

Effectiveness of Patient Navigation for Colorectal Cancer Screening: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Background: Colorectal cancer is highly preventable through early screening, but disparities in screening create a negative impact on the lives of those at risk. One approach to address this is patient navigation. This systematic review and meta-analysis therefore aimed to provide evidence of the effectiveness of patient navigation in increasing colorectal cancer screening uptake.

Objectives: This study aimed to determine the effectiveness of patient navigation on colorectal cancer screening uptake. Specifically, it aimed to study the effects of different methods of navigation on the uptake of initial screening tests among persons with average risk.

Methods: The studies included were randomized clinical trials conducted within 2011-2021 and involving only humans as participants. Data were analyzed by calculating the risk ratio and 95% confidence intervals of each successful outcome, and the investigators independently appraised each study's risk of bias. Subgroup analysis was conducted to assess consistency of study effects. Certainty of evidence was assessed using the GRADE standard.

Results: Eleven (11) studies were included in this systematic review and meta-analysis. All studies encompassed health systems of different countries, and they utilized different means of navigation to achieve outcome measure of colorectal cancer screening uptake. Results show a statistically significant increase in screening uptake with patient navigation in a forest plot. However, there is a high level of heterogeneity among the studies, hence a subgroup analysis was conducted among these studies according to navigation method.

Conclusion. This systematic review and meta-analysis show an increase in screening rates in those who were navigated. Results in favor of patient navigation was consistent when all studies were analyzed together and when they were analyzed according to navigation method. Increase in screening uptake is more statistically significant among patients navigated via face-to-face and via phone call, but data is more consistent for patient navigation via phone call alone.

Key words: Colorectal cancer, patient navigation

INTRODUCTION

Colorectal cancer is the third most common medical diagnosis in the world, and the second deadliest form of cancer for both male and female.¹ In the Philippines, it ranks second among males of all ages, about 11.8% as of 2018, and third among females of all ages at 8.7%.² This form of disease is highly preventable through early screening, detection, and intervention. Early warning signs for colorectal cancer

includes persistent change in bowel habit, narrow stools, rectal bleeding, persistent abdominal pain or discomfort, sensation of incomplete bowel emptying, and unexplained weight loss and fatigue.¹ This medical condition could present as sporadic (70%), the average age diagnosis of which is older than 50 years and mostly linked to environmental factors, while only a smaller percentage is due to familial clustering (20%) and inherited syndromes (10%).³ Early detection includes education on the modifiable risk factors such as proper diet and lifestyle, and timely screening procedures for the average-risk population. However, for developing countries like the Philippines, lack of proper implementation of cancer prevention, screening, and treatment as well as information dissemination decreases the odds for quality cancer care and survival.

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Hence, the U.S. Preventive Services Task Force⁴ recommends screening for colorectal cancer at the age of 50 up to 75, placing huge significance on the use of the different modalities to identify it while it is still in its initial stages.

Because colorectal cancer is supposedly a highly preventable type of cancer through early and effective screening, disparities in screening create a huge negative impact on the lives of those at risk, and they exist based on race, ethnicity, income, education, and health insurance status. To address these barriers and improve the provision of timely and comprehensive medical assistance, a system called the Patient Navigation program was developed. It is defined as "individualized assistance to help patients overcome personal and healthcare system barriers, and to facilitate understanding and timely access to quality screening."^{5,14,15} Patient navigation helps the patient at any point in the continuum of a disease, from prevention to screening, to treatment and rehabilitation. In the Philippines, the Patient Navigation Program (PNaP) implemented by the Philippine Cancer Society started catering to breast cancer patients in 2011, in cooperation with the Department of Health.⁵ It is mostly manned by highly trained nurses who "navigate" the patients through the complicated healthcare system. Services offered include assistance for diagnostic examinations, chemotherapy and radiotherapy, patient education and family counseling.⁵ The patient navigation system has already been around since 1990 and was created as an innovative approach to reduce cancer disparities.⁶ The prevention, screening, diagnosis, treatment, and even rehabilitation of cancer involves multiple and complex processes that leave most of those who need to undergo them overwhelmed and at a disadvantage. However, early on in its evolution, there was little consensus about what patient navigation really means and what it comprises of. There was also a question on its efficacy and what specific outcomes it aimed to achieve. With that, several studies have cropped up over the past years, thus coming up a consensus on the effects of patient navigation on several outcomes along the continuum of cancer management. In the United States, statistics have found that colorectal cancer incidence and mortality declined due to screening and improvements and early detection, hence a meta-analysis was conducted by Nelson, et al.⁷ on the effectiveness of patient navigation to increase cancer screening in populations adversely affected by health disparities, and they have concluded that colorectal, breast, and cervical cancer screening rates were higher in patients provided navigation services. In their study, however, subgroup analysis was focused on the types of screening tests that the patients took after navigation services. A systematic review was conducted by Jermy-Leigh Domingo and Kathryn Braun⁸, wherein they reviewed studies of colorectal cancer screening completion among navigated and non-navigated federally qualified health center clients through experimental and quasi-experimental study designs. Their primary outcome was broader, though, with uptake of screening test without any time limit from the start of patient navigation application. A study conducted by Charles R. Rogers, et al.⁹ focused on African American men, seeing as they have a higher risk of colorectal cancer than any other ethnicity, and the lowest survival rate for colorectal cancer of any racial group. They stated that aside from the big genetic influence, low screening adherence partly causes this poor rate. In their meta-analysis, patient navigation was not the only intervention of interest,

and the specific methods of patient navigation were not specified. They have concluded, though, that interventions utilizing patient navigation and stool-based kits were most effective at increasing colorectal cancer screening completion. A systematic review and meta-analysis were also conducted by Dr. Michael Dougherty, et al.¹⁰, wherein they attempted to determine which intervention increased completion of colorectal cancer screening tests in the United States. Multicomponent programs that were evaluated included patient navigation, patient education only, FOBT outreach, patient reminders, clinician interventions of academic detailing, and clinician reminders. A combinations of these interventions (clinician interventions or navigation added to FBT outreach) were also investigated. Their primary outcomes were completion of any colorectal cancer screening modality, a follow-up colonoscopy after a positive FOBT, and continued annual FOBTs. The limitations of their study, however, is that they were focused solely on US population and health care setting. There was also substantial heterogeneity probably due to the number of interventions and their combinations. A systematic review by Muliira JK, et al.¹¹ showed the effectiveness of patient navigation interventions on the successful uptake of colorectal cancer screening in primary care settings. They included published studies of various research designs, such as randomized controlled trials, quasi-experimental trial, interventional projects, cohort and multi-level studies, and retrospective analysis, hence majority of these studies were not randomized.

The results from previous studies and the lack of updated reviews and meta-analysis of studies that are strictly randomized controlled trials and the effects of specific methods of patient navigation on the uptake of a colorectal cancer screening test within a shorter time period therefore prompted the researchers to conduct this systematic review and meta-analysis. This study, therefore, will provide an updated literature on patient navigation which will help medical professionals and policymakers further enhance the implementation of this program to increase colorectal cancer screening rates and completion especially here in the Philippines, thus help improve the morbidity and mortality picture of a supposedly largely preventable and treatable disease. Furthermore, it will encompass how patient navigation is performed in other health care settings of other countries. It will also aim to systematically evaluate the different methods of patient navigation.

The general objective was to conduct a systematic review and meta-analysis of randomized controlled trials regarding the effectiveness of patient navigation on colorectal cancer screening.

It specifically aimed to study the effects of different methods of navigation on the uptake of colorectal cancer screening tests among persons with average risk.

