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## COLONOSCOPIC SCREENING IN AVERAGE RISK INDIVIDUALS AGES 40 TO 49 VERSUS 50 TO 59 YEARS

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### Abstract

**Background and Aims**—Screening guidelines for colorectal cancer include colonoscopy starting at age 50 based on the prevalence of adenomas and the incidence of colon cancer at that age. However, only one prior study has investigated the prevalence of colorectal neoplasia with colonoscopic screening in asymptomatic average-risk individuals ages 40-49 years in the United States.

**Methods**—We analyzed the results of screening colonoscopies offered to patients of a healthcare provider that offers screening services as part of an employer-provided wellness program. The primary endpoints were prevalence of adenomas and cancers for those aged 40-49 years versus those 50-59 years.

**Results**—We analyzed 553 screening colonoscopies for patients ages 40-49 and 352 screening colonoscopies for patients ages 50-59. In the 40-49 age group, 79 patients (14%) had one or more adenomas, of which 11 (2% of screened) had an advanced neoplasm (>1cm). In the 50-59 age group, 56 patients (16%) had one or more adenomas detected. Of those patients, 13 (3.7% of screened) had an advanced neoplasm, and one patient (0.3%) had an adenocarcinoma detected.

**Conclusions**—We found on colonoscopic screening that the prevalence of total adenomas was similar in individuals ages 40-49 and in those 50-59 years, although the prevalence of advanced neoplasia in the 50-59 age group may be higher than that in the 40-49 age group.

### INTRODUCTION

Colonoscopy is an effective and widely-endorsed modality for screening for colorectal cancer. In recent years, colonoscopy was the primary driving force for the overall increase in colorectal cancer screening.<sup>(1)</sup> There is compelling evidence that screening colonoscopy with removal of detected polyps leads to a substantial reduction in the incidence of

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colorectal cancer, with its efficacy rivaling or superior to annual fecal occult blood testing, flexible sigmoidoscopy, and double contrast barium enema.(2-4)

Guidelines from multiple professional societies recommend screening colonoscopy beginning at age 50 for average-risk individuals.(5-7) This age cutoff is based largely on the fact that the incidence of colorectal cancer begins to rise in the sixth decade of life.(8) However, given the long lead time associated with the adenoma to carcinoma progression, the increased number of colorectal cancers diagnosed in this age group may reflect the end result of adenomas present in individuals in their forties. Hence, these cancers may be prevented by colonoscopy with polypectomy of premalignant lesions in the preceding decade. Despite this theoretical argument for screening individuals in their forties, only one prior study has investigated the prevalence of colorectal neoplasia with colonoscopic screening in asymptomatic average-risk individuals aged 40-49 years in the United States. (9)

In this study, we investigated the prevalence of colorectal neoplasia, including potentially premalignant adenomas, in asymptomatic individuals at average risk aged 40-49 years undergoing colonoscopic screening, and compared it to findings in individuals aged 50-59 years.

## METHODS

Executive Health Exams International, Inc. (EHE) is a company that provides annual physical exams to individuals employed at corporations who offer EHE services as part of its corporate wellness plan. The exams are offered to the employees of participating companies at no cost to the employee. Companies differ in their policies regarding which levels of employees are eligible for the physical exam, but many companies offer it to all levels of employees and their spouses. The physical exams take place at six EHE owned centers (New York City, NY; Stamford, CT; Morristown, NJ; Houston, TX; Chicago II; and Boston, MA) and at a network of over 60 physician offices across the country. The network offices meet EHE quality control standards for the exam procedures. Exam data are recorded electronically in a centralized digital medical record system maintained by EHE. Data can be retrieved from the centralized digital medical record system and are stripped of identifiers before being compiled into files that can be read by standard statistical programs. The Columbia University Medical Center Institutional Review Board approved the study protocol and designated it as Non-Human Research involving de-identified records previously collected for other purposes.

Colonoscopy screening is provided as part of the wellness exam for all adults over age 40. At the time of their initial exam, they fill out a questionnaire, which collects demographic, risk factor, and clinical history information. Those 40 and older who are eligible and agreeable are then scheduled to return for their colonoscopic examination.

