engl J Med 2006;355:2533-41.
88. Chen SC, Rex DK. Endoscopist can be more powerful than age and male gender in predicting adenoma detection at colonoscopy. Am J Gastroenterol 2007;102:856-61.
89. Wang HS, Pisegna J, Modi R, et al. Adenoma detection rate is necessary but insufficient for distinguishing high versus low endoscopist performance. Gastrointest Endosc 2013;77:71-8.
90. Rex DK, Hardacker K, MacPhail M, et al. Determining the adenoma detection rate and adenomas per colonoscopy by photography alone: proof-of-concept study. Endoscopy 2015.
91. Kaminski MF, Wieszczy P, Rupinski M, et al. Increased Rate of Adenoma Detection Associates With Reduced Risk of Colorectal Cancer and Death. Gastroenterology 2017;153:98-105.
92. Shaukat A, Rector TS, Church TR, et al. Longer Withdrawal Time Is Associated With a Reduced Incidence of Interval Cancer After Screening Colonoscopy. Gastroenterology 2015;149:952-7.
93. Kaminski MF, Anderson J, Valori R, et al. Leadership in training to improve adenoma detection rate in screening colonoscopy: a nationwide randomized trial. United European Gastroenterol J 2014;2:A44.
94. Coe SG, Crook JE, Diehl NN, et al. An endoscopic quality improvement program improves detection of colorectal adenomas. Am J Gastroenterol 2013;108:219-26; quiz 227.
95. Atkins L, Hunkeler EM, Jensen CD, et al. Factors influencing variation in physician adenoma detection rates: a theory-based approach for performance improvement. Gastrointest Endosc 2016;83:617-26.e2.
96. Barclay RL, Vicari JJ, Greenlaw RL. Effect of a time-dependent colonoscopic withdrawal protocol on adenoma detection during screening colonoscopy. Clin Gastroenterol Hepatol 2008;6:1091-1098.
97. Waldmann E, Gessl I, Sallinger D, et al. Trends in quality of screening colonoscopy in Austria. Endoscopy 2016;48:1102-1109.
98. Shaukat A, Oancea C, Bond JH, et al. Variation in detection of adenomas and polyps by colonoscopy and change over time with a performance improvement program. Clin Gastroenterol Hepatol 2009;7:1335-40.
99. Rex DK. Colonoscopic withdrawal technique is associated with adenoma miss rates. Gastrointest Endosc 2000;51:33-6.
100. Desai M, Bilal M, Hamade N, et al. Increasing adenoma detection rates in the right side of the colon comparing retroflexion with a second forward view: a systematic review. Gastrointest Endosc 2019;89:453-459.e3.
101. Williet N, Tournier Q, Vernet C, et al. Effect of Endocuff-assisted colonoscopy on adenoma detection rate: meta-analysis of randomized controlled trials. Endoscopy 2018.
102. Rex DK, Repici A, Gross SA, et al. High-definition colonoscopy versus Endocuff versus EndoRings versus Full-Spectrum Endoscopy for adenoma detection at colonoscopy: a multicenter randomized trial. Gastrointest Endosc 2018.