METHODS

This systematic review and meta-analysis only included randomized controlled trials involving humans as participants. The articles published during the period of 2011 to 2021 were searched and retrieved from databases including MEDLINE/Pubmed, Cochrane Library, Google Scholar, Embase, ClinicalTrials.gov, and the local database HERDIN. A 'snowball' search was also conducted, wherein the reference lists of the articles eligible for full text review were

reviewed to find additional articles that might have been missed during database searches. Grey literature search was also conducted to look for studies not indexed in the databases listed above. The following grey literature databases were also searched: Open Grey (www.opengrey.eu), Grey Literature Report of the New York Academy of Medicine (www.greylit.org), Agency for Healthcare Research and Quality (www.ahrq.gov), National Institute for Health and Clinical Excellence (www.nice.org.uk). The key words 'patient navigation' and 'colorectal cancer screening' were used in all the databases and search engines used. In the MEDLINE/Pubmed database, the Boolean term "AND" was used to yield articles with both these key words. The 10-year filter and randomized controlled trial filter were then employed to narrow the search results. The titles and abstracts of these articles were perused for full-text review, and articles with titles and/or abstracts not fitting this study's inclusion criteria, duplicate studies, and repeated entries were excluded. In Google Scholar, an advanced filter search specifying the key words above was utilized. Furthermore, articles were extracted from the reference list of the articles found in the primary search. The investigators included studies of adult (≥ 50 years old) patients, who are defined by the U.S. Preventive Services Task Force as having average risk for colorectal cancer, as long as they do not have active gastrointestinal symptoms or any comorbidities that would necessitate a medical consult prior to undergoing a colonoscopy, a history of inflammatory bowel disease or colorectal cancer, and family history of known genetic disorders that predispose them to a high lifetime risk of colorectal cancer. These patients are also those who were not able to complete any colorectal screening test according to US Preventive Services Task Force guidelines, which is defined as colonoscopy in the past 10 years, sigmoidoscopy or double-contrast barium enema in the past 5 years, or FIT/FOBT in the past year. In line with the definition by Dr. Harold Freeman, who pioneered Oncology Patient Navigation, navigators help patients overcome practical barriers to cancer screening, provide culturally appropriate patient education, offer counseling, provide linkages to financial and community resources, offer client reminders and outreach; and reduce structural/practical barriers.^{6,12,14} Hence, this review acknowledges any form of patient navigation given by a study as long as they appear to fulfill these characteristics. Control as comparator is usual or standard care as defined by the specific health system in a particular country or area, as long as these forms of usual or standard care do not involve any form of navigation. For the primary outcome, a study was included if it mentioned the uptake of any form of colorectal screening test within 12 months of initiation of patient navigation, using either FOBT, colonoscopy or flexible sigmoidoscopy. We included studies that are randomized controlled trials, and written in the English language. These studies were published within the years 2011-2021, in keeping with the objective of reviewing and analyzing the latest studies on patient navigation and updating relevant literature. There were no limitations to study setting.

The two investigators conducted the search in all the databases and search engines previously mentioned, and they assessed for relevance to the focus of this study among the titles and abstracts of the articles. If an investigator deemed the title of an article as relevant, the abstract was reviewed. The two investigators then independently appraised these abstracts and selected the studies that met the eligibility

criteria. Articles with the following characteristics were excluded from the review: colorectal screening uptake was not one of the outcomes measured, studies with any form of navigation in the control group, studies who compared one form of navigation with another, studies that focused on diagnostic resolution or completion after an initial screening test was already performed or if the test yielded a positive result, studies focusing on complications associated with colorectal cancer screening tests and procedures, studies with other outcomes such as cost-effectiveness, patient satisfaction, perceived benefits and barriers, proportion of screening test results that turned out positive, change in decision change, and adequacy of bowel preparation, and studies that are not of RCT research design. Any disagreements between the two investigators regarding the eligibility of each article was settled through discussion, and further indecision was resolved by the consultant co-author.

The investigators assessed risk of bias in the included studies using the Cochrane Collaboration Risk of Bias Tool. This tool addresses five specific domains: 1) bias arising from the random sequence generation; 2) bias arising from allocation concealment; 3) bias arising from blinding of participants and personnel; 4) bias arising from outcome assessment; 5) bias arising from incomplete outcome data; and 6) bias arising from selective reporting. The two investigators independently applied the tool to each included study, and recorded supporting information and justifications for judgements of risk of bias for each domain (low risk; high risk; unclear risk). Any discrepancies in judgements of risk of bias or justifications for judgements were resolved by discussion to reach consensus between the two investigators, with a third author (consultant co-author) acting as an arbiter if necessary. To assess for reporting bias, the study protocols of each included article were searched in Pubmed, Cochrane Library, Google Scholar, Embase and ClinicalTrials.gov. If the protocol of an article is available, then the outcomes in the protocol and the published report are compared.

Data extracted from each included article are dichotomous. Therefore, the investigators analyzed these data by calculating the risk ratio and the 95% confidence intervals of each successful outcome, as reflected in the forest plot produced in the Review Manager (RevMan) application. The overall analysis was based on results at the 12-month mark after randomization, and this also applies to studies that reported outcomes at more than one time point. In studies with 2 intervention arms involving patient navigation, the results of the 2 arms were not combined, and the results from the longer follow-up time were the only values included in the meta-analysis. Statistical heterogeneity was assessed, with its magnitude measured using the I² statistic. Subgroup analysis was conducted to obtain effect estimates according to the method of patient navigation used. Finally, a funnel plot was generated to assess for publication bias or other causes of systematic heterogeneity.

The two investigators of this study independently assessed the certainty of evidence. The Grades of Recommendations Assessment, Development and Evaluation (GRADE) standard was utilized, wherein the certainty of the evidence was evaluated using the five GRADE considerations: risk of bias, consistency of effect, indirectness, imprecision and publication bias. The quality of evidence would be

downgraded if any of the factors above are found, and the levels of downgrading depended on how large the effects of these factors have on the outcome. Finally, all the decisions to down-grade were justified for each consideration.

This study was approved by the Cluster Ethics Review Committee (CERC) of the Department of Health Region XI Southern Philippines Medical Center. It was exempted from ethics review with a protocol registration number of P20121501. Furthermore, this study was registered in the Health Research and Development Information Network with a registration code of PHRR201125-003173.

RESULTS

MEDLINE/Pubmed, Cochrane Library, Google Scholar, Embase, ClinicalTrials.gov, and the local database HERDIN, grey literatures and registers namely Open Grey, Grey Literature Report of the New York Academy of Medicine, Agency for Healthcare Research and Quality (www.ahrq.gov), and National Institute for Health and Clinical Excellence were perused for eligible articles. A total of 172,293 articles were searched in

all the databases after the key words 'patient navigation' and 'colorectal cancer screening' were used. After duplicates, nonrelevant studies, and studies published earlier than 2011 were removed, 115 records were screened, and 91 of which were excluded due to the following reasons: colorectal cancer screening was not one of the outcomes measured, studies were focused on diagnostic resolution after a positive initial screening result, articles were of quasi-experimental/prospective/descriptive research designs, studies were about treatment for colorectal cancer, systematic review/meta-analysis articles, articles were about cost-efficiency of patient navigation, articles with navigation given to control group, articles with participants at high risk for colorectal cancer, articles with participants less than 50 years old, and studies that are ongoing or still in protocol form. 24 full-text articles were assessed, and 13 of these were excluded, leaving 11 studies eligible for review. The process of selecting the articles is illustrated in Figure 1.

A total of 115 articles were initially identified from all the databases searched, and 11 were included in the final sample for the systematic review and meta-analysis. All studies were randomized controlled trials encompassing health systems in different countries.

