



## Strategies to Increase Colorectal Cancer Screening Rates in Moderate-Risk Population: A Systematic Review

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### Abstract

Evidence from randomized intervention studies indicates that colorectal cancer (CRC) screening is effective in reducing mortality. Thus, this systematic review is aimed to evaluate the factors associated with the success of strategies that increased the adherence to CRC screening tests by medium-risk patients. We grouped each strategy in clusters according to its interventions. Two articles addressing screening by recommendation/education of medical professionals presented an increase of 12.4% and 2.2 times more chance of patients completing screening tests; three resorted to recommendation/education of non-medical health professionals or assistant researchers, in which compliance went from 1% to 29% and 1.6 times more chance of following it through; four used recommendation/education of trained members of the community, in which there were an increase from 6.6% to 26.4%; two provided free FOBT kits available at post offices and pharmacies, in which the increase was of 29.8% to 30%; one sent pamphlets/invitations by mail or inviting patients by phone, in which growth varied from 1.1% to 13.7%; three educated the population via multimedia, which increased the rate to 14% or 15%; five used a mix of interventions, resulting in a growth from 1.7% to 76.9%. The rate increase in adherence to CRC screening tests relates to the guidance provided by a trained multidisciplinary team. Also, the patient-centered clinical method attends to the patient's singularities and thereby uses the best screening methodology based on updated scientific evidence for each population. Moreover, sending personalized newsletters and strengthening contact with patients via phone call/multimedia also increase success chances.

**Keywords:** Cancer; Colorectal Neoplasms; Diagnosis; Early Intervention; Health Education; Screening; Strategy

### Abbreviations

CRC: Colorectal Cancer; FS: Flexible Rectosigmoidoscopy; FOBT: Fecal Occult Blood Test; PROSPERO: International Prospective Register of Systematic Reviews; MESH: Medical Subject Headings; AOR: Adjusted Odds Ratio; FIT: Fecal Immunochemical Test; LHW: Lay Health Worker; OR: Odds Ratio; IG: Intervention Group; CG: Control Group; CI: Confidence Interval; CHW: Community Health Workers

### Introduction

Colorectal cancer (CRC) is the third most common cancer found in men and the second in women [1-3]. Worldwide, there were 1.8 million new cases and  $\approx$  881000 cancer-related deaths in 2018 - according to the Global Cancer Observatory database. The risk factors for developing CRC are genetic [4] and environmental, such as excessive alcohol consumption; smoking and obesity [5,6].

Screening is recommended to prevent CRC in patients aged  $\geq 50$  years old, regardless of any signs or symptoms of illness or family history - considered to be at medium-risk for CRC - through the investigation of the presence of blood in the stool (FOBT) and the analysis of the intestinal mucosa with flexible rectosigmoidoscopy (FS) or with colonoscopy [7-9]. Screening is associated with decreased CRC incidence in the United States [10] and survival rates  $> 90\%$  for colon cancer and  $> 80\%$  for rectal cancer, indicating the efficiency of comprehensive intervention approaches that promote increase of screening among individuals  $> 50$  years old [7,11].

However, barriers hinder adherence to screening [11]. These barriers are multifactorial [8,9,11,12], highlighting individual factors, such as financial issues [11]; anxiety; depression [12]; absence of symptoms; fear of having a colonoscopy done [9,12] or feeling pain; and lack of time [11]. There are also interpersonal issues, as lack of spousal, family, or friends support [12]. Environmental factors are also relevant, as the absence of transportation [8,12] and hardship accessing health services specially for rural areas residents [12]. Additionally, insufficient knowledge about CRC and the importance of screening is closely related to low adherence [9,11].

