



# Primary and secondary prevention of colorectal cancer: An evidence-based review

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## Abstract

Colorectal cancer (CRC) is a common cancer that affects one in three men and one in four women worldwide. Late-stage detection is associated with significantly lower 5-year survival rates. Although it is well established that CRC mortality rates have decreased in the past several decades, adoption of routine screening continues to lag behind screening for other common cancers such as cervical and breast cancer. The decrease in overall rates has been attributed, in part, to improved primary and secondary prevention efforts, including smoking prevention and cessation programs, nutritional counseling, and the use of evidence-based screening protocols, as well as access to better treatment. Despite the increased screening rates, it is estimated that at least one-third of eligible people do not receive appropriate screening. The objective of this review is to describe the current epidemiology of CRC and to demonstrate effective primary and secondary prevention strategies for the primary care provider.

**Keywords:** Colorectal cancer; adenocarcinoma; modifiable risk factors; primary prevention; secondary prevention; primary care

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## Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed type of cancer in men and women [1]. The American Cancer Society forecast for 2017 is for 95,520 new cases of colon cancer and 39,910 new cases of rectal cancer in the United States. Although CRC morbidity and mortality rates in the United States have been steadily declining in the past 20 years, the rates remain high relative to those in many other industrial nations [1]. There are a number of risk factors that have been associated with CRC, including inactivity, obesity/overweight, nutrition, smoking,

and excessive alcohol consumption [2]. The decrease in overall rates has been attributed, in part, to improved primary and secondary prevention efforts, including smoking prevention and cessation programs, nutritional counseling, and the use of routine screening tests, as well as access to better treatment (tertiary prevention) [3]. Primary and secondary prevention strategies can be used by primary care providers to reduce the rate at which new disease occurs as well as disease burden as reflected in morbidity, mortality, financial costs, and diminished quality of life.



## Epidemiology

In 2012 there were nearly 1.4 million new CRC cases worldwide [4, 5]. CRC is the third most common cancer in men (746,000 cases, 10.0% of the total) and the second in women (614,000 cases, 9.2% of the total) [5]. In the United States the highest rates of diagnosis were in people aged 65–84 years, with a greater incidence and disproportionately high mortality rate in black males and females [1]. In addition, incidence rates differ tenfold in both sexes worldwide, with almost 55% of new cases arising in more developed countries. The highest incidence rates are found in Australia/New Zealand [age-standardized rates (ASR) 44.8 and 32.2 per 100,000 in men and women respectively], and the lowest are found in western Africa (4.5 and 3.8 per 100,000) [5] (Fig. 1). The vast majority of CRC cases develop in individuals with average risk factors, whereas only about 20% of cases develop in people who have a family history [1]. Nonetheless, the lifetime risk of developing CRC is two to three times higher in people with a first-degree relative who has colon cancer or an adenomatous polyp than in the general population [6]. CRC has been associated with the Western diet and lifestyle factors, which

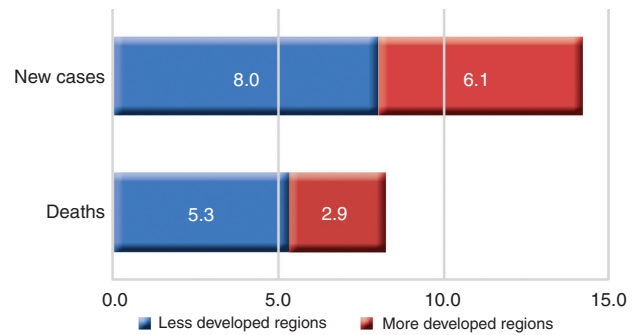


Fig. 1. Number of cancer cases and deaths worldwide in 2012 (in millions).

Source: GLOBOCAN 2012

include consumption of foods that are high in red and processed meats and physical inactivity [7].

