

ARTICLE

Protection From Right- and Left-Sided Colorectal Neoplasms After Colonoscopy: Population-Based Study

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- Background** Colonoscopy is used for early detection and prevention of colorectal cancer, but evidence on the magnitude of overall protection and protection according to anatomical site through colonoscopy performed in the community setting is sparse. We assessed whether receiving a colonoscopy in the preceding 10-year period, compared with no colonoscopy, was associated with prevalence of advanced colorectal neoplasms (defined as cancers or advanced adenomas) at various anatomical sites.
- Methods** A statewide cross-sectional study was conducted among 3287 participants in screening colonoscopy between May 1, 2005, and December 31, 2007, from the state of Saarland in Germany who were aged 55 years or older. Prevalence of advanced colorectal neoplasms was ascertained by screening colonoscopy and histopathologic examination of any polyps excised. Previous colonoscopy history was obtained by standardized questionnaire, and its association with prevalence of advanced colorectal neoplasms was estimated, after adjustment for potential confounding factors by log-binomial regression.
- Results** Advanced colorectal neoplasms were detected in 308 (11.4%) of the 2701 participants with no previous colonoscopy compared with 36 (6.1%) of the 586 participants who had undergone colonoscopy within the preceding 10 years. After adjustment, overall and site-specific adjusted prevalence ratios for previous colonoscopy in the previous 10-year period were as follows: overall, 0.52 (95% confidence interval [CI] = 0.37 to 0.73); cecum and ascending colon, 0.99 (95% CI = 0.50 to 1.97); hepatic flexure and transverse colon, 1.21 (95% CI = 0.60 to 2.42); right-sided colon combined (cecum to transverse colon), 1.05 (95% CI = 0.63 to 1.76); splenic flexure and descending colon, 0.36 (95% CI = 0.16 to 0.82); sigmoid colon, 0.29 (95% CI = 0.16 to 0.53); rectum, 0.07 (95% CI = 0.02 to 0.40); left colon and rectum combined (splenic flexure to rectum, referred to as left-sided elsewhere), 0.33 (95% CI = 0.21 to 0.53).
- Conclusion** Prevalence of left-sided advanced colorectal neoplasms, but not right-sided advanced neoplasms, was strongly reduced within a 10-year period after colonoscopy, even in the community setting.

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With more than 1 million new diagnoses and more than 500 000 deaths each year, colorectal cancer is the third most common cancer and the fourth most common cancer cause of death globally (1). Colonoscopy, which enables detection and removal of precancerous lesions, has been shown to be an effective method for colorectal cancer prevention under highly standardized trial conditions. In particular, the National Polyp Study (2) demonstrated colonoscopy to be associated with a 76%–90% risk reduction for colorectal cancer among people with colorectal polyps. However, the effectiveness of colonoscopy in preventing colorectal cancer is less clear in the community setting. In fact, results of several studies (3–6) have indicated that effectiveness of colonoscopy in the community setting may be substantially lower than in clinical trials, possibly because colorectal adenomas may be missed more frequently in the community. A recent study (7) that was conducted in a community setting in Canada and used administrative

claims data to define colonoscopy history found that a history of colonoscopy at least 6 months before diagnosis was associated with a reduction in colorectal cancer mortality of approximately 40%, which was restricted essentially to left-sided colorectal cancers. In a community setting in Germany, we investigated the prevalence of colorectal cancers and advanced adenomas, overall and at specific sites, in patients with colorectal cancer who had received a colonoscopy in the 10-year period before diagnosis compared with those who never had a colonoscopy.

Patients and Methods

Study Design and Study Population

A statewide cohort study was initiated in 2005 in Saarland, a small state (1 million inhabitants) located in southwestern Germany, to monitor colorectal cancer incidence and mortality

CONTEXT AND CAVEATS

Prior knowledge

Although colonoscopy is used for early detection and prevention of colorectal cancer, data are sparse on protection from colorectal cancer overall and by anatomical site of colonoscopy performed in the community setting.

Study design

A cross-sectional study of the effectiveness of colonoscopy was conducted among participants in screening colonoscopy from the German state of Saarland who were aged 55 years or older. Advanced colorectal neoplasms were detected by screening colonoscopy. Previous colonoscopy history was obtained by questionnaire. The association of previous colonoscopy with prevalence of advanced colorectal neoplasms was estimated overall and by site.