103. Fuccio L, Frazzoni L, Hassan C, et al. Water exchange colonoscopy increases adenoma detection rate: a systematic review with network meta-analysis of randomized controlled studies. Gastrointest Endosc 2018;88:589-597.e11.
104. Lee SW, Chang JH, Ji JS, et al. Effect of Dynamic Position Changes on Adenoma Detection During Colonoscope Withdrawal: A Randomized Controlled Multicenter Trial. Am J Gastroenterol 2016;111:63-9.
105. Barclay RL, Vicari JJ, Doughty AS. Colonoscopic withdrawal times and adenoma detection during screening colonoscopy. N Engl J Med 2006;355:2533-2541.
106. Butterly L, Robinson CM, Anderson JC, et al. Serrated and adenomatous polyp detection increases with longer withdrawal time: results from the New Hampshire Colonoscopy Registry. Am J Gastroenterol 2014;109:417-26.
107. Sawhney MS, Cury MS, Neeman N, et al. Effect of institution-wide policy of colonoscopy withdrawal time > or = 7 minutes on polyp detection. Gastroenterology 2008;135:1892-8.
108. Subramanian V, Mannath J, Hawkey CJ, et al. High definition colonoscopy vs. standard video endoscopy for the detection of colonic polyps: a meta-analysis. Endoscopy 2011;43:499-505.
109. Pioche M, Denis A, Allescher HD, et al. Impact of 2 generational improvements in colonoscopes on adenoma miss rates: results of a prospective randomized multicenter tandem study. Gastrointest Endosc 2018;88:107-116.
110. Zimmermann-Fraedrich K, Groth S, Sehner S, et al. Effects of two instrument-generation changes on adenoma detection rate during screening colonoscopy: results from a prospective randomized comparative study. Endoscopy 2018;50:878-885.
111. Brown SR, Baraza W. Chromoscopy versus conventional endoscopy for the detection of polyps in the colon and rectum. Cochrane Database Syst Rev 2010:CD006439.
112. Repici A, Wallace MB, East JE, et al. Efficacy of Per-oral Methylene Blue Formulation for Screening Colonoscopy. Gastroenterology 2019;156:2198-2207.e1.
113. Pasha SF, Leighton JA, Das A, et al. Comparison of the Yield and Miss Rate of Narrow Band Imaging and White Light Endoscopy in Patients Undergoing Screening or Surveillance Colonoscopy: A Meta-Analysis. Am J Gastroenterol 2012;107:363-370.
114. Atkinson NSS, Ket S, Bassett P, et al. Narrow-Band Imaging for Detection of Neoplasia at Colonoscopy: A Meta-analysis of Data From Individual Patients in Randomized Controlled Trials. Gastroenterology 2019;157:462-471.
115. Paggi S, Mogavero G, Amato A, et al. Linked color imaging reduces the miss rate of neoplastic lesions in the right colon: a randomized tandem colonoscopy study. Endoscopy 2018;50:396-402.
116. Adler J, Toy D, Anderson JC, et al. Metachronous Neoplasias Arise in a Higher Proportion of Colon Segments From Which Large Polyps Were Previously Removed, and Can be Used to Estimate Incomplete Resection of 10-20 mm Colorectal Polyps. Clin Gastroenterol Hepatol 2019.
117. Pohl H, Srivastava A, Bensen SP, et al. Incomplete polyp resection during colonoscopy-results of the complete adenoma resection (CARE) study. Gastroenterology 2013;144:74-80 e1.
118. Duloy AM, Kaltenbach TR, Keswani RN. Assessing colon polypectomy competency and its association with established quality metrics. Gastrointest Endosc 2018;87:635-644.
119. Gupta S, Anderson J, Bhandari P, et al. Development and validation of a novel method for assessing competency in polypectomy: direct observation of polypectomy skills. Gastrointest Endosc 2011;73:1232-9 e2.