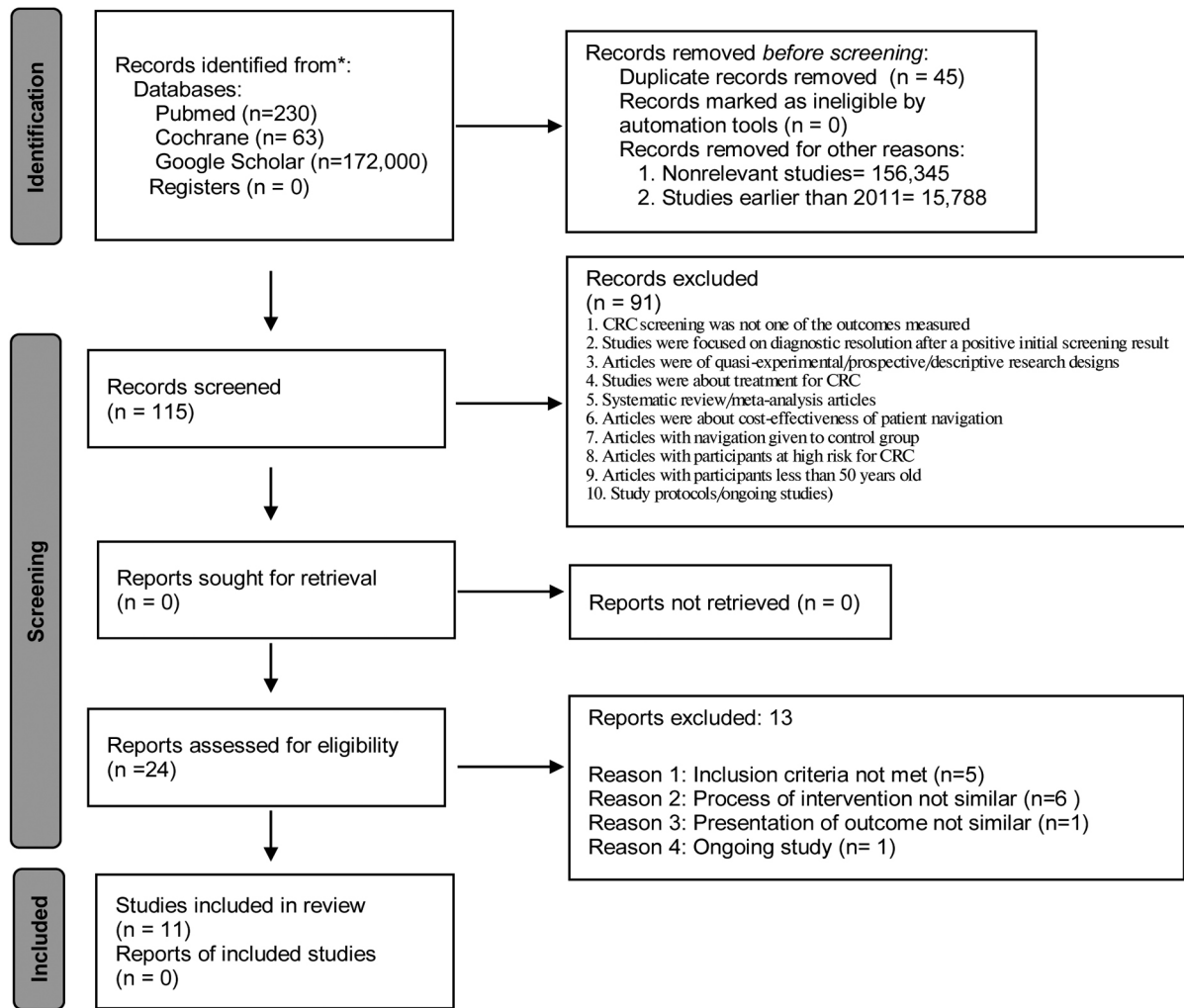


Figure 1. Flow chart of selection of articles according to PRISMA 2020 Guidelines.

Table 1. The summary of characteristics of the included studies.

Author	Author	Sample size and Population	Study Design	Interventions (I) (and Controls (C))	Outcome Measures and Key Results	Study Conclusions
Ritvo, PG, et al, 2014 ⁷	21 primary care practices in Ontario, Canada	n= 5,240 1. 50 to 74 y/o 2. No prior or current diagnosis of bowel cancer screening), or underscreened (no fecal occult blood test (FOBT) within the preceding 2 years and no colonoscopy or barium enema or flexible sigmoidoscopy within the preceding 5 years Intervention group: n= 2,629 Control group: n= 2,611	Randomized Controlled Trial	I: Patient navigation= Participants were contacted by a trained nurse navigator C: usual care (not specified)	Outcome Measures and Key Results Colorectal cancer screening uptake within 12 months (48 weeks) after the initial mailing of the invitation letter. Screening uptake was defined as performance of either SBT or colonoscopy during this interval.	Study Conclusions In the intervention group, 923 individuals were screened within 12 months (35% of all intervention subjects) compared with 533 control subjects (20% of all control subjects).
Temucin, E, et al, 2018 ⁸	Family health center in Uskudar, South of Istanbul.	n= 110 1. Aged 50–70 y/o 2. No prior cancer diagnosis, 3. No family member with colorectal cancer 4. Being covered by health insurance, 5. No apparent cognitive impairment (MMSE ≥ 25), 6. Not up to date on CRC screening (colonoscopy in the past 10 years or FOBT in the past 2 years). Nurse-navigated: n= 55 Non-navigated: n= 55	Randomized Controlled Trial	I: Nurse Navigation Program (CRC education, CRC screening counseling, motivational interview, reminder phone calls, nurse-assisted call guidance) according to individuals' readiness stage C: Usual care (not specified)	Outcome Measures and Key Results Primary: CRC screening (FOBT and colonoscopy) adherence at 3 and 6 months after the nurse navigation program. FOBT screening behavior evaluated whether participants brought their fecal samples to a family health center and whether they had FOBT test results on the record. Colonoscopy screening behavior was evaluated based on whether colonoscopy results for the participants were brought to the family health center. Secondary: Progression in adoption stages for each CRC screening test was assessed to evaluate changes between stages. The perceived benefits of and barriers to CRC screening were measured for FOBT and colonoscopy	Study Conclusions At 6 months, the FOBT screening completion rates were 83.6% in the nurse-navigated group, 10.9% in the non-navigated group. Following the nurse navigation program, there were statistically significant differences in CRC screening (FOBT and colonoscopy) between the nurse-navigated and non-navigated groups at both 3 and 6 months ($p < .05$). The screening (FOBT and colonoscopy) completion rates were significantly higher in the nurse-navigated group compared with the non-navigated group ($p < .05$)
Lasser, KE, et al, 2011 ⁹	Cambridge Health Alliance- composed of 15 community health centers. The health centers serve a multicultural, low-income population in Cambridge, Somerville, and Everett, Massachusetts.	n=465 1. 52 to 74-years 2. Had 1 visit to a primary care provider, ie, a physician or nurse practitioner, in each of the 2 previous years at 1 of the study sites. 3. Not completed CRC screening according to USPSTF (defined as colonoscopy in the past 10 years, sigmoidoscopy or double-contrast barium enema in the past 5 years, or fecal occult blood testing [FOBT] in the past year) 4. Spoke English, Haitian Creole, Portuguese, or Spanish, as their primary language Intervention group: n= 235 Control group: n= 230	Randomized Controlled Trial	I: Patient navigation for 6 months: 6 hours was spent contacting patients, educating them regarding CRC and CRC screening tests (FOBT and colonoscopy), motivating them to get screened, helping them decide which test to undergo, helping them obtain health insurance coverage, educating them regarding the correct way to complete FOBT cards, helping them make colonoscopy appointments and finding someone to accompany them home after the procedure, educating them regarding the required bowel preparation, and meeting them on the day of their colonoscopy. C: Usual care (not specified)	Outcome Measures and Key Results Primary: Completion of CRC screening (colonoscopy, FOBT, flexible sigmoidoscopy, or double-contrast barium enema) within 1 year. Secondary: Proportion of patients screened by colonoscopy and the proportion in whom the screening detected adenomas or cancer. Another secondary outcome was the proportion of patients with high-risk lesions (classified as a dichotomous yes/no variable), defined as 3 or more adenomas of any type, adenomas 1 cm or larger, or adenomas with any villous features.	Study Conclusions A total of 33.6% of intervention patients had been screened by 1 year after study entry vs 20.0% of control patients ($P < .001$) Intervention patients were more likely to have adenomas detected than were controls, and high-risk adenomas were more frequently detected among intervention patients than among controls.
Reuland, DS, et al, 2017 ¹⁰	2 community health centers, 1 in Albuquerque, New Mexico, and 1 in Charlotte, North Carolina. The sites serve diverse	n= 265 1. Aged 50 to 75 years 2. English or Spanish	Randomized Controlled Trial	I: Decision aid and patient navigation *Decision aid: Videos with approx. 15 minutes long and consist of 3 parts: (1) overview of importance of CRC screening and review of fecal testing (FOBT/FTT) and colonoscopy; (2) head-to-head comparison of screening	Outcome Measure: Completion of a CRC screening test within 6 months after the initial study visit	Study Conclusions Main result: in this randomized clinical trial that included 265 patients, the rate of CRC screening completion at 6 months was greater in the intervention arm (68%) than in the control arm (27%), a significant

