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A systematic review of repeat fecal occult blood tests for colorectal cancer screening

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Abstract

Screening with fecal occult blood tests (FOBT) reduces colorectal cancer mortality. Failure to complete repeat tests may compromise screening effectiveness. We conducted a systematic review of repeat FOBT across diverse healthcare settings. We searched MEDLINE, Embase, and the Cochrane Library for studies published in 1997 – 2017 and reported repeat FOBT over ≥2 screening rounds. Studies (n=27 reported in 35 articles) measured repeat FOBT as (1) proportion of Round 1 participants completing repeat FOBT in Round 2; (2) proportion completing two, consecutive FOBT; or (3) proportion completing ≥3 rounds. Among those who completed FOBT in Round 1, 24.6 – 89.6% completed repeat FOBT in Round 2 (median: 82.0%, IQR: 73.7 – 84.6%). The proportion completing FOBT in two rounds ranged from 16.4 – 80.0% (median: 46.6%, IQR: 40.5 – 50.0%), and in studies examining ≥3 rounds, repeat FOBT ranged from 0.8 – 64.1% (median: 39.2%, IQR: 19.7 – 49.4%). Repeat FOBT appeared higher in mailed outreach (69.1 – 89.6%) compared to opportunistic screening (24.6 – 48.6%). Few studies examined correlates of repeat FOBT. In summary, we observed a wide prevalence of repeat FOBT, and

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prevalence generally declined in successive screening rounds. Interventions that increase and maintain participation in FOBT are needed to optimize effectiveness of this screening strategy.

Keywords

colorectal neoplasia; population screening; patient adherence

Introduction

Colorectal cancer (CRC) incidence and mortality has declined in the U.S. since the late 1980s,[1] largely due to increasing uptake of screening.[2, 3] Guidelines recommend screening with colonoscopy, sigmoidoscopy, fecal occult blood test with high-sensitivity guaiac (gFOBT), or fecal immunochemical test (FIT) starting at age 50 for average-risk adults.[4] gFOBT and FIT (hereafter collectively referred to as "FOBT") have become increasingly common in population-based screening programs in Europe,[5] as well as large U.S. healthcare systems implementing mailed outreach.[6, 7] FOBT also plays a critical role in CRC screening for underserved or rural populations,[8, 9] where access to colonoscopy may be limited.[10]

Stool-based screening strategies rely on patients completing regular, on-schedule tests,[11–13] and failure to complete repeat exams may compromise effectiveness.[14] Most European countries, Canada, and Australia recommend stool-based screening every two years, while annual screening is recommend in the U.S. and Asian countries.[15] Compared with the 80 – 85% of participants in randomized trials of screening efficacy completing two or more exams,[11–13] repeat FOBT in clinical practice settings may be very low or vary widely.[16] Repeat FOBT in clinical practice is also complex because it involves reassessing eligibility, considering recommended intervals (annual vs. biennial), and identifying patients due for screening at each round.

Few have characterized repeat FOBT patterns in real-world settings, particularly in light of the growing number of healthcare systems transitioning to stool-based screening strategies[17] for population health. To address this gap, we conducted a systematic review of the literature to estimate prevalence of repeat FOBT across diverse healthcare settings and populations.

Methods

Data sources and searches

We conducted all search methods according to the Preferred Reporting of Systematic Reviews and Meta-Analysis (PRISMA) Statement guidelines.[18] With the assistance of a health sciences librarian, we searched MEDLINE (via Ovid; 1997 to September Week 4 2017, In-Process & Other Non-Indexed Citations September 28, 2017 and Epub Ahead of Print September 28, 2017, searched September 29, 2017), Embase (via Ovid; 1997 to September Week 4, searched September 29, 2017), and the Cochrane Library (via Wiley; Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials, Issue 9 of 12 Sept 2017, searched September 29, 2017) for articles published between 1997 and 2017. General concepts that comprised the search included: colorectal cancer,

mass screening, screening program, and patient adherence. We adapted search terms for each database's unique keywords and subjects headings; strategies were pre-tested and refined through an iterative process by screening citations for relevance to our eligibility criteria. Search strategies for each database are listed as Supplementary Material We also hand searched reference lists from eligible articles and Scopus (via Elsevier) to determine whether eligible articles had been cited by others not identified by our search strategy.