120. Patel SG, Duloy A, Kaltenbach T, et al. Development and validation of a video-based cold snare polypectomy assessment tool (with videos). Gastrointest Endosc 2019.
121. Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2017;49:270-297.
122. Patel K, Rajendran A, Faiz O, et al. An international survey of polypectomy training and assessment. Endosc Int Open 2017;5:E190-e197.
123. Sakata S, Klein K, Stevenson ARL, et al. Measurement Bias of Polyp Size at Colonoscopy. Dis Colon Rectum 2017;60:987-991.
124. van Doorn SC, Hazewinkel Y, East JE, et al. Polyp morphology: an interobserver evaluation for the Paris classification among international experts. Am J Gastroenterol 2015;110:180-7.
125. Patel K, Faiz O, Rutter M, et al. The impact of the introduction of formalised polypectomy assessment on training in the UK. Frontline Gastroenterol 2017;8:104-109.
126. van Doorn SC, Bastiaansen BA, Thomas-Gibson S, et al. Polypectomy skills of gastroenterology fellows: can we improve them? Endosc Int Open 2016;4:E182-9.
127. Duloy AM, Kaltenbach TR, Wood M, et al. Colon polypectomy report card improves polypectomy competency: results of a prospective quality improvement study (with video). Gastrointest Endosc 2019;89:1212-1221.
128. Britto-Arias M, Waldmann E, Bannert C, et al. Forceps Versus Snare Polypectomies - Low Adherence to Guideline Results in Incomplete Resection. Gastrointest Endosc 2014;79:AB129.
129. Ansell J, Hurley JJ, Horwood J, et al. The Welsh Institute for Minimal Access Therapy colonoscopy suitcase has construct and concurrent validity for colonoscopic polypectomy skills training: a prospective, cross-sectional study. Gastrointest Endosc 2014;79:490-7.
130. Boo SJ, Jung JH, Park JH, et al. An adequate level of training for technically competent colonoscopic polypectomy. Scand J Gastroenterol 2015;50:908-15.
131. Valori R, Rey JF, Atkin WS, et al. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition--Quality assurance in endoscopy in colorectal cancer screening and diagnosis. Endoscopy 2012;44 Suppl 3:SE88-105.
132. Sheffield KM, Han Y, Kuo YF, et al. Potentially inappropriate screening colonoscopy in Medicare patients: variation by physician and geographic region. JAMA Intern Med 2013;173:542-50.
133. Schoen RE, Pinsky PF, Weissfeld JL, et al. Utilization of surveillance colonoscopy in community practice. Gastroenterology 2010;138:73-81.
134. Lieberman DA, Rex DK, Winawer SJ, et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2012;143:844-57.
135. Hassan C, Quintero E, Dumonceau JM, et al. Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2013;45:842-51.
136. Djinbachian R, Dube AJ, Durand M, et al. Adherence to post-polypectomy surveillance guidelines: a systematic review and meta-analysis. Endoscopy 2019.
137. Boolchand V, Olds G, Singh J, et al. Colorectal screening after polypectomy: a national survey study of primary care physicians. Ann Intern Med 2006;145:654-9.

138. van Heijningen EM, Lansdorp-Vogelaar I, Steyerberg EW, et al. Adherence to surveillance guidelines after removal of colorectal adenomas: a large, community-based study. Gut 2015;64:1584-92.
139. Bugajski M, Wieszczy P, Pisera M, et al. The European Society of Gastrointestinal Endoscopy key performance measures for colonoscopy in the Polish Colonoscopy Screening Program – a retrospective analysis. Endoscopy 2019.
140. Lauby-Secretan B, Vilahur N, Bianchini F, et al. The IARC Perspective on Colorectal Cancer Screening. N Engl J Med 2018;378:1734-1740.
141. Atkin W, Rogers P, Cardwell C, et al. Wide variation in adenoma detection rates at screening flexible sigmoidoscopy. Gastroenterology 2004;126:1247-1256.
142. Pinsky PF, Schoen RE, Weissfeld JL, et al. Variability in flexible sigmoidoscopy performance among examiners in a screening trial. Clinical Gastroenterology and Hepatology 2005;3:792.e1-792.e.
143. Rogal SS, Pinsky PF, Schoen RE. Relationship Between Detection of Adenomas by Flexible Sigmoidoscopy and Interval Distal Colorectal Cancer. Clinical Gastroenterology and Hepatology 2013;11:73-78.
144. Bevan R, Blanks RG, Nickerson C, et al. Factors affecting adenoma detection rate in a national flexible sigmoidoscopy screening programme: a retrospective analysis. The Lancet Gastroenterology and Hepatology 2019;4:239-247.
145. Rutter MD, Rees CJ. Quality in gastrointestinal endoscopy. Endoscopy 2014;46:526-8.
146. Levin TR, Farraye FA, Schoen RE, et al. Quality in the technical performance of screening flexible sigmoidoscopy: recommendations of an international multi-society task group. Gut 2005;54:807-13.
147. Robertson DJ, Imperiale TF. Stool Testing for Colorectal Cancer Screening. Gastroenterology 2015;149:1286-93.
148. de Klerk CM, Vendrig LM, Bossuyt PM, et al. Participant-Related Risk Factors for False-Positive and False-Negative Fecal Immunochemical Tests in Colorectal Cancer Screening: Systematic Review and Meta-Analysis. The American Journal of Gastroenterology 2018.
149. Nieuwenburg SAV, Vuik FER, Kruip M, et al. Effect of anticoagulants and NSAIDs on accuracy of faecal immunochemical tests (FITs) in colorectal cancer screening: a systematic review and meta-analysis. Gut 2018.
150. Randel KR, Botteri E, Romstad KMK, et al. Effects of Oral Anticoagulants and Aspirin on Performance of Fecal Immunochemical Tests in Colorectal Cancer Screening. Gastroenterology 2019;156:1642-1649.e1.
151. Tinmouth J, Lansdorp-Vogelaar I, Allison JE. Faecal immunochemical tests versus guaiac faecal occult blood tests: what clinicians and colorectal cancer screening programme organisers need to know. Gut 2015;64:1327-37.
152. Daly JM, Bay CP, Levy BT. Evaluation of fecal immunochemical tests for colorectal cancer screening. J Prim Care Community Health 2013;4:245-50.
153. Toes-Zoutendijk E, van Leerdam ME, Dekker E, et al. Real-Time Monitoring of Results During First Year of Dutch Colorectal Cancer Screening Program and Optimization by Altering Fecal Immunochemical Test Cut-Off Levels. Gastroenterology 2017;152:767-775 e2.
154. Imperiale TF, Gruber RN, Stump TE, et al. Performance Characteristics of Fecal Immunochemical Tests for Colorectal Cancer and Advanced Adenomatous Polyps: A Systematic Review and Meta-analysis. Ann Intern Med 2019.

