

EARLY DETECTION OF COLORECTAL CANCER AT PRIMARY CARE LEVEL HEALTH SERVICES



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Protecting populations from the risk of illness by prevention and promoting a healthy lifestyle are core objectives of primary care (PC). Frequent interaction with PC personnel promotes cancer prevention, screening and early diagnosis as well as follow-up care for treated patients. Given the increasing burden and risk of colorectal cancer (CRC) in low- and middle-income countries, involving PC in its early detection and prevention is a pragmatic implementation option for CRC control. PC practitioners who can identify people with persistent symptoms, provide a CRC-related examination, faecal occult blood tests and refer patients with suspected CRC to specialists will promote CRC early detection.

Primary health care, hereafter referred as primary care (PC), involves providing universally accessible essential health care based on acceptable, pragmatic, scientifically sound and socially acceptable methods and technology to individuals and families in the community.¹ PC is about caring for people, rather than specific diseases, constitutes the foundation of health services for the population at large and has become a core concept of World Health Organization's (WHO) goal of "Health for All". PC is often the first point of contact between people and health care providers in the health care system. A primary health care approach is the single most efficient and cost-effective foundation to build a health system on. International evidence overwhelmingly demonstrates that health systems oriented towards primary health care produce better outcomes, at lower costs and with higher user satisfaction.

Protecting populations from risks to health and illness by prevention and health promotion is the core objective of PC. The aim is to provide an easily accessible route to care for people with common illnesses, as well as for chronic diseases such as diabetes, and the prevention of future ill-health

through advice, immunization and early detection. Professionals working in PC are general doctors, nurses, midwives and health workers, dealing with a broad range of physical, psychological and social problems, rather than highly qualified specialists in any particular disease area.

The most common source of PC in rural areas are government health services. In many low- and middle-income countries these services are found at the primary health centre (PHC), a dispensary or a polyclinic in urban areas, and with the general practitioners (GPs) in these centres or in the private/voluntary sector. More than 80% of clinical care in the United Kingdom is delivered in general practice and the PC practitioners refer less than 5% of their patients each year for specialist consultations, opinions and hospital investigations.^{2,3} Recently, there has been renewed interest in the potential of PC to deliver the global health policy agendas with the new focus on non-communicable diseases.⁴ The frequent interaction of apparently healthy people with PC provides important opportunities for cancer prevention, screening and early diagnosis as well as for providing follow-up care for treated cancer patients.

There is increasing emphasis on involving PC in the control of chronic diseases, including cancer, as part of the new integrated non-communicable disease (NCD) control policy evolved by WHO. PHCs in more and more low- to middle-income countries are currently being equipped with essential medications to control diabetes, hypertension, dyslipidemia, chronic respiratory illness and facilities for the early detection of cervical cancer by visual screening. However, cancer is a heterogeneous disease involving several organs and controlling cancer requires a multipronged approach involving several stakeholders. We discuss the global role of primary care practitioners in contributing to the early detection and prevention of colorectal cancer (CRC) within the context of integrating cancer control in primary care. CRC accounts for 1,360,602 cases and 693,881 deaths globally; 347,395 cases and 198,242 deaths in developing countries and the risk is steadily increasing in many developing countries.⁵⁻⁷

Clinical suspicion of CRC in PC

Early detection of cancer is about finding it early when there is a better chance of cure. The PC practitioner's awareness of symptoms and signs of cancer, referral pathways and skills in providing a cancer-related physical examination, taking advantage of the opportunities provided by clients' interaction in PC, are critical to trigger referral to secondary or tertiary care for early diagnosis and treatment. Identification of the symptoms and signs of cancer form the core of the competency required for urgent referral of patients suspected of having cancer. This could be challenging, given the fact the symptoms are not specific to many cancers and the evidence linking certain symptoms to particular cancers is rather weak. Since the diagnosis of cancer is relatively rare for PC practitioners, they need to sort out the minority of patients who need urgent referral from the majority who are unlikely to have the disease. They should also take into account the harm associated with a false-positive referral. This means that the PC practitioners need in-service training and re-orientation for the clinical suspicion of cancer and facilitating early diagnosis. These "skills-building" exercises for PC personnel are often overlooked and less emphasized when introducing cancer early detection initiatives in primary care, particularly in low- and middle-income countries.

