Screening for colorectal cancer: the role of the primary care physician

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In recent years, the role of primary care physicians (PCPs) in the diagnosis and management of gastrointestinal disorders, including screening for colorectal cancer (CRC), has been recognized as very important. The available data indicate that PCPs are not adequately following CRC screening guidelines because a number of factors have been identified as significant barriers to the proper application of CRC screening guidelines. These factors include lack of time, patient reluctance, and challenges related to scheduling colonoscopy. Further positive engagement of PCPs with CRC screening is required to overcome these barriers and reach acceptable levels in screening rates. To meet the expectations of modern medicine, PCPs should not only be able to recommend occult blood testing or colonoscopy but also, under certain conditions, able to perform colonoscopy. In this review, the authors aim to provide the current knowledge of the role of PCPs in increasing the rate and successfully implementing a screening program for CRC by applying the relevant international guidelines. Eur J Gastroenterol Hepatol 29:e1–e7 Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

Introduction

Colorectal cancer (CRC) represents one of the most important malignant digestive neoplasms, harboring significant morbidity and mortality. As the majority of CRC appear in the context of pre-existing polyps, the endoscopic removal of these polyps reduces the incidence of CRC. International guidelines recommend that all men and women should be screened for CRC beginning at the age of 50 years and that successful screening should start with primary care [1]. Unfortunately, the majority of the populations in almost all countries do not follow the guidelines provided by scientific organizations and health authorities.

During the last few years, the role of primary care physicians (PCPs) in the prevention, diagnosis, and management of a number of benign and malignant gastrointestinal disorders has been recognized as very important. The role of PCPs becomes even more significant in the case of CRC as, with suitable screening programs, the rate of this neoplasm could be diminished markedly.

However, the role of PCPs differs according to the screening scheme in a respective country or region. In many European countries, their role has been changing recently with the introduction of population-based

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programs, in which PCPs do not perform screening, but have a rather supportive, informative, or facilitating role.

The aim of this review is to provide the current knowledge of the role of PCPs in successfully performing and increasing the rate of screening programs for CRC.

Literature search

The relevant evidence has been derived from a thorough search of computerized medical databases, including Medline, EMBASE, and Cochrane Review Library (2000–2016). A combination of the following MeSH subject headings and text-words was applied: 'primary care', 'primary care physician', 'screening for colorectal cancer', 'prevention of colorectal cancer', 'general practitioner,' 'colorectal cancer screening in primary care', 'fecal blood test', and 'colonoscopy'. Two authors (J.K.T. and A.G.) performed the literature search according to the above strategy.

The studies selected were clinical and cohort studies as well as reviews referring to CRC screening in primary care. They were included only if PCPs were actively involved in carrying out the study.

Bearing in mind the increasing proportion of PCPs in most countries, their growing role in diagnosing and treating various disorders, and the changes in the epidemiology of digestive diseases in many parts of the world, we also underscore the ways to update PCPs awareness.

Participation rates of colorectal cancer screening programs

The participation rate in CRC screening programs worldwide is generally low, although recent data suggest that it could be characterized in some countries as satisfactory, especially during the last 6 years.

In the Czech Republic, a European country with CRC incidence among the highest worldwide, only 25% of individuals eligible for screening undergo regular screening: $\sim 500\,000$ immunologic fecal occult blood tests

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(IFBTs) a year [2]. However, in a study that included 50 primary healthcare centers in Serbia, 50 894 individuals were invited to participate in a CRC screening program using IFBT. The participation rate was quite satisfactory (67.8%). Among individuals with a positive test, 69.7% agreed to undergo colonoscopy [3].

Recently, Klabunde *et al.* [4] asked representatives of 12 countries participating in the International Cancer Screening Network program to describe their G-fecal occult blood test (FOBT)/fecal immunochemical test (FIT)-based CRC screening programs. They found that the overall uptake/ participation rate varied markedly: from 7 to 67.7%. In a population-based randomized clinical trial conducted in four countries (Poland, Norway, the Netherlands, and Sweden), in which colonoscopy screening versus no screening was compared, it was found that among 31 420 eligible participants randomized to the colonoscopy group, only 12 574 (40.0%) underwent screening. The participation rates vary significantly among the four countries [5].

Finally, in a systematic review of the data available up to the end of 2009, it was found that studies comparing invitation methods showed higher participation rates with the involvement of a general practitioner, a more personalized recruitment approach, and reduction of barriers that discourage participation [6].

The conclusion derived from these figures is that, during the last years, the cooperation of the target population with health professionals (especially PCPs) would increase the rate of participation in CRC screening programs, although steps should be taken to further increase the motivation of individuals to participate in these programs.