155. Vart G, Banzi R, Minozzi S. Comparing participation rates between immunochemical and guaiac faecal occult blood tests: a systematic review and meta-analysis. Prev Med 2012;55:87-92.
156. Grobbee EJ, van der Vlugt M, van Vuuren AJ, et al. Diagnostic Yield of One-Time Colonoscopy Vs One-Time Flexible Sigmoidoscopy Vs Multiple Rounds of Mailed Fecal Immunohistochemical Tests in Colorectal Cancer Screening. Clin Gastroenterol Hepatol 2019.
157. Dominitz JA, Robertson DJ, Ahnen DJ, et al. Colonoscopy vs. Fecal Immunochemical Test in Reducing Mortality From Colorectal Cancer (CONFIRM): Rationale for Study Design. Am J Gastroenterol 2017;112:1736-1746.
158. van Roon AH, Goede SL, van Ballegooijen M, et al. Random comparison of repeated faecal immunochemical testing at different intervals for population-based colorectal cancer screening. Gut 2013;62:409-15.
159. De Girolamo G, Goldoni CA, Corradini R, et al. Ambient temperature and FIT performance in the Emilia-Romagna colorectal cancer screening programme. J Med Screen 2016;23:186-191.
160. Doubeni CA, Jensen CD, Fedewa SA, et al. Fecal Immunochemical Test (FIT) for Colon Cancer Screening: Variable Performance with Ambient Temperature. J Am Board Fam Med 2016;29:672-681.
161. Cha JM, Suh M, Kwak MS, et al. Risk of Interval Cancer in Fecal Immunochemical Test Screening Significantly Higher During the Summer Months: Results from the National Cancer Screening Program in Korea. Am J Gastroenterol 2018;113:611-621.
162. Grazzini G, Ventura L, Zappa M, et al. Influence of seasonal variations in ambient temperatures on performance of immunochemical faecal occult blood test for colorectal cancer screening: observational study from the Florence district. Gut 2010;59:1511-5.
163. van Roon AH, Hol L, van Vuuren AJ, et al. Are fecal immunochemical test characteristics influenced by sample return time? A population-based colorectal cancer screening trial. Am J Gastroenterol 2012;107:99-107.
164. Zorzi M, Baracco S, Fedato C. Limited effect of summer warming on the sensitivity of colorectal cancer screening. Gut 2012;61:162; author reply 162.
165. Dancourt V, Hamza S, Manfredi S, et al. Influence of sample return time and ambient temperature on the performance of an immunochemical faecal occult blood test with a new buffer for colorectal cancer screening. Eur J Cancer Prev 2016;25:109-14.
166. Fraser CG, Allison JE, Halloran SP, et al. A proposal to standardize reporting units for fecal immunochemical tests for hemoglobin. J Natl Cancer Inst 2012;104:810-4.
167. Rubeca T, Rapi S, Deandrea S, et al. Guidance for faecal occult blood testing: quantitative immunochemical method (FIT-HB) in colorectal cancer screening programmes. Epidemiol Prev 2017;41:1-31.
168. Toes-Zoutendijk E, Bonfrer JMG, Ramakers C, et al. Quality Monitoring of a FIT-Based Colorectal Cancer Screening Program. Clin Chem 2019;65:419-426.
169. Cheng C, Ganz DA, Chang ET, et al. Reducing Rejected Fecal Immunochemical Tests Received in the Laboratory for Colorectal Cancer Screening. J Healthc Qual 2019;41:75-82.
170. Zalis ME, Barish MA, Choi JR, et al. CT colonography reporting and data system: a consensus proposal. Radiology 2005;236:3-9.
171. Hansmann A, Burling D. Essential requirements of a CT colonography service. Eur J Radiol 2013;82:1187-91.