We collected de-identified data on colonoscopies performed on individuals ages 40-49 as well as individuals ages 50-59 during the 27 month period from January 2004 through March 2006. We excluded colonoscopies that did not reach the cecum as well as colonoscopies for which the clinical indication was other than for screening purposes (e.g. anemia, abdominal pain, or diarrhea). So as to ensure that the population was of average risk, we excluded from the analysis individuals who had a family history of colon cancer, or a personal history of inflammatory bowel disease or any malignancy other than skin cancer. We collected data on the size, location, and number of adenomas per patient from the colonoscopy reports. The presence of adenomatous polyps, villous features, high-grade dysplasia, and carcinoma was defined by pathology review.

Adenoma size was determined by visual estimate with the use of the open biopsy forceps, or was determined after removal. Adenomas considered advanced were those that were  $\geq 1$  cm in diameter or that contained villous features or high grade dysplasia. In instances where an individual had multiple adenomas, we reported information on the largest. In instances where two or more adenomas were the same size, information on the most distal was reported.

We compared the prevalence and location of colorectal adenomas, advanced adenomas, and carcinomas among individuals 40-49 years to those 50-59 years. We used the chi-square and Fischer exact tests for comparisons of proportions.

## RESULTS

A total of 905 colonoscopies were performed during the study period that were eligible for analysis. Of these, 553 colonoscopies were of patients 40-49 years and 352 colonoscopies were of patients 50-59 years. The demographics of the subjects included in the analysis are listed in Table 1. Both groups were predominantly male (75% in the 40-49 group and 77% in the 50-59 group), and were drawn largely from New York City and Houston, Texas. The preparation was characterized as excellent or average in 87% of patients in the 40-49 age bracket and in 85% of the 50-59 age bracket ( $p=0.70$ ). Moderate or extreme technical difficulty was reported in 11% and 13% of the patients in the 40-49 and 50-59 age brackets, respectively ( $p=0.56$ ).

A total of 135 patients had one or more adenomas with a uniform prevalence of findings by age group. The prevalence of adenomas in the two age brackets is illustrated in Table 2. Among the 40-49 year olds, 79 (14%, 95% CI 12-18%) individuals had one or more adenomas and among the 50-59 year olds, 56 (16%, 95% CI 12-20%) had one or more adenomas ( $p=0.50$ ). After controlling for sex, race, body size, and clinical facility location, age group remained unassociated with adenoma prevalence ( $p=0.52$ ). In the 40-49 year age group, 11 of these patients (2% of the total screened, 95% CI 1-4%) had an advanced neoplasm, while in the 50-59 year old age group, 13 of the patients had an advanced neoplasm (4% of the total screened, 95% CI 2-6%). The number needed to screen to find one advanced neoplasm in the 40-49 year old age group is 50 (95% CI 29-100) and in the 50-59 year old age group is 27 (95% CI 16-50). Among the 40-49 year old group men accounted for 73% of the advanced lesions and among the 50-59 year old group men accounted for 69% of the advanced lesions ( $p=0.85$ ). There was one adenocarcinoma found in the entire cohort, occurring in the 50-59 year old age group, yielding a carcinoma prevalence of 0.3% in this age group. The prevalence of advanced colorectal neoplasia did not differ significantly between the two age groups ( $p=0.12$ ). In the 40-49 age group the prevalence of one or more adenomas among women was 11% and among men was 15% ( $p=0.21$ ), and in the 50-59 age group the prevalence was 15% in men and 16% in women ( $p=0.76$ ).

The distribution of the number of adenomas per patient is illustrated in Table 3. Of the 40-49 year olds with adenomas, 57 (72%) had one adenoma, 17 (22%) had two adenomas, and 5 (6%) had three or more adenomas. Of the 50-59 year olds with adenomas, 45 (80%) had one adenoma, 8 (14%) had two adenomas, and 3 (5%) had three or more adenomas. The difference in adenoma number between these two age groups was not statistically significant ( $p=0.53$ ). The average and median adenoma size did not vary by group (40-49 year olds mean = 4.82 mm, median = 4.00 mm; 50-59 year olds mean = 5.05 mm, median = 4.00 mm,  $p=0.78$ ). The prevalence of adenomas greater or equal to 5mm in size was 43% in the 40-49 age bracket and 45% in 50-59 age bracket ( $p=0.85$ ).