**Aim of the Study**

Therefore, the present study aims to better understand and evaluate strategies to promote increased adherence to screening

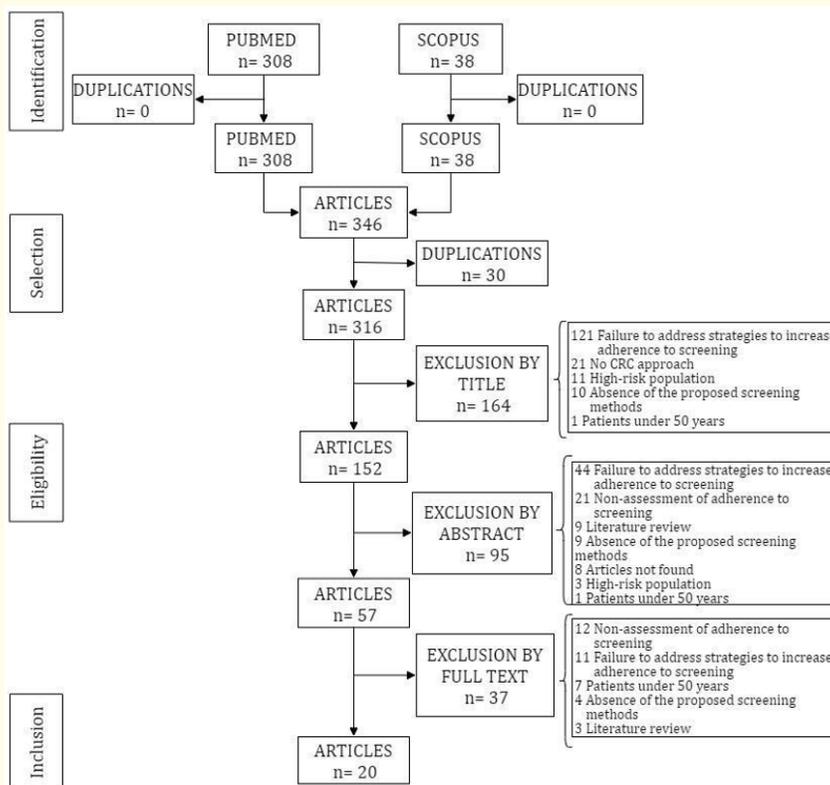
methods at medium-risk patients for CRC either by colonoscopy, stool occult blood testing or rectosigmoidoscopy.

**Materials and Methods**

A systematic literature review was conducted between May and November of 2020, using Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) protocol [13] as a methodological basis to guarantee quality and reasonable fidelity to this study. We registered this systematic review with the International prospective register of systematic reviews (PROSPERO) under the protocol number CRD42020205012.

We used PubMed and Scopus databases and we consulted the Medical Subject Headings (MESH) platform to choose the following descriptors: colorectal neoplasms AND health education AND mass screening AND early detection of cancer. We selected only articles written in English and papers that were focused on strategies to increase adherence to CRC screening rates through the previously mentioned methods at medium-risk populations. We excluded non-systematic literature reviews, experimental studies in animals and those which studied people at low or high risk for CRC, as well as articles not available in full version.

We found a total of 346 articles in both databases and we excluded the papers that did not fit the established criteria. Finally, we selected 20 texts to write this article (Figure 1).



**Figure 1:** Addresses the partial numbers of articles excluded from the writing of this paper and each justification for removal.

To do the risk of bias analysis, we used the Cochrane Risk of Bias Tool [14] so we could study each of the 20 articles under the following aspects: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; selective reporting; and other bias. We classified each aspect of risk of bias as high, low, or unclear, and we ratified each judgment using a sentence extracted from the text or written as the researcher’s conclusion after studying the text. Each article was blindly classified by two reviewers, while a third researcher analyzed disagreements. We assessed each article’s risk of bias using the Collaboration’s Risk of bias tool from Cochrane Handbook for Systematic Reviews of Interventions (version 5.1) (Figure 2A and 2B).