<p>low-income communities including substantial numbers of Latino patients and had baseline CRC screening rates of approximately 35%</p>	<p>3. Were at average CRC risk (no personal or family history of CRC, polyps, or inflammatory bowel disease) 4. Not up-to-date with recommended CRC screening, and had upcoming appointments</p> <p>Intervention group: n = 133 Control group: n = 132</p>	<p>test options (after which viewers are asked to consider which test features are important to them); and (3) selection of a colored brochure corresponding to their screening readiness.</p> <p>*Patient Navigation: Navigators met participants immediately after their clinician encounter and assisted in carrying out the screening plan. Support was tailored based on individual patient factors, including preferred test strategy (FOBT/FIT or colonoscopy), screening barriers, and stage of readiness for screening. Navigators also offer and distribute FOBT/FIT kits using standing orders. Navigators periodically tracked intervention participants and attempted to contact unscreened participants at roughly 2-week intervals until participants refused, completed screening, or were deemed unreachable (after 5 attempts).</p> <p>C: food safety (attention control) video</p>	<p>Other outcomes: Review of the patient navigation logs, and semiquantitative description of the findings regarding decision aid video viewing, telephone contacts, FOBT/FIT distribution, and barriers addressed; Summary of screening test results from participant laboratory and/or pathology reports.</p>	<p>difference: vs 27% (21% FOBT/FIT, 6% colonoscopy) in controls (n = 132) (adjusted difference 40 percentage points; 95% CI, 29-51 percentage points; number needed to be offered the intervention to screen 1 additional patient. Implementation findings: Common barriers to screening were competing health priorities, for- getting about the stool tests, the time required to complete screening, and losing the FOBT/FIT kit.</p> <p>Screening test results: Among 100 study participants who completed FOBT/FIT, 5 results (5%) were positive. Among the 28 study participants who underwent colonoscopy either as the primary screening test or for follow-up of an abnormal FOBT/FIT test result, 19 (18 had a primary colonoscopy; 1 had follow-up) had normal or hyper- plastic polyps; 5 had 1 to 2 small adenomas (low risk), and 3 had 3 or more adenomas or large (≥ 1 cm) adenoma or villous histologic abnormalities (high-risk adenomas) (2 had a primary colonoscopy; 1 had follow-up).</p>
<p>Myers, RE, et al., 2018²¹</p>	<p>Randomized Controlled Trial</p> <p>n=400</p> <ol style="list-style-type: none"> Participants of Hispanic/Latino ethnicity 50 to 75 years of age Had not been diagnosed with colorectal cancer Had no personal or family history of colon cancer or polyps Not up-to-date with colorectal cancer screening (i.e., no SBT within 12 months or colonoscopy within 10 years) <p>DSNI: n = 197 SI: n = 203</p>	<p>I-Decision Support and Navigation Intervention (DSNI): colorectal cancer screening kit (bilingual informational booklet, fecal immunochemical stool blood test (SBT), and colonoscopy screening instructions) plus telephone contact from a patient navigator who clarified screening test preference and likelihood of test performance, helped to develop a screening plan, and provided guidance through test performance.</p> <p>C-Standard intervention: colorectal cancer screening kit (bilingual informational booklet, fecal immunochemical stool blood test (SBT), and colonoscopy screening instructions)</p>	<p>Primary: Overall colorectal cancer screening was adherence within 12 months after the individual's randomization date.</p> <p>Secondary: A secondary study endpoint was defined as screening test-specific adherence; Additional secondary end- points included the baseline-to-endpoint change in colorectal cancer screening decision stage and the endpoint scores on knowledge (percent correct of 10 true/false items) and perceptions screening.</p>	<p>At 12 months, colorectal cancer screening was substantially higher in the DSNI Group than the SI Group (78% vs. 43%), with an adjusted OR of 4.8 (95% confidence interval (CI), 3.1–7.6; P: 1/4 0.001). Furthermore, compared with the SI Group, the DSNI Group was more likely to screen with both an SBT (57% vs. 37% and a colonoscopy (20% vs. 6%).</p>
<p>Myers, RE, et al., 2014²²</p>	<p>Randomized Controlled Trial</p> <p>n=761</p> <ol style="list-style-type: none"> African Americans 50 to 75 y/o No prior diagnosis of colorectal neoplasia or inflammatory bowel disease Had visited a participating practice within the previous 2 years Had complete contact information Not compliant with American Cancer Society (ACS) CRC screening guidelines. <p>TNI group: n = 382 SI group: n = 379</p>	<p>I- Mailed CRC screening informational booklet, with a personalized message page that noted PHM barriers to screening the individual identified on the baseline survey (eg, low social support for screening) and a barrier-specific response. The page also identified the individual's screening test preference. For patients who preferred colonoscopy screening, a toll-free telephone number was included for use in arranging a colonoscopy appointment. An SBT kit was included for those who preferred at-home SBT screening. Colonoscopy instructions were sent to participants who had an equal preference for colonoscopy and SBT screening. A trained navigator would then call each participant to: 1) review the mailed materials, 2) reassess screening test preference, 3) discuss concerns or barriers to test performance, 4) help to develop a plan to complete the preferred screening test, and 5) arrange a follow-up call. If the navigator found that the participant's screening test preference had changed from baseline, new</p>	<p>Primary: CRC screening adherence within six months after randomization.</p> <p>Secondary: CRC screening at 12 months.</p> <p>For both outcomes, adherence was defined as performance of any CRC screening test recommended in ACS and United States Preventive Services Task Force (USPSTF) guidelines that applied when the study was initiated.</p>	<p>The TNI group exhibited a statistically significantly higher level of six-month screening adherence than the SI group (38.0% vs 23.7%, OR = 2.1, CI = 1.5 to 2.9, P = .001). At 12 months, adherence was also statistically significantly higher in the TNI group than the SI group (43.5% vs 32.2%, OR = 1.7, CI = 1.2 to 2.3, P = .001).</p> <p>As treated analysis findings: Screening adherence at six months in the TNI group among those who were navigated was substantially higher than those who were not navigated (45.7% vs 12.4%, respectively). An adherence difference of similar magnitude was noted at 12 months (50.9% vs 19.1%, respectively).</p>

<p>Goldman, SN, et al, 2017³³</p>	<p>Erie Family Health Center (EFHC) in Chicago, Illinois with 8 clinics serving adult patients. At EFHC, 55% of patients are best served in Spanish, 95% fall below 200% of the federal poverty line, and 35% are uninsured.</p>	<p>n= 420 1. 50–75 y/o 2. Preferred language of English or Spanish 3. At least 2 Erie Family Health Center visits over 2 years before the study 4. No prior CRC screening 5. No conditions suggesting FOBT may be inappropriate (e.g., chronic diarrhea, inflammatory bowel disease, iron deficiency, metastatic cancer, and previous total colectomy) 6. No pending or completed referral for colonoscopy, completed FIT, or precluding diagnosis. Intervention group: n= 210 Control group: n= 210</p>	<p>Randomized controlled trial</p>	<p>screening materials related to the current preferred test were sent. Finally, a reminder was sent at 45 days. C: Standard intervention group received a mailed CRC screening informational booklet, a personalized letter that included a contact telephone number to schedule a colonoscopy appointment, and an SBT kit. A reminder letter was mailed at 45 days post-randomization to those who had not returned the SBT kit. I: Multi-faceted outreach, wherein each week, patients randomized to the outreach group had FIT kits mailed to their homes, including provider letters and plain language FIT instructions. A few days after the mailing, an automated phone call was sent, and 2 days later, a text message via a contracted commercial system. After 2 weeks, HER was assessed to identify patients who had not completed a FIT and sent those individuals another automated phone call and text message. Three months after the mailing, patients who had not completed a FIT were identified, and EFHC's CRC Screening Navigator contacted them by phone. Patients who verbalized willingness to complete the FIT were mailed another kit. The central EFHC laboratory processed all returned FITs and entered test results into the EHR. If a FIT was negative, the Navigator mailed a letter with the test result and a reminder to repeat the test in 1 year. If the FIT was positive, the Navigator worked with patients' providers to arrange diagnostic colonoscopy.</p>	<p>Primary: FIT completion within 6 months Secondary: Differences in the rate of FIT completion at different time points corresponding to receipt of outreach components (0–2 weeks; >2–13 weeks; >13–26 weeks).</p>	<p>Over the first 6 months of follow-up, 77 (36.7%) patients in the outreach group and 31 (14.8%) in the usual care group completed a FIT (p<0.001). During each time period over the first 6 months of follow-up, the rate of FIT completion was higher for the outreach group compared to the usual care group. However, the difference between the outreach and usual care groups between weeks 13 and 26 was small (9.1% vs. 7.1%, respectively).</p>
<p>DeGroot, Amy, et al, 2017³⁴</p>	<p>Boston Medical Center's Section of Gastroenterology in Boston, Massachusetts, where patients are largely medically underserved population; approx. 70% are from racial and ethnic minority populations and 30% are non-English speakers. Participants were recruited from BMC's Section of General Internal Medicine and Family Medicine Department. Recruitment was also expanded to East Boston Neighborhood Health Center, a community health center serving a large Spanish-speaking population.</p>	<p>n= 840 1. 50–75 y/o 2. Referred by a primary care provider to the BMC GI for colonoscopy screening 3. Speaks English or Spanish 4. No previous diagnosis of colon cancer or adenomatous polyps 5. No active substance abuse or acute psychiatric diagnosis as determined by medical records/primary care provider. Navigation group: n= 419 Control group: n= 421</p>	<p>Randomized Controlled Trial</p>	<p>C: Usual care (not specified) I: Navigators primarily worked with participants via telephone, although some activities were conducted in person and by mail. Typical activities included assessing for barriers, informing and educating patients about the colonoscopy procedure and bowel preparation, addressing emotional concerns about the procedure, making appointments, and arranging for escorts and transportation services. Navigators assisted participants with obtaining bowel preparation materials by ensuring they received their prescription and picked up the medication along with the appropriate type of liquid to mix with the medication and, if needed, accompanying them to the pharmacy. Navigators called participants to remind them about bowel preparation and their screening appointment date and, following the procedure, ensure they received screening results. Additionally, navigators supported communication within the healthcare system confirming that the referring primary care provider received the endoscopy report on colonoscopy completion. C: For participants in the control group, usual care generally involved telephone contact by an administrative staff person in BMC GI to schedule an appointment after the referral was received</p>	<p>Primary: colonoscopy completion measured by the percentage of patients in each group completing the procedure within 6 months. Secondary: Adequacy of bowel preparation, as determined by the performing endoscopist</p>	<p>Overall, 57.1% completed colonoscopy within 6 months, with the percentage significantly higher for the patient navigation group (61.1%) than the control group (53.2%, p140.021). The odds of completing colonoscopy for navigated patients were 1.51 times greater (95% CI 1.14, 1.2, 2.03) than the odds for control patients (p140.007). Navigated patients were one and a half times more likely to complete colonoscopy than patients receiving usual care. Researchers did not demonstrate an effect of PN on the quality of bowel preparation, a secondary outcome.</p>

