Comparing Current Screening Modalities for Colorectal Cancer and Precancerous Lesions: Is Colonoscopy the Method of Choice?

Puneet K. Singh*

Saba University School of Medicine, Saba, Dutch Caribbean

*Corresponding author: Puneet K. Singh; pun33t.singh@gmail.com

Colorectal cancer (CRC) is the third most common form of cancer and the second leading cause of cancer death in the Western world. Presently, screening tools such as colonoscopy, sigmoidoscopy, fecal occult blood test (FOBT) and computed tomographic colonography (CTC) are available for CRC screening. The debate over which screening tool is most effective in detecting CRC and precancerous lesions is ongoing. Many recent studies have identified colonoscopy as the most sensitive and specific screening modality for CRC. However, a number of factors have prevented colonoscopy from being widely accepted. Less invasive techniques such as sigmoidoscopy and CTC are growing in popularity among physicians and patients who are apprehensive about colonoscopy screening; although many still are yet to experience the procedure first-hand. This literature review will attempt to validate the growing theory that colonoscopy is superior to other modalities for the diagnosis and screening of CRC and reduces the risk of CRC mortality. In order to do so, the paper will compare the risks and benefits of colonoscopy to sigmoidoscopy and CTC. It will further look at the different aspects that encompass a patient's decision to partake in screening, such as basic knowledge about CRC, history of CRC in the family, advice from physicians and individual beliefs about what screening entails. Finally, this paper will propose ways in which colonoscopy screening can be improved and thus surpass other screening modalities to universally become the first choice for CRC screening.

Keywords: *colonoscopy; colorectal neoplasms; sigmoidoscopy; CT colonography; mass screening.*

INTRODUCTION

Colorectal cancer (CRC) is the third most common form of cancer and the second leading cause of cancer death in the Western world, equally affecting both men and women.[1] In 2012, the United States had an estimated 143,460 individuals diagnosed with CRC and 51,690 related deaths.[2] The vast majority of CRCs within North America are sporadic with fewer than 5% directly related to chronic inflammatory diseases or hereditary causes of CRC, such as familial adenomatous polyposis (FAP) and hereditary non-polyposis colon cancer (HNPCC).[1] Sporadic CRC is due to mutations causing histological changes within the luminal aspect of colonic mucosa which slowly progress to benign adenomatous polyps of varying types: tubular, tubulovillous and villous.[3] These precancerous lesions can increase in size, become dysplastic and eventually transform into overt carcinomas. The slow progression of these changes causes age to be one of the greatest risk factors for CRC. It is estimated that 90% of all CRC cases occur after the age of 50 in both men and women.[4] Along with family history and age, other significant risk factors for CRC include obesity, tobacco and alcohol abuse, stress, inflammatory bowel diseases (e.g., ulcerative colitis) and diet.[3] With its long list of risk factors and worldwide prominence, it is imperative that health care providers and patients become more knowledgeable about CRC and the ways in which to detect its precursor lesions at early and docile stages.

A number of different techniques are currently employed to screen for polyps and CRC. Epidemiological studies have shown a decline in the incidence and mortality of CRC over the years, which is primarily attributed to increases in screening test use.[5] Specific guidelines outlining which tests should be used and when they should be administered have been established by a number of prominent medical societies and organizations. The United States Preventative Services Task Force (USPSTF) recommends three main screening methods: high-sensitivity fecal occult blood test (FOBT) annually, flexible sigmoidoscopy every 5 years with FOBT every 3 years or colonoscopy every 10 years.[5] The American Cancer Society and The American College of Physicians' (ACP) recommendations mirror those of USPSTF. These bodies also agree that patients with one

or more first-degree relatives with CRC, or a hereditary syndrome that predisposes them to CRC, should receive screening in the second or third decade of life,[6] while in average-risk patients, screening should be done between the ages of 50 and 75.[7] There is a strong belief that screening after the age of 75 may no longer be beneficial for patients and may in fact cause harm.[4,6]

Since the 1990s, the dominant screening test for CRC in the United States has been colonoscopy.[8] Colonoscopy allows for direct visualization of the entire colon, from the appendiceal orifice to the dentate line, and also facilitates biopsy sampling or polypectomy of lesions that may appear abnormal. However, there is still an ongoing debate in the medical community over which screening test is superior in the prevention and detection of CRC. Moreover, with the introduction of newer screening methods such as Computed Tomographic Colonography (CTC) and fecal DNA testing, choosing the best screening method has become more difficult for both physicians and patients.

This paper will review both the advantages and disadvantages of colonoscopy, sigmoidoscopy and CTC. The paper will forgo discussion of FOBT as it attempts to focus on invasive screening techniques that are more procedurally similar to colonoscopy so that aspects of the patient experience during each technique can be appropriately compared. Other factors affecting a patient's decision to engage in regular CRC screening and the role of primary care providers in informing their patients about each method will also be analyzed.

Through a contemporary literature review, this paper will examine whether colonoscopy is the superior method for the diagnosis and screening of CRC, and thus whether it has a greater capacity to reduce the risk of death from CRC as compared to other screening modalities.

METHODS

The main database used to obtain scholarly articles cited in this literature review was PubMed at www.pubmed.org. A number of different search strategies were used to narrow down articles. One strategy included keywords such as: ((colon cancer) AND (colonoscopy) AND (surveillance)). Another strategy used 'colonoscopy', 'epidemiology' and 'colorectal neoplasms' as MeSH terms with 'mass screening OR screening.' Subsequent searches focused on other modalities of CRC screening with the use of 'sigmoidoscopy' and 'CT colonography' as MeSH terms and with the subheading 'therapeutic use.' The filters used in all searches included: past 5 years (2008–2013), clinical trial, randomized control trials (RCTs), humans, English and full text available. A few articles were also attained from other databases such as Medscape, EBSCOhost and Google Scholar using variations of the search strategies, keywords and filters described above.

In all articles selected, the study population of interest was high- and low-risk patients, aged 50 or older, living within North America and other developed nations. Other inclusion criteria included choosing articles that were published in prominent journals or by recognized and valued medical organizations.