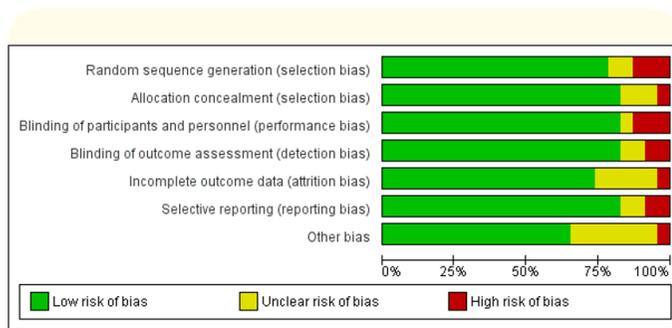


Figure 2A

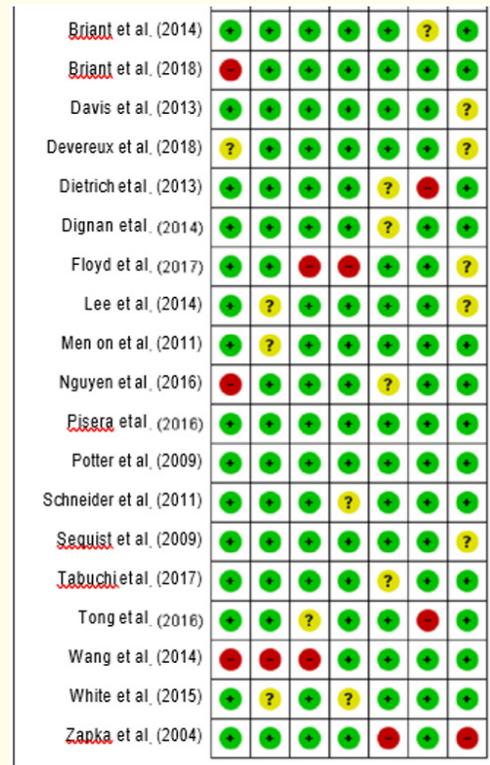
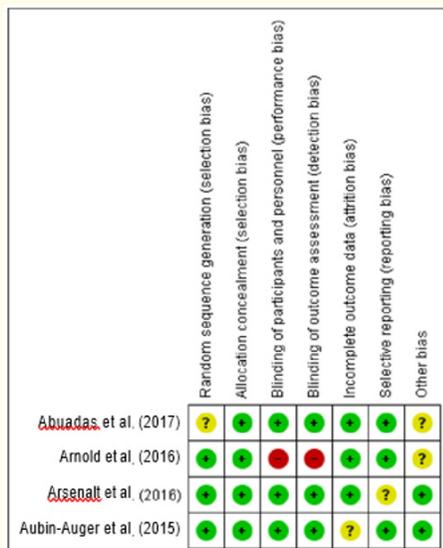


Figure 2B

Figure 2A and 2B: Risk of bias assessment. A red dot is the symbol which indicates high risk of bias, yellow unclear risk, and green low risk in each domain evaluated. Both tables were made with Review Manager (RevMan) [Computer program]. Version 5.4, The Cochrane Collaboration, 2020.

To enable a thorough study of the strategies that granted success to the interventions to increase CRC screening rates, we subdivided the articles according to their methodologies, analyzing each cluster in detail. The clusters are 1. Screening by recommendation/education of medical professionals; 2. Screening by recommendation/education of non-medical health professionals or assistant researchers; 3. Screening by recommendation/education of trained members of the community; 4. Screening by providing free FOBT kits available at post offices and pharmacies; 5. Encouragement for screening by sending pamphlets/invitations by mail or by phone call; 6. Encouragement for screening by population education via multimedia; 7. Encouragement for screening by a mix of interventions.

## Results

### Screening by recommendation/education of medical professionals

Aubin-Auger, *et al.* (2016) [15] patient participation rate per general practitioner among eligible patients during the study was 36.7 ( $\pm$  20.3) in the intervention group and 24.5 ( $\pm$  10.1) in the control group ( $p = 0.03$ ). It is important to show that two years before the study started the patient participation rate per general practitioner was 24.3 ( $\pm$  9.1) in the intervention group and 24.7 ( $\pm$  9.5) in the control group ( $p = 0, 8$ ), considering previous data from the same doctors.