There were an estimated 694,000 deaths worldwide (8.5% of the total number of cancer deaths, fourth most common cause of cancer-related deaths). Although mortality rates were lower in 2012 (Table 1), disparities persisted, showing more than half of deaths (52%) occurred in the less developed regions of the

Table 1. Epidemiology of colorectal cancer worldwide

Parameter	Males	Females	All
<b>Incidence data</b>			
Number of new cases	746,298	614,304	1,360,602
Number of new cases per 100,000 population	21.0	17.6	19.3
ASR(W)	20.6	14.3	17.2
Proportion of all newly diagnosed cancers <sup>a</sup> (%)	10.0	9.2	9.7
Rank among all newly diagnosed cancers <sup>a</sup>	Third	Second	Third
<b>Mortality data</b>			
Number of deaths	373,639	320,294	693,933
Number of deaths per 100,000 population	10.5	9.2	9.8
ASR(W)	10.0	6.9	8.4
Proportion of all cancer-related deaths <sup>a</sup> (%)	8.0	9.0	8.5
Rank among all cancer-related deaths <sup>a</sup>	Fourth	Third	Fourth
<b>Prevalence data (patients still alive 5 years after diagnosis)</b>			
Absolute number of survivors	1,953,431	1,590,151	3,543,582
Number per 100,000 population	75.3	61.2	68.2
Cumulative risk of developing colorectal cancer from birth until 75 years (%)	2.36	1.57	1.95

From Ferlay et al. [8].

<sup>a</sup>Excluding nonmelanoma skin cancer.



world, reflecting poorer survival in these regions [5]. In 2012, central and eastern Europe showed the highest estimated mortality rates for both sexes (20.3 per 100,000 for men, 11.7 per 100,000 for women), while western Africa showed the lowest (3.5 per 100,000 for men and 3.0 per 100,000 for women). The 5-year prevalence of CRC (i.e. the number of CRC patients who were still alive 5 years after diagnosis) was estimated at 3,543,582 worldwide (68.2 CRC survivors per 100,000 population), and the cumulative risk of CRC in individuals younger than 75 years was 1.95% worldwide (2.36% in men, 1.57% in women) [5] (Table 1).

### Primary prevention of CRC

Much of primary cancer prevention is designed to avert cancer by living a healthy lifestyle and avoiding cancer-causing substances, such as tobacco. Although the benefit of screening (secondary prevention) is clear, there is also extensive evidence to support the impact of primary prevention activities, primarily through lifestyle modification. The annual report to the nation on the status of cancer estimated that increased screening in combination with a significant but achievable reduction in lifestyle risk factor prevalence from the rates in 2000 could reduce CRC mortality by as much as 50% in 2020 [9]. Compelling evidence indicates that avoidance of smoking and heavy alcohol consumption, prevention of weight gain, and the maintenance of a reasonable level of physical activity are associated with markedly lower risks of CRC [10]. Modifying lifestyle risk factors such as obesity [11], high red meat consumption [12], cigarette smoking [13, 14], and alcohol abuse [15] have been associated with a decreased risk of CRC development [10, 16]. Thus to achieve a meaningful reduction in CRC incidence, primary prevention is an essential complement to CRC screening and early intervention [17] (Fig. 2). Data suggest that cessation of smoking late in life does not necessarily eliminate the increased risk of CRC; it is critical to prevent smoking in adolescents and young adults and to convince smokers to quit as early as possible [10]. Smokers have an approximately twofold increased risk of receiving a diagnosis of an adenoma and higher risk of CRC-related death associated with current smoking [14]. In addition to lifestyle modification, it is also important to note that colonoscopy, while generally considered as part of screening (or secondary