Contribution

Advanced colorectal neoplasms were detected in 308 (11.4%) of the 2701 participants with no previous colonoscopy compared with 36 (6.1%) of the 586 participants who had undergone colonoscopy within the preceding 10 years. Prevalence of left-sided advanced colorectal neoplasms, but not right-sided advanced neoplasms, was substantially lower within a 10-year period after colonoscopy, even in the community setting.

Implications

Results of this study need to be validated in independent populations. Additional research, including both randomized and observational studies, is warranted to determine the best type of endoscopy, the optimum screening and surveillance intervals, and risk-adapted screening strategies.

Limitations

Previous colonoscopies were self-reported. Screening colonoscopies were performed in the community setting by many endoscopists. Histopathologic examination was performed by various pathology laboratories. Numbers of advanced neoplasms at specific sites were rather small.

From the Editors

among individuals who participated in screening colonoscopy. In this article, results of a cross-sectional analysis of baseline data from participants recruited in 33 gastroenterology practices in Saarland from May 1, 2005, through December 31, 2007, are reported.

Screening colonoscopy has been offered by the Statutory Health Insurance System in Germany since October 1, 2002. Women and men aged 55 years or older are eligible to receive up to two screening colonoscopies at least 10 years apart. Annual participation is approximately 3% of eligible people, which, if maintained, would correspond to a participation rate of approximately 30% within the 10-year time window offered. Screening is almost exclusively performed in practices of gastroenterology or internal medicine. Only experienced endoscopists, who have conducted at least 200 colonoscopies and at least 50 polypectomies under supervision in the preceding two calendar years, become eligible to conduct screening colonoscopies. To maintain eligibility, these endoscopists must conduct at least 200 colonoscopies per year and at least 10 polypectomies per year. Histopathologic examination of

any polyps removed is performed decentrally; endoscopists send the polyps to a certified pathological laboratory of their choice that is typically located in the same region as the endoscopist's practice, although endoscopists may select a laboratory in another region.

With few exceptions, all practices conducting screening colonoscopies in Saarland ($n = 33$) agreed to recruit patients for the study cohort. To be eligible, patients had to be residents of Saarland who were aged 55 years or older and to undergo screening colonoscopy in one of the participating practices. Patients with a history of colorectal cancer or previous colorectal surgery were not eligible. Overall, 5181 patients were recruited between May 1, 2005, and December 31, 2007. The study was approved by ethics committees of the University of Heidelberg and of the Medical Association of Saarland. Written informed consent was obtained from each participant.

Data Collection

After providing informed consent but before screening colonoscopy, patients were asked to fill out a short standardized questionnaire on their own and their family's medical history and also socioeconomic, demographic, and lifestyle factors. In particular, participants were asked if they ever had had a previous colonoscopy for any reason. We did not ask for other endoscopic examinations of the large bowel, such as flexible sigmoidoscopy, which are rarely done in Germany (8). Patients were asked to return the completed questionnaire before receiving their colonoscopy. However, 699 (13.5%) of the 5181 participants returned their questionnaire later by mail, as did 678 (13.1%) who could not be recruited before receiving their colonoscopy because of the work overload in the practices and so were invited to participate by mail shortly after their colonoscopy.

Results of each screening colonoscopy were abstracted from colonoscopy and histology reports and transferred to a standardized form by two independent trained investigators who were blinded with respect to questionnaire data. Items recorded included number, location, and the size and histological classification of polyps. In addition, completeness of colonoscopy (cecum reached in the first attempt) and quality of bowel preparation (fully adequate, partly inadequate, or inadequate) were recorded. Records from the two investigators were compared, and any initial discrepancy was resolved by consensus. Participants were classified according to occurrence of the most advanced of the following findings: colorectal cancer, advanced adenoma (defined as presence of at least one adenoma with at least one of the following features: >1 cm in diameter, tubulovillous or villous components, or high-grade dysplasia), other adenoma, hyperplastic or unspecified polyp, or none of the aforementioned findings.