Criteria used to exclude articles from this paper include factors such as a small study population and articles categorized as 'review articles', although a limited number were consulted to obtain relevant background information on the pathophysiology, epidemiology and diagnosis of CRC.

Articles that met these criteria were then compiled into an 'Evidence Table' (Table 1) that outlines the key findings of each.

RESULTS

Comparing Colonoscopy to Sigmoidoscopy and CTC

Colonoscopy

Colonoscopy is a screening method that allows inspection of the entire colon and enables biopsy of neoplastic lesions through polypectomy. This method is conducted under sedation and is currently the leading tool for CRC screening.[8] Many of the presently known benefits of colonoscopy stem from population-based cohort studies that analyze the effects of colonoscopy on incidence and mortality among communities around the world. In Ontario, Canada, Rabeneck et al[9] conducted a large prospective study between 1993 and 2006 where they found the rates of complete colonoscopy screening increased in all regions of the province. Within the population that underwent screening, the incidence rates and mortality rates of CRC were lower in the younger age group (50–69 years) and lower for women within all age groups. When mortality rate was adjusted for confounding factors associated with increased risk of CRC death, such as increased age, male gender, lower income and rural residence, greater colonoscopy use was overall associated with decreased mortality from CRC. Furthermore, the study identified that for every 1% increase in colonoscopy rates in the cohort's individual region of residence (each participant was assigned to 1 of 13 regions based on their address in Ontario), there

Table 1. Evidence table outlining articles analyzed in this review

First author	Date of publication	Study design	Level of evidence	Study population	Therapy or exposure	Outcome/results
Adler, Andreas	2013	Prospective cohort without controls	4	21 colonoscopists were studied from private practices in Berlin, between Oct. 2006 and Mar, 2008. Overall, a total of 12,134 colonoscopies were examined.	Colonoscopy	Three patient factors correlated with adenoma detection rate (ADR): age, sex and low quality of bowel preparation. Factors that accounted for 41.4% of inter-physician variability in ADR included: the number of CME meetings attended and differences in equipment used during screening.
Atkin, Wendy	2013	RCT	1	1,580 patients, 55 years or older (median age was 68 years; range 61–75), with symptoms suggestive of CRC (change in bowel habits, rectal bleeding or abdominal pain) from 21 UK hospitals. 1,047 were randomly assigned to colonoscopy and 533 assigned to CTC. 864 (55%) of the cohort were women. Patients were recruited between Mar. 2004 and Dec. 2007.	CTC and colonoscopy	160 (30%) patients in the CTC group had additional colonic investigation compared with 86 (8.2%) in the colonoscopy group. Almost half the referrals after CTC were for small (<10 mm) polyps or clinical uncertainty. Detection rates of CRC or large polyps were 11% for both procedures. CTC missed 1 of 29 CRC and colonoscopy missed none (of 55)
Baxter, Nancy N.	2009	Case control	3	10,292 case patients and 51,460 controls were part of this study population. Five controls matched by age, sex, geographic location and socioeconomic status were randomly selected for each case patient. Participants were between the ages of 52 and 90 who received a CRC diagnosis from Jan. 1996 to Dec. 2001 and died of CRC by Dec. 2003.	Colonoscopy	Complete colonoscopy was strongly associated with fewer deaths from left-sided CRC but not from right-sided CRC
Baxter, Nancy N.	2012	Case control	3	A total of 9,458 cases were identified. Patients were aged 70–89 and diagnosed with CRC between Jan. 1998 and Dec. 2002. Three controls (patients without CRC) were matched to each case. The primary exposure in the cases was colonoscopy preformed from 1 Jan. 1991 to 6 months before the reference date. All case and control data were collected from the SEER-Medicare data.	Colonoscopy	Colonoscopy is associated with a reduced risk of death from CRC, with a stronger detection rate for distal vs. proximal CRC. The overall association of reduced risk of death was strongest if colonoscopy was performed by a gastroenterologist, as opposed to surgeons or primary care providers.

Table 1 (*Continued*)

First author	Date of publication	Study design	Level of evidence	Study population	Therapy or exposure	Outcome/results
Bretagne, Jean-Francois	2010	Retrospective cohort	3	Eighteen endoscopists were used in this study; 14 worked in private practice and 4 worked in public hospitals. The screening group included asymptomatic men and women aged between 50 and 74 with no other risk factor for CRC. The study was conducted between 2003 and 2007 in Illeet-Vilane, Brittany. The first round of screening was in 2003 and 2004 with 213,635 participants and the second round in 2005 and 2006 with 224,504 participants.	Colonoscopy	Interendoscopic variability had no effect on cancer detection in a screening program with a high compliance rate with colonoscopy after FOBT; however, it did influence the identification of adenomas.
Courtney, Ryan J.	2013	Case series without controls	4	1,592 at-risk individuals (56–88 years of age) were randomly selected from the Hunter Community Study (a longitudinal community cohort in Australia) between Dec. 2004 and Dec. 2007 to take part in a questionnaire by mail. 1,117 participants returned the questionnaires; 760 respondents were eligible for screening and analysis.	Colonoscopy	63% of participants received CRC screening, with the majority being 'potentially high risk' participants (84%). Those significantly more likely to have received testing were aged between 65 and 74 and who had at some point received screening advice from their family physician, or had discussed family history of CRC with their doctor. 21% of those in the 'at or slightly above average-risk' group had received screening as per official screening guidelines. Guidelines were significantly more likely to be followed in the 'moderately increased risk or potentially high risk' groups (45%). Colonoscopy within 5 years was the most commonly recommended guideline and was significantly more likely to be recommended to individuals with private insurance or who had discussed family history of CRC with a doctor.
de Wijkerslooth, Thomas R.	2012	RCT	1	This study was of 8,844 Dutch citizens aged 50–74, invited by mail for population-based CRC screening in Amsterdam and Rotterdam, between Jun. 2009 and Aug. 2010. Invitations were randomly allocated 2:1 to colonoscopy (5,924) or CTC (2,920)	Colonoscopy and CTC	Before screening, individuals expected colonoscopy and bowel preparation to be more burdensome than CTC screening. However, when individuals participated in screening, CTC was scored as more burdensome than colonoscopy.