Study selection

We considered articles eligible if they: 1) were written in English; 2) reported data from a primary study (i.e., not a review, commentary, or editorial); and 3); measured repeat FOBT over at least two screening rounds. We focused on studies conducted in average-risk populations (e.g., no personal history of inflammatory bowel disease, CRC, hereditary syndromes, or polyps/adenomas, no family history of CRC or polyps/adenomas), for whom guidelines at the time recommended initiating screening with FIT or gFOBT at age 50 years.[19] To best characterize repeat FOBT in *real world* settings, we excluded trials of screening efficacy or intervention studies requiring informed patient consent. We also excluded studies in which the primary outcome was test performance (i.e., sensitivity and specificity).

We screened articles in a multi-step process. First, two authors (AS and BS) independently reviewed the titles and abstracts of all articles identified by the search strategy, assigning a rating of "not eligible" or "potentially eligible" for inclusion. A third author (CCM) reviewed the title and abstracts of all "potentially eligible" abstracts. Discrepancies in "potentially eligible" ratings across co-authors occurred in fewer than 5% of all abstracts reviewed; all discrepancies were discussed until consensus was reached. Finally, two authors independently evaluated full-text articles of all "potentially eligible" abstracts.

In cases where eligible articles reported data from the same or overlapping patient cohorts, we selected the most recently published article or the article with the most complete data. For example, we identified three articles of overlapping cohorts in the Kaiser Permanente healthcare system,[6, 20, 21] and we report results from the most recent of the three articles.[20]

Data extraction and quality assessment

Using an abstraction form created for this review, two authors (AS and BS) extracted relevant information from all eligible articles, including: study setting, sample size, eligibility criteria, and outcome measures. A third author (CCM) was available to resolve any discrepancies between the two sets of extracted data. Discrepancies in coding occurred in <5% of all studies and were adjudicated through discussion until consensus was reached across the three co-authors.

Repeat FOBT and relevant outcomes were reported in a variety of ways (e.g., completion of all screening rounds, completion of subsequent screening rounds) across studies. The considerable heterogeneity between studies (I^2=99%) precluded the use of meta-analysis to aggregate effect sizes of repeat FOBT. Therefore, we used reported numbers to manually calculate repeat FOBT as the: 1) proportion of Round 1 participants who completed repeat FOBT in Round 2; 2) proportion of patients who completed two, consecutive FOBT; or 3) proportion of patients who completed FOBT in three or more screening rounds (Table 1).

When possible, we excluded from our calculation patients with a positive index test, prior colonoscopy, or prior sigmoidoscopy and who would therefore be ineligible for repeat FOBT.

Using the STROBE checklist,[22] two authors (AGS and CCM) assessed completeness of reporting on nine selected aspects of internal and external validity related to representativeness, intervention, outcome ascertainment, follow-up period, and eligibility criteria. Each characteristic was assigned a rating[23, 24] of "Y, reported by authors," "N, not reported by authors," or "I, inferred by raters but not explicitly reported by authors." We resolved any discrepancies in rating by discussion until consensus was reached.

There was considerable heterogeneity between studies (I2), and the wide-ranging prevalence estimates precluded the use of meta-analysis to aggregate effect sizes of repeat FOBT.

Results

Study selection and patient characteristics

Our search strategy identified 6,258 potentially eligible articles, of which we reviewed the full text of 312 (see Supplementary Figure 1 for PRISMA flow diagram). Common reasons for exclusion included evaluating screening performance or efficacy and requiring patient consent. From the full text review, we identified 35 articles that met inclusion criteria, representing 27 unique studies. As described above, for the eight articles reporting overlapping cohorts, we selected the most recently published article or the article with the most complete data.

Study characteristics are shown in Table 2. Studies were conducted in Europe (n=12), United States (n=8), Asia (n=2), Australia (n=3), and Canada (n=2) and represented a variety of healthcare systems (59.3% mailed, population-based screening outreach, 18.5% mailed outreach in integrated systems, and 25.9% opportunistic screening). Most studies measured repeat FOBT using government health plan or population registry data (n=17, 63.0%), while others used electronic health records (n=9, 33.3%). Only one study[25] relied on patient self-report. Studies examined repeat FOBT over a range of 2 to 5 screening rounds. About half (n=13, 48.1%) of studies evaluated repeat FOBT across three or more screening rounds, and the remaining studies (n=14, 51.9%) evaluated repeat FOBT in only two rounds.

