

Colon Cancer Screening in North Carolina

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Colorectal cancer (CRC) is the 2nd leading cause of cancer death both in North Carolina and in the United States. The goal of CRC screening is early detection and prevention. This commentary reviews the evidence for screening, discusses current screening options, and explores which options are best suited for use in North Carolina.

Colorectal cancer (CRC) is the 3rd most common cancer and the 2nd leading cause of cancer death in the United States [1]. However, we have witnessed great improvement nationally, with a 47% decline in CRC death rates since the 1970s. The largest reduction was likely due to increased screening made possible by the introduction of the colonoscope into clinical practice in the early 1970s [2]. It has been estimated that around 60% of CRC deaths could be prevented with screening. Indeed, the CRC death rate decreased from 29.2 deaths per 100,000 in 1970 to 15.1 deaths per 100,000 in 2011 [3]. The Medicare program began reimbursing for colonoscopy of high-risk individuals in 1998, and Medicare expanded coverage to average-risk beneficiaries in 2001. The rapid decline in late-stage disease since 2000 is likely due to increases in screening colonoscopy (4% or more per year from 2008 to 2011) [2, 4].

The goal of CRC screening is early detection and prevention of CRC through the removal of adenomatous polyps. The National Polyp Study showed that removal of adenomatous polyps prevents the development of colon cancer [5], and it was later shown that this translated into a mortality benefit [6]. However, navigating the options and recommendations for screening can be confusing, as multiple societies have proposed slightly different guidelines. Additionally, tests are divided into cancer *prevention* tests (ie, colonoscopy, computed tomography [CT] colonography, flexible sigmoidoscopy, and double contrast barium enema) versus cancer *detection* tests (ie, various stool tests). Recommendations for screening are also split between presenting the patient with multiple options versus singling out colonoscopy as the preferred screening strategy; the latter approach is endorsed by multiple gastroenterology societies.

Colon cancer screening should begin at age 45 years for African Americans and at age 50 years for average-risk individuals of other races. The US Preventive Services Task Force (USPSTF) recommends routine screening between the ages of 50 and 75 years. Routine screening between the ages of

75 and 85 years is not universally recommended but should be considered on an individual basis after taking into account the patient's health problems and prior screening history. Screening after the age of 85 years is not recommended by the USPSTF. Although smoking and obesity are risk factors for colon cancer, these factors do not currently necessitate screening at an earlier age.

Options for colon cancer prevention screening include colonoscopy every 10 years, CT colonography every 5 years, flexible sigmoidoscopy every 5 years, and double contrast barium enema every 5 years. These are primarily structural exams aimed at detecting cancer and precancerous polyps. Other options for screening, which fall into the category of cancer detection tests, include various stool tests: annual fecal occult blood testing (FOBT), annual fecal immunochemical testing (FIT), or fecal DNA testing every 3 years. In order for these stool tests to be efficacious, they need to be repeated at regular intervals, and a colonoscopy is required if the test is positive [7].

A careful family history should be performed when deciding on colon cancer screening. The American College of Gastroenterology (ACG) recommends that individuals who have a single first-degree relative with CRC or advanced adenoma diagnosed before the age of 60 years and those who have 2 first-degree relatives with CRC or advanced adenomas should begin screening with colonoscopy at age 40 years and repeat it every 5 years or, alternatively, start screening 10 years younger than the age of diagnosis of the youngest affected relative [8]. Individuals with a single first-degree relative with CRC or advanced adenoma diagnosed after the age of 60 years should be treated as an average-risk patient and should undergo screening colonoscopy at the age of 50 years and every 10 years thereafter, according to the ACG guidelines. Difficulties in ascertaining risk from family history often arise when patients do not know the types of polyps that have occurred in their family members or when patients' knowledge of their family medical history is incomplete. It has been my experience that patients occasionally confuse prostate cancer and colon cancer when reporting their family history, and patients sometimes

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equate a digital rectal exam with a colonoscopy when they are questioned about having had a prior colonoscopy.

Colon Cancer Prevention Screening

Colonoscopy is currently the gold standard for preventive screening, and its greatest benefit lies in its ability to remove polyps. Indeed, other screening methods ultimately achieve their cancer-preventive benefit by referring patients for colonoscopy when the initial screening test is positive. It is important to note, however, that colonoscopy is an imperfect test. One study noted that colonoscopy has a 12% miss rate for large adenomas (1 cm or greater), and others have noted a miss rate for colon cancer of around 4% [9, 10]. Some recent studies have suggested that, although colonoscopy is a very important part of the CRC screening picture, its protective effect is lower than the 76–90% decreased risk of CRC noted in the 1993 National Polyp Study; a follow-up to the National Polyp Study found only 53% reduction in CRC mortality [6]. In addition to missed polyps, another risk of colonoscopy is the small but nonzero risk of perforation; a study using Medicare claims data estimated this rate at 5–7 perforations per 10,000 procedures [11].

CT colonography has also been shown to be effective in screening for CRC. One study showed 94% sensitivity for polyps 1 cm or greater [12], such that 1 in 13 patients screened would subsequently have been referred for a colonoscopy to remove the polyps. Issues related to CT colonography include how to address small polyps, the undetermined risk associated with radiation exposure, and the possibility for extracolonic findings that may lead to additional procedures and testing. The USPSTF has concluded that there is insufficient evidence to recommend for or against CT colonography at this time. Currently, Medicare does not cover CT colonography for routine screening, but it is often covered if prior colonoscopy has failed.