Table 1 (*Continued*)

First author	Date of publication	Study design	Level of evidence	Study population	Therapy or exposure	Outcome/results
				Allocation was stratified for age, sex, SES status based on data of Statistics Netherlands		
de Wijkerslooth, Thomas R.	2012	RCT	1	Between Jun. 2009 and Aug. 2010, 8,844 individuals aged 50–75, never before screened for CRC, were randomly allocated to undergo either colonoscopy screening (5,924) or CTC (2,920). Allocation was based on age, sex and socioeconomic status; data from Statistics Netherlands. Patients were from the Amsterdam and Rotterdam region.	Colonoscopy and CTC	The most frequently cited reasons to accept screening were early detection of precursor lesions and CRC, and contribution to science. The most frequently cited reasons to decline were the unpleasantness of the examination, the inconvenience of the preparation, a lack of symptoms and 'no time/too much effort'. Elderly individuals cited the absence of symptoms as a more significant reason to not undergo colonoscopies as compared to the overall study population. The most frequently cited reason for declining colonoscopy was the unpleasantness of the examination.
Fenton, Joshua J.	2011	Prospective cohort	3	The study population included patients attending appointments at 2 academic primary care clinics – University of California, Davis, and Medical Center in Sacramento, CA., between Sept. 2008 and Dec. 2009. 50 patients aged between 50 and 75 were eligible for CRC based on the criteria that they had never had: FOBT during the past year, flexible sigmoidoscopy during the past 5 years, colonoscopy in 10 years. In addition, 20 family care physicians were selected from the 2 clinics.	Colonoscopy	As compared to patient visits without CRC screening discussion, visits with discussion were associated with increased perceived and screening intention after the visit but no significant change in perceived benefits, barriers or self-efficacy. Within 6 months, 17 of 38 patients (45%) who discussed screening completed screening compared with 0 of 12 patients who did not discuss screening.
Graser, A.	2009	Prospective cohort without controls	4	311 asymptomatic, average-risk adults (171 men and 140 women), aged between 50 and 81 underwent same day screening of 5 different screening interventions. Only 307 patients completed it in full, as 4 subjects withdrew.	Sigmoidoscopy CTC, FIT, FOBT, Colonoscopy	Sensitivities of OC, CTC, FS, FIT and FOBT for advanced colonic neoplasia were 100,96.7. 83.3, 32 and 20%, respectively. Combination of FS with FIT or FOBT did not increase sensitivity for advanced CRC.

Table 1 (*Continued*)

First author	Date of publication	Study design	Level of evidence	Study population	Therapy or exposure	Outcome/results
				Exclusions criteria included the absence of specific symptoms of colonic disease (melena, hematochezia, diarrhea, relevant changes in stool frequency or abdominal pain). Subjects were also excluded if they had prior OC within the last 5 years, positive family history for CRC, a history of or present IBD, hereditary CRC syndromes, a body weight greater than 150 kg or severe cardiovascular or pulmonary disease.		CTC had low sensitivity for lesions <6 mm in size, but detection of large and advanced lesions, sensitivity was comparable to OC. 46% of subjects preferred CTC, while 37% preferred OC for future screening.
Hoff, Geir	2009	RCT	1	The study included 13, 653 subjects in the screening group (of which only 8,846 attended screening), and 41,092 subjects were in the control group. Groups consisted of an equal number of men and women, aged 55–64, who were randomly selected from 2 areas in Norway; city of Oslo and Telemark county (urban and mixed urban and rural populations). The study was conducted from Jan. 1999 to Dec. 2000.	Sigmoidoscopy	Reduction in incidence of CRC with flexible sigmoidoscopy screening was not seen after 7-year follow-up. Mortality from CRC was not significantly reduced in the screening group.
Johnson, C. Daniel	2008	Case series without controls	4	The study included 2,531 asymptomatic patients, 50 years or older who underwent CTC followed by same day colonoscopy between Feb. 2005 and Dec. 2006. Patients were excluded if they presented any symptoms of CRC (anemia, melena, hematochezia) more than once in the past 6 months, if they had IBD, hereditary colorectal disease, if they had received colonoscopy in the past 5 years or had a positive FOBT result.	CTC and colonoscopy	CTC identified 90% of the adenomas or cancers measuring 10 mm or more in subjects.
Ko, Cynthia W.		Retrospective cross-sectional study	4	A total of 328,167 colonoscopies were conducted by 12,910 providers (either gastroenterologists, surgeons (general or colorectal) or primary care physician	Colonoscopy	Gastroenterologists were most likely and general surgeons were least likely to detect polyps during colonoscopy. Diagnostic biopsy rates were highest for family physicians and lowest for colorectal surgeons.

Table 1 (*Continued*)

First author	Date of publication	Study design	Level of evidence	Study population	Therapy or exposure	Outcome/results
						Snare polypectomy and polyp removal rates were highest for gastroenterologists and lowest for family physicians.
Leiberman, David A.	2000	Case control	3	Asymptomatic adults were selected from 13 Veterans Affairs medical centers in the United States, between Feb. 1994 and Jan. 1997. 17,732 patients were screened for enrolment, 3,196 were enrolled; 3,121 of the enrolled patients (97.7%) underwent complete colonic examination. The mean age of the patients was 62.9 years, and 96.8% were men.	Colonoscopy	Colonoscopy can detect advanced colonic neoplasms in asymptomatic adults which cannot be detected with sigmoidoscopy.
Manser, Christine N.	February 2012	Non-randomized prospective cohort	2	1912 screened and 20,774 control participants from a rural area of Switzerland	Colonoscopy	Colonoscopy with polypectomy significantly reduced CRC incidence and cancer-related mortality in the general population.
Rabeneck, Linda	2010	Population-based prospective cohort	3	This study included 2,412,077 participants aged between 50 and 90 (mean age of 64) in Ontario, Canada. Of the cohort, 84.2% lived in an urban area, 53.7% were women and 86.5% had a co-morbidity score of 0. Each member of the cohort was assigned to 1 of 13 regions based on their address in the province. Patients were excluded if they had a previous diagnosis of CRC, ulcerative colitis, Crohn's disease or had their residence in the South East Local Health Integration Network during the time of the study.	Colonoscopy	Increased colonoscopy use was associated with mortality reduction from CRC at the population level.
Singh, Harminder	2010	Population-based prospective cohort	3	32,306 individuals from Manitoba, Ontario, who had negative results on initial colonoscopy screening between Apr. 1, 1987 and Sept. 30, 2007. Study population included patients aged between 50 and 80. Individuals outside this age range, those with prior sigmoidoscopy, IBD, resective colorectal surgery or CRC were excluded.	Colonoscopy	There was a 29% reduction in overall CRC mortality and a 47% reduction in mortality from distal CRC (SMR, but no reduction in mortality from proximal CRC) The reduction in mortality from distal CRC remained significant for greater than 10 years