Prevalence of repeat FOBT

Prevalence of repeat FOBT is described in Table 3. Among those who completed FOBT in Round 1, 24.6 – 89.6% (median: 82.0%, IQR: 73.7 – 84.6%) completed repeat FOBT in Round 2.[16, 26–43] Repeat FOBT appeared higher in mailed outreach programs[27–30, 32, 33, 36–42, 44–47] compared to opportunistic screening (Supplementary Figure 2).[16, 35, 36, 43] Specifically, the proportion of Round 1 participants who completed repeat FOBT in Round 2 ranged from 69.1% to 89.6% in studies with mailed outreach, whereas repeat FOBT was less than 50% in studies with opportunistic screening. Notably, two pragmatic, randomized controlled trials[36, 48] compared mailed outreach to opportunistic screening in low-income settings. In both trials, a higher proportion of patients randomized

to mailed outreach completed repeat FOBT in Round 2 (82.2 vs. 37.3%)[36] and across all screening rounds (30.8 vs 2.3%)[48] compared to opportunistic screening. There appeared to be only small differences in repeat FOBT in studies with annual (range 34.5 – 89.6%) vs. biennial (range 24.6 – 88.4%) screening (Supplementary Figure 3), and in studies of FIT vs. gFOBT (Supplementary Figure 4).

The proportion of patients who completed two, consecutive FOBT varied widely across studies, ranging from 16.4% to 80.0% (median: 46.6%, IQR: 40.5 – 50.0%).[20, 26–30, 34, 37, 38, 46, 49] Most studies reported repeat FOBT between 40% and 60%. Notable outliers were studies by Garcia and Janda (both <20% completion) and Wong (>80% completion).

Repeat FOBT across all screening rounds also varied, ranging from 0.8% to 64.1% (median: 39.2%, IQR: 19.7 – 49.4%).[20, 25, 29, 30, 34, 40, 46–48, 50–52] Prevalence generally decreased across screening rounds. For example, Gellad et al.[53] reported 42.1%, 26.0%, 17.8%, and 14.1% completed one, two, three, and four tests, respectively, over five rounds of screening. Similarly, Pornet et al.[54] identified a greater proportion of never (33.6%) or occasional participants (27.7%) – those who completed no or one test over three screening rounds – than consistent participants (38.8%).

Completeness of reporting

Supplementary Table 1 describes the completeness of reporting of each included study. All or the majority of studies described test type, defined repeat FOBT, and used EHR or registry data to ascertain the outcome. We identified eight studies[6, 20, 21, 25, 35, 37, 38, 40, 41, 48, 53] that did not report type of FOBT, and the study by Bae et al.[25] assessed repeat FOBT by patient self-report. Studies were more variable with respect to reporting the number of patients eligible in each screening round or the number who were lost to follow-up, were diagnosed with CRC or died, or received colonoscopy. Although all studies included patients who were age-eligible for screening (i.e., age 50–75 years), fewer studies made an attempt to exclude patients at higher-risk (e.g., family history of CRC). Some studies[25, 30, 41, 51] required patients to complete a brief questionnaire as part of inclusion criteria.

Discussion

Success of stool-based screening relies on patients completing regular, on-schedule screening, every one to two years. Studies included in our review report a wide range of repeat FOBT – between 14 and 90% – and prevalence generally declined across successive screening rounds. Our synthesis of data across studies highlight two key challenges: 1) ensuring patients initiate and repeat FOBT consistently as part of stool-based screening strategies; and 2) increasing the already substantial prevalence of repeat FOBT among patients who have previously initiated screening. As such, interventions that maintain consistent participation in FOBT are needed to optimize the effectiveness of this CRC screening strategy. Our findings also point to a number of areas for future research and the need for more transparent results reporting.

Although tightly controlled screening efficacy trials report up to 85% of trial participants complete two or more tests, we observed varying prevalence of repeat FOBT across *real world* settings. The wide variation in repeat FOBT across studies included in our review underscores potential differences in data collection and quality and highlights the need for better summary measures. Reasons for such wide-ranging prevalence estimates may be related to a variety of factors, including test type and frequency, screening delivery, and intensity of reminders for test completion. Most studies included in our review examined repeat FOBT every two years (i.e., biennial screening), but prevalence in these studies did not appear to differ dramatically from studies of annual screening. Studies also used a variety of test types, and differences in patient handling and collection may have contributed to the wide range of prevalence estimates. In randomized trials of gFOBT vs. FIT, participation in FIT screening is about 10% higher than for FOBT.[55, 56] Some of have suggested three-sample tests deter patients from completing repeat screening and introduce more opportunity for sampling and collection error.[57] Only four studies[16, 46, 48, 50] reported using a three-sample test, and prevalence of repeat FOBT in these studies ranged from 0.8 – 49.8% across all screening rounds. Differences in repeat FOBT by test type (FIT vs. gFOBT) also appeared to be small.