Awareness about people at increased risk of CRC such as being over 50 years old, complaining of rectal bleeding, having recent changes in bowel habits, a personal history or family history of colorectal polyps and CRC and a family history of hereditary CRC syndromes, familial adenomatous

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polyposis (FAP) or hereditary non-polyposis colon cancer (HNPCC), and patients with inflammatory bowel disease (IBD), such as ulcerative colitis and Crohn's disease, is conducive to early detection. Since more than 90% of CRCs occur in those aged over 50, ageing is considered the major risk factor in people without IBD. For patients with a family history of CRC in a first-degree relative, especially with a relative diagnosed before age 55, the risk of CRC is nearly double that of patients without a family history.

The symptoms associated with CRC are given in Table 1. Patients presenting with rectal bleeding or change in bowel habits are more likely to be referred by PC practitioners for specialist consultation, sigmoidoscopy or colonoscopy.⁸⁻¹⁰ More often than not, these symptoms may be caused by conditions other than CRC such as gastrointestinal infection, haemorrhoids, irritable bowel syndrome or inflammatory bowel disease. As many patients presenting in PC present with abdominal symptoms, it is important that PC practitioners can identify those at increased risk of CRC, yet they may not encounter more than one or two CRC patients in a year. It is often suggested that symptoms persisting for more than 6 weeks should trigger prompt referral for diagnostic investigations that include specialist consultation and endoscopy. Among the symptoms, rectal bleeding, dark stools or blood in the stools and changes in bowel habits are the most common and well-recognized alarm symptoms for CRC with a high predictive value for cancer.⁸⁻¹² Positive predictive value indicates the probability of diagnosis of the condition when one has the symptom.

In a cohort study involving 762,325 patients aged 15 years or above, registered with 128 United Kingdom general practices between 1994 and 2000, a first occurrence of rectal bleeding, with no previous cancer diagnosis, occurred in 15,289 (2.0%) patients and 338 were diagnosed with CRC in the following three years, yielding a positive predictive value of 2.2%; the predictive value increased significantly with increasing age (Table 2).⁹ Rectal bleeding was associated with a higher risk of CRC diagnosis within 90 days immediately after presentation: 257 of 338 (76%) of diagnosed CRC

Table 1: Symptoms of colorectal cancer

- ▶ Blood in stools, from bright red (more distal tumours) to dark and tarry (more proximal cancers) or dark stools.
- ▶ A persistent change in bowel habits, such as diarrhoea, increased frequency of stools, constipation or narrowing of the stool that lasts for more than 10 days.
- ▶ A feeling that one needs to have a bowel movement that is not relieved by doing so.
- ▶ Feeling of incomplete evacuation after defecation.
- ▶ Inability to pass stools for a prolonged period of time (e.g. 1 week).
- ▶ Abdominal pain, cramps or bloating.
- ▶ Vomiting, especially after prolonged constipation.
- ▶ General weakness and fatigue.
- ▶ Unintended weight loss and/or loss of appetite.

occurred within 3 months from the bleeding episode.⁹ Given the fact that rectal bleeding affects 8–20% of the population the characteristics of the bleeding requires attention: painless bleeding or dark blood mixed with faeces are significantly associated with CRC diagnosis.^{9,10} Changes in bowel habits towards increased looseness or increased stool frequency is more predictive than constipation.⁸ Research evidence indicates that a combination of rectal bleeding, with change in bowel habits, or one of these symptoms in persons aged 60 and above should prompt urgent referral.^{8,10} A recent review indicated rectal bleeding and weight loss as symptoms with high positive predictive value for CRC diagnosis.¹¹ Other concomitant symptoms and signs with rectal bleeding doubles the likelihood of a CRC diagnosis and, in contrast, other symptoms in isolation have very low predictive value for CRC.¹²

Symptoms of CRC differ depending on the location of the tumour, from proximal to distal bowel. Those presenting with proximal cancers may present without changes in bowel habits, as the highly liquid stool may pass easily around even large masses. Patients with cancers of the sigmoid and rectum may pass bright red blood in stools which might be mistaken by the patient as bleeding from haemorrhoids. Difficulty on defecation or constipation can result from the

mass effect of tumours in the distal colon where the stool is more bulky and unable to pass.

Early detection tests for CRC

Early detection tests for CRC include the chemical faecal occult blood test (cFOBT), the immunochemical FOBT (iFOBT), a digital rectal examination (DRE), a double contrast barium enema, sigmoidoscopy, endoscopic colonoscopy and virtual colonoscopy. FOBT and DRE are feasible in PC, whereas the other procedures can only be done in specialized services at secondary or tertiary care centres by highly trained specialists.