Inclusion and Exclusion Criteria

For this analysis, we compared participants who had had a previous colonoscopy in the 10-year period before the screening colonoscopy examination with participants who had not had a previous colonoscopy. We excluded participants who were recruited or returned the questionnaire after their screening colonoscopy from this analysis, so that knowledge of the screening colonoscopy result could not affect answers to items on the questionnaire. We also excluded participants with a history of inflammatory bowel disease [who have a strongly increased risk of colorectal cancer and are

advised to undergo regular surveillance by colonoscopy (9)], participants with missing information on the year of their only or their latest colonoscopy, and participants who indicated that their only or their latest colonoscopy was conducted in the same year as the screening colonoscopy. The latter exclusion was made to prevent potential bias by erroneous reporting of the current screening colonoscopy as a preceding colonoscopy. In addition, participants who had their only or their latest previous colonoscopy more than 10 years ago were excluded, which indicates that that previous colonoscopy was probably negative; otherwise, a follow-up colonoscopy would have been recommended (10,11). Thus, this subgroup may be a highly selective group in whom the previous colonoscopy was mostly “negative.” Any risk reduction observed in this group would be expected to reflect primarily the inherent low risk associated with the absence of colorectal neoplasia rather than a protective effect of colonoscopy (8).

Statistical Analysis

We described the two groups of participants (those without a previous colonoscopy [group 1] and those who had had a colonoscopy in the 10 years before the screening colonoscopy [group 2]) with respect to sociodemographic characteristics and the following potential colorectal cancer risk factors: history of colorectal cancer in a first-degree relative (yes or no), smoking (current, former, or never), school education (≥ 10 or < 10 years), and body mass index (< 25 , 25 – 29.9 , or ≥ 30 kg/m²).

We compared the prevalences of colorectal cancer and advanced adenomas in participants with and without a previous colonoscopy. Because the prevalence of cancer was very low, cancers and advanced adenomas were combined to form a common endpoint termed advanced colorectal neoplasm. Prevalence of advanced colorectal neoplasms by specific locations within the colon and rectum (ie, cecum and ascending colon, hepatic flexure and transverse colon, splenic flexure and descending colon, sigmoid colon, and rectum) was determined in participants with and without previous colonoscopy. Additional analyses were performed for right-sided (cecum to transverse colon) and left-sided (splenic flexure to rectum) locations. The association of previous colonoscopy with prevalence of advanced colorectal neoplasms was quantified by crude and adjusted prevalence ratios. Adjustments were made for age, sex, and potential colorectal cancer risk factors that were found to be differentially distributed ($P < .20$) between the two groups of participants compared. Apart from age and sex, the following potential colorectal cancer risk factors or risk indicators were considered: school education (< 10 or ≥ 10 years), history of colorectal cancer in a first-degree relative (no or yes), smoking (never, current, or former), and body mass index (< 25 , 25.0 – 29.9 , or ≥ 30 kg/m²). Analyses were carried out with the SAS statistical software package version 9.1 (12) using log-binomial regression for multivariable estimation of prevalence ratios as previously described (13). All statistical tests were two-sided.

Additional sensitivity analyses were carried out by excluding participants with more than one previous colonoscopy or participants with an incomplete screening colonoscopy (ie, cecum not reached, no additional attempt made) or not fully adequate bowel preparation for screening colonoscopy according to the colonoscopy report.

Results

Overall, 5181 participants were recruited from May 1, 2005, through December 31, 2007 (Figure 1). After exclusions were complete, 3287 participants were included in the analysis: 2701 with no previous colonoscopy (ie, group 1) and 586 with a previous colonoscopy that had been conducted 1–10 years before the screening colonoscopy (ie, group 2). Screening colonoscopy was reported to be complete (cecum reached) in 3239 (98.5%) of the 3287 participants and bowel preparation was reported to be fully adequate in 3063 (93.2%).

Characteristics of participants with and without previous colonoscopy are shown in Table 1. Among those with previous colonoscopies, 315 (56.7%) had had one previous colonoscopy and only 36 (6.5%) had more than three previous colonoscopies. Mean time since the only or last previous colonoscopy was 5.7 years, and the median time was 5 years. The sex distribution was about even and the distribution of educational level was also about the same among participants with and without previous colonoscopy. However, participants with a previous colonoscopy were on average older (65.6 vs 63.8 years), and a larger proportion of them had a history of colorectal cancer in a first-degree relative (16.6% vs 11.6%). The distribution of smoking habits and body mass index was similar in both groups. Almost half of the participants had ever smoked, but only 325 (10.0%) continued smoking. Two thousand two hundred fifteen (68.4%) participants were overweight (body mass index = 25 – 25.9 kg/m²) or obese (body mass index ≥ 30 kg/m²).