Menon, *et al.* (2011) [7] highest occurrence of CRC screening tests was due to the personalized education group (23.8%,  $p < 0.02$ ); in which participants were 2.2 times more likely to complete a post-intervention CRC screening than the control group [Adjusted Odds Ratio (AOR) = 2.2, CI = 1.2 - 4.0]. After managing the effects of sociodemographic characteristics, there were only two significant post-intervention CRC screening predictors: intervention group and physician's recommendation.

### Screening by recommendation/education of non-medical health professionals or assistant researchers

After the intervention of Dignan, *et al.* (2014) [16], FOBT increased from 11.2% to 12.2% regarding the baseline values, and colonoscopy from 29.6% to 31.8%. They found the results of FOBT screening in  $< 20\%$  of cases, and the rates of FS were deficient. Colonoscopy was the most commonly found screening method, with 30% of participants performing it. Notably, FOBT rates appeared to decline throughout the study. Colonoscopy rates at six-month follow-up increased by  $\approx 5\%$ , and there were no statistically significant differences in rates of "early" intervention group and "overdue" intervention group for FOBT or colonoscopy. Colonoscopy test rates at the six-month evaluation were 15.7% higher in the "early" intervention and only 2.4% higher in "overdue" intervention clinics ( $p = 0.01$ ).

Davis, *et al.* (2013) [17] had a FOBT return rate of 38.6% in the control group, 57.1% in the education segment, and 60.6% in the nurse's support segment. There were differences between the study groups concerning compliance to FOBT among patients with limited literacy levels ( $p = 0.006$ ), but not among those with adequate literacy levels ( $p = 0.064$ ).

Before the intervention, in Abuadas, *et al.* (2018) [18] study, 56.9% of the participants had never read or heard about CRC; 84.8% had not read about FOBT; nor 65.5% colonoscopy; nor 72.6% sigmoidoscopy. After the research started, 21.8% underwent the FOBT (18.6% in the control group and 81.4% in the intervention group).

### Screening by recommendation/education of trained members of the community

Nguyen, *et al.* (2017) [19] divided the intervention participants into two groups: one group received only printed material (Print), and the second received printed material and follow-up by lay health workers (LHW) (LHW + Print).

LHW + Print group reported increases on all days that FOBT (68.6% - 82.5%); sigmoidoscopy or colonoscopy (40.6% - 47.2%) were done; as well as any CRC screening (73.9% - 88.3%) (all  $p < 0.0001$ ).

Print group reported minor, but still significant, increases in FOBT (65.8% - 70.7%,  $p = 0.032$ ); sigmoidoscopy or colonoscopy (37.5% - 43.0%,  $p = 0.0003$ ); or any CRC screening (72.3% - 79.5%,  $p = 0.0003$ ).

In Wang, *et al.* (2014) [20] study, the proportion of participants who reported having had a FOBT increased significantly, from 66.7% to 79.0% ( $p < 0.001$ ). Likewise, having already done any CRC screening increased significantly, from 71.9% to 82.5% ( $p < 0.001$ ). The proportion of those who were up to date with CRC screening increased from 70.2% to 79.0% ( $p = 0.04$ ).

Tong, *et al.* (2017) [21] intervention group showed greater increases in post-intervention awareness compared to the control group (IG: 69.6% - 90.7%; CG: 74.4% - 79.8% [ $p = 0.0017$ ]). Between pre and post-intervention periods, the IG also exhibited greater increases than the CG in relation to having ever performed a FOBT (IG: 67.7% - 79.5%; CG: 68.5% - 70.8% [ $p = 0.039$ ]) and sigmoidoscopy or colonoscopy (IG: 26.1% - 36.0%; CG: 18.5% - 17.9% [ $p = 0.0052$ ]). The IG was superior to the CG, which did not show significant changes in the screening results, as for continuous screening (OR = 1.73; CI = 95%, 1.07 - 2.79) and being updated with screening (OR = 1.71; CI = 95%, 1.26 - 2.32).

In Briant, *et al.* (2018) [22], in the beginning of the study, 30.9% of the participants were not up to date with CRC screening (via

FOBT, sigmoidoscopy, or colonoscopy). Of those participants not adhering to the screening, 86.7% (n = 26) received a FOBT kit at the first meeting and returned it for analysis. There was an increase in CRC screening awareness among all participants ( $p < 0.0001$ ).