The role of primary care physicians in colorectal cancer screening programs

During the last few years, it became evident that PCPs have all the available resources to ensure high standards of care for their patients. In particular, clearly articulated clinical practice guidelines, effective medications, accurate noninvasive investigations, and evidence-based primary care management plans are available to support PCPs who aim to increase their threshold for referring patients with gastrointestinal symptoms [7]. PCPs play an important role across the cancer continuum, from encouraging screening and accurate diagnosis to providing care during and after treatment for cancer and any comorbid conditions. The improvement in CRC screening rates largely depends on the efforts of PCPs to implement effective systems and procedures for screening delivery. An active engagement and support of practices are essential for the potential of CRC screening to be realized.

However, it must be emphasized from the beginning that the roles of PCPs differ in each country or geographic region according to the screening scheme. As mentioned before, the initiation of population-based programs in Europe has changed significantly compared with other continents as PCPs play a rather supportive, informative, or facilitating role.

Several randomized-controlled trials have shown PCPsled follow-up to be equivalent to hospital-led care in terms of patient well-being, recurrence rates, and survival, and might be less costly [8]. However, a large proportion of PCPs did not consider CRC screening practice as a part of the periodic health examination, whereas only 25% recommended evidence-based screening tests during usual check-up visits, despite the fact that the personal involvement of PCPs has a positive impact on the participation of individuals in screening programs.

It seems that the personal involvement of the PCPs produces better results. In a study in Australia, letters calling for participation in CRC screening programs led to better results if they were accompanied by the personal involvement of PCPs [9]. Another study showed that participants who received the FOBT kit from their PCPs were more likely to participate in the study [10]. Patient prompting of their physician resulted in a significant increase in referral in CRC screening in both underinsured and insured patient populations [11].

The role of PCPs is better emphasized in studies showing that the presentation of individualized CRC risk information by a nonphysician assistant as a decision aid did not result in higher CRC screening rates in primary care patients compared with the presentation of general CRC screening information [12].

An interactive training seminar increased the proportion of physicians with the intention to prescribe FIT and colonoscopy in equal proportions [13]. Asking patients questions about their specific risk factors and providing them and their providers information just before an appointment may increase participation in CRC testing [14].

In Asia, CRC testing compliance is quite low, probably because the knowledge of CRC symptoms and risk factors is low. An interesting study found that perceived health, psychological, and access barriers to CRC testing in Asian countries are high. It is of interest that the physician's recommendation might increase testing. However, physicians mainly recommend testing only in individuals with a positive family history for CRC [15].

Although in Europe medical assistants are not generally part of the health professional staff devoted to screening programs, in other countries, including the USA, they can play a key role in improving CRC screening rates as part of a redesigned system of primary care. A relevant study showed that education providers and electronic reminders had minimal immediate impact on screening rates. The addition of the expanded medical assistant role was associated with a sustained increase in the colonoscopy referral order rate to 13.4%, a relative improvement of 123% [16]. Powerful strategies to increase CRC screening rates include a recommendation to perform the test from the PCPs and focusing efforts on patients aged 50-59 years to ensure that they complete their first FOBT [17]. One of the key roles of PCPs currently recognized in CRC screening is to provide information to patients for their choices and decision making on screening.

In conclusion, the data available indicate that PCPs play a key role in increasing the participation rate in CRC screening programs.

Compliance of primary care physicians with colorectal cancer screening guidelines

The role of PCPs in each country reflects the rules of an established national/regional program rather than scientific guidelines. Extensive literature shows that there is a wide geographic variation among and within countries in the use of CRC screening approaches that are mainly explained by physician preferences, local medical culture, and available resources. Comparing the USA and Europe, there may be a greater variation in CRC screening recommendation and practice within each continent rather than between them, but there seems to be a stronger emphasis on programmatic screening in Europe, facilitating quality assurance. The much-debated need for randomized trials, as new screening modalities emerge, could be handled more easily if running screening programs are considered natural platforms for testing out and evaluating presumed improvements in the service, including new emerging screening modalities [18].

The PCP is a medical doctor responsible for the prevention of almost all human diseases. Consequently, this role represents the most important element of all advanced primary care health systems. A PCP's failure to inform patients on the usefulness and the availability of routine screening tests could result in significant delays in early cancer diagnosis, thus having an important impact on patients' survival. Consequently, PCPs must provide the best medical care in all patients and individuals under their care on the basis of the most current scientific data. Therefore, their role should not just be 'supportive' and must not be limited from 'national screening schemes'. In other words, each PCP must adopt and apply the most current knowledge and skills derived from the relevant international approaches and experiences.

It seems that generally PCPs do not adequately follow CRC screening guidelines published so far either in Europe for example, European guidelines for quality assurance in CRC screening and diagnosis, the European Code Against Cancer and the European Colorectal Cancer Screening Guidelines Working Group [19–22], or in other continents, including Asia [23].