We also observed variability in the proportion of patients completing repeat FOBT depending upon how the outcome was defined. For example, when defined as the proportion of Round 1 participants completing FOBT in Round 2, approximately 75% of patients completed repeat screening. Repeat FOBT was much lower when defined as completion across multiple screening rounds – about 45% of patients completed FOBT in two, consecutive rounds. Repeat FOBT appeared even lower when considering patterns over three or more rounds. These differences in outcome suggest two possible phenomena: 1) prior cancer screening experience predicts repeat, on-schedule screening; and 2) those who initially refuse are unlikely to participate in subsequent rounds. In the context of interventions, the former suggests FOBT participants should be actively engaged to encourage repeat screening, and non-participants may instead benefit from an alternate screening test.[58] This variability in outcome is also important when comparing results across studies, which used different definitions for repeat FOBT.

Few studies examined correlates of repeat FOBT, and those that did generally included non-modifiable factors (e.g., age, sex). This is consistent with studies on correlates and predictors of FOBT *initiation*, in which sociodemographic variables such as younger age, non-white race/ethnicity, low socioeconomic status, poor educational attainment, and lack of insurance are negatively associated with screening uptake.[59–61] Although demographic factors may help identify a target population in which to promote screening, they do not identify strategies that can be used to modify or change behavior. Repeat FOBT may depend highly on patient behavior. For example, in our review, Duncan et al.[51] found greater perceived barriers and lower levels of response efficacy were associated with drop-out from FOBT screening. Others have shown self-efficacy distinguishes patients engaged in consistent, on-schedule screening from those never screened.[51, 62]

Repeat FOBT was generally higher in studies of mailed outreach (either in integrated healthcare systems or population-based programs) compared to studies of opportunistic

screening. Our search strategy also identified two pragmatic trials[26, 48] of screening outreach; both demonstrated the effectiveness of mailed FOBT outreach (i.e., test kits with postage-paid return envelope) to increase patient adherence to two or more tests over multiple screening rounds. Other trials not included in our review similarly show mailed FOBT kits increase one-time screening, regardless of patient factors or preferences.[63–67] Incorporating elements of mailed outreach may optimize efforts to implement population health and cancer screening programs. Learning from system-level interventions[68] to promote repeat breast[69] and cervical cancer screening, such as tracking screening utilization and reports to primary care providers, may also help achieve comparable adherence for repeat FIT or FOBT.

Our findings also underscore the importance of transparent results reporting to facilitate comparison among studies and healthcare systems. For example, few studies reported the number of persons eligible at each screening round, and confusion surrounding the appropriate denominator can make it difficult to determine prevalence of repeat FOBT and compare prevalence estimates across studies. Others failed to describe the number of patients completing a prior screening test, creating challenges for measuring the true yield of screening programs. Allison et al.[70–72] have developed several standards to improve FIT results reporting, including fecal hemoglobin concentration, sample handling, storage, and transport. Adapting these standards, we have proposed a checklist (Table 4) to strengthen reporting of FOBT screening completion, particularly when assessed across multiple screening rounds. Most importantly, studies of repeat FOBT should report the number eligible at each screening round, including those who become ineligible for a repeat test due to CRC diagnosis, death, move away from healthcare system or geographic region, prior positive FOBT and/or diagnostic colonoscopy, and prior colonoscopy for some other reason. These standards will allow researchers to compare and contrast the results of published studies and improve translation of results into clinical practice.

We observed considerable heterogeneity between studies (e.g., different countries, healthcare systems, test type), and the wide-ranging prevalence estimates precluded the use of meta-analysis to aggregate effect sizes of repeat FOBT. Similarly, because few studies examined correlates, it was not feasible to provide summary estimates. We excluded screening intervention trials requiring informed patient consent, and repeat FOBT may differ in intervention vs. clinical practice settings. However, recent post hoc analyses[62, 73, 74] of these trials suggest prevalence of repeat screening is similar to what we reported. Further, many of the studies included in our review reflect European or predominantly insured, white American populations, thereby excluding a number of patients at risk of CRC and among whom screening uptake remains low (e.g., Hispanics, non-Hispanic blacks). Although we have demonstrated that many patients, including those completing an index FOBT, fail to complete repeat screening, these data do not illustrate specific reasons for suboptimal screening.