### Screening by providing free FOBT kits available at post offices and pharmacies

In the work of Potter, *et al.* (2009) [23], CRC screening rates using FOBT kits increased in the control group from 52.9% to 57.3% ( $p = 0.07$ ). It grew from 54.5% to 84.3% ( $p < 0.001$ ) in the intervention group, with the change between intervention participants, 25.4 percentage points higher than among control group participants ( $p < 0.001$ ). Among patients initially in delay with CRC screening, researchers screened 20.7% in the control group and 68% in the intervention group until the study's completed version ( $p < 0.001$ ). In multivariate analysis, the odds ratio for updating with screening in the intervention group (vs. the control group) was 11.3 (CI 95%, 5.8 - 22.0).

In Schneider, *et al.* (2011) [24], participants who received randomly persuasive instructions had a 16% increase in returning the FOBT results while personalized instructions had a 30% increase in returning. As for the total number of FOBT kits distributed (n = 14464; which includes beginners and repeat participants), persuasive instructions increased by 188, while personalized instructions increased by 347 during CRC screening by FOBT. There was a tendency for those who received the combined instructions to present a higher return rate on the result, but it did not reach significance. Therefore, they found that the instructions' persuasive and personalized material increases adherence to screening compared to the baseline participants' control group.

### Encouragement for screening by sending pamphlets/invitations by mail or by phone call

Dietrich, *et al.* (2013) [25] baseline CRC screening rates were 35% in Intervention group (IG) 1, 42% in IG 2, and 57% in IG 3. Women in the intervention group were significantly more likely than women in the control group to catch up on CRC screening during the intervention period, with 6% higher screening rates in the intervention group and a significant adjusted global OR of 1, 32 (95% CI, 1.08 - 1.62). The rates of taking FOBT at home were not significantly different between the two study groups (12.5% in the intervention and 12.2% in control; OR = 1.03; CI 95%, 0.76 - 1.38).

### Encouragement for screening by population education via multimedia

Lee, *et al.* (2014) [26] revealed that the DVD and the brochure (sent to the control group) were not significantly different ( $p > 0.005$ ) in their impact on screening rates, with both interventions playing an essential role in increasing the use of CRC screening.

Zapka, *et al.* (2004) [27] general screening rates were the same in the intervention and control groups (55%). In regression modeling, intervention participants were not significantly more likely to complete sigmoidoscopy alone or in combination with another test (OR = 1.22 [CI 95%, 0.88 - 1.70]). The "intervention dose" (considered as viewing  $\geq 50\%$  of the video) showed significant relation to receiving sigmoidoscopy with or without another test (OR = 2.81 [CI, 1.85 - 4.26]). An uploaded video did not affect colorectal cancer's overall screening rate.

Devereux, *et al.* (2019) [28] recruited 414 people. Of these, 56 were considered not eligible by the program, with 358 remaining. Of these, 61% were screened. Higher education participants were more likely to be screened than those with lesser education (90% vs. 75%,  $p = 0.009$ ).

### Encouragement for screening by a mix of interventions

In Sequist, *et al.* (2009) [29], patients who received mail containing an educational pamphlet presented higher screening rates than those who did not (44.0% vs. 38.1%;  $p < 0.001$ ). Screening rates were similar among patients who had been assisted by doctors who received electronic reminders or not (control group) (41.9% vs. 40.2%;  $p = 0.47$ ).

Arsenault, *et al.* (2016) [30] in 2014, completed a manual review of archived graphics and achieved an increase in the screening rate from 28% to 57.75%. Community Health Workers (CWH) were trained, and more than 75% of patients who participated in CHW educational talks went through CRC screening.