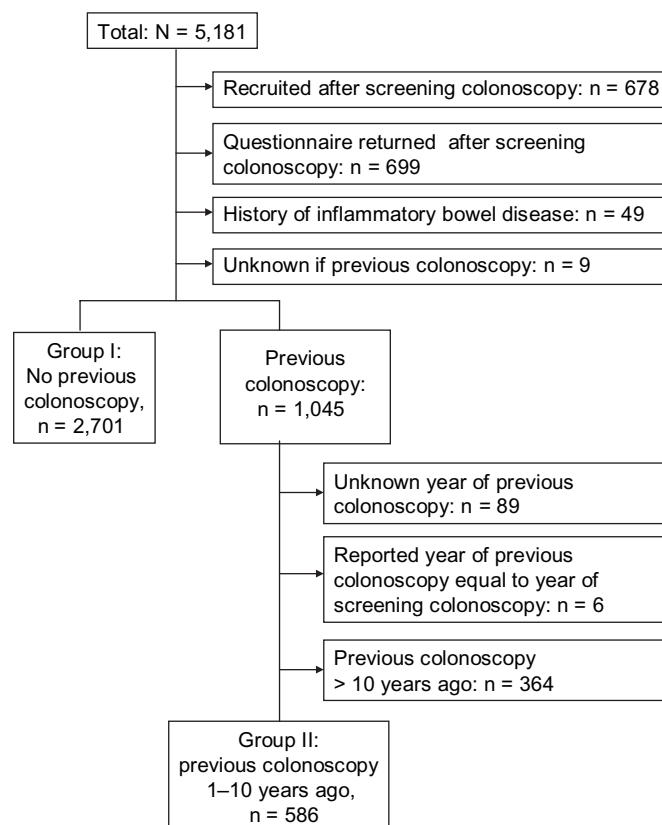


Figure 1. Flow diagram illustrating the exclusion of study participants from this analysis for the reasons indicated.

Table 1. Characteristics of study participants with and without a previous colonoscopy who were included in this study (N = 3287)

Characteristic	Previous colonoscopy*		P†
	No (n = 2701)	Yes, 1–10 years ago (n = 586)	
No. of previous colonoscopies, No. (%)			
1	—	315 (56.7)	
2	—	154 (27.7)	
3	—	51 (9.2)	
>3	—	36 (6.5)	
Time since last colonoscopy, No. (%)			
1–5 y	—	302 (51.5)	
6–10 y	—	284 (48.5)	
Sex, No. (%)			
Men	1330 (49.2)	277 (47.3)	
Women	1371 (50.8)	309 (52.7)	.39
Age, No. (%)			
55–59 y	888 (32.9)	131 (22.4)	
60–64 y	614 (22.7)	129 (22.0)	
65–69 y	666 (24.7)	172 (29.4)	
70–74 y	330 (12.2)	89 (15.2)	
≥75 y	203 (7.5)	65 (11.1)	<.001
School education, No. (%)			
<10 y	1836 (68.7)	390 (67.5)	
≥10 y	837 (31.3)	188 (32.5)	.57
History of colorectal cancer in a first-degree relative, No. (%)			
No	2388 (88.4)	489 (83.5)	
Yes	313 (11.6)	97 (16.6)	.001
Smoking, No. (%)			
Never	1378 (51.4)	315 (54.3)	
Current	271 (10.1)	54 (9.3)	
Former	1032 (38.5)	211 (36.4)	.44
Body mass index, No. (%)			
<25 kg/m ²	858 (32.2)	164 (28.5)	
25–29.9 kg/m ²	1249 (46.9)	285 (49.5)	
≥30 kg/m ²	554 (20.8)	127 (22.1)	.21

* Numbers do not add up to the expected total numbers because of missing values for some variables. Numbers of missing values for participants without or with previous colonoscopy are as follows: values for number of previous colonoscopies were zero and 30, for school education were 28 and eight, for smoking were 20 and six, and for body mass index were 40 and 10.

† P value for χ^2 test, comparing proportions between the two groups. All statistical tests were two-sided.