<p>electronically or by fax from their primary care physician. During this call, participants were also given brief verbal instructions about the bowel preparation and need for escorted transportation. Participants were sent a mailing with a prescription for bowel preparation materials and related instructions, instructions to arrange escorted transportation, and directions to the hospital. Participants who could not be contacted directly by phone after multiple attempts were sent non-negotiated appointment dates and times in the mail along with the other materials noted above. Participants were encouraged to call BMC GI with questions or problems (e.g., arranging escorted transportation, canceling and rescheduling appointments). Participants in the control group had no additional contact with BMC GI staff until a reminder call 3 days prior to the scheduled exam, at which time the bowel preparation instructions and need for escorted transportation were reviewed. Navigated patients did not receive usual care.</p>	<p>Primary: participation in CRC screening (e.g. FOBT performed). The uptake was whether the FOBT was performed before 1 November 2013. This allowed a 9-month delay after the last information letter sent by the SMS in February 2013.</p>	<p>In the screening population, the intervention was associated with a non-significant increase in the participation rate of 1.5%. This increase was greater in rural strata (RD and RA) than in urban ones (UD and UA), and was greater in affluent strata (RA and UA) than in deprived ones (UD and RD). In the navigable population, the intervention was associated with a significant increase in the participation rate of 3.2%. This increase was greater in affluent strata (RA and UA).</p>
<p>electronically or by fax from their primary care physician. During this call, participants were also given brief verbal instructions about the bowel preparation and need for escorted transportation. Participants were sent a mailing with a prescription for bowel preparation materials and related instructions, instructions to arrange escorted transportation, and directions to the hospital. Participants who could not be contacted directly by phone after multiple attempts were sent non-negotiated appointment dates and times in the mail along with the other materials noted above. Participants were encouraged to call BMC GI with questions or problems (e.g., arranging escorted transportation, canceling and rescheduling appointments). Participants in the control group had no additional contact with BMC GI staff until a reminder call 3 days prior to the scheduled exam, at which time the bowel preparation instructions and need for escorted transportation were reviewed. Navigated patients did not receive usual care.</p>	<p>I: As a first step, an information letter with SN availability and a free phone number was sent 4 months after the first usual invitation. After 10 days, the SN contacted the subject by phone. The calls were repeated three to four times at different times and on different days. Once contact was established, the SMS presented and discussed the CRC screening FOBT. Each contact was personalized to identify and eliminate barriers to CRC screening. Depending on the difficulties expressed or felt by the subject, personalized assistance was given. At any time, the subject could refuse contact and the intervention would stop. The SN intervention was guided by a dedicated tool specifically developed for this study and allowing all SN actions undertaken to be recorded (letters, call phone, home visit).</p> <p>C: subjects aged 50– 74 years are invited by post by a local screening structure to ask their general practitioner for CRC screening at the occasion of a regular consultation. The general practitioner checks for the absence of medical contra-indication to CRC screening (symptoms, history of CRC...) and informs the subject about screening and distributing the FOBT kit. The patient can then perform the test at home and send it to the laboratory. A first postal reminder is sent by the local screening structure to non-participants, 3–4 months after the initial invitation, and finally the FOBT is mailed at 8 months to the subject's home. In case of positive test, a colonoscopy is realized.</p>	<p>Overall CRC screening adherence at 6 months (TNI Group: 38%, S1 Group: 33%, Control Group: 12%, Table 2) was significantly higher in both intervention groups than in the Control Group (adjusted $p = 0.001$ for both comparisons). However, adherence was not significantly different in the TNI Group and the S1 Group (adjusted $p = 0.207$). Screening rates at 12 months were higher across all</p>
<p>Guillaume, E, et al, 2017⁵</p>	<p>France</p> <p>n= 16, 267 (navigable population)</p> <ol style="list-style-type: none"> 1. 50-74 y/o 2. No prior history of disease or colorectal cancer screening, in clusters from the most affluent to the most deprived quartiles, with socioeconomic levels determined using an accredited index (Townsend index) <p>Intervention group: n= 8121 Control group: n= 8146</p>	<p>Randomized Controlled Trial</p>
<p>Myers, RE, et al, 2013⁶</p>	<p>10 primary care practices affiliated with the Christiana Care Health System (CCHS) in Delaware that used a common medical record system (Centricity).</p> <p>n= 945</p> <ol style="list-style-type: none"> 1. Aged 50 to 79 years of age 1. Had no prior diagnosis of colorectal neoplasia or inflammatory bowel disease 2. Had visited one of the participating practices within the previous two years 3. Had complete contact information 	<p>Randomized Controlled trial</p>

<p>4. Were not compliant with American Cancer Society CRC screening guidelines.</p> <p>TMJ group: n= 312 SI group: n= 316 Control group: n= 317</p>	<p>Three departments of the Picardy region in northern France</p>	<p>n= 16,250 Those aged 50-74 years old coming from four strata: urban deprived (UD), rural deprived (RD), urban affluent (UA), and rural affluent (RA).</p> <p>Navigation group: n= 8105 Control group: n= 8145</p>	<p>Randomized Controlled trial</p>	<p>participant to verify and update (if necessary) the individual's test preference, discuss any concerns or barriers that the participant may have, and encourage performance of the preferred test. Finally, reminders were then sent to the participants.</p> <p>C:</p> <p>1. <i>Standard Intervention (SI)</i>: Participants received a mailed informational booklet on CRC screening, a personalized letter that included a nurse contact telephone number that could be used to obtain information about scheduling a colonoscopy appointment, and an stool blood test kit.</p> <p>2. <i>Control group</i>: Usual care (not specified)</p> <p>I: Navigation began with an information letter sent by the patient navigator or about 4 months after the initial screening invitation letter. The information letter contained a toll-free phone number and an email address to contact the patient navigator if the participant wished. Approximately 10 days after this mailing, the patient navigator initiated a structured phone call aimed at identifying barriers to screening. Navigation services essentially included telephone follow-up, home visits, and mailing of the FOBT kit. If a participant could not be reached by telephone after three or four attempts, a postal reminder was sent containing a reply coupon with a prepaid envelope on which participants could provide their phone number or indicate their wish for a home visit.</p> <p>C: Participants were mailed invitations by the local screening structure to see their general practitioner, who gives them a FOBT kit if it is indicated. Patients can perform the FOBT at home and send it to the laboratory. A first postal reminder is sent by the local screening structure to nonparticipants 3 to 4 months after the initial invitation; at 8 months' time, the FOBT kit is mailed to each nonparticipant at home.</p>	<p>Secondary: A 12-month window after randomization was also considered to assess delayed screening performance as an additional endpoint of interest. Also, Change in overall screening decision stage (SDS) between the baseline and the endpoint surveys (secondary analyses) to explore the impact of baseline screening test preference and study group on overall adherence at 6 months)</p> <p>Screening adherence rate (i.e., FOBT completed or not)</p>	<p>three study groups than rates at 6 months (TMJ Group: 43%, SI Group: 36%, Control Group: 18%, Table 2), but the pattern of intervention effects across the study groups was comparable. Adherence at 12 months was not significantly different between the TMJ and SI Groups ($p = 0.118$).</p> <p>Navigation was globally associated with a significant increase in participation of 3.3% (P 14 0.003; 95% CI 1.5%-5.0%; 24.4% in the intervention group vs. 21.1% in the control group).</p>
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Methods of Patient Navigation