In a relevant study, it was reported that although 77.5% of PCPs reported using national screening guidelines, only 51.7% reported recommendations consistent with the guidelines. Younger physicians were significantly more likely to report compliance with screening guidelines. PCPs practicing in solo group or community health centers were significantly less likely to report following guidelines compared with those in academic practice. Guideline compliance is higher for FOBT than colonoscopy [24].

In another study, it was found that the annual FOBT was correctly suggested and performed by 40% of PCPs, the suggestion for flexible sigmoidoscopy every 3–5 years by 12%, and the concurrent application of both examinations by 8% [25]. In Greece, only 50% of PCPs recommend screening for CRC, whereas the percentage of PCPs recommending FOBT and sigmoidoscopy was 24 and 4%, respectively [26].

The situation in other European countries might be considered satisfactory. According to Mauri *et al.* [27] CRC screening is recommended by 65–95% of PCPs in Europe. In more detail, FOBT was advised by 42–83% and prescription of screening endoscopic modalities was inconsistent (6–48%).

In conclusion, the available data indicate that a large effort is required to persuade PCPs to consider CRC screening programs as a very important part of their clinical practice.

Screening modalities for colorectal cancer applied by primary care physicians

Studies from the USA, Canada, and Australia indicate that the performance of large bowel endoscopy by PCPs represents a usual practical screening approach possibly because of the existence of the accredited colonoscopy training in family medicine programs. It must be emphasized, however, that in Europe, the potential of PCPs in performing sigmoidoscopy or colonoscopy is marginal. Nevertheless, it could be supported that this experience could be applied (after modifications) in certain geographical areas with lower specialist capacity (e.g. remote geographical areas and islands).

Flexible sigmoidoscopy and colonoscopy performed by primary care physicians

Colonoscopy remains the gold standard for the investigation and management of large bowel CRC and polyps. Nevertheless, with the current need for greater access to CRC screening, PCPs trained in colonoscopy could play a role in providing access to colonoscopy for CRC screening.

In a systematic review and meta-analysis aiming to characterize the quality and outcome of flexible sigmoidoscopy, colonoscopy, or upper gastrointestinal endoscopy performed by a nonphysician (nurse, nurse practitioner, physician assistant), it was shown that nurses and nurse-practitioners/physician assistants performing flexible sigmoidoscopies achieved pooled polyp detection rates of 9.9 and 23.7%, adenoma detection rates of 2.9 and 7.2%, CRC detection rates of 1.3 and 1.2%, and adverse event rates of 0.3 and 0/1000 sigmoidoscopies, respectively. No significant differences were found between polyp and adenoma detection rates in sigmoidoscopy performance studies comparing nurses or nursepractitioners/physician assistants with physicians. Data from the three studies of nonphysician performance of colonoscopy showed that the pooled adenoma detection rate was 26.4%, the cecal intubation rate was 93.5%, and the adverse event rate was 2.2/1000 colonoscopies [28]. Other data from different settings in many countries show that adequately trained PCPs can provide safe and technically competent colonoscopies. Their results compare favorably with the currently reported comparative data from specialist endoscopists [29,30].

Family physicians or specialized nurses are in a privileged position to learn and use sigmoidoscopy to screen patients, especially in resource-deprived areas, where colonoscopic capacity is limited. Flexible sigmoidoscopy represents an endoscopic skill that has been developed and successfully performed by suitably trained nonmedical staff in the USA and to a lesser degree in other parts of the world, including Europe, Asia, and Canada.

In the UK, a multidisciplinary committee of nurses and clinicians developed a structured training program involving a staged process of observations, withdrawals, and finally, full procedures. The training program required 35 observations, 35 withdrawals, and 35 supervised full procedures to be performed before the real sigmoidoscopy. Almost all the examinations were completed successfully with no complications [31].

In a study carried out in six hospitals in the UK, it was found that there was no significant difference between doctors and nurses in outcome at 1 day, 1 month, or 1 year after upper and/or lower gastrointestinal endoscopy, leading to the conclusion that diagnostic endoscopy can be performed safely and effectively by nurses [32]. However, above-mentioned European randomized multithe institution nurse endoscopy trial also showed that endoscopy performed by nurses is not cost-effective compared with endoscopy performed by doctors [33]. In these clinical trials, the nurses began their practical training on the first day with a real endoscope to familiarize themselves with its various functions. This preliminary stage was followed by training in simulators. Subsequently, the nurses were introduced to the practical aspects of performing flexible sigmoidoscopy. After 1 week, the nurses returned to their hospitals to commence practical training under the supervision of experienced gastroenterologists or surgeons.

It seems that colonoscopies performed by PCPs are both safe and effective. Quality indicators are within the range of the published literature for those performed by specialists and the parameters recommended by expert consensus. Also, the complication rate as well as the rate of success of flexible sigmoidoscopy performed by nonspecialists fall into the range of those of gastroenterologists-endoscopists. However, for most European healthcare systems, this suggestion is, at present, not relevant.