In summary, adherence to repeat screening is critical to the effectiveness of stool-based tests, but few patients complete regular, on-scheduling testing over multiple screening rounds. Our review of repeat FOBT showed a wide range of repeat FOBT across 27 studies, as well as varying measures and definitions of repeat screening. Understanding reasons for these

patterns may identify strategies to promote regular CRC screening at recommended intervals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Definition of repeat FOBT outcomes across studies

Outcome	Screening rounds	Numerator	Denominator	Key example
Proportion of Round 1 participants who completed repeat FOBT in Round 2	2	Completed FOBT in Round 2	Completed FOBT with negative result in Round 1	Baker, 2015[26]
Proportion of patients who completed two, consecutive FOBT	2	Completed consecutive FOBT in Rounds 1 and 2	Eligible to complete FOBT in two screening rounds; negative result or did not complete FOBT in Round 1	Singal, 2018[20]
Proportion of patients who completed FOBT in all screening rounds	≥3	Completed FOBT in all screening rounds	Eligible to complete FOBT in three or more screening rounds; negative result or did not complete FOBT in all but final round	Denis, 2015[50]

Table 2.

Characteristics of included studies (n=27 unique studies reported in 35 articles)

Author, year	Study setting	Eligibility criteria	Sample size	FOBT/FIT	Screening delivery
Tazi, 1997 [40]	Burgundy, France 1988 – 1996	Age 45–74 yrs	45,642	Biennial	Mailed outreach population-based
Weller, 2007 [39]	UK CRC Screening Pilot Evaluation, England 2000 – 2004	Ages 50–69 yrs; completed negative index test	107,434	Biennial Hema-screen	Mailed outreach population-based
Fenton, 2010 [16]	Group Health Cooperative, Seattle, WA, USA 2000 – 2003	Age 52–78 yrs; completed negative index test; continuously enrolled in health plan	10,132	Biennial Hemoccult II SENSA	Opportunistic
Janda, 2010 [38]	Queensland, Australia 2000 – 2002	Age 50–74 yrs; completed negative index test Excluded hx SIG or COL	3,406	Biennial	Mailed outreach population-based
Gellad, 2011 [53]	Veterans Health Administration (136 sites), USA 1999 – 2005	Age 50–75 yrs Excluded hx SIG, COL, or CRC	394,996	Annual	Opportunistic
Cole, 2012 [27]	National Bowel Cancer Screening Pilot Program, Australia 2003 – 2005	Age 55–74 yrs	16,433	Annual Detect™	Mailed outreach population-based
Crotta, 2012 [52]	Aosta Valley, Italy 2001 – 2008	Age 50–74 yrs Excluded hx SIG, COL, IBD, polyps, CRC, or severe comorbid conditions	2,959	Biennial OC-Sensor	Mailed outreach population-based
Garcia, 2012 [37]	Catalonia, Spain 2004 – 2006	Age 50–69 yrs; completed negative index test	11,969	Biennial	Mailed outreach population-based
Liss, 2013 [35]	Erie Family FQHC, Chicago, IL, USA 2010 – 2011	Age 50–74 yrs; completed negative index test Excluded hx SIG, COL, IBD, CRC, or lower GI symptoms	281	Annual	Opportunistic
Bae, 2014 [25]	University Hospital at Gangdong, South Korea 2002 – 2011	Age ≥50 yrs; completed ≥1 FOBT in prior decade; completed baseline survey	237	Biennial	Opportunistic
Baker, 2014 [36]	Erie Family FQHC, Chicago, IL, USA 2010 – 2011	Age 51–75 yrs; completed negative index test Excluded hx SIG, COL, IBD or lower GI symptoms	225	Annual OC-Light	Opportunistic
Baker, 2014 [36]	Erie Family FQHC, Chicago, IL, USA 2010 – 2011	Age 51–75 yrs; completed negative index test Excluded hx SIG, COL, IBD or lower GI symptoms	225	Annual OC-Light	Mailed outreach
Duncan, 2014 [51]	Bowel Health Service, Australia 2008 – 2010	Age 50–75 yrs; completed baseline survey Excluded hx SIG, COL, IBD or CRC, family hx CRC	1,540	Annual OC-Sensor	Mailed outreach population-based
McNamara, 2014 [28]	Tallaght Hospital-Trinity College CRC Screening Program, Ireland 2008 – 2012	Age 50–75 yrs Excluded hx COL, serious illness, or CRC	9,863	Biennial OC-Sensor	Mailed outreach
Steele, 2014 [34]	UK CRC Screening Pilot Evaluation, Scotland 2000 – 2006	Age 50–69 yrs	251,578	Biennial Hema-screen	Mailed outreach population-based
Wong, 2014 [30]; Wong, 2013 [31]	Hong Kong 2008 – 2012	Age 50–70 yrs	5,832	Annual Hemosure	Mailed outreach population-based