The distribution of adenomas throughout the colon in the two groups is detailed in Table 4 and did not vary by age group ( $p=0.37$ ). The largest adenomas found within an individual were present proximal to the splenic flexure in 47% and 59% of the 40-49 and 50-59 age groups, respectively ( $p=0.17$ ). Among those with adenomas, the prevalence of individuals without adenomas at or distal to the splenic flexure was 41% in the 40-49 year old group and 54% in the 50-59 year old group ( $p=0.13$ ).

## DISCUSSION

Despite the substantial morbidity associated with colorectal cancer and the widespread adoption of screening recommendations that apply to asymptomatic average-risk persons at age 50, the prevalence of preneoplastic colorectal adenomas in the preceding decade has had little study. The sole previous analysis of the prevalence of adenomas in this age group in the United States found an adenoma prevalence of 11%, with a prevalence of advanced adenomas of 3.5%, rates similar to our findings (Table 5).<sup>(9)</sup> Similar findings in this age group were reported among average risk men in South Korea, though in that study the prevalence of adenomas and advanced neoplasia among women was significantly lower.<sup>(10)</sup>

Prior studies of asymptomatic patients older than 50 years found a prevalence of adenoma and advanced neoplasia that was considerably higher than those in our cohort. For example, in one large cohort, the prevalence of colorectal neoplasia was 37.5%.<sup>(4)</sup> However, more than two thirds of this cohort consisted of subjects between 60 and 75 years. Moreover, 13.9% of individuals in that population had one or more first degree relatives with a history of colorectal cancer. Other cohorts demonstrating a similarly high prevalence of adenomas among asymptomatic patients older than 50 years had a large proportion of patients older than 59 and included those with a family history of colorectal cancer.<sup>(11, 12)</sup> Our study excluded such patients so as to compare the prevalence of colorectal neoplasia in two age deciles in an average-risk population. This most likely accounts for the relatively lower prevalence of adenomas in our cohort as compared to prior studies.

We did not find a significant difference in the overall prevalence of adenomas between the 40-49 age group and the 50-59 age group. However, we did observe an increase in the prevalence of advanced neoplasms in the 50-59 age group compared to the 40-49 age group. Although this near-doubling of the prevalence of advanced neoplasms was not statistically significant, we suspect that there is a true rise in the prevalence of advanced neoplasms between these two decades that our study was not adequately powered to observe. Post-hoc power analyses show that the smallest difference in the prevalence of advanced tumors that could be observed with 80% power was 2% in the 40-49 year old group versus 6% in the 50-59 year old group. This rise was noted as well in the study by Imperiale, et al, in which the rise in prevalence of advanced neoplasms continued in subsequent decades of life. <sup>(9)</sup> A rise in the prevalence of advanced neoplasms in the 50-59 age group as compared to the 40-49 age group would account for the well-established subsequent parallel rise in the prevalence of colorectal cancer in later decades.

An actuarial analysis of colonoscopy for colorectal cancer screening is required to determine whether screening the asymptomatic population beginning at age 40 would prevent enough morbidity and mortality to be cost effective; such cost efficacy analyses have been performed on colonoscopy as a screening modality, but have generally considered age 50 to be the age of initiation of screening,<sup>(13, 14)</sup> with only one such analysis considering one-time screening at age 45-49.<sup>(15)</sup>

A recent study by Regula, et al, analyzing the results of a national screening program in Poland, found that the prevalence of advanced colorectal neoplasia in men age 40-49 was

similar to that of women age 50-59, suggesting that the age at which to commence screening should be gender-specific.<sup>(16)</sup> However, individuals in the 40-49 age bracket in that study were eligible for screening only if there were a family history of cancer of any kind; this does not represent the average risk population, even when limiting the analysis to those with a family history of malignancy other than colorectal cancer. Nonetheless, our results are similar in that, among men the prevalence of adenoma was the same in the two age groups, and was slightly higher among 50-59 year old women than among 40-49 year old women.