Table 1 (*Continued*)

First author	Date of publication	Study design	Level of evidence	Study population	Therapy or exposure	Outcome/results
Schoen, Robert E.	2012	RCT	1	A total of 154,900 men and women aged 55–74 participated in this study from 1993 through 2001. Individuals were randomly assigned to either an intervention group (screening with flexible sigmoidoscopy with repeat screening at 3–5 years) or to the usual care group.	Sigmoidoscopy	Incidence of CRC after a median follow-up of 11.9 years was 11.9 cases per 10,000 person-years in the intervention group, as compared with 15.2 cases per 10,000 person-years in the usual-care group. Reductions were seen in incidence of CRC in both proximal and distal colon. Mortality was reduced by 50% only in distal CRC with no change in proximal.
von Wagner, Christian	2012	RCT	1	547 patients with symptoms suggestive of CRC who were randomly assigned at a ratio of 2:1 to undergo either colonoscopy (362) or CTC (185) Of these, 388 responded to a post-test questionnaire; 212 women (55–87 years old) and 176 men (55–96 years old). 337 patients responded to the follow-up questionnaire; 199 women (55–87 years old) and 138 men (55–92 years old).	Colonoscopy and CTC	In the short-term analysis, patients are more likely to accept CTC as a better method of surveillance than colonoscopies. However, after long-term follow-up, patients noted that colonoscopy offered some benefits
Zalis, Michael E.	2012	Prospective cohort without controls	4	605 asymptomatic men and women, aged 50–85, with moderate to average risk of CRC were recruited from four institutions: Massachusetts General Hospital; Brigham and Women's Hospital; University of California, San Francisco Veterans Affairs Medical Center; and North Shore Medical Center, between Jun. 2005 and Oct. 2010	Non-cathartic CTC and colonoscopy	Non-cathartic CTC was able to accurately detect adenomas 10 mm or greater but less accurate for smaller lesions when compared to colonoscopy screening of same cohort

RCT = randomized control trials; CTC = computed tomographic colonoscopy; OC = optical colonoscopy; FS = flexible sigmoidoscopy; FIT = fecal immunochemical stool testing; FOBT = fecal occult blood testing; CRC = colorectal cancer; IBD = inflammatory bowel disease.

was a statistically significant decrease in the hazard of death by 3%.[9]

Similar results showing significantly decreased CRC incidence and mortality in groups undergoing colonoscopy screening were found in two other population-based prospective studies conducted by Manser et al[10], in Switzerland, and by Singh et al[11] in Manitoba, Canada. Singh et al[11] analyzed a cohort of individuals who had previously undergone CRC screening with only colonoscopy between April 1984 and September 2007 and had received negative results (no polyps/CRC). The overall reduction in CRC mortality within the screened population of this study was 29%, with the largest reduction in mortality rates (39%) seen during a 5–10 year follow-up, as compared to the general population.[11] Importantly, the study also found there were differences in the morality rates associated with specific locations in the colon. There was a statistically significant 47% reduction in distal CRC deaths, but no reduction in deaths from proximal CRC.[11] The reduction in mortality due to distal CRC remained significant for up to 10 years following the study's conclusion.[11] A case-control study carried out by Baxter et al[12] presented mirroring results, finding that colonoscopy screening not only decreased CRC mortality in cases vs. controls but also that this screening was associated with fewer deaths from left-sided CRC as compared to right-sided.[12]

Many recent studies have discovered that discrepancies during colonoscopy-specific detection of CRC and precancerous lesions may be operator dependent. Bretagne et al[13] identified that differences in the performance of 18 endoscopists analyzed in their study resulted in large ranges of adenoma detection rates (ADR). However, when assessing the detection rate of actual CRC, these operant-dependent factors did not independently influence the varied range of rates, as patient age and sex also played a role.[13] Another study by Adler et al[14] went on to identify what it believed were the specific factors that defined the efficacy and quality of screening by colonoscopists. The most statistically significant associations, with 41.4% of the inter-physician variability in ADR, were the number of Continuing Medical Education (CME) meetings each colonoscopist attended and the characteristics of their individual instruments.[14]

Some researchers investigated if the specific specialties of those carrying out colonoscopies played any role in the variability of ADR and CRC detection. Baxter et al[15] found that although colonoscopy screening reduced the risk of CRC mortality (regardless of the specialty of the endoscopist), there was a stronger association if a gastroenterologist performed the colonoscopy as opposed to a non-gastroenterologist (e.g., a surgeon or primary care provider). Conclusively, gastroenterologists provided significantly more protection from CRC death than other providers.[15] A study by Ko et al[16] further identified variability in frequency of procedures performed by each specific specialty (Fig. 1). Overall, multivariate analysis determined that non-gastroenterologists were least likely to detect and remove polyps, and likelihood of diagnostic biopsy was significantly lower for all surgeons (general/colorectal).[16]

Sigmoidoscopy

Unlike colonoscopy, flexible sigmoidoscopy is performed without sedation, has limited bowel preparation and is thus more often provided by general practitioners or non-physicians.[1] The use of flexible sigmoidoscopy CRC screening was analyzed in a German observational study by Graser et al[17] and two RCTs: the PLCO trial conducted by Schoen et al[18] and the first of the three Norwegian Colorectal Cancer Prevention (NORCCAP) trials carried out by Hoff et al.[19]