Fecal occult blood tests: the role of primary care physicians

It is well established that screening using FOBT can detect CRC at an earlier stage than symptomatic presentation and significantly decrease mortality from this malignancy. It is noteworthy that the type of FOBT used by PCPs is usually directed by the program and the reimbursement rules. In the UK, the uptake of screening is currently low, despite the introduction of the Bowel Cancer Screening Program. In this country, the success of population-based screening for CRC might largely be determined by PCPs' attitudes and support, particularly with respect to FOBT, which is considered to be the most appropriate for population-based screening [34]. In some countries of Southern Europe, approximately only one-third of the general practitioner population recommended FOBT screening.

Moreover, many PCPs in many countries continue to use inappropriate methods to screen for FOBT. In a study from the USA, it was reported that most of the 1134 PCPs used standard guaiac tests, whereas higher sensitivity guaiac tests and immunochemical tests were used only by 22.0 and 8.9%, respectively. Moreover, few PCPs recommend repeating the FOBT (17.8%) or using tests other than colonoscopy for the diagnostic work-up (6.6%) [35].

In terms of the preferred method of screening for CRC, the available data in the USA indicate that PCPs' CRC screening recommendations and practices have changed markedly during the last decade. Colonoscopy is now the most frequently (95%) recommended test to asymptomatic, average-risk individuals, whereas 80% of PCPs recommend FOBT. Most PCPs do not recommend the full list of test options prescribed in national guidelines [36]. In another study, it was found that in the USA, colonoscopy was promoted as the preferred CRC screening method.

FOBT was recommended for patients who could not afford or did not wish to undergo colonoscopy. Flexible sigmoidoscopy or barium enemas are rarely recommended. Experienced PCPs use brief CRC screening promotion scripts, including counseling techniques that improve CRC screening performance [37].

Reminder systems

Reminder systems are an essential element of an effective program performed by PCPs. There are two reminder systems: one targeting physicians and another targeting patients.

Evidence from various meta-analyses proves that many reminder options are effective. These options will assist PCPs in choosing their own strategy and tools to attain a high level of consistency and impact.

In a relevant systematic review, five comparative studies involving 25 287 patients comparing physician reminders with controls were identified and analyzed to obtain a summary outcome. The results showed that in all studies, a higher percentage uptake was obtained when physician reminders were provided [38].

In a trial aiming to assess the costs and costeffectiveness of a mailed educational reminder on FOBT adherence, it was found that a simple mailed educational reminder increases the FOBT card return rate at a reasonable cost. Compared with other patient-directed interventions, including telephone, letters from physicians, and mailed reminders for CRC screening, this intervention was both more effective and cost-effective [39].

Various reminder systems for FOBT have been shown to be beneficial, especially those focused on the family physician. Using an intent-to-screen analysis, the screening rate in the physician and patient reminder groups was significantly higher than that in the control group (16.5 and 11.9 vs. 1.2%, respectively) and phone reminders were more effective than letters (14.7 vs. 9.2%) [40].

The web offers novel possibilities to educate patients and improve health behaviors, such as cancer screening. However, a study showed that a web-based educational intervention was no more effective than a print-based one or control (no educational intervention) in increasing CRC screening rates in women at average risk of CRC. Risk messages tailored to attentional style had no effect on screening uptake. In average-risk populations, the use of the internet for health communication without additional enhancement is unlikely to improve screening participation [41].

The use of an alert in an individual's primary care electronic medical records is associated with a significantly increased uptake of an organized, FIT-based CRC screening program in patients attending primary care centers [42].

A recent European study showed that an interactive training seminar could increase the proportion of physicians with the intention to prescribe FIT and colonoscopy in equal proportions [13]. Asking patients questions about their specific risk factors and providing them information just before an appointment may increase participation in CRC testing [17].

In conclusion, the use of reminder systems depends on the mode of invitation and performance of screening. The role of PCPs in this varies across Europe.

Barriers to screening

A number of factors referring both to PCPs and to individuals have been identified internationally as significant barriers to CRC screening. These factors include lack of time, patient reluctance, and challenges related to scheduling colonoscopy. Clinicians identified communication skills and the convenience of office-based screening procedures as facilitators of CRC screening.

In a relevant study, it was found that physician recommendation and knowing someone who has/had cancer were the most common factors motivating patients' decision to complete CRC screening [43]. Pre-existing medical conditions, physician recommendation, and psychosocial factors could represent potential barriers to CRC screening. However, a relevant study found that CRC screening referrals were similar for all patients, irrespective of comorbidities or clinical visits. Comorbidities, rated as having an extreme influence on CRC screening, showed a trend toward lower screening rates, suggesting that, although comorbidities did not predict colonoscopy completion, they may play a role in relation to other factors [44]. Other factors, such as patient's obesity, birthplace outside of Western Europe and North America and physician's male sex, were associated with lower CRC screening rates in a Swiss university primary care setting. Physicians' perception of obesity and its impact on their recommendation for CRC screening might be a target for further research [45].