All of the studies included an intervention arm and control arm in conducting their studies, and they utilized the patient navigation intervention but through different means in order to achieve outcome measure of colorectal cancer screening uptake. De Groff, et al. Guillaume, et al. Lasser, et al. and De Mil, et al. conducted navigation primarily through phone calls. The usual activities were discussing colorectal cancer screening tests, motivating them to get screened and helping them decide which test to undergo. Lasser, et al. even helped the participants to obtain health insurance coverage. Barriers to screening were also asked during telephone interview. There were four studies who utilized mailed informational materials and screening kits followed by a phone call from a navigator (Myers, et al. 2013, 2014, 2018 and Goldman, et al. 2015). Informational booklets on colorectal cancer screening and screening test kits according to individual's preferred CRC screening test were mailed, and later on navigators called them to discuss screening test preference and concerns or barriers to test uptake. Myers, et al. (2018) mailed colorectal cancer screening kit [bilingual informational booklet, fecal immunochemical stool blood test (SBT), and colonoscopy screening instructions] plus telephone contact from a patient navigator who clarified screening test preference and likelihood of test performance, helped to develop a screening plan, and provided guidance through test performance.

There were also three studies that had patient navigation either through phone call or face-to-face with the participants. Reuland, et al. provided decision aids which included videos explaining the importance of CRC screening and comparison of screening test options. The navigators then met participants immediately after, and assisted them in carrying out the screening plan. Support was tailored based on individual patient factors, including preferred test strategy (FOBT/FIT or colonoscopy), screening barriers, and stage of readiness for screening. Navigators also offer and distribute FOBT/FIT kits using standing orders. Temucin, et al. made use of the nurse navigation program,

which involved multiple interventions (colorectal cancer screening and education, motivational interview and reminder phone calls were done depending on the individuals' readiness stage. In the conducted by Ritvo, et al. participants were met by a trained nurse navigator either face-to-face or via phone, who elicited participant's screening test preference (colonoscopy or SBT), provided a stool blood test when preferred, and directly scheduled a colonoscopist's consultation, when colonoscopy was the preference.

Figure 2 shows the summary statistics (number of events and sample size) for Patient Navigation and usual care rendered to patients at average risk of having colorectal cancer, with a risk ratio of 1.28 and a 95% confidence interval for the dichotomous outcome, which is the uptake of any colorectal cancer screening test. The events are defined as the number of participants, either in the intervention (patient navigation) or control (usual care) group, who utilized a screening test within 12 months of randomization.

In De Groff, et al. (2017), 61.1% from the navigation group vs 53.2% from the control group completed colonoscopy. In De Mil, et al. (2018), 24.4% from the intervention group vs 21.1% in the control group adhered to screening. Goldman (et al, 2015) showed that 36.7% from the intervention group vs 14.8% from the control group completed a FIT. In Guillaume's (et al, 2017) study, he had an initial sample population of 28,929, which was narrowed down to 16,267 after excluding participants who underwent screening after being informed by their general practitioners about screening and the distribution of FOBT kits. These 16,267 participants (intervention= 8121; control= 8146) were included in the analysis of results following the rendition of patient navigation and usual care. 24.3% of those navigated completed a screening test as compared to 21.1% from the control group. Lasser, et al. (2011) study showed that 33.6% of intervention patients had been screened within 1 year after study entry vs 20.0% of control patients. Ronald Myers and his colleagues conducted 3 different studies over a span of 6 years. In his 2013 study, he randomized his sample population to 3 groups, namely the tailored navigation, standard intervention, and

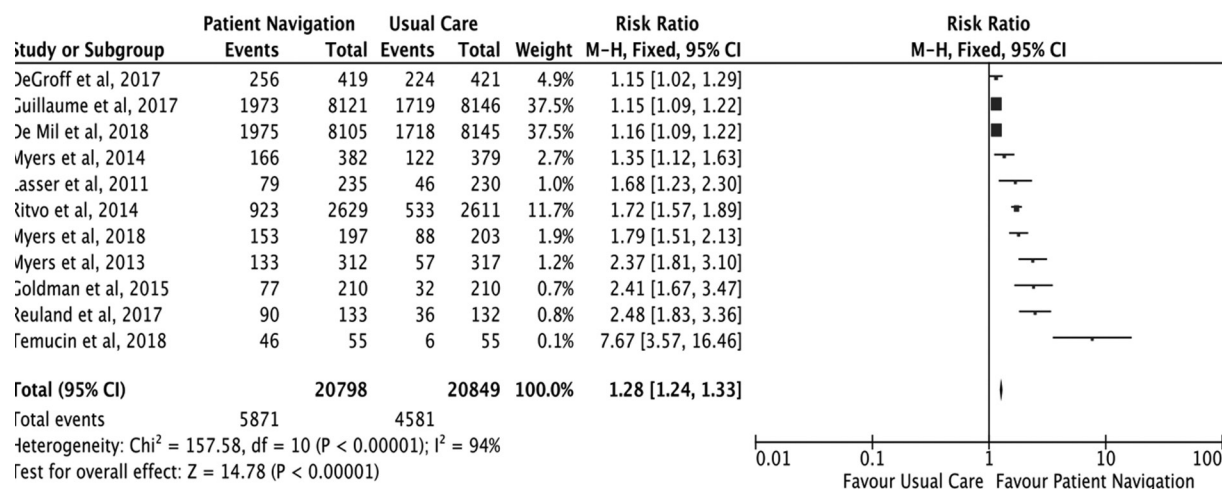


Figure 2. Meta-analysis of randomized controlled trials of the effect of patient navigation on colorectal cancer screening test uptake.

control group. Overall, colorectal cancer screening adherence was higher in both intervention groups than in the control group (TNI Group: 38%, SI Group: 33%, Control Group: 12%). In this meta-analysis, however, the investigators only included the events from the TNI and the control groups, in fulfillment of the intervention and outcome criteria. In his 2014 study, Myers showed that the tailored navigation group had a 38% adherence rate as compared to 23.7% from the control group. Finally, in his 2018, Myers showed that 78% of those who were navigated took up screening, as compared to 43% from the control group. Reuland, et al. (2017) showed that the rate of screening at 6 months was greater in the intervention arm (68%) than in the control arm (27%). Ritvo, et al. (2014) also concluded that 35% of all intervention participants were screened, as compared to 20% of that in the control group. Temucin, et al. (2018) also concluded that at 6 months, the FOBT screening completion rates were 83.6% in the nurse-navigated group and 10.9% in the non-navigated group.

Combining the results of the studies in a forest plot shows a statistically significant increase in colorectal cancer screening with patient navigation (RR 1.28; 95% CI 1.24 to 1.33; $I^2 = 94\%$; 11 trials). However, there is a high level of heterogeneity ($I^2 = 94\%$) among the studies, hence a subgroup analysis was conducted among these studies according to the method of patient navigation utilized.