Arnold, *et al.* (2016) [31] had three branches: enhanced service, health education, and nursing support. First-year FOBT completion rates among eligible participants improved from 3% before the intervention to 39% with enhanced assistance, 57% with health education, and 61% with educational tools and additional support of nurses ( $p < 0.012$ ). In the second year, among 461 participants who completed the initial FOBT with a negative result,

38% in enhanced assistance completed a second annual FOBT, 33% in health education, and 59% in nursing support ( $p < 0.0003$ ). Of the participants with negative FOBT results in the first and second years, 48% completed the third consecutive annual FOBT. FOBT rates in the third year were 34.2% in enhanced care, 59.6% in health education, and 47.4% in nursing support ( $p = 0.21$ ).

White., *et al.* (2015) [32] observed the most significant gains when the three interventions (pamphlet, enhancement package, and outdoor advertising) were combined (49.5% vs. 43.4%, OR = 1.28,  $p < 0.001$ ). In Pisera., *et al.* (2016) [33], each individual in the screening group received an invitation letter with the colonoscopy appointment date and time. The participation rate in the colonoscopy screening was statistically higher in the Invitation resubmit group compared with the Educational meetings group (5.2 and 2.1%, respectively;  $p = 0.015$ ). The response rate was also statistically significantly higher in the Invitation resubmit group than in the Educational meeting group (16.5 and 4.3%, respectively;  $p < 0.001$ ).

## Discussion

The studies' duration ranged from one month [24] to a maximum of five years [20], with an average duration of  $\approx 17$  months. The authors promoted specific interventions, such as the delivery of information pamphlets and Pisera., *et al.* (2016) stated that sending a letter to the patient, reminding him/her of the need of screening for CRC by colonoscopy, achieved greater adherence to it than sending an educational meeting invitation instead [33].

Arsenalt., *et al.* (2016) claims that there is evidence that confirms that offering just colonoscopy as an available option for CRC screening can decrease patient compliance. On the one hand, in two studies in which the only available examination option for screening was colonoscopy [28,33], the main justifications for low patient compliance were the high cost of the examination [28]; the belief that screening is ineffective or potentially harmful [33]; the lack of knowledge about the importance of screening for the early diagnosis of CRC [28,33]. On the other hand, according to Pisera., *et al.* (2016), the annual performance of tests such as FOBT may have less patient compliance when compared to colonoscopy every ten years. In some studies that offered colonoscopy, FOBT, or sigmoidoscopy as screening options, more participants opted for colonoscopy [16,17,21,26]. In other studies, however, FOBT had greater adherence [20,29]. In general, in studies that offered the

screening option of sigmoidoscopy, few patients chose this method compared to the other available tests [16,17,20,21,26,29]. Zapka., *et al.* (2004) did not report any compromise in the adherence rate to sigmoidoscopy, obtaining a high index compared to the control group [27].

According to Little., *et al.* (2001), a patient-centered approach is essential to obtain better results in the screening of CRC, especially in primary health care [34]. The study carried out by Aubin-Auger., *et al.* (2016) confirms this idea, presenting an increase of 12.4% in screening rates. According to it, these results could have been even better if care strategies focused on the person/patient had been adopted [15]. Another example - a study by Menon., *et al.* (2011) - concluded that having a doctor recommending the screening test increases in two times the chances of patients adhering to the strategy and completing screening after the intervention compared to those who had not received medical recommendations [7]. This could be explained by the Health Belief Model, which maintains that an individual can change its behavior around the action of interest (in this context, CRC screening) if the knowledge about the test, the perceiving risks of developing the disease, the perceived benefits (positive results associated with CRC screening) and self-efficacy (confidence in performing a CRC screening test) are high and the barriers (obstacles to CRC screening) are low [7].

Also, Berkhof., *et al.* (2011) conducted a systematic review of previous communication skills programs in continuing medical education. Training programs are useful if they last at least one day [35]. Thus, according to the authors, the fact that training lasted only four hours in the study carried out by Aubin-Auger., *et al.* (2016) due to the lack of doctors' availability, this may have contributed to not obtaining better screening rates [15]. Therefore, medical recommendations notably positively impact increasing CRC screening rates.