Barriers to CRC screening are not the same in every country; for example, in Thailand, patients' ignorance, unavailability of the test, unawareness of physician, and financial problems are the main barriers for CRC screening [46].

Both PCPs and average-risk adults identified the lack of patient awareness and physician recommendation as key barriers to obtaining CRC screening. PCPs also frequently cited patient embarrassment/anxiety about testing and test cost/lack of insurance coverage, but few adults identified these as major barriers. Of adults not current with testing, those who had visited a doctor in the past year or had health insurance were more likely to report lack of physician recommendation as the main reason why they were not updated compared with their counterparts with no doctor visit or health insurance. Only 10% of adults not current with testing, who had a doctor visit in the past year, reported receiving a screening recommendation [47].

Many studies have shown that not all individuals with positive FOBT are prompt to undergo colonoscopy and decision making by PCRs has a major effect on nonperformance of a complete diagnostic evaluation after a positive FOBT result [48].

A systematic review aiming to characterize patients' own experience of colonoscopy in the screening context showed that most patients perceived the laxative bowel preparation to be the most burdensome part of colonoscopy. Other reported difficulties including anxiety, anticipation of pain, feelings of embarrassment, and vulnerability. Inadequate knowledge and fear of finding cancer were identified as obstacles to the uptake of screening colonoscopy. Physician endorsement, presence of a family history, knowing someone with cancer, and perceived accuracy of the test were incentives to having a colonoscopy [49].

Older individuals represent another target group with many peculiarities. PCPs often individualize their CRC screening recommendations for older women by selecting to engage patients in discussions and seeking their input before making a CRC recommendation. PCPs are more likely to select to engage the patients represented by the good and fair health vignette where the potential benefits outweigh the potential harms than patients in poor health, where the potential harms outweigh the potential benefits [50].

Finally, barriers dealing with the PCPs themselves are also important and include lack of time, privacy and confidentiality concerns, and family dynamics. It seems that adherence to CRC screening is based on a supportive 'patient-physician' dialogue that is separate from assistive 'patient-family member' relations [51].

In other parts of the world with lower participation rates in CRC screening programs, it has been found that specific barriers to participation included language barriers, logistical challenges to attending screening tests, and cultural beliefs [52].

In conclusion, many barriers referring to both patients and physicians certainly exist. These barriers might be different in various parts of the world and must be taken into account when planning a CRC screening program.

Suggestions for more effective screening programs

In countries with low rates of CRC screening, targeted actions are needed to improve the situation. These should include adaptations to the invitation and follow-up protocol by the implementation of an active call-recall system. PCPs should be flexible in their suggestions by changing to or adding another screening modality, and gastroenterology and PCRs societies should enhance these efforts in cooperation with the health authorities. Associating PCPs with an invitation to screen achieves better participation and reparticipation than does an invitation from a centralized screening unit [53].

Quality assurance and evaluation are very important parameters to ensure a minimal burden and a balanced use of resources. A more comprehensive discussion of CRC screening can increase the rates of CRC screening [54].

Systematic reminders to patients and physicians could increase screening rates and electronic reminders to physicians may increase screening among adults who have more frequent primary care visits [55,56]. Other sources of information, such as videotapes, written material, and even an endorsement of CRC screening by the clinic's office staff, can help patients to decide to undergo screening [57].

As time passes and we gain increasingly more experience in CRC screening programs, it becomes obvious that a need for a multidisciplinary team approach is of paramount importance for the success of a screening program. A multidisciplinary team, including PCPs, nurses, physician assistants, nurse practitioners, clerical personnel, health educators, and behavioral scientists, should work together. Teamwork and tenacity have been considered to be especially influential in the delivery of preventive services in primary care settings in the USA [58]. The adoption of advanced information systems, including electronic health records, is crucial because they could transform patients' role by empowering them to make decisions on prevention.

Conclusion

A team approach, the use of information systems, the involvement of the patients in decisions about their own care, monitoring practice performance, reimbursement for services such as telephone and e-mail contacts, training opportunities in communication, cultural competence, and the use of information technologies would improve the rate of CRC screening. The improvement in CRC screening rates largely depends on the efforts of PCPs to implement effective systems and procedures for screening delivery. Appropriate guidelines must be incorporated by the PCPs [59].

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Conflicts of interest

There are no conflicts of interest.