Overall, advanced neoplasia was found in 36 (6.1%) of the 586 participants who had had a previous colonoscopy 1–10 years before their screening colonoscopy (including one participant with colorectal cancer) compared with 308 (11.4%) of the 2701 participants with no previous colonoscopy (including 41 participants with colorectal cancer), which translates to a crude prevalence ratio of 0.54 (95% confidence interval [CI] = 0.39 to 0.75) (Table 2). Adjustment for age, sex, and family history of colorectal cancer hardly changed the results (adjusted prevalence ratio = 0.52, 95% CI = 0.37 to 0.73). However, in site-specific analyses, previous colonoscopy was strongly and inversely associated with prevalence of advanced neoplasia in the left-sided colon and rectum but not with prevalence of advanced neoplasia in the right-sided colon. Adjusted prevalence ratios were 0.99 (95% CI = 0.50 to 1.97) for the cecum and ascending colon, 1.21 (95% CI = 0.60 to 2.42) for the hepatic flexure and transverse colon, 0.36 (95% CI = 0.16 to 0.82) for the splenic flexure and descending colon, 0.29 (95% CI = 0.16 to 0.53) for the sigmoid colon, and 0.07 (95% CI = 0.02 to 0.40) for the rectum. Respective estimates of adjusted prevalence ratios for the right-sided colon combined and the left-sided colon and rectum combined were 1.05 (95% CI = 0.63 to 1.76) and

0.33 (95% CI = 0.21 to 0.53), respectively. Prevalence ratios for advanced neoplasms were similar for previous colonoscopies conducted 1–5 years ago and 6–10 years ago (0.89 and 1.23 for the right-sided colon, and 0.35 and 0.31 for the left colon and rectum, respectively).

These results did not materially change in sensitivity analyses that excluded participants with more than one previous colonoscopy (241 [41.1% of the 586 participants in group 2 and 7.3% of all 3287 participants]) or participants with incomplete screening colonoscopy (cecum not reached, 48 [1.5%] of 3287 participants) or not fully adequate bowel preparation for screening colonoscopy (224 [6.8%] of 3287 participants). With the latter exclusions, estimated risk reduction of advanced neoplasia appeared to be even slightly more pronounced (adjusted prevalence ratio for advanced neoplasia at any location = 0.45, 95% CI = 0.31 to 0.66).

Discussion

In this large study that was conducted in the community setting in Germany, previous colonoscopy that took place in the

Table 2. Associations of previous colonoscopy with prevalence of advanced colorectal neoplasia (cancer or advanced adenoma) detected at screening colonoscopy, overall and by anatomical sites*

Location	Previous colonoscopy†		Prevalence ratio (95% CI)‡	
	No (n = 2701), No. (%)	Yes, 1–10 years ago (n = 586), No. (%)	Crude	Adjusted§
Any	308 (11.4)	36 (6.1)	0.54 (0.39 to 0.75)	0.52 (0.37 to 0.73)
Cecum and ascending colon	42 (1.6)	10 (1.7)	1.10 (0.55 to 2.18)	0.99 (0.50 to 1.97)
Hepatic flexure and transverse colon	36 (1.3)	10 (1.7)	1.28 (0.64 to 2.57)	1.21 (0.60 to 2.42)
Splenic flexure and descending colon	78 (2.9)	6 (1.0)	0.35 (0.16 to 0.81)	0.36 (0.16 to 0.82)
Sigmoid colon	172 (6.4)	11 (1.9)	0.29 (0.16 to 0.54)	0.29 (0.16 to 0.53)
Rectum	91 (3.4)	2 (0.3)	0.07 (0.03 to 0.41)	0.07 (0.02 to 0.40)
Right-sided (cecum to transverse colon)	73 (2.7)	18 (3.1)	1.14 (0.68 to 1.89)	1.05 (0.63 to 1.76)
Left-sided (splenic flexure to rectum)	246 (9.1)	18 (3.1)	0.34 (0.21 to 0.54)	0.33 (0.21 to 0.53)

* CI = confidence interval.

† Sum of site-specific numbers may exceed total number because of detection of neoplasms at more than one anatomical site.

‡ For previous colonoscopy vs no previous colonoscopy.

§ Adjusted for age, sex, and history of colorectal cancer in a first-degree relative.