The PLCO trial mirrored findings presented in many older observational trials that showed flexible sigmoidoscopy conferring protection against CRC mortality and incidence.[8] In this study, a 21% reduction in CRC incidence was observed in the intervention group as compared to the usual care group, and CRC incidence in specific locations of the colon also showed significant reductions: 29% in the distal colon and 19% in the proximal.[18] Overall, CRC mortality was reduced by 26% in the intervention group as compared to the usual-care group. However, when observing location-specific mortality rates in distal and proximal parts of the colon, the PLCO trial found that distal CRC mortality was reduced by 50%, but no significant change in mortality was observed for proximal CRC (143 and 147 deaths; relative risk, 0.97; 95% CI, 0.77–1.22; $P = 0.81$).[18]

Compared to the PLCO trial, the NORCAPP trial observed a larger reduction in mortality rates (59%) among subjects who took part in sigmoidoscopy screening.[19] Nevertheless, like the PLCO trial, some findings of NORCAPP also substantiated discrepancies in cancer mortality rates among discrete locations of the colon when sigmoidoscopy was performed. Among the intervention group, a greater reduction in both incidence and mortality (76%) of rectosigmoidal cancer was found as opposed to CRC.[19] Thus, benefits of sigmoidoscopy

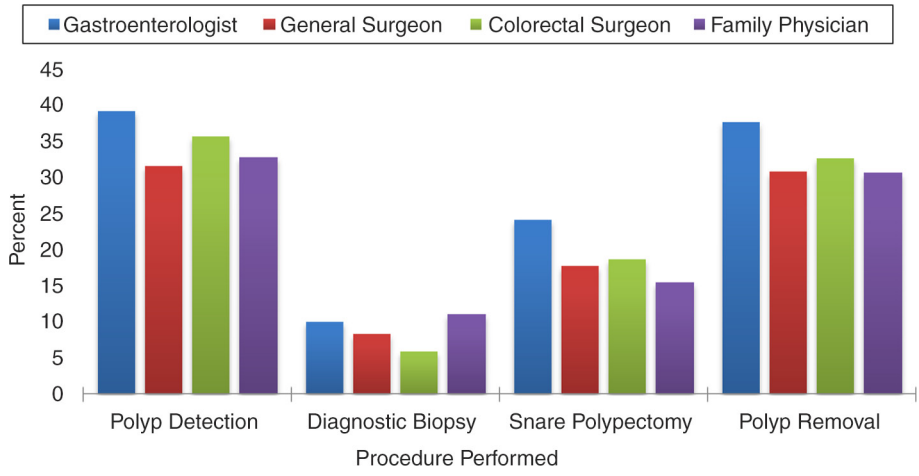

Figure 1. Variability in rate of polyp detection, biopsy and polyp removal among provider specialty. Gastroenterologists have the highest rate of polyp detection, polypectomy and polyp removal. General surgeons are least likely to detect polyps, while colorectal surgeons have the lowest diagnostic biopsy rate. Family physicians have the highest rate of biopsy, but lowest rate of polyp removal. (Modified from Ko et al.[16])

were once again shown to be limited to areas of the distal colon.

The last study analyzing sigmoidoscopy screening was a prospective study carried out by Graser et al.[17] The sensitivities of five different screening methods: sigmoidoscopy, CTC, colonoscopy, fecal immunochemical stool testing (FIT) and FOBT were all tested in parallel among asymptomatic subjects. Flexible sigmoidoscopy was 83.3% sensitive for advanced colonic neoplasia (CRC) and only 68% sensitive to adenomas $\geq$10 mm. Combining sigmoidoscopy with FOBT or FIT enabled an increased detection of large adenomas (76.2 and 71.4%, respectively) as compared to sigmoidoscopy alone (68%). However, when these tests were combined for the detection of advanced CRC, no increase in sensitivity was observed. Although flexible sigmoidoscopy showed to be a superior test to FOBT and FIT, it was unable to surpass the advanced sensitivity of colonoscopy and CTC in detection of CRC and adenomas of all sizes.[17]

Computed Tomographic Colonography

CTC is a minimally invasive screening tool that is currently undergoing testing in a number of trials. Like colonoscopy, CTC provides examination of the entire colon and rectum; however, it allows for computerized 3D and advanced 2D imaging not available with colonoscopy.[1] In order to compare the efficiency of CTC to colonoscopy in CRC screening and detection, three observational studies and one UK-based multicenter RCT were analyzed.[17,20,21]

All three observational studies focused on comparing the sensitivity and specificity of CTC in detecting adenomas of various sizes and neoplastic lesions to that of colonoscopy, with additional comparison to other screening modalities (sigmoidoscopy, FIT and FOBT) completed by Graser et al.[17] The study populations assessed in all three studies were comparable and included average risk, asymptomatic patients (each study using similar exclusion criteria) who were aged 50 or older.[17,20,21] All studies presented similar results (Table 2).

Although similarities between the sensitivity and specificity of CTC and colonoscopy for the detection of large neoplastic lesions were found, discrepancies became evident in all studies when detecting adenomas of smaller sizes, specifically between 5 and 6 mm in diameter (Table 2). All three studies concluded that CTC was significantly less sensitive for smaller lesions than colonoscopy. Measurements of specificity showed similar trends.[17,20,21] In two of the studies, the median sizes of missed lesions were 7 mm[21] and 6 mm.[20] Graser et al[17] found that CTC only missed one adenoma with advanced histology in the $<$10 mm size group.