References

- 1 Fletcher RH. Successful colorectal cancer screening starts with primary care. *Rev Gastrointerol Disord* 2002; 2 (Suppl 1):S27–S34.
- 2 Azeem K, Ševčíková J, Kyselý Z, Horáková D, Vlčková J, Kollárová H. Primary and secondary prevention of colorectal cancer in the Czech Republic. *Prz Gastroenterol* 2016; 11:1–5.
- 3 Scepanovic M, Jovanovic O, Keber D, Jovanovic I, Miljus D, Nikolic G, et al. Faecal occult blood screening for colorectal cancer in Serbia: a pilot study. Eur J Cancer Prev 2016. [Epub ahead of print].
- 4 Klabunde C, Blom J, Bulliard JL, Garcia M, Hagoel L, Mai V, et al. Participation rates for organized colorectal cancer screening programmes: an international comparison. J Med Screen 2015; 22:119–126.
- 5 Bretthauer M, Kaminski MF, Løberg M, Zauber AG, Regula J, Kuipers EJ, et al. Nordic-European Initiative on Colorectal Cancer (NordICC) Study Group. Population-based colonoscopy screening for colorectal cancer: a randomized clinical trial. JAMA Intern Med 2016; 176:894–902.
- 6 Khalid-de Bakker C, Jonkers D, Smits K, Mesters I, Masclee A, Stockbrügger R. Participation in colorectal cancer screening trials after first-time invitation: a systematic review. *Endoscopy* 2011; 43: 1059–1086.
- 7 Gikas A, Triantafillidis JK. The role of primary care physicians in early diagnosis and treatment of chronic gastrointestinal diseases. *Int J Gen Med* 2014; 7:159–173.
- 8 Emery JD, Shaw K, Williams B, Mazza D, Fallon-Ferguson J, Varlow M, et al. The role of primary care in early detection and follow-up of cancer. *Nat Rev Clin Oncol* 2014; 11:38–48.
- 9 Cole SR, Young GP, Byrne D, Guy JR, Morsom J. Participation in screening for colorectal cancer based on fecal occult blood test is improved by endorsement by the primary care practitioner. *J Med Screen* 2002; 9:147–152.
- 10 Davis TC, Arnold CL, Rademaker AW, Platt DJ, Esparza J, Liu D, et al. FOBT completion in FQHCs: impact of physician recommendation, FOBT information, or receipt of the FOBT kit. J Rural Health 2012; 28:306–311.
- 11 Le V, Syed S, Vega KJ, Sharma T, Madhoun MF, Srinivasan N, et al. Patient prompting of their physician resulted in increased colon cancer screening referrals. World J Gastrointest Oncol 2014; 6:257–262.