172. Rutter MD, Beintaris I, Valori R, et al. World Endoscopy Organization Consensus Statements on Post-Colonoscopy and Post-Imaging Colorectal Cancer. Gastroenterology 2018;155:909-925 e3.
173. Ahlquist DA. Multi-target stool DNA test: a new high bar for noninvasive screening. Dig Dis Sci 2015;60:623-33.
174. Lidgard GP, Domanico MJ, Bruinsma JJ, et al. Clinical performance of an automated stool DNA assay for detection of colorectal neoplasia. Clin Gastroenterol Hepatol 2013;11:1313-8.
175. Kaminski MF, Kraszewska E, Rupinski M, et al. Design of the Polish Colonoscopy Screening Program: a randomized health services study. Endoscopy 2015.
176. Bretthauer M, Hoff G. Comparative effectiveness research in cancer screening programmes. BMJ 2012;344:e2864.

Figure legends

Figure 1. Summary of CRC screening quality measures and key optimization strategies.
Figure 2. Solutions and interventions to optimize CRC screening adherence

Table 1. **Application of FIT in Trials and National Screening Programs**

Program or Study	**Target age**	**Frequency**	**Number of FITs per cycle**	**FIT type**	**Brand**	**Threshold**
ColonPrev RCT (Spain)	50–69	biennial	single	quantitative	OC sensor	15 ug Hb/g feces
Screesco randomized controlled trial (Sweden)	59–62 years old	biennial	single	quantitative	OC sensor	10 ug Hb/g feces
CONFIRM RCT (US)	50–75	annual	single	quantitative	OC sensor	20 ug Hb/g feces
Denmark National Screening Program	50–74	biennial	single	quantitative	OC sensor	20 ug Hb/g feces
Dutch National Screening Program	55–75 year old	biennial/	single	quantitative	FOB-gold	47 ug Hb/g feces
Italy National Screening Program	50–74 years old	biennial	single	quantitative	OC-hemodia	20 ug Hb/g feces
National Cancer Screening Program of Korea	50 years or older	annual	single	quantitative	OC-sensor	20 ug Hb/g feces
Taiwanese National Screening Program	50–75 year old	biennial	single	quantitative	OC-sensor and HM-Jack	20 ug Hb/g feces
US/Kaiser Permanente	51–75 year old	annual	single	quantitative	OC sensor	20 ug Hb/g feces