The UK-based RCT carried out by Atkin et al[22] presented similar findings to those seen in the observational studies. The sensitivity of CTC to CRC was 85% in this RCT as compared to 93% with colonoscopy. Still, the most significant discrepancy in CTC screening presented by this study was its discovery that a greater number of patients assigned to the CTC screening

Table 2. Differences in sensitivity and specificity of CTC and colonoscopy in detecting adenomatous lesions of various sizes

	CTC (large lesions; >10 mm)		CTC vs. Colonoscopy (small lesions; 5–6 mm)	
Study	Sensitivity (%)	Specificity	Sensitivity (%)	
Graser et al[17]	96.7	n/a	59.2	94.6
Johnson et al[20]	90	86%	78	100
Zalis et al[20]	91	85%	59	76

Colonoscopy and CTC have similar efficacy in detecting large lesions; however, colonoscopy is significantly more sensitive than CTC for smaller lesions.

group needed to undergo additional colonic investigations (after initial screening) as compared to the colonoscopy group (30.0% vs. 8.2%).[22] Within the colonoscopy group, the major reason for additional screening was incomplete colonoscopy (did not reach the cecum) as seen in 11.3% of patients. In contrast, the major causes for additional CTC investigations were low predictive value for CRC or polyps $\geq$10 mm (15.6%) and failure to confirm the presence of small ($<$10 mm) polyps (9.2%). In both cases, the additional investigation was a new or repeat colonoscopy; a more invasive procedure than CTC. Finally, this RCT was the only study to identify a statistically significant difference in men and women with regard to the need for additional investigations after screening. Men were six times more likely to need further investigation after CTC compared to colonoscopy, while women were only two times more likely.[22]

Patient Experience, Education and Compliance

Patient experiences, perspectives on CRC screening and compliance to screening guidelines were also analyzed. Research conducted by von Wagner et al[23] found that individuals undergoing colonoscopy were significantly less satisfied, more worried, experienced more physical discomfort and reported more adverse effects such as 'feeling faint or dizzy' than those taking part in CTC screening. This study further noted that patients had a better experience with CTC screening than with colonoscopy.[17,20–22] However, this initial dissatisfaction with colonoscopy was not absolute, as von Wagner et al[23] identified that patients undergoing CTC had a greater number of post-procedure referral rates as compared to those who took part in colonoscopy screening (33% vs. 7%). Thus, the study concluded that after 3 months, patients reported greater satisfaction with the long-term outcomes of their colonoscopy screening compared to CTC[23]; a result also found by Atkin et al.[22]

It is likely that because the overall benefits of colonoscopy are not known by patients initially, the negative connotations surrounding CRC screening are factors that deter patients from actually fulfilling screening guidelines. A RCT conducted by de Wijkerslooth et al[24] examined the reasons for participation and non-participation in CRC screening among a study population who had never undergone screening in two regions of the Netherlands. This study found that the most significant reason to participate in CRC screening (either colonoscopy or CTC) was 'it allows early detection of precursor lesions' (the most decisive reason in both screening modalities; 72% for colonoscopy vs. 68% for CTC).[24] The most significant reason for non-participation with respect to colonoscopy was 'the examination strikes me as unpleasant' (66%) while for CTC the reasons were both lack of time and absence of symptoms.[24] A second RCT looked at the 'expected' burden of screening before colonoscopy or CTC and compared it to the actual ('perceived') burden experienced during either procedure.[25] This research discovered that although participants expected colonoscopy to be more burdensome than CTC, in reality they experienced significantly more overall burden with CTC (79% with colonoscopy vs. 82% with CTC).[25]

Many of the reasons mentioned for and against screening participation stem from a lack of patient knowledge about CRC and its prevention, and most importantly from a lack of doctor–patient communication about specific guidelines for screening. A case series by Courtney et al[26] identified that within their study population, only 63% of the cohort had ever received any sort of CRC screening (FOBT/ sigmoidoscopy or colonoscopy), with the majority of this subset being 'potentially high risk' participants (84%). Overall, individuals significantly more likely to have received testing were those who were either between the ages of 65 and 74, had at some point received screening

advice from their family physician or had discussed family history of CRC with their doctor.[26]

Similar results permeated from a prospective study by Fenton et al[27] which took a deeper look at what a group of physicians actually discussed with patients during visits. In 76% of the interactions, physicians discussed CRC screening for a median time of 2.5 min. Physicians described one or two modalities for screening, with colonoscopy always being mentioned. Doctors discussed benefits of CRC screening in more than half of the encounters, but less often commented on risks/susceptibility to CRC, barriers to screening, or self-efficacy of screening. After all visits were complete, it was found that patients in the discussion group had a significantly increased knowledge of risk/susceptibility to CRC and had an increased intention to undergo screening. Unfortunately, there was no significant change in perceived benefits of screening, barriers or self-efficacy in this discussion group compared to when they initially began the visit. Finally, a 6-month follow-up revealed that 45% of patients within the group that discussed CRC screening actually underwent screening, as compared to the non-discussion group in which no patient was screened.[27]

DISCUSSION

Screening for CRC is an integral part of cancer prevention and has the capacity to positively impact CRC mortality rates. Colonoscopy has proven to be a leading method of CRC screening and its use has increased in many regions across North America.[9,11] However, detection of CRC via colonoscopy does not occur uniformly within the colon, and specific 'burdens' of screening are discouraging individuals from participating in colonoscopy. Thus, prematurely accepting colonoscopy to be the superior screening modality is erroneous. Many factors must be considered when defining a tool as superior including patient preferences, user-dependent skills, success of CRC detection and cost-effectiveness. Until research can address these factors and clearly define superiority, the debate over which method to choose for CRC screening remains.

Unlike research on sigmoidoscopy and CTC, current scholarly literature analyzed in this study has not produced RCTs studying colonoscopy as a method of CRC screening. Many of the colonoscopy-focused studies analyzed in this review were observational (level 4) studies – a major limitation of this paper. Some studies lacked control groups, and their cohorts were often too small. In addition, each study focused on only one or two screening modalities at a time, thus preventing grouped analysis of common variables. The initiation of RCTs with large cohorts comparing each specific modality in parallel and with more universal data analysis techniques is necessary. In addition, more prospective studies looking at the long-term benefits of colonoscopy are needed as current research shows many of the benefits of colonoscopy are observed several years following the initial procedure.[11] However, to accurately determine long-term benefits, studies must also focus on populations closer to the age of 50 as loss to follow-up due to death can negatively impact results.

Other limitations of this review included restricting search strategies with the filter 'full text available' during data collection and also focusing on only a select group of screening modalities. Studies on FOBT or FIT could have expanded the scope of this paper and enabled a more comprehensive comparison of all screening tools recommended by current guidelines.