10-year period before a screening colonoscopy was associated with a 67% reduced risk of advanced neoplasia in the left colon and rectum, but no risk reduction for advanced neoplasia in the right colon was found. However, because most neoplasms in the colon and rectum are located on the left side, substantial overall risk reduction for colorectal cancers and advanced adenomas was observed.

Few previous studies (7,14–16) have addressed the preventive potential of colonoscopy stratified according to anatomical site in the large bowel, and those that have had focused on colorectal cancer incidence and mortality as outcome measure. Our study addressed this issue by examining preclinical colorectal lesions (ie, the association between previous colonoscopy and site-specific prevalence of colorectal cancer and advanced adenomas as detected by screening colonoscopy) and thus provides an important complement to current evidence. Interestingly, despite the different outcome measures, the findings of our study and of the other studies (7,14–16), all of which found the reduction of colorectal cancer incidence and mortality to be stronger for left-sided than for right-sided cancers, are consistent. In particular, our finding of a strongly reduced prevalence of left-sided advanced colorectal neoplasms (prevalence ratio = 0.33), along with absence of an association for right-sided advanced colorectal neoplasms (prevalence ratio = 1.05), is remarkably consistent with the odds ratios (ORs) of deaths from right- and left-sided colorectal cancer recently reported by Baxter et al. (7) in a large record linkage study from Canada (OR = 0.33 and 0.99, respectively). The observed patterns are also consistent with clinical observations that a greater proportion of colorectal cancer is right sided among those who have had a previous colonoscopy than among the general population (17,18).

Possible explanations for the lack of association of previous colonoscopies with prevalence of right-sided neoplasms include the following: First, some right-sided adenomas may be missed by incomplete colonoscopies or worse bowel preparation in the right colon. Second, a much larger proportion of adenomas in the right colon than in the left colon and rectum are sessile or flat, and such adenomas are more often missed and are more difficult to remove

at colonoscopy (19). Third, right- and left-sided neoplasms differ with respect to histology and molecular features, as do flat, sessile, and polypoid adenomas whose prevalence varies strongly between both locations (20–22).

As for overall (ie, non-site-specific) risk reduction, our results are consistent with and of similar magnitude to those reported in previous studies (7,14,23–27) that were conducted in the community setting in Canada, Germany, and the United States. These studies focused on reduction of colorectal cancer incidence and mortality.

Our study has several limitations. First, previous colonoscopies were self-reported, which implies a potential for “exposure misclassification.” However, in a recent validation study from Southern Germany, we found self-reports of colonoscopy to be highly valid (28). Furthermore, only participants who completed and returned their questionnaires before their screening colonoscopy were included, and differential recall according to findings at screening colonoscopy, therefore, was avoided. Second, screening colonoscopies were performed in the community setting by many endoscopists, which may increase the potential for missed polyps (29), despite the high qualification criteria for endoscopists required for admission to screening colonoscopy along with the measures of quality assurance. Third, histopathologic examination was likewise performed by different pathology laboratories, which may increase the potential for misclassification of polyps. Potential misclassification, if relevant, would though be expected to be nondifferential with respect to history of colonoscopy, so that the true associations may even have been underestimated. Fourth, numbers of advanced neoplasms by location were rather small. Nevertheless, consistent patterns of risk reduction in all parts of the left colon and rectum were observed, with absence of risk reduction in all parts of the right colon, and confidence intervals for combined categories of left-sided advanced colorectal neoplasms and right-sided advanced colorectal neoplasms did not overlap.

Fifth, our results pertain to colorectal neoplasms that were prevalent and detected at a screening colonoscopy. Although we used statewide recruitment rather than recruitment in selected special

centers, participants of screening colonoscopy may not be representative of the general population but rather be on average more health conscious. By focusing on prevalent disease, cases of colorectal cancer that might have become clinically detected before screening colonoscopy were not considered. However, major selection bias from this source appears unlikely because of the low rate at which colorectal cancer is clinically detected in individuals who are younger than 64 years, the median age of our study population. Also, the associations between previous colonoscopy and right- and left-sided colorectal neoplasms that we found are remarkably consistent with those found in studies (7,14–16) focusing on colorectal cancer incidence and mortality, which are not affected by this potential selection bias. Not all of the detected cancers and advanced adenomas would have been detected clinically during an individual's lifetime. It is conceivable that slower growing neoplasms, which may be more readily detected and removed at screening colonoscopy, were somewhat overrepresented and that potential effects of colonoscopy in prevention of colorectal neoplasms may be somewhat overestimated in this setting. Nevertheless, inclusion of advanced colorectal adenomas may also be considered a strength of our study because these lesions are now considered the primary target for preventive colonoscopy (10).