As can be seen in the figure above, the test for subgroup differences suggests that there is a statistically significant subgroup effect ($p < 0.00001$), meaning that the different methods of patient navigation significantly modifies the effect of colorectal cancer screening uptake among the intervention group in comparison to the control group. Increase in screening uptake is more statistically significant among patients navigated via face-to-face and via phone call (RR 1.83; 95% CI 1.68 to 2.00; $I^2 = 90\%$; 4 trials), followed by navigation via mailed materials and kits followed by phone call (RR 1.79; 95% CI 1.60 TO 2.00; $I^2 = 95\%$; 3 trials) and lastly navigation via phone call alone (RR 1.16; 95% CI 1.12 to 1.20; $I^2 = 55\%$; 4 trials). A sufficient number of trials and participants were included in each subgroup, so the covariate distribution is not concerning for this subgroup analysis. However, there is still a substantial amount of unexplained heterogeneity in the subgroups for navigation via phone call and face-to-face, and mailed materials and kits followed by phone call.. Heterogeneity in the subgroup for navigation via phone call ($I^2 = 45\%$) has significantly reduced. Therefore, the validity of the treatment effect estimate for each subgroup is uncertain, as individual trial results are inconsistent.

The Cochrane Collaboration Risk of Bias Tool was used to assess risk of bias for each of the included studies. Table 2 displays for each included study the risk-of-bias judgement for each of 6 domains of bias.

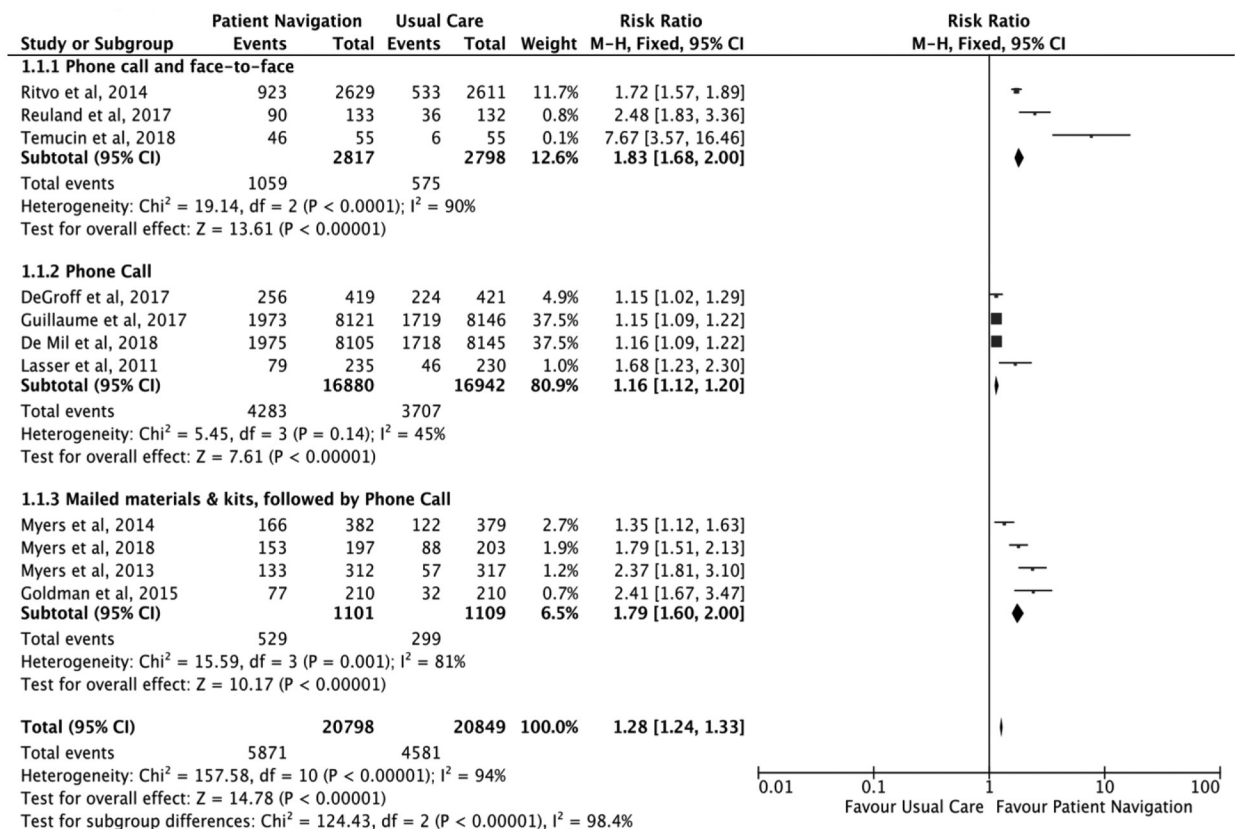


Figure 3. Subgroup analysis: Different methods of patient navigation

Table 2. Assessment of Bias in each study.

Study	Random Sequence Generation (Selection bias)	Allocation Concealment (Selection bias)	Selective Reporting (Reporting bias)	Blinding Of Participants & Personnel (Performance bias)	Blinding Of Outcome Assessment (Detection bias)	Incomplete Outcome Data (Attrition bias)	Other Bias
De Groff et al, 2017	Low risk	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Unclear risk
De Mil et al, 2018	Unclear risk	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Unclear risk
Goldman et al, 2015	Unclear risk	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Unclear risk
Guillaume et al, 2017	Low risk	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Unclear risk
Lasser et al, 2011	Low risk	Unclear risk	Low risk	High risk	Low risk	Low risk	Unclear risk
Myers et al, 2013	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Unclear risk
Myers et al, 2014	Low risk	Low risk	Low risk	High risk	Unclear risk	Low risk	Unclear risk
Myers et al, 2018	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Unclear risk
Reuland et al, 2017	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Unclear risk
Ritvo et al, 2014	Low risk	Unclear risk	Low risk	High risk	Low risk	Low risk	Unclear risk
Temucin et al, 2018	Low risk	Low risk	Unclear risk	High risk	High risk	Low risk	Unclear risk

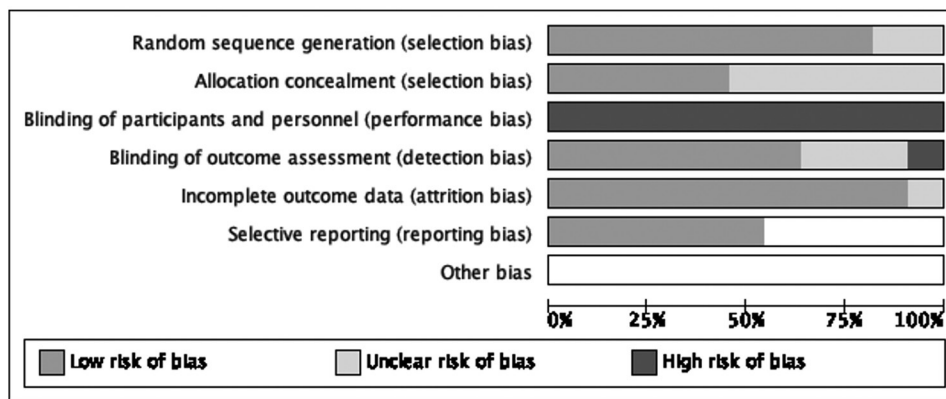


Figure 4. Review of authors' judgements about each risk of bias item presented as percentages across all included studies.

Eleven (11) randomized controlled trials (RCTs) directly compared uptake of a colorectal cancer screening test between patient navigation and usual care groups. 9 out of 11 studies had low risk of selection bias, while 6 of these studies did not explicitly state the concealment of the participant allocation to intervention and control groups. 6 out of 11 studies had accessible study protocols, and their outcomes that are of interest in the review have been reported completely. 7 studies successfully avoided detection bias arising from knowledge of the allocated interventions by outcome assessors, and in all the studies, all subjects were analyzed in the group to which they were randomized, lowering the risk for attrition bias. However, because all the participants, particularly those assigned in the intervention groups, were not blinded as they were actively navigated, all the studies understandably are at high risk for performance bias.

Small study effects were assessed using a funnel plot. The figure above displays asymmetry (skewed to the right). This suggests the possibility of missing studies in the middle and to the left of the funnel, probably indicating the presence of publication bias where small studies with null or negative results were not published. It could also be due to reporting bias (as evidenced by 5 studies yielding unclear risk in the

reporting bias domain in Table 2), or statistical heterogeneity caused by the huge differences in study sizes and their corresponding intervention effects.

The quality of evidence for the entire study was assessed independently by the 2 reviewers using the Grades of Recommendations Assessment, Development and Evaluation (GRADE) standard established by the World Health Organization (WHO). The reviewers assessed the certainty of the evidence using the five GRADE considerations (risk of bias, consistency of effect, indirectness, imprecision, and publication bias).