Author, year	Study setting	Eligibility criteria	Sample size	FOBT/FIT	Screening delivery
		Excluded hx SIG, COL, IBD, CRC, or lower GI symptoms			
Baker, 2015 [26]	Erie Family FQHC, Chicago, IL, USA 2012 – 2013	Age 51–75 yrs; completed negative index test Excluded hx SIG, COL, or CRC in Round 1	225	Annual OC-Light	Mailed outreach
Bujanda, 2015 [33]	Basque, Spain 2009 – 2013	Age 50–69 yrs; completed negative index test Excluded hx SIG, COL, IBD, or CRC, family hx CRC	100,135	Biennial OC-Sensor	Mailed outreach population-based
Denis, 2015 [50]; Pornet 2014 [54]	Haut-Rhin, France 2003 – 2012	Age 50–74 yrs Excluded hx of SIG, COL, serious illness, or high risk CRC features	242,271	Biennial Hemoccult II	Mailed outreach population-based
Lo, 2015 [29]; Lo, 2016 [75]; Lo, 2015 [76]	NHS Bowel Cancer Screening Program, England 2006 – 2012	Age 60–64 yrs	62,099	Biennial Hema-screen	Mailed outreach population-based
Schlichting, 2015 [32]	Veterans Health Administration, Iowa City, IA, USA 2011 – 2013	Age <65 yrs; completed negative index test Excluded self-reported screen up-to-date	159	Annual OC FIT-CHEK	Mailed outreach
Paszat, 2016 [43]	ColonCancerCheck Program, Ontario, Canada 2008 – 2012	Age 50–74 yrs; completed negative index test Excluded hx SIG, COL, or CRC, family hx CRC	294,329	Biennial Hema-Screen	Opportunistic
Telford, 2016 [42]	Colon Check Program, British Columbia, Canada 2009 – 2013	Age 50–74 Excluded hx SIG, COL, CRC, IBD, or rectal bleeding	16,234	Biennial OC-Auto Micro	Mailed outreach population-based
Knudsen, 2017 [41]	Bowel Cancer Screening in Norway, Southeast Norway 2012 – 2016	Age 50–74 yrs; completed negative index test; completed lifestyle survey Excluded hx SIG, COL, or CRC	3,114	Biennial	Mailed outreach population-based
Saraste, 2017 [46]	Stockholm-Gotland Region, Sweden 2008–2015	Age 60–69 yrs; invited to ≥3 screening rounds	48,959	Biennial Hemoccult	Mailed outreach population-based
Singal, 2017 [48]	Parkland Health & Hospital System, Dallas, TX, USA 2013 – 2016	Age 50–64 yrs; not up-to-date with screening Excluded hx SIG, COL, CRC, or IBD	1,199	Annual Hemoccult ICT	Opportunistic
Singal, 2017 [48]	Parkland Health & Hospital System, Dallas, TX, USA 2013 – 2016	Age 50–64 yrs; not up-to-date with screening Excluded hx SIG, COL, CRC, or IBD	2,400	Annual FIT-CHEK	Mailed outreach
van der Vlugt, 2017 [49]; Denters, 2013 [77]; Grobbee, 2017 [78]	Southwest and Northwest Netherlands 2006 – 2014	Age 50–74 yrs; eligible for ≥2 screening rounds Excluded hx SIG, COL, IBD, CRC, or severe comorbid conditions	17,132	Biennial OC-Sensor	Mailed outreach population-based
Singal, 2018 [20]; Jensen, 2016 [6]; Gordon, 2015 [21]	Parkland Health & Hospital System, Dallas, TX; Kaiser Permanente Washington, Seattle, WA; Kaiser Permanente Northern and Southern California, USA 2010 – 2013	Age 50–71 yrs; completed negative index test; 2–3 yrs follow-up Excluded hx SIG, COL, or CRC	273,182	Varied across sites	Varied across sites
Singal, 2018 [20]; Jensen, 2016 [6]; Gordon, 2015 [21]	Parkland Health & Hospital System, Dallas, TX; Kaiser Permanente Washington, Seattle, WA; Kaiser Permanente Northern and Southern California, USA 2010 – 2013	Age 50–71 yrs; completed negative index test; ≥3 yrs follow-up Excluded hx SIG, COL, or CRC	344,103	Varied across sites	Varied across sites