Despite its limitations, our study provides further evidence that strong protection from colorectal neoplasms by colonoscopy is possible in the community setting. It is notable that the previous colonoscopies, whose impact is assessed in this analysis, were mostly performed for diagnostic purposes before the introduction of screening colonoscopy, with its high standards of quality assurance, in late 2002.

Although a strong protective effect of colonoscopy from colorectal neoplasms has been established through previous studies, our results add to the evidence that this effect is much stronger in, if not confined to, the left colon and rectum, at least in the community setting. Possibly, the lack of effect in the right colon could be overcome to some extent by enhanced training of endoscopists, by enhanced measures of quality assurance, and by development of technology that enhances inspection of the right colon (30). Nevertheless, the possibility that cancer in the right colon simply does not lend itself equally well to early detection on biological grounds has to be considered. If this possibility could be demonstrated in other investigations, then the relative merits of sigmoidoscopy and colonoscopy in the early detection and prevention of colorectal cancer would need to be reevaluated.

In conclusion, our results provide further evidence that colonoscopy provides strong protection against advanced neoplasms in the left colon and rectum, even in the community setting. Despite the lack of data from randomized trials, screening for colorectal cancer by endoscopy of the large bowel is among the most powerful measures for reducing the cancer burden in Western societies. Although efforts to ensure quality and to increase utilization of endoscopic screening for colorectal cancer should be continued and intensified (10), additional research, including both randomized and observational studies, is needed to delineate effects of various screening modalities more specifically (31) (eg, with respect to type of endoscopy, screening and surveillance intervals, and risk-adapted screening strategies).

References

1. Parkin DM, Bray F, Ferlay J, et al. Global cancer statistics. 2002. *CA Cancer J Clin*. 2005;55(2):74–108.
2. Winawer SJ, Zauber AG, Nah Ho M, et al. Prevention of colorectal cancer by colonoscopic polypectomy. *N Engl J Med*. 1993;329(27):1977–1981.
3. Hosokawa O, Shirasaki S, Kaizaki Y, Hayashi H, Douden K, Hattori M. Invasive colorectal cancer detected up to 3 years after a colonoscopy negative for cancer. *Endoscopy*. 2003;35(6):506–510.
4. Robertson DJ, Greenberg ER, Beach M, et al. Colorectal cancer in patients under close colonoscopic surveillance. *Gastroenterology*. 2005;129(1):34–41.
5. Bressler B, Paszat LF, Vinden C, Li C, He J, Rabeneck L. Colonoscopic miss rates for right-sided colon cancer: a population-based analysis. *Gastroenterology*. 2004;127(2):452–456.
6. Bressler B, Paszat LF, Chen Z, Rothwell DM, Vinden C, Rabeneck L. Rates of new or missed colorectal cancers after colonoscopy and their risk factors: a population-based analysis. *Gastroenterology*. 2007;132(1):96–102.
7. Baxter NN, Goldwasser MA, Paszat LF, Saskin R, Urbach DR, Rabeneck L. Association of colonoscopy and death from colorectal cancer: a population-based, case-control study. *Ann Intern Med*. 2009;150(1):1–8.
8. Brenner H, Chang-Claude J, Seiler CM, Stürmer T, Hoffmeister M. Does a negative screening colonoscopy ever need to be repeated? *Gut*. 2006;55(8):1145–1150.
9. Ahmadi AA, Polyak S. Endoscopy/surveillance in inflammatory bowel disease. *Surg Clin North Am*. 2007;87(3):743–762.
10. Levin B, Lieberman DA, McFarland B, et al. American Cancer Society guidelines for the early detection of cancer, 2006. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *CA Cancer J Clin*. 2008;58(3):130–160.
11. Schmigel W, Reinacher-Schick A, Arnold D, et al. Update S3 guidelines colorectal cancer 2008 [in German]. *Z Gastroenterol*. 2008;46(8):799–840.
12. SAS Institute, Inc. *SAS Software for Windows. Version 9.1*. Cary, NC: SAS Institute, Inc; 1999.
13. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol*. 2005;162(3):199–200.
14. Brenner H, Arndt V, Stürmer T, Stegmaier C, Ziegler H, Dhom G. Long-lasting reduction of risk of colorectal cancer following screening endoscopy. *Br J Cancer*. 2001;85(7):972–976.
15. Brenner H, Chang-Claude J, Seiler CM, Stürmer T, Hoffmeister M. Potential for colorectal cancer prevention of sigmoidoscopy versus colonoscopy. *Cancer Epidemiol Biomarkers Prev*. 2007;16(3):494–499.
16. Singh G, Mannalithara A, Wang HJ, Graham DJ, Gerson LB, Triadafilopoulos G. Is protection against colorectal cancer good enough: a comparison between sigmoidoscopy and colonoscopy in the general population. *Gastroenterology*. 2007;132(4):A81.
17. Farrar WD, Sawhney MS, Nelson DB, Lederle FA, Bond JH. Colorectal cancers found after a complete colonoscopy. *Clin Gastroenterol Hepatol*. 2006;4(10):1259–1264.
18. Singh H, Turner D, Xue L, Targownik LE, Bernstein CN. Risk of developing colorectal cancer following a negative colonoscopy examination: evidence for a 10-year interval between colonoscopies. *JAMA*. 2006;295(20):2366–2373.
19. Heresbach D, Barrioz T, Lapalus MG, et al. Miss rate for colorectal neoplastic polyps: a prospective multicenter study of back-to-back video colonoscopies. *Endoscopy*. 2008;40(4):284–290.
20. Azzoni C, Bottarelli L, Campanini N, et al. Distinct molecular patterns based on proximal and distal sporadic colorectal cancer: arguments for different mechanisms in the tumorigenesis. *Int J Colorectal Dis*. 2007;22(2):115–126.
21. Sugai T, Habano W, Jiao YF, et al. Analysis of molecular alterations in left- and right-sided colorectal carcinomas reveals distinct pathways of carcinogenesis: proposal for new molecular profile of colorectal carcinomas. *J Mol Diagn*. 2006;8(2):193–201.