- 12 Wilkins T, Gillies RA, Panchal P, Patel M, Warren P, Schade RR. Colorectal cancer risk information presented by a nonphysician assistant does not increase screening rates. *Can Fam Physician* 2014; 60:731–738.
- 13 Selby K, Cornuz J, Gachoud D, Bulliard JL, Nichita C, Dorta G, et al. Training primary care physicians to offer their patients faecal occult blood testing and colonoscopy for colorectal cancer screening on an equal basis: a pilot intervention with before-after and parallel group surveys. *BMJ Open* 2016; 6:e011086.
- 14 Skinner CS, Halm EA, Bishop WP, Ahn C, Gupta S, Farrell D, et al. Impact of risk assessment and tailored versus nontailored risk information on colorectal cancer testing in primary care: a randomized controlled trial. *Cancer Epidemiol Biomarkers Prev* 2015; 24: 1523–1530.
- 15 Sung JJ, Choi SY, Chan FK, Ching JY, Lau JT, Griffiths S. Obstacles to colorectal cancer screening in Chinese: a study based on the health belief model. *Am J Gastroenterol* 2008; 103:974–981.
- 16 Baker AN, Parsons M, Donnelly SM, Johnson L, Day J, Mervis A, et al. Improving colon cancer screening rates in primary care: a pilot study emphasizing the role of the medical assistant. *Qual Saf Health Care* 2009; 18:355–359.
- 17 Clouston K, Katz A, Martens PJ, Sisler J, Turner D, Lobchuk M, et al. CIHR/CCMB Team in Primary Care Oncology (PCO-NET). Does access to a colorectal cancer screening website and/or a nurse-managed telephone help line provided to patients by their family physician increase fecal occult blood test uptake?: results from a pragmatic cluster randomized controlled trial. *BMC Cancer* 2014; 14:263.
- 18 Hoff G, Dominitz JA. Contrasting US and European approaches to colorectal cancer screening: which is best? *Gut* 2010; 59:407–414.
- 19 Halloran SP, Launoy G, Zappa M. International Agency for Research on Cancer. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First edition – faecal occult blood testing. *Endoscopy* 2012; 44 (Suppl 3):SE65–SE87.
- 20 Valori R, Rey JF, Atkin WS, Bretthauer M, Senore C, Hoff G, et al. International Agency for Research on Cancer. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition – Quality assurance in endoscopy in colorectal cancer screening and diagnosis. Endoscopy 2012; 44 (Suppl 3):SE88–SE105.
- 21 Armaroli P, Villain P, Suonio E, Almonte M, Anttila A, Atkin WS, et al. European code against cancer, 4th edition: cancer screening. Cancer Epidemiol 2015; 39 (Suppl 1):S139–S152.
- 22 European Colorectal Cancer Screening Guidelines Working Group, von Karsa L, Patnick J, Segnan N, Atkin W, Halloran S, Lansdorp-Vogelaar I, *et al.* European guidelines for quality assurance in colorectal cancer screening and diagnosis: overview and introduction to the full supplement publication. *Endoscopy* 2013; 45:51–59.
- 23 Sung JJ, Ng SC, Chan FK, Chiu HM, Kim HS, Matsuda T, et al. Asia Pacific Working Group. An updated Asia Pacific consensus recommendations on colorectal cancer screening. Gut 2015; 64:121–132.
- 24 Nodora JN, Martz WD, Ashbeck EL, Jacobs ET, Thompson PA, Martínez ME. Primary care physician compliance with colorectal cancer screening guidelines. *Cancer Causes Control* 2011; 22:1277–1287.
- 25 Schattner A, Gilad A. Primary care physicians' awareness and implementation of screening guidelines for colorectal cancer. *Prev Med* 2002; 35:447–452.
- 26 Xilomenos A, Mauri D, Kamposioras K, Gkinosati A, Zacharias G, Sidiropoulou V, et al. Colorectal cancer screening awareness among physicians in Greece. BMC Gastroenterol 2006; 6:18.
- 27 Mauri D, Pentheroudakis G, Milousis A, Xilomenos A, Panagoulopoulou E, Bristianou M, et al. Colorectal cancer screening awareness in European primary care. *Cancer Detect Prev* 2006; 30:75–82.
- 28 Day LW, Siao D, Inadomi JM, Somsouk M. Non-physician performance of lower and upper endoscopy: a systematic review and meta-analysis. *Endoscopy* 2014; 46:401–410.
- 29 Azzopardi J, DeWitt DE. Quality and safety issues in procedural rural practice: a prospective evaluation of current quality and safety guidelines in 3000 colonoscopies. *Rural Remote Health* 2012; 12:1949.
- 30 Kolber MR, Wong CK, Fedorak RN, Rowe BH; APC-Endo Study Physicians. Prospective study of the quality of colonoscopies performed by primary care physicians: the Alberta primary care endoscopy (APC-Endo) study. *PLoS One* 2013; 8:e67017.
- 31 Duthie GS, Drew PJ, Hughes MA, Farouk R, Hodson R, Wedgwood KR, Monson JR. A UK training programme for nurse practitioner flexible sigmoidoscopy and a prospective evaluation of the practice of the first UK trained nurse flexible sigmoidoscopist. *Gut* 1998; 43:711–714.

- 33 Richardson G, Bloor K, Williams J, Russell I, Durai D, Cheung WY, et al. Cost effectiveness of nurse delivered endoscopy: findings from randomised multi-institution nurse endoscopy trial (MINuET). BMJ 2009; 338: b270.
- 34 Damery S, Clifford S, Wilson S. Colorectal cancer screening using the faecal occult blood test (FOBt): a survey of GP attitudes and practices in the UK. *BMC Fam Pract* 2010; 11:20.
- 35 Nadel MR, Berkowitz Z, Klabunde CN, Smith RA, Coughlin SS, White MC. Fecal occult blood testing beliefs and practices of US primary care physicians: serious deviations from evidence-based recommendations. J Gen Intern Med 2010; 25:833–839.
- 36 Klabunde CN, Lanier D, Nadel MR, McLeod C, Yuan G, Vernon SW. Colorectal cancer screening by primary care physicians: recommendations and practices, 2006–2007. *Am J Prev Med* 2009; 37:8–16.
- 37 Scheid DC, Hamm RM, Ramakrishnan K, McCarthy LH, Mold JW. Oklahoma. Physicians Resource/Research Network. Improving colorectal cancer screening in family medicine: an Oklahoma Physicians Resource Network (OKPRN) study. J Am Board Fam Med 2013; 26:498–507.
- 38 Siddiqui MR, Sajid MS, Khatri K, Kanri B, Cheek E, Baig MK. The role of physician reminders in faecal occult blood testing for colorectal cancer screening. *Eur J Gen Pract* 2011; 17:221–228.
- 39 Lee JK, Groessl EJ, Ganiats TG, Ho SB. Cost-effectiveness of a mailed educational reminder to increase colorectal cancer screening. *BMC Gastroenterol* 2011; 11:93.
- 40 Vinker S, Nakar S, Rosenberg E, Kitai E. The role of family physicians in increasing annual fecal occult blood test screening coverage: a prospective intervention study. *Isr Med Assoc J* 2002; 4:424–425.
- 41 Weinberg DS, Keenan E, Ruth K, Devarajan K, Rodoletz M, Bieber EJ. A randomized comparison of print and web communication on colorectal cancer screening. *JAMA Intern Med* 2013; 173:122–129.
- 42 Guiriguet C, Muñoz-Ortiz L, Burón A, Rivero I, Grau J, Vela-Vallespín C, et al. Alerts in electronic medical records to promote a colorectal cancer screening programme: a cluster randomised controlled trial in primary care. Br J Gen Pract 2016; 66:e483–e490.
- 43 Feeley TH, Cooper J, Foels T, Mahoney MC. Efficacy expectations for colorectal cancer screening in primary care: identifying barriers and facilitators for patients and clinicians. *Health Commun* 2009; 24:304–315.
- 44 Lukin DJ, Jandorf LH, Dhulkifl RJ, Thélémaque LD, Christie JA, Itzkowitz SH, et al. Effect of comorbid conditions on adherence to colorectal cancer screening. J Cancer Educ 2012; 27:269–276.
- 45 Fischer R, Collet TH, Zeller A, Zimmerli L, Gaspoz JM, Giraudon K, et al. Obesity and overweight associated with lower rates of colorectal cancer screening in Switzerland. *Eur J Cancer Prev* 2013; 22:425–430.