Risk of Bias. Based on Table 2 and Figure 4 showing risks of bias, more than 50% of the studies have unclear allocation concealment. Almost half of the studies are also likely to have reporting bias, and these are considered limitations that likely reduce confidence in effects, hence we downgrade the quality of evidence by 1 level.

Consistency of Effect. When studies yield widely differing estimates of effect or heterogeneity, the confidence in the results, and hence the quality of evidence, becomes lower. In this meta-analysis, the I^2 was

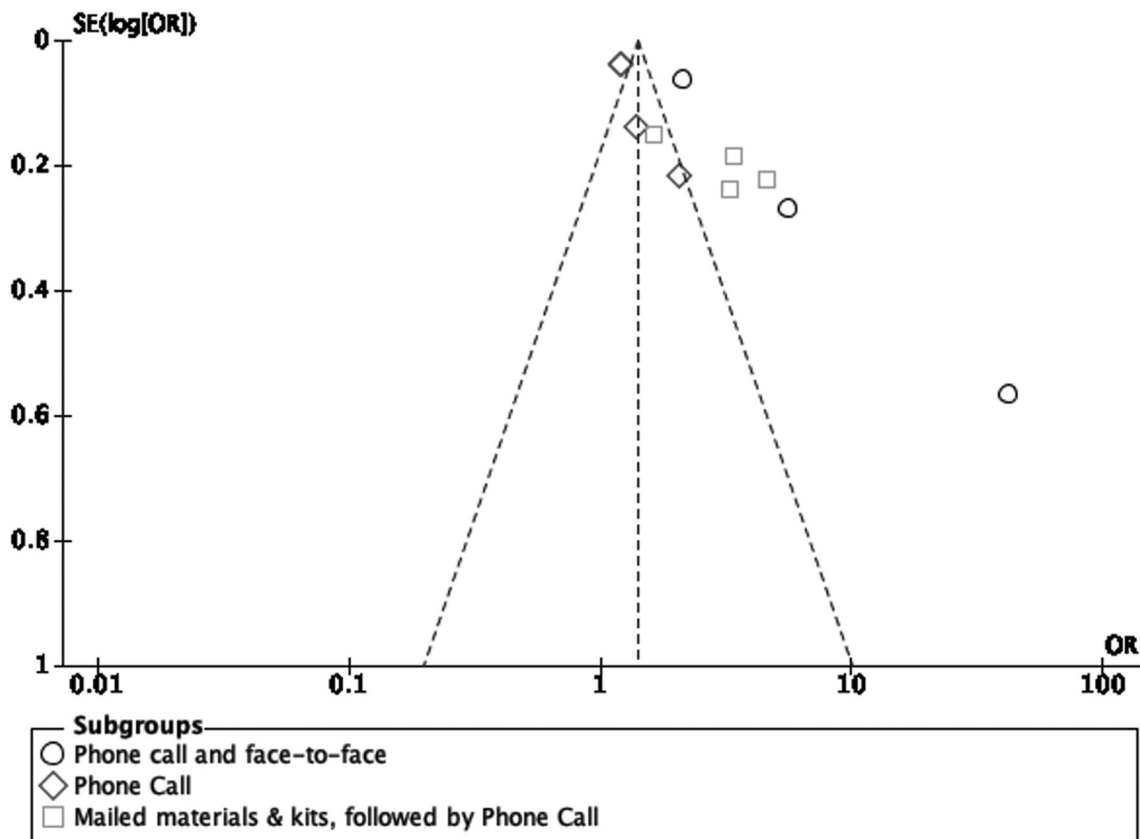


Figure 5. Funnel plot.

at 95% (Figure 2). Hence, a subgroup analysis according to specific methods of patient navigation was conducted thereafter to investigate this. Figure 3 shows that heterogeneity was substantial in 2 subgroups. This, therefore, indicates a downgrade of the level of quality of evidence of the study.

Indirectness. Each of the studies were appraised on their directness with the research question. All fulfilled the criteria for a population with an average risk of developing colorectal cancer. Directness for intervention is also judged as fulfilled if each study defines it as a form of patient navigation. This is also true for control, however one study (Myers, et al. 2013) divided the sample population into 3 groups, and 2 of these were considered interventions and separate from control. However, in this review, only one intervention arm (tailored navigation) was analyzed against control. Finally, directness for outcome was also fulfilled, as all studies aimed for uptake of any colorectal cancer screening tool within 12 months of the start of the study.

Imprecision. The total relative risk or risk ratio for all 11 studies is at 1.28 (95% CI 1.24 to 1.33). Hence, to determine the preciseness of the results, the confidence intervals of the included studies were assessed. Five studies (De Groff, Guillaume, De Mil, Myers 2014, Lasser) had confidence intervals that cross the 1.28 risk ratio. Under these

circumstances, one may reasonably think to downgrade the quality of evidence, however the number of events and number of participants in this review are large enough that it is more reasonable not to downgrade for imprecision.

Publication bias. This was assessed using a funnel plot (Figure 5).

DISCUSSION

The purpose of this systematic review and meta-analysis was to ascertain the effectiveness of patient navigation on increasing colorectal cancer screening uptake among those with average risk, and to determine which specific method of navigation was most effective. The 11 studies reviewed and analyzed in this study show favor to patient navigation, and this result was consistent when subgroup analysis was conducted according to method of navigation. These findings are congruent with results of majority of systematic reviews and meta-analysis previously conducted on patient navigation. In a systematic review and meta-analysis conducted by Dougherty, et al.¹⁰ evaluating different interventions to increase colorectal cancer screening in the United States, they have concluded that navigation and FOBT outreach are more effective than other interventions in increasing screening rates.

The magnitude of the observed effects was highest for those navigated via both phone call and face-to-face, then by mailed

materials and kits followed by a phone call, and lastly navigation via phone call alone. Although there was significant heterogeneity, it was markedly decreased to below substantial levels upon subgroup analysis for patient navigation conducted via phone call alone, indicating less variability of data and more consistency of observed effects of an increase in uptake of colorectal cancer screening when patients were navigated via phone call. This result is consistent with the findings of a systematic review by Roy, et al.²⁸, wherein they reviewed interventions to increase stool blood colorectal cancer screening in African Americans, and they have concluded that a tailored navigation approach either by telephone or in person can be a potentially effective strategy for increasing CRC screening in African American communities.

Limitations found in this study include publication and other reporting biases that may have affected the findings. There is substantial heterogeneity in the study effects, which diminished the precision of the estimates for intervention effect sizes, although the heterogeneity significantly decreased for patient navigation via phone call alone after subgroup analysis. The variation in the delivery and components of the navigation services and the navigators themselves, and the difference in culture and ethnicity in the population receiving them may have likely contributed to the heterogeneity. This study is also limited to reviewing the effects of patient navigation as compared to usual care, and it was not compared to other forms of services that could also increase screening test uptake. In addition, the effects of navigation in completion of tests after an abnormal result was not included in this study, although several other reviews have studied them. Despite this, patient navigation has evidently broken through barriers and has customized its methods to accommodate the needs of each individual. It has shown its effectiveness across multiple reviews, and it has proven to be more useful now more than ever, as a way to work around the present global circumstances in order to still provide optimal care to those at risk of colorectal cancer.

CONCLUSION AND RECOMMENDATION

In conclusion, this systematic review and meta-analysis show an increase in screening rates in those who were navigated. Increase in screening uptake is more statistically significant among patients navigated via face-to-face and via phone call, but data is more homogenous for patient navigation via phone call alone. This study therefore provides some evidence for future strategies to promote colorectal cancer screening, especially in the Philippines. At present, only 7 government hospitals are known to have been implementing the Patient Navigation Program (PNAP) in the country, namely: Philippine General Hospital, Jose Reyes Memorial Medical Center, East Avenue Medical Center, Rizal Medical Center, Amang Rodriguez Memorial Medical Center, Philippine Children's Medical Center and Bicol Regional Training and Teaching Hospital.¹⁶ Hence, the findings of this study are significant in that it can boost the implementation of navigation programs for colorectal cancer screening in all the other areas of the country. In addition, at the present times, patient navigation via phone call is very relevant, as less physical interaction is needed to prevent the COVID-19 virus spread. Hence, this method is the most efficient way to navigate patients as a form of teleconsultation, in order to continue

providing optimum care despite the limitations brought about by the pandemic.

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