Nevertheless, this paper addresses several important aspects of colonoscopy screening. First, a number of problems still remain in the actual effectiveness of colonoscopy screening. Many articles determined that colonoscopy was more beneficial in detecting distal CRC as opposed to proximal. Two RCTs identified that sigmoidoscopy also presented with similar caveats.[18,19] Although both screening tools were limited in the location they could optimally perform, sigmoidoscopy proved to cause a greater reduction in distal CRC mortality as compared to colonoscopy**.** The PLCO trial found that mortality was reduced by 50% in the distal colon using sigmoidoscopy compared to colonoscopy,[18] while the NORCAPP trial also identified that sigmoidoscopy's greatest reduction of mortality (76%) was seen for rectosigmoidal cancer (specific to the distal colon).[19] Both values were higher than the 47% reduction in distal CRC mortality found via colonoscopy.[11] Identifying ways to optimize screening of both the proximal and distal colon is therefore necessary to enable colonoscopy to surpass the strengths of sigmoidoscopy.

Another major issue associated with colonoscopy was the variations in results due to the level of expertise of each colonoscopist. Gastroenterologists proved to be the most efficient when compared to surgeons and primary care physicians (Table 2). These performance differences can greatly impact the accurate detection of CRC and precancerous lesions. Furthermore, these differences in expertise may prevent the

significantly at-risk populations from being screened by the most skilled provider. Individuals from higher-income households ($>$\$70,000 compared to $\leq$\$39,999)[26] are more likely to take part in CRC screening, as a specialist appointment is more costly than a primary care visit. This is an unfortunate fact considering low income is a significant risk factor for CRC mortality.[9] It is imperative that all health care professionals performing colonoscopies attain standardized training and continually strive to advance their skills so every patient can receive screening from an equally qualified colonoscopist. One way in doing so may be to increase attendance at CME meetings, as this had a positive association with ADR in primary care providers.[14]

In spite of the disadvantages of colonoscopy use, this screening modality is still the most sensitive and specific test for detecting CRC and precancerous lesions of all sizes. Studies comparing colonoscopy to CTC and sigmoidoscopy identified that the rank from highest to lowest for specificity and sensitivity was colonoscopy $>$ CTC $>$ sigmoidoscopy. Although CTC was the closest to colonoscopy in sensitivity and specificity for CRC, it was 20–30% less sensitive for lesions $<$6 mm in size than colonoscopy. Thus, exclusive use of CTC over colonoscopy risks missing small lesions that can present similar threats of cancerous growth as large ones. As many articles have noted, this failure to detect small lesions forces patients to endure additional investigations via colonoscopy in order to identify all those that are missed. Patients thus become burdened with extra tests leading to unnecessary stress and worry.

Currently only 65.1% of the US population is up-to-date on screening for CRC as recommended by standard guidelines.[7] Among studied populations, the major reason for participation in both colonoscopy and CTC was to identify precancerous lesions, while the main reason to not participate was the thought that the colonoscopy procedure would be unpleasant and the belief that a lack of symptoms did not warrant undergoing CTC. Furthermore, when looking at reasons to choose specific screening modalities patients also assumed colonoscopy screening to be more burdensome than CTC due to its preparation and unpleasantness. However, patients admitted that in the long run colonoscopy was less burdensome,[25] suggesting that patient expectations or beliefs may often be due to a lack of knowledge and guidance. Understanding the factors that shape a patient's views on CRC screening is essential in learning how to present screening in a positive light and how to create educational material that may further empower patients to comply with guidelines.

Much research has shown that the most significant factor in promoting screening is the interaction between a physician and patient. In one study, discussions about the risks and benefits of CRC, options for screening and family history of CRC occurred in only 76% of patient–doctor meetings.[27] Nevertheless, of the group of patients whose physicians did make an attempt to provide educational information, 45% went on to take part in colonoscopy screening. This study highlighted the fact that a simple conversation can enable individuals to take action. If physicians take adequate time to have detailed discussions with all at-risk patients and eliminate any myths of the procedure, it is likely that participation in colonoscopy screening will significantly increase.

CONCLUSION

In conclusion, colonoscopy has proven to be the most sensitive and specific tool for CRC screening and has allowed for significant reductions in CRC incidence and mortality. In order to ascertain that colonoscopy is superior to sigmoidoscopy and CTC in all aspects of CRC such as effectiveness in detecting both distal and proximal CRC, convenience of screening, efficiency of screening and patient preference, a number of factors must be addressed. First, large-scale RCTs looking at all three screening modalities together must be initiated in order to understand the exclusive benefits of colonoscopy and to move away from observational studies that are clouding current research. Next, eliminating the weakness of colonoscopy in detecting proximal CRC is imperative in order to ensure that it provides the greatest advantage possible. In addition, in order to enable patients to understand the life saving benefits of colonoscopy, misconceptions and narrowed views about this modality must be thoroughly addressed. Empowerment can start within the doctor–patient relationship. Once patients become more aware of their health and more knowledgeable about all of the preventative procedures available to maintain their wellbeing, they may be more inclined to take action. Finally, performing colonoscopies must become a more standardized procedure. All colonoscopists should ideally learn the same techniques and have access to the same quality of screening tools to ensure that operant-dependent differences do not confound the results of colonoscopy screening.

Conflict of interest and funding: The author declares no conflict of interest.