Our study has a number of limitations. As noted above, the population is predominantly male and Caucasian, limiting the ability to evaluate gender and race as a risk factor for colorectal neoplasia due to a relative lack of comparators. Dietary and medication data, which may affect development of adenomas, were not collected; nevertheless, one would not expect there to be a large difference in diet or medication use between the two age brackets that would have a substantial impact on our findings. As this was an observational study, the decision of the patient to proceed with colonoscopy during age 40-49 years may have been due to factors associated with an increased risk of adenoma or carcinoma, such as rectal bleeding. We excluded from our analysis those patients who were noted to have an indication for colonoscopy other than screening, but the possibility remains that some of the patients in the 40-49 bracket were of above-average risk for colorectal neoplasia. Furthermore, our study focused on an employed population provided with wellness exams by their employers. Thus, the results may not be generalizable to other groups.

Our analysis demonstrates that there is little difference in the overall prevalence of colorectal adenomas when we compared asymptomatic individuals age 40-49 to those age 50-59 years. Despite the similar adenoma prevalence between the two age groups, we detected an increased prevalence of advanced neoplasia in the 50-59 age group that was not statistically significant, possibly due to sample size limitations. We suspect that future sufficiently powered studies will demonstrate a true rise in the prevalence of advanced neoplasia when comparing these two age groups. Future studies are also required to determine the cost-efficacy of screening with colonoscopy at age 40, and to develop non-invasive methods to further risk-stratify those whom we currently consider to be at average risk for colorectal cancer.

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**Table 1**

Demographics of subjects undergoing screening colonoscopy

	<b>Age 40-49</b> N=553	<b>Age 50-59</b> N=352
Age	Median=45.58 Range=40.13 – 49.99	Median=53.71 Range=50.03-59.74
Gender		
Male	417 (75%)	271 (77%)
Female	136 (25%)	81 (23%)
Race		
Caucasian	393 (71%)	258 (73%)
Non-Caucasian	160 (29%)	94 (27%)
Body Size		
Normal weight	191 (36%)	110 (33%)
Overweight	258 (49%)	154 (47%)
Obese	79 (15%)	68 (21%)

**Table 2**

Number of patients (%) with no adenoma, one or more adenoma, and one or more advanced neoplasm. There was no statistically significant difference between the two age brackets with regard to prevalence of adenomas ( $p=0.50$ ) or prevalence of advanced adenomas ( $p=0.12$ ).

	Age 40-49	Age 50-59
No adenoma	474 (86)	296 (84)
Non-advanced adenoma	68 (12)	43 (12)
Advanced neoplasia	11 (2)	13 (4)



**Table 3**

Number (%) of patients with 1, 2, or 3 adenomas among among patients with adenomas in the two age brackets. P=0.53 for the difference in adenoma number.

Number of adenomas	Age 40-49	Age 50-59
One adenoma	57 (72)	45 (80)
Two adenomas	17 (22)	8 (14)
Three or more adenomas	5 (6)	3 (5)

**Table 4**

Prevalence of adenomas by location and age group. Figures are expressed as N (%). The difference in distribution of adenomas in these two age groups was not statistically significant ( $p=0.37$ ).

Age Group	Location							
	Rectum	Sigmoid	Descending Colon	Splenic Flexure	Transverse Colon	Hepatic Flexure	Ascending Colon	Cecum
40-49	8 (10)	13 (17)	10 (13)	11 (14)	12 (15)	8 (10)	11 (14)	6 (8)
50-59	5 (9)	8 (14)	4 (7)	6 (11)	6 (11)	6 (11)	8 (14)	13 (23)

**Table 5**

Prevalence of adenomas, advanced neoplasms, and colorectal cancer among patient groups aged 40-49 and 50-59.

Study	Percentage of patients with adenomas	Percentage of patients with advanced neoplasms	Percentage of patients with colorectal cancer
Current study	40-49: 14	40-49: 2	40-49: 0
	50-59: 16	50-59: 4	50-59: 0.3
Imperiale, et al(9)	40-49: 11	40-49: 3.5	40-49: 0
	50-59: not stated	50-59: 4.1	50-59: 0.5