- 46 Thanapirom K, Treeprasertsuk S, Rerknimitr R. Awareness of colorectal cancer screening in primary care physicians. J Med Assoc Thai 2012; 95:859–865.
- 47 Klabunde CN, Vernon SW, Nadel MR, Breen N, Seeff LC, Brown ML. Barriers to colorectal cancer screening: a comparison of reports from primary care physicians and average-risk adults. *Med Care* 2005; 43:939–944.
- 48 Jimbo M, Myers RE, Meyer B, Hyslop T, Cocroft J, Turner BJ, et al. Reasons patients with a positive fecal occult blood test result do not undergo complete diagnostic evaluation. Ann Fam Med 2009; 7:11–16.
- 49 McLachlan SA, Clements A, Austoker J. Patients' experiences and reported barriers to colonoscopy in the screening context – a systematic review of the literature. *Patient Educ Couns* 2012; 86:137–146.
- 50 Lewis CL, Esserman D, DeLeon C, Pignone MP, Pathman DE, Golin C. Physician decision making for colorectal cancer screening in the elderly. *J Gen Intern Med* 2013; 28:1202–1207.
- 51 Lobchuk MM, Bapuji SB, McClement SE, Sisler JJ, Katz A, Martens P, et al. What is the role of family in promoting faecal occult blood test screening? Exploring physician, average-risk individual and family perceptions. *Cancer Epidemiol* 2012; 36:e190–e199.
- 52 Honein-AbouHaidar GN, Kastner M, Vuong V, Perrier L, Daly C, Rabeneck L, et al. Systematic review and meta-study synthesis of qualitative studies evaluating facilitators and barriers to participation in colorectal cancer screening. Cancer Epidemiol Biomarkers Prev 2016; 25:907–917.
- 53 Whibley AH, Cole SR, Byrne D, Guy J, Morcom J, Young GP. Endorsement by the primary care practitioner consistently improves participation in screening for colorectal cancer: a longitudinal analysis. *J Med Screen* 2010; 17:19–24.
- 54 Mosen DM, Feldstein AC, Perrin NA, Rosales AG, Smith DH, Liles EG, et al. More comprehensive discussion of CRC screening associated with higher screening. Am J Manag Care 2013; 19:265–271.
- 55 Sequist TD, Zaslavsky AM, Marshall R, Fletcher RH, Ayanian JZ. Patient and physician reminders to promote colorectal cancer screening: a randomized controlled trial. *Arch Intern Med* 2009; 169:364–371.
- 56 Lee JK, Reis V, Liu S, Conn L, Groessl EJ, Ganiats TG, *et al.* Improving fecal occult blood testing compliance using a mailed educational reminder. *J Gen Intern Med* 2009; 24:1192–1197.
- 57 Goldsmith G, Chiaro C. Colorectal cancer screening: how to help patients comply. *J Fam Pract* 2008; 57:E2–E7.
- 58 Hudson SV, Ohman-Strickland P, Cunningham R, Ferrante JM, Hahn K, Crabtree BF. The effects of teamwork and system support on colorectal cancer screening in primary care practices. *Cancer Detect Prev* 2007; 31:417–423.
- 59 Klabunde NC, Lanier D, Breslau SE, Zapka GJ, Fletcher RH, Ransohoff DF, et al. Improving colorectal cancer screening in primary care practice: innovative strategies and future directions. J Gen Internal Med 2007; 22:1195–1205.