In a DRE, the anal canal and rectum are examined with a lubricated, gloved finger. Although a DRE is often included as part of a routine physical examination, when patients complain of rectal bleeding or other abdominal symptoms, it is not recommended as a stand-alone test for CRC. This simple test, which is not usually painful, can detect masses in the anal canal or lower rectum. By itself, however, it is not a good test for detecting CRC because its reach is limited and negative DRE does not exclude CRC. A small amount of stool in the rectum when doing a DRE is used by some general practitioners for cFOBT or iFOBT. However, simply checking the stool obtained in this fashion for bleeding with an FOBT is not an acceptable method of early detection of CRC as the stool collected has not recently transited through the colon and, therefore, is not a representative sample of faeces. Research has shown that this type of FOBT will miss more than 90% of CRC and polyps. All patients with bright red blood in the stool should undergo a DRE to assess if haemorrhoids are present. Any blood in the stool in the absence of haemorrhoids should prompt an immediate referral for colonoscopy.

Early detection tests such as FOBT could help general practitioners in the early diagnosis of CRC. Such tests, especially the iFOBT, should be accessible for PC practitioners. The iFOBT is an early detection test that detects occult (hidden) blood in the faeces. This test reacts with globin, which is part of the human haemoglobin protein

Table 2: Frequency of colorectal cancer (CRC) among people with rectal bleeding in a cohort study in the United Kingdom

Age group	Number of people with a first episode of rectal bleeding	People with CRC, diagnosed within 3 years from rectal bleeding	Positive predictive value (%) for CRC diagnosis
15–44 years	5,489	8	0.15%
45–64 years	5,314	109	2.1%
65+	4,494	221	4.9%
Total	15,289	338	2.2%

Adapted from reference⁹

found in red blood cells. iFOBT is not subject to false-negative results in the presence of high-dose vitamin C supplements and no dietary restriction is required because dietary constituents such as red meat, cruciferous vegetables and fruits do not affect the test. Since globin is degraded by digestive enzymes in the upper gastrointestinal tract, iFOBT is more specific for lower gastrointestinal bleeding and not affected by bleeding from stomach, thus improving their specificity to detect CRC and polyps. Hence, it is easier to use iFOBT rather than cFOBT. Since FOBT may not detect a tumour that is not bleeding, multiple stool samples should be tested. The probability of CRC is clearly higher in patients with positive rather than negative findings on FOBT testing.¹⁰ It is also suggested that iFOBT is more sensitive than cFOBT in detecting early stage CRC¹⁰, and if the results are positive for hidden blood, a colonoscopy is required to investigate further. In order to be beneficial, the test must be repeated approximately every 2 years.

The role of PC in promoting CRC screening programmes

PC practitioners and health workers are ideally positioned to improve participation of subjects in CRC screening programmes with FOBT screening. Since a large number of people above the age of 50 years interact with primary care for routine health care, FOBT screening may be carried out during these visits. All national organized screening programmes initiate screening at age 50, as symptoms of CRC may not be evident until late in the disease process.

A pilot CRC screening programme using iFOBT was implemented through 154 primary care units and 12 community hospitals, at the PC level of Government Health Services, in Lamphang Province, to research the acceptability, feasibility and scaling-up of screening in Thailand.¹³ A target population 127,301 people aged 50–65 years were informed about and invited to undergo CRC screening by community health workers (HWs). The HWs provided the faecal sample collection kits and explained how to use them and participants brought their samples either to one of the primary health units or community hospitals where nurses performed iFOBT. Of the 127,301 target population, 80,012 (62.9%) were screened using iFOBT and 873 (1.1%) were found positive and were referred to undergo colonoscopy at the Lamphang Cancer Hospital and endoscopic polypectomy/biopsies were performed according to colonoscopic findings. Of the 627 (72.0%) iFOBT-positive persons who underwent colonoscopy, 23 were diagnosed with CRC, 75 with advanced adenoma and 112 with non-advanced adenoma.¹³ The stage-distribution of the detected

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invasive cancers was as follows: 2 stage I, 12 stage II, 7 stage III and 2 missing stage information. Those with confirmed CRC received appropriate treatment. The successful implementation of the pilot CRC screening with satisfactory process measures indicates the feasibility of scaling up organized CRC screening through PHC services in Thailand.