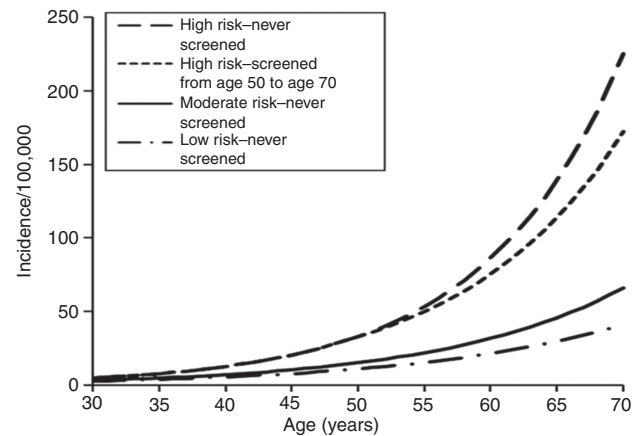


Fig. 2. Age-specific incidence of colon cancer per 100,000 person-years from age 30 years to age 70 years, according to screening behavior, for 1) a “high-risk” participant (one who accrued 10 pack-years, of smoking before age 30 years, had a consistently high relative body weight, had physical activity of 2 metabolic equivalent (MET)-hours/week, consumed 1 serving of red or processed meat per day, was never screened for colon cancer, and had a folate intake of 150  $\mu\text{g}/\text{day}$ ); 2) a “high-risk” participant who was screened from age 50 years to 70 years; 3) a “moderate-risk” participant (one who was a nonsmoker, had an average body mass index, had physical activity of 13.5 MET-hours/week, did not consume red or processed meat, was never screened, and had a folate intake of 300  $\mu\text{g}/\text{day}$ ); and 4) a “low-risk” participant (one who was a nonsmoker, had a consistently low relative body weight, had physical activity of 21 MET-hours/week, did not consume red or processed meat, was never screened, and had a folate intake of 400  $\mu\text{g}/\text{day}$ ), Nurses’ Health Study, 1980–2004.

Source: Wei EK et al. *Am J Epidemiol* 2009; 170:863–72

prevention), may also play a part in primary prevention since removal of noncancerous polyps from the colon may prevent CRC from starting in the first place [18].

### Secondary prevention and screening for early detection of CRC

Factors such as obesity, nutrition, and smoking are most closely associated with the primary prevention of ascending colon cancer [19]. Secondary prevention, in the form of CRC screening, is most closely associated with successful descending colon cancer and CRC prevention [19]. So any comprehensive CRC prevention program must also



incorporate CRC screening, a service whose ‘A’ rating from the US Preventive Services Task Force on a regular basis for people aged 50–75 years and on an individual basis for people aged 76–85 years was reiterated in June 2016. The US Preventive Services Task Force also recognized a number of critical barriers to screening, which is recognized as a widely underused service: “Screening is a cascade of activities that must occur in concert, cohesively, and in an organized way for benefits to be realized, from the point of the initial screening examination (including related interventions or services that are required for successful administration of the screening test, such as bowel preparation or sedation with endoscopy) to the timely receipt of any necessary diagnostic follow-up and treatment” [20]. At the same time, the US Preventive Services Task Force addressed a variety of screening strategies in its recommendation and stated that “there are no empirical data to demonstrate that any of the reviewed strategies provide a greater net benefit” [21] (Table

2). A number of evidence-based strategies have also been recognized by the Community Preventive Services Task Force, including clinician and patient reminder systems, use of small media (e.g. videos, letters, and brochures), reduction of structural barriers to screening (e.g. time or distance to screening setting or offering extended or nonstandard clinic hours), and provision of clinician assessment and feedback about screening rates [20]. There is also evidence that patient navigators increase screening rates, decrease no-show rates, and improve patients’ preparation for screening tests [22].

Current cancer screening rates are particularly disappointing among ethnic minorities and individuals with low socioeconomic status, who often present with late-stage diagnoses and have high mortality rates [23]. Decreases in CRC rates are attributed to improved screening, removal of precancerous lesions, and reduction in modifiable risk factors such as smoking and excessive alcohol consumption [4]. Despite these decreases, a recent survey found that only two-thirds of all

Table 2. Effect of screening intervention on reducing mortality from colorectal cancer

Screening intervention	Study design	Internal validity	Consistency	Magnitude of effect	External validity
Fecal occult blood test (guaiac based) <sup>a</sup>	Randomized controlled trials [1]	Good	Good	15%–33%	Fair
Sigmoidoscopy	Randomized controlled trials	Good	Good	About 25%; 50% for descending colon	Fair
Digital rectal examination	Case-control studies	Fair	Good	No effect	Poor
Colonoscopy	Case-control studies; observational cohort studies that use historical/other controls; randomized controlled trials in progress	Poor	Poor	About 60%–70% for descending colon; uncertain for ascending colon	Fair

From National Cancer Institute [21].

There are no data from randomized controlled trials on the effect of other screening interventions (i.e. fecal occult blood test combined with sigmoidoscopy, barium enema, colonoscopy, computed tomographic colonography, and stool DNA mutation tests) on mortality from colorectal cancer.