According to Davis., *et al.* (2013), some of the most effective interventions include using a multidisciplinary team to communicate with patients with lower educational levels, low income and composed of minority and ethnic groups, because, in general, they present the lowest levels of screening [16,17,23]. In the study written by Davis., *et al.* (2013), group participants who were instructed by a nurse were 1.6 times more likely to be screened compared to other participants who did not have such guidance [17]. Also, in Abuadas., *et al.* (2018), after the educational discussion group in-

intervention, there was an increase of 21.8% in the total compliance to FOBT testing, being that 81.4% of this increase was due to the individuals who had participated on the discussion group [18]. Consequently, recommendations by non-medical health professionals and educational discussion groups increase the screening rates for the CRC. In addition to it, in the study by Nguyen, *et al.* (2017), there was statistically significant evidence that leaflets' delivery is less effective than interventions made by trained community lay people to encourage screening through face-to-face meetings and telephone calls and who did follow-ups with the participants after the intervention [19].

Encouraging patients to go through CRC screening by sending pamphlets/invitations by mail or by invitation via phone call contributed to increasing the screening rate, establishing it as a good strategy to attract patients. Good communication between the patient and the health care professional/institution and also the dissemination of screening [30] ensured greater adherence to interventions aiming at the early diagnosis of CRC, either by colonoscopy, rectosigmoidoscopy or FOBT.

Communication via pamphlet, personal invitation or phone call aims not only to get in touch with patients but to teach them about what CRC is and how the screening tests work. Warnings are made about the seriousness of the disease and its level of incidence, raising patients' awareness about their leading role in their own health care [30].

Further, when the invitation or the educational pamphlet are customized, it results in greater patient receptivity and understanding about the importance of going in for CRC screening. This customization can be done either by culturally adapting the information, translating it into the patient's native language [19] and addressing their beliefs and customs [26] or by sending an attached personalized letter of identification identifying the patient by name.

In Japan, where the screening CRC rate is already considered satisfactory, yet there was an increase in the screening rate after the implementation of a government program, where it was sent an explanatory brochure about the importance of carrying out FOBT to the patients' homes. A voucher for a free exam was attached to this brochure.

The free exam is undoubtedly another factor of undeniable impact in increasing adherence to screening. Another study credited the increase in screening rates to the education of target patients through pamphlets in their native language, advising the patient on how and where the exam could be done, in addition to informing how the patient could obtain free or low-cost exams [19].

Health education interventions using multimedia have not proved to be very effective for the patient's adequate understanding of the severity of CRC and the importance of screening methods for early diagnosis and treatment and, consequently, they were proven less effective for the target population's adherence to the most appropriate screening methods [18,26].

In studies conducted by Dietrich (2013) and Schneider (2011), the costs of interventions were less than US \$ 500.00 in studies [24,25] that the main intervention did not directly involve training people, whether they were health care professionals or not. Examples of it are: the usage of personalized letters and educational pamphlets [29,32,33], educational videos [26,27], questionnaires answered via phone calls [27], FOBT kits and test instructions [23,24,29,32], reminder calls to patients [23,25] and electronic reminders for doctors [29]. In these low-cost interventions studies, rates of adherence to screening were obtained and ranged from 1.7% up to 27% [23-27,29,32,33].

As for the limitations, it was reported in almost half of the studies the impossibility of attributing the results to other populations. It is because there are significant differences among the groups of other studies regarding ethnicity, nationality [7,17,22], gender [19], or financial status of patients [27], in addition to hospital infrastructure or the HealthCare System where the intervention was conducted [26] and the fact that some patients' samples are small [18,20,22]. Some authors reported difficulty in gathering information about screening before and after the intervention, either because of inconsistent data reported by patients [7,19,20] or noted in medical records [16] as well as insufficient patient follow-up time [21] and limited financial resources [30].

## Conclusion

The rate increase in adherence to CRC screening tests relates to the guidance provided by a trained multidisciplinary team. Also,

the patient-centered clinical method attends to the patient's singularities and thereby uses the best screening methodology based on updated scientific evidence for each population. Moreover, sending personalized newsletters and strengthening contact with patients via phone call/multimedia also increase success chances.

### Conflict of Interest

There is no financial interest or conflict of interest.

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