22. Soetikno RM, Kaltenbach T, Rouse RV, et al. Prevalence of nonpolypoid (flat and depressed) colorectal neoplasms in asymptomatic and symptomatic adults. *JAMA*. 2008;299(9):1027–1035.
23. Selby JV, Friedman GD, Quesenberry CP, Weiss NS. A case control study of screening sigmoidoscopy and mortality from colorectal cancer. *N Engl J Med*. 1992;326(10):653–657.
24. Müller AD, Sonnenberg A. Protection by endoscopy against death from colorectal cancer. A case-control study among veterans. *Arch Intern Med*. 1995;155(16):1741–1748.
25. Müller AD, Sonnenberg A. Prevention of colorectal cancer by flexible endoscopy and polypectomy. A case-control study of 32,702 veterans. *Ann Intern Med*. 1995;123(12):904–910.
26. Newcomb PA, Storer BE, Morimoto LM, Templeton A, Potter JD. Long-term efficacy of sigmoidoscopy in the reduction of colorectal cancer incidence. *J Natl Cancer Inst*. 2003;95(8):622–625.
27. Kahi CJ, Imperiale TF, Juliar BE, Rex DK. Effect of screening colonoscopy on colorectal cancer incidence and mortality. *Clin Gastroenterol Hepatol*. 2009;7(7):770–775.
28. Hoffmeister M, Chang-Claude J, Brenner H. Validity of self-reported endoscopies of the large bowel and implications for estimates of colorectal cancer risk. *Am J Epidemiol*. 2007;166(2):130–136.
29. van Rijn JC, Reitsma JB, Stoker J, Bossuyt PM, van Deventer SJ, Dekker E. Polyp miss rate determined by tandem colonoscopy: a systematic review. *Am J Gastroenterol*. 2006;101(2):343–350.
30. Rex DK. Maximizing detection of adenomas and cancers during colonoscopy. *Am J Gastroenterol*. 2006;101(12):2866–2877.
31. Schoen RE. Surveillance after positive and negative colonoscopy examinations: issues, yields, and use. *Am J Gastroenterol*. 2003;98(6):1237–1246.

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