Table 3.

Prevalence of repeat FOBT across studies (n=27 unique studies reported in 35 articles) by screening delivery

Author, year	Data source	Screening rounds	Relevant outcome	Sample size	Prevalence (95% CI)
Mailed outreach, population-based					
Tazi, 1997 [40]	Pop. Registry	5	% completed among Round 1 participants % completed across all screening rounds	36,573/ 43,852 13,951/ 37,502	83.4% (83.1 – 83.7%) 37.2% (36.7 – 37.7%)
Weller, 2007 [39]	Gov't health plan	2	% completed among Round 1 participants	87,129/ 107,434	81.1% (80.9 – 81.3%)
Janda, 2010 [38]	Pop. Registry	2	% completed among Round 1 participants % completed two, consecutive tests	874/ 1,163 874/ 3,406	75.2% (72.7 – 77.6%) 25.7% (24.2 – 27.1%)
Cole, 2012[27]	Gov't health plan	2	% completed among Round 1 participants % completed two, consecutive tests	6,656/ 8,345 6,656/ 16,433	79.8% (78.9 – 80.6%) 40.5% (39.8 – 41.3%)
Crotta, 2012 [52]	Pop. Registry	4	% completed across all screening rounds	713/ 2,109	33.8% (31.8 – 35.8%)
Garcia, 2012 [37]	Pop. Registry	2	% completed among Round 1 participants % completed two, consecutive tests	10,415/ 11,969 10,415/ 63,685	87.0% (86.4 – 87.6%) 16.4% (16.1 – 16.6%)
Duncan, 2014[51]	Gov't health plan	3	% completed across all screening rounds	860/ 1,540	55.8% (53.4 – 58.3%)
Steele, 2014 [34]	Gov't health plan	3	% completed among Round 1 participants % completed two, consecutive tests % completed across all screening rounds	114,063/ 139,274 114,063/ 251,578 98,494/ 251,578	81.9% (81.7 – 82.1%) 45.3% (45.1 – 45.5%) 39.2% (39.0 – 39.3%)
Denis, 2015[50]; Pornet 2014[54]	Gov't health plan	4	% completed across all screening rounds	34,556/ 242,271	14.3% (14.1 – 14.4%)
Wong, 2014[30]; Wong, 2013[31]	Gov't health plan	3	% completed among Round 1 participants % completed two, consecutive tests % completed across all screening rounds	4,426/ 5,391 4,426/ 5,534 3,519/ 5,488	82.1% (81.1 – 83.1%) 80.0% (78.9 – 81.0%) 64.1% (62.9 – 65.4%)
Bujanda, 2015 [33]	Gov't health plan	2	% completed among Round 1 participants	69,193/ 100,135	69.1% (68.8 – 69.4%)
Lo, 2015[29]; Lo, 2016[75]; Lo, 2015[76]	Gov't health plan	3	% completed among Round 1 participants % completed two, consecutive tests % completed across all screening rounds	30,182/ 35,611 30,182/ 62,099 27,587/ 62,099	84.8% (84.4 – 85.1%) 48.6% (48.2 – 49.0%) 44.4% (44.0 – 44.8%)
Telford, 2016 [42]	Pop. Registry	2	% completed among Round 1 participants	5,378/ 6,255	86.0% (85.1 – 86.8%)
Knudsen, 2017 [41]	Pop. Registry	2	% completed among Round 1 participants	2,574/ 3,114	82.7% (81.3 – 84.0%)
Saraste, 2017 [46]	Pop. registry	3	% completed among Round 1 participants % completed two, consecutive tests % completed across all screening rounds	26,098/ 29,113 26,098/ 48,959 24,373/ 48,959	89.6% (89.3 – 90.0%) 53.3% (52.9 – 53.7%) 49.8% (49.3 – 50.2%)
van der Vlugt, 2017 [49]; Denters, 2013 [77]; Grobbee, 2017 [78]	Pop. Registry	4	% completed two, consecutive tests % completed across all screening rounds % completed in 3 of 3 screening rounds	2,561/ 5,232 4,345/ 8,795 1,365/ 3,285	48.9% (47.6 – 50.3%) 49.4% (48.4 – 50.4%) 41.6% (39.9 – 43.2%)
Mailed outreach, integrated healthcare systems					
Baker (intervention), 2014[36]	EHR	2	% completed among Round 1 participants	185/219	84.5% (79.7 – 89.3%)