Flexible sigmoidoscopy and barium enema are 2 additional options for preventive screening, although they have been used with less frequency in the United States in recent years. In flexible sigmoidoscopy, only the lower half of the colon is evaluated, and this procedure is often performed without sedation. The disadvantages are that it does not evaluate the right side of the colon, an area of increased neoplasia (particularly in later life); patients are often uncomfortable due to the lack of sedation; and there is a small risk of perforation, estimated at less than 1 per 20,000 procedures [13]. A barium enema can evaluate the whole colon, but it requires a colon preparation, and enthusiasm for this test is often limited due to patient discomfort, reduced sensitivity for polyps as compared to colonoscopy or CT colonography, and the need for a follow-up colonoscopy (including another colon preparation) if the test is positive.

Colon Cancer Detection Tests

Other options for screening include various stool tests: FOBT, FIT, and fecal DNA testing. Although these tests may

detect premalignant adenomatous polyps, their main goal is the detection of CRC; thus the opportunity for prevention of CRC is more limited [7]. FOBT relies on the detection of blood in the stool through measurement of pseudoperoxidase activity of heme or hemoglobin [7]. Trials of FOBT have shown a CRC mortality reduction of 15–33%, with a range of sensitivity for cancer—from 37% for rehydrated Hemoccult II to 79% for Hemoccult II SENSE, although other studies have shown a much lower sensitivity [7]. However, FOBT performed on a sample collected by digital rectal exam at the time of a medical appointment, which is still widely performed today, is highly inaccurate and not recommended. This method was shown to have 5% sensitivity for detection of advanced neoplasia and 9.5% sensitivity for cancer [14].

FIT relies on the detection of human globin, a part of hemoglobin. One advantage of FIT is that, unlike with FOBT, patients do not have to adhere to dietary restrictions prior to testing. In one study, the sensitivity for FIT to detect advanced neoplasia was 40% for distal lesions and 28% for proximal colon lesions, with an overall sensitivity of 55% and a negative predictive value for CRC of 99.8% [15].

Stool DNA testing looks for tumor-specific alterations in the DNA shed in the stool. One study showed 92% sensitivity for detecting CRC and 42% sensitivity for detecting advanced neoplasia with stool DNA testing [16]. One important question that has been raised is whether a patient with a negative colonoscopy in the setting of a positive stool DNA test truly has a negative result, or whether the positive DNA test is a harbinger of future malignancy or indicative of upper gastrointestinal malignancy. Stool DNA testing shows great promise and is a reasonable option for screening, but it is not endorsed by all organizations or covered by all insurance companies at this time.

Colon Cancer Screening in North Carolina

Historically, CRC death rates were highest in the Northeast and Mid-Central United States and lowest in the South [3]. However, a recent study noted that rates had become fairly even across the United States by the 2000s, with the exception of 3 hot spots—the Lower Mississippi Delta, west-central Appalachia, and eastern North Carolina/Virginia—all of which are primarily rural areas [3]. This fits with the finding of increased risk of death from CRC among patients from rural areas and the shift of CRC burden to low-income individuals, who have higher CRC incidence, morbidity, and mortality [3]. This closely mirrors findings in countries with more limited health resources [3]. This study thus highlights the need to increase CRC screening, especially among the rural population of North Carolina.

In North Carolina, African Americans have a higher rate of CRC, are more likely to be diagnosed at an advanced stage, and have a higher mortality rate than whites [17]. This disparity is possibly due to higher screening rates among whites; the North Carolina Behavioral Risk Factor Surveillance System indicated that the rate of sigmoidos-

copy or colonoscopy among whites was 69% in 2008, versus 62% for African Americans; in 2014, these rates were 75% and 71%, respectively [18]. North Carolina needs to make concerted efforts to increase CRC screening rates in the state's African American population.

Overall, a comprehensive approach to screening cannot rely exclusively on colonoscopy. There are many counties in North Carolina that do not have an endoscopy unit, and there are also social, economic, and cultural factors that impede colonoscopy screening in North Carolina's population. Based on 2007 estimates, 6.5% of households in North Carolina have no vehicle, 14% of the population has

less than a high school education, 14% of households earn less than \$15,000 per year, and roughly 9.6% of the population speaks a language other than English at home [19]. Also, part of North Carolina's population is transient, due to movements in the agricultural workforce. These are all factors that may hinder access to screening colonoscopy.

The Patient Protection and Affordable Care Act of 2010 requires coverage of CRC screening for health plans that started on or after September 23, 2010. Medicare covers screening colonoscopy at no cost; if a polyp is removed, however, Medicare then labels the procedure as diagnostic and the patient becomes responsible for the coinsurance and/or

copayment. There is a legislative push at the national level to change this rule with the Removing Barriers to Colorectal Cancer Screening Act [20].

A comprehensive CRC screening approach for North Carolina also cannot rest solely on physicians referring patients for colonoscopy, as many patients do not have access to primary care or do not see a physician regularly; in a 2014 survey, only 62% of respondents indicated having a personal physician [18]. Despite data showing a considerable benefit to screening, approximately 1 in 3 Americans aged 50–75 years still have not been screened for CRC. In 2014, the National Colorectal Cancer Roundtable, a collective action of multiple organizations, announced its goal to increase screening by any method to 80% by 2018 [21]. This is an important goal for the people of North Carolina, and a

strategy for reaching this goal will need to be creative and must factor in patients' preferences, local expertise, and social and economic variables. **NCMJ**

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