Primary prevention of CRC

There is compelling data regarding an inverse relationship of physical exercise and risk of CRC. A meta-analysis of 52 studies found an overall relative risk (RR) of 0.76 (95% confidence interval (CI): 0.72, 0.81) for CRC associated with physical activity.¹⁴ The most motivating means of getting patients to exercise regularly is to speak with them about what activities they enjoy, or enjoyed in the past, focusing on deriving pleasure from the activity. A vast amount of information exists regarding the role of diets and dietary components in relation to development of CRC, which indicates that diets high in trans-fatty acids and saturated fat, sugar and refined starches and low in fruits and vegetables are associated with a higher risk of CRC.¹⁵

Advising people interacting with PC on being physically active for at least 30 minutes, at least five days a week, on maintaining a healthy weight, avoiding tobacco use in any form, drinking no more than one drink a day for women or two drinks a day for men and eating a diet rich in fruits, vegetables and whole grains and less in red and processed meat can be conducive to reducing the risk of CRC. Many of the recommendations regarding diet, exercise and normalization of weight will have ramifications far beyond prevention of CRC and must be implemented as part of an overall healthy lifestyles initiative.

Conclusion

Early detection of CRC at the PC level heavily relies on symptoms, medical history, physical examination, clinical

signs, faecal occult blood tests and appropriate referral. The diagnosis of CRC in its early stages has immense potential to improve survival, with 5-year exceeding 90% for stage I CRC. Given the increasing burden of CRC in low- and middle-income countries⁷, assessing symptoms by careful history taking and physical examination and using early detection tests such as iFOBT at the PC level are of paramount importance in the early diagnosis and control of CRC in such countries in view of the resource constraints in organizing population-based screening programmes. However, the challenge is that PC services in many low- and middle-income countries are already over-crowded and over-extended with a multitude of tasks added each year without matching augmentation of resources provided to cope up with increased demands for additional services. In middle-income countries, with increasing risk of CRC, early detection services for CRC at the PC level should be extended by providing appropriate additional resources and in-service training for the care providers, as has been shown in the Lampang pilot introduction of CRC screening through PC services in Thailand.¹³ ●

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References

- World Health Organization 1978. Primary Health care. Report of the International Conference on Primary Health Care. Alma-Ata, USSR, 6-12 September 1978. Geneva: WHO.
- O'Donnell CA. Variation in GP referral rates: what can we learn from the literature? *Fam Pract* 2000;17:462-71.
- Sullivan CO, Omar RZ, Ambler G, et al. Case-mix and variation in specialist referrals in general practice. *Br J Gen Pract* 2005;55:529-33.
- Rule J, Ngo DA, Oanh TT, et al. Strengthening Primary Health Care in Low- and Middle-Income Countries: Generating Evidence Through Evaluation. *Asia Pac J Public Health* 2013.
- Ferlay J, Soerjomataram I, Dikshit R, et al. 2013. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon: IARC <http://globocan.iarc.fr>.
- Forman D, Bray F, Brewster DH, et al. 2013. Cancer Incidence in Five Continents, Vol. X (electronic version). Lyon: IARC. <http://ci5.iarc.fr>
- Jemal A, Center MM, DeSantis C, et al. Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol Biomarkers Prev* 2010;19:1893-907.
- Hamilton W, Sharp D. Diagnosis of colorectal cancer in primary care: the evidence base for guidelines. *Fam Pract* 2004;21:99-106.
- Jones R, Latinovic R, Charlton J, et al. Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. *BMJ* 2007;334:1040.
- Jellema P, van der Windt DA, Bruinvels DJ, et al. Value of symptoms and additional diagnostic tests for colorectal cancer in primary care: systematic review and meta-analysis. *BMJ* 2010;340:c1269.
- Adelstein BA, Macaskill P, Chan SF, et al. Most bowel cancer symptoms do not indicate colorectal cancer and polyps: a systematic review. *BMC Gastroenterol* 2011;11:65.
- Lawrenson R, Logie J, Marks C. Risk of colorectal cancer in general practice patients presenting with rectal bleeding, change in bowel habit or anaemia. *Eur J Cancer Care (Engl)* 2006;15:267-71.
- Khuhaprema T, Sangrajrang S, Lalitwongsa S, et al. Organized colorectal cancer screening in Lampang Province, Thailand: Preliminary results from a pilot implementation programme. *BMJ Open* (in press).
- Wolin KY, Yan Y, Colditz GA, et al. Physical activity and colon cancer prevention: a meta-analysis. *Br J Cancer* 2009;100:611-6.
- Gingras D, Beliveau R. Colorectal cancer prevention through dietary and lifestyle modifications. *Cancer Microenviron* 2011;4:133-9.