REFERENCES

1. Holt PR, Kozuch P, Mewar S. Colon cancer and the elderly: from screening to treatment in management of GI disease in the elderly. Best Pract Res Clin Gastroenterol 2009; 23: 889–907. doi: 10.1016/j.bpg.2009.10.010
2. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012; 62: 10–29. doi: 10.3322/caac.20138
3. Manne U, Shanmugam C, Katkoori VR, Bumpers HL, Grizzle WE. Development and progression of colorectal neoplasia. Cancer Biomark 2010; 9: 235–65. doi: 10.3233/CBM-2011-0160
4. Qaseem A, Denberg TD, Hopkins RH, Jr., et al. Screening for colorectal cancer: a guidance statement from the American College of Physicians. Ann Intern Med 2012; 156: 378–86. doi: 10.7326/0003-4819-156-5-201203060-00010
5. Centers for Disease Control and Prevention. Vital signs: colorectal cancer screening, incidence, and mortality–United States, 2002–2010. MMWR Morb Mortal Wkly Rep 2011; 60: 884–9.
6. Lieberman D. Colorectal cancer screening: practice guidelines. Dig Dis 2012; 30(Suppl 2): 34–8. doi: 10.1159/000341891
7. Centers for Disease Control and Prevention. Vital signs: colorectal cancer screening test use – United States, 2012. MMWR Morb Mortal Wkly Rep 2013; 62: 881–8.
8. Kahi CJ, Anderson JC, Rex DK. Screening and surveillance for colorectal cancer: state of the art. Gastrointest Endosc 2013; 77: 335–50. doi: 10.1016/j.gie.2013.01.002
9. Rabeneck L, Paszat LF, Saskin R, Stukel TA. Association between colonoscopy rates and colorectal cancer mortality. Am J Gastroenterol 2010; 105: 1627–32. doi: 10.1038/ajg.2010.83
10. Manser CN, Bachmann LM, Brunner J, Hunold F, Bauerfeind P, Marbet UA. Colonoscopy screening markedly reduces the occurrence of colon carcinomas and carcinoma-related death: a closed cohort study. Gastrointest Endosc 2012; 76: 110–17. doi: 10.1016/j.gie.2012.02.040
11. Singh H, Nugent Z, Demers AA, Kliewer EV, Mahmud SM, Bernstein CN. The reduction in colorectal cancer mortality after colonoscopy varies by site of the cancer. Gastroenterology 2010; 139: 1128–37. doi: 10.1053/j.gastro.2010.06.052
12. Baxter NN, Goldwasser MA, Paszat LF, Saskin R, Urbach DR, Rabeneck L. Association of colonoscopy and death from colorectal cancer. Ann Intern Med 2009; 1501–8
13. Bretagne JF, Hamonic S, Piette C, et al. Variations between endoscopists in rates of detection of colorectal neoplasia and their impact on a regional screening program based on colonoscopy after fecal occult blood testing. Gastrointest Endosc 2010; 71: 335–41. doi: 10.1016/j.gie.2009.08.032
14. Adler A, Wegscheider K, Lieberman D, et al. Factors determining the quality of screening colonoscopy: a prospective study on adenoma detection rates, from 12,134 examinations (Berlin colonoscopy project 3, BECOP-3). Gut 2013; 62: 236–41. doi: 10.1136/gutjnl-2011-300167
15. Baxter NN, Warren JL, Barrett MJ, Stukel TA, Doria-Rose VP. Association between colonoscopy and colorectal cancer mortality in a US cohort according to site of cancer and colonoscopist specialty. J Clin Oncol 2012; 30: 2664–9. doi: 10.1200/JCO.2011.40.4772
16. Ko CW, Dominitz JA, Green P, Kreuter W, Baldwin LM. Specialty differences in polyp detection, removal, and biopsy during colonoscopy. Am J Med 2010; 123: 528–35. doi: 10.1016/j.amjmed.2010.01.016
17. Graser A, Stieber P, Nagel D, et al. Comparison of CT colonography, colonoscopy, sigmoidoscopy and faecal occult blood tests for the detection of advanced adenoma in an average risk population. Gut 2009; 58: 241–8. doi: 10.1136/gut.2008.156448
18. Schoen RE, Pinsky PF, Weissfeld JL, et al. Colorectal-cancer incidence and mortality with screening flexible sigmoidoscopy. N Engl J Med 2012; 366: 2345–57. doi: 10.1056/NEJMoa1114635
19. Hoff G, Grotmol T, Skovlund E, Bretthauer M, Norwegian Colorectal Cancer Prevention Study G. Risk of colorectal cancer seven years after flexible sigmoidoscopy screening: randomised controlled trial. BMJ 2009; 338: b1846. doi: 10.1136/bmj.b1846
20. Johnson CD, Chen MH, Toledano AY, et al. Accuracy of CT colonography for detection of large adenomas and cancers. N Engl J Med 2008; 359: 1207–17. doi: 10.1056/NEJMoa0800996
21. Zalis ME, Blake MA, Cai W, et al. Diagnostic accuracy of laxative-free computed tomographic colonography for detection of adenomatous polyps in asymptomatic adults: a prospective evaluation. Ann Intern Med 2012; 156: 692–702. doi: 10.7326/0003-4819-156-10-201205150-00005
22. Atkin W, Dadswell E, Wooldrage K, et al. Computed tomographic colonography versus colonoscopy for investigation of patients with symptoms suggestive of colorectal cancer (SIGGAR): a multicentre randomised trial. Lancet 2013; 381: 1194–202. doi: 10.1016/S0140-6736(12)62186-2
23. von Wagner C, Ghanouni A, Halligan S, et al. Patient acceptability and psychologic consequences of CT colonography compared with those of colonoscopy: results from a multicenter randomized controlled trial of symptomatic patients. Radiology 2012; 263: 723–31. doi: 10.1148/radiol.12111523
24. de Wijkerslooth TR, de Haan MC, Stoop EM, et al. Reasons for participation and nonparticipation in colorectal cancer screening: a randomized trial of colonoscopy and CT colonography. Am J Gastroenterol 2012; 107: 1777–83. doi: 10.1038/ajg.2012
25. de Wijkerslooth TR, de Haan MC, Stoop EM, et al. Burden of colonoscopy compared to non-cathartic CT-colonography in a colorectal cancer screening programme: randomised controlled trial. Gut 2012; 61: 1552–9. doi: 10.1038/ajg.2012
26. Courtney RJ, Paul CL, Sanson-Fisher RW, et al. Individual- and provider-level factors associated with colorectal cancer screening in accordance with guideline recommendation: a community-level perspective across varying levels of risk. BMC Public Health 2013; 13: 248. doi: 10.1186/1471-2458-13-248
27. Fenton JJ, Jerant AF, von Friederichs-Fitzwater MM, Tancredi DJ, Franks P Physician counseling for colorectal cancer screening: impact on patient attitudes, beliefs, and behavior. J Am Board Fam Med 2011; 24: 673–81. doi: 10.3122/jabfm.2011.06.110001