<sup>a</sup>The US Preventive Services Task Force (USPSTF) adds that “there are numerous screening tests to detect early-stage colorectal cancer, including stool-based tests (gFOBT [Guaic Fetal Occult Blood Testing], FIT [Fetal Immunochemical Testing], and FIT-DNA), direct visualization tests (flexible sigmoidoscopy, alone or combined with FIT; colonoscopy; and CT [(Computerized Tomographic)] colonography, and serology tests (*SEPT9* DNA test).” The USPSTF found no head-to-head studies demonstrating that any of these screening strategies are more effective than others, although they have various levels of evidence supporting their effectiveness, as well as different strengths and limitations [20]. Additional information may be found in a recent evidentiary review by the USPSTF [1].



eligible patients received screening from their health care provider [24]. Although primary care physicians are most likely to deliver preventive services, they are often doing so within systems that are already taxed by time constraints, administrative tasks, and lower reimbursement [25]. A number of effective strategies have been identified to address these challenges, including use of a team-based approach, optimization of the use of electronic medical records, and creation of patient registries [25, 26]. The concepts are concordant with the patient-centered medical home model of service delivery that has taken hold in many health systems across the United States in the past decade [27]. Using a team-based approach, physicians can work closely with all members of their team to ensure that eligible patients are identified and screened in a timely manner. A pilot study involving seven community-based primary care clinics in Utah found that the use of electronic medical record reminders, provider and medical assistant education on screening, and an expanded role for the medical assistant was associated with an increase in the colonoscopy referral rate from 6.0% at the baseline to 13.4% [28].

### Primary care role

Primary care providers have key roles in the prevention, diagnosis, and management of CRC. Previous authors have reinforced the fact that successful screening should start with primary care [29, 30]. A systematic review of strategies for CRC screening at the population level showed higher participation rates with the involvement of a primary care practitioner, a more personalized recruitment approach, and reduction of barriers that discourage participation [31]. However, the increase in CRC screening rates largely depends on implementation of effective systems of decision support (e.g. electronic medical record reminders) and procedures for screening delivery (e.g. registries) in primary care practices. CRC screening recommendations by primary care providers targeting high-risk patients to ensure that they complete their first fecal occult blood test has proven to be effective [32]. A primary care provider's failure to inform patients of 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.

### Other perspectives

CRC is also an important health problem in countries with a Westernized lifestyle outside the United States. In European countries, for example, CRC mortality has been observed to be much higher than that in the United States, leading, in part, to recommendations for "program screening" (requiring public responsibility by law or official regulation) in addition to screening obtained outside programmatic settings [33]. For public organized programs, it is recommended that there be a regional or national team responsible for implementation, quality, and reporting, and that the screening test, examination interval, and eligible population group are also specified [33]. Screening approaches in these programs have differed according to country. In 2007, for example, guaiac-based fecal occult blood testing was the only screening method in 12 countries, while six countries used two types of test from among both guaiac and immunochemical fecal occult blood testing as well as flexible sigmoidoscopy. In most countries, colonoscopy is used for follow-up of positive screening test results, but in Poland, colonoscopy was the only method used. Screening intervals also differ widely – anywhere from 1 year to 10 years – with the latter reflecting reliance on CRC screening. These variations reflect, in part, the evolving nature of knowledge of CRC screening.

### Conclusion

CRC risk can be lowered through a comprehensive approach that includes both primary and secondary prevention strategies. Primary care providers are in an ideal position to help patients identify lifestyle risks that may place them at an elevated risk of developing CRC. The use of a team-based approach, which includes physicians, nurse practitioners, physicians' assistants, nurses, patient navigators, and behaviorists, may alleviate common barriers such as time constraints, and provide patients with more comprehensive, whole-person care [25]. Adoption of evidence-based tobacco and alcohol screening and brief intervention programs can assist primary care providers in identifying individuals at risk [34, 35].

### Conflict of interest

The authors declare no conflict of interest.





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### Related Information

For more information about colorectal cancer, please read the following articles published in *Family Medicine and Community Health*.

- Temporal trends in colorectal cancer incidence among Asian American populations in the United States, 1994-2013  
<http://www.ingentaconnect.com/content/cscript/fmch/2017/00000005/00000001/art00006>
- Stool DNA-based versus colonoscopy-based colorectal cancer screening: patient perceptions and preferences  
<http://www.ingentaconnect.com/content/cscript/fmch/2015/00000003/00000003/art00002>