Author, year	Data source	Screening rounds	Relevant outcome	Sample size	Prevalence (95% CI)
McNamara, 2014 [28]	EHR	2	% completed among Round 1 participants % completed two, consecutive tests	3,767/ 4,549 3,767/ 9,359	82.8% (81.7 – 83.9%) 40.3% (39.3 – 41.2%)
Baker, 2015 [26]	EHR	2	% completed among Round 1 participants % completed two, consecutive tests	114/ 129 114/ 189	88.4% (82.8 – 93.9%) 60.3% (53.3 – 67.3%)
Schlichting, 2015 [32]	EHR	2	% completed among Round 1 participants	126/ 159	79.2% (72.9 – 85.5%)
Singal (intervention), 2017[48]	EHR	3	% completed across all screening rounds	395/ 2,007	19.7% (17.9 – 21.4%)
Opportunistic					
Fenton, 2010 [16]	EHR	2	% completed among Round 1 participants	4,928/ 10,132	48.6% (47.7 – 49.6%)
Gellad, 2011 [53]	EHR	5	% completed in 4 of 5 screening rounds	55,652/ 394,996	14.1% (14.0 – 14.2%)
Liss, 2013 [35]	EHR	2	% completed among Round 1 participants	69/ 281	24.6% (19.5 – 29.6%)
Bae, 2014 [25]	Self-report	5	% completed across all screening rounds	105/ 237	44.3% (38.0 – 50.6%)
Baker (usual care), 2014	EHR	2	% completed among Round 1 participants	84/ 219	38.3% (31.9 – 44.8%)
Paszat, 2016 [43]	Gov't health plan	2	% completed among Round 1 participants	101,526/ 294,329	34.5% (34.3 – 34.7%)
Singal (usual care), 2017	EHR	3	% completed across all screening rounds	8/ 1,044	0.8% (0.2 – 1.3%)
Varied					
Singal, 2018 [20]; Jensen, 2016 [6]; Gordon, 2015 [21]	EHR	2	% completed two, consecutive tests	127,188/ 273,182	46.6% (46.4 – 46.7%)
Singal, 2018 [20]; Jensen, 2016 [6]; Gordon, 2015 [21]	EHR	3	% completed two, consecutive tests	160,252/ 344,103	46.6% (46.4 – 46.7%)

NOTE: For studies with three or more screening rounds (e.g., Saraste, 2017[46]), the outcome describing completion of two, consecutive tests corresponds to FOBT completion in the first two screening rounds (i.e., in Rounds 1 and 2); confidence intervals estimated using Wald method based on a normal approximation

Table 4.

Proposed checklist for reporting studies of repeat stool-based screening

Outcome variable	
	• Explicitly defined, with numerator and denominator
Test characteristics	
	• Test name, manufacturer
	• Quantitative or qualitative
	• Number of samples
	• Cut-off concentration
Study population	
	• Age at study entry
	• Number with high risk features: family history, personal history, IBD or UC
	• Proportion previously screened
Screening round	
	• Number of screening rounds
	• Follow-up period
	• Distinguish new invitees from previous participants
	• Number ineligible: positive FOBT or diagnostic colonoscopy in prior screening round, aged out, moved away from healthcare system or geographic region, colonoscopy for other reason, CRC diagnosis, death
Screening delivery	
	• Organized outreach vs. opportunistic
	• Frequency, timing, and intensity of patient reminders
	• Patient education materials (if any)
	• Out-of-pocket costs or financial incentives