

Long-term Risk of Colorectal Cancer and Related Deaths After a Colonoscopy With Normal Findings

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IMPORTANCE Guidelines recommend a 10-year rescreening interval after a colonoscopy with normal findings (negative colonoscopy results), but evidence supporting this recommendation is limited.

OBJECTIVE To examine the long-term risks of colorectal cancer and colorectal cancer deaths after a negative colonoscopy result, in comparison with individuals unscreened, in a large, community-based setting.

DESIGN, SETTING, AND PARTICIPANTS A retrospective cohort study was conducted in an integrated health care delivery organization serving more than 4 million members across Northern California. A total of 1 251 318 average-risk screening-eligible patients (age 50-75 years) between January 1, 1998, and December 31, 2015, were included. The study was concluded on December 31, 2016.

EXPOSURES Screening was examined as a time-varying exposure; all participants contributed person-time unscreened until they were either screened or censored. If the screening received was a negative colonoscopy result, the participants contributed person-time in the negative colonoscopy results group until they were censored.

MAIN OUTCOMES AND MEASURES Using Cox proportional hazards regression models, the hazard ratios (HRs) for colorectal cancer and related deaths were calculated according to time since negative colonoscopy result (or since cohort entry for those unscreened). Hazard ratios were adjusted for age, sex, race/ethnicity, Charlson comorbidity score, and body mass index.

RESULTS Of the 1 251 318 patients, 613 692 were men (49.0%); mean age was 55.6 (7.0) years. Compared with the unscreened participants, those with a negative colonoscopy result had a reduced risk of colorectal cancer and related deaths throughout the more than 12-year follow-up period, and although reductions in risk were attenuated with increasing years of follow-up, there was a 46% lower risk of colorectal cancer (hazard ratio, 0.54; 95% CI, 0.31-0.94) and 88% lower risk of related deaths (hazard ratio, 0.12; 95% CI, 0.02-0.82) at the current guideline-recommended 10-year rescreening interval.

CONCLUSIONS AND RELEVANCE A negative colonoscopy result in average-risk patients was associated with a lower risk of colorectal cancer and related deaths for more than 12 years after examination, compared with unscreened patients. Our study findings may be able to inform guidelines for rescreening after a negative colonoscopy result and future studies to evaluate the costs and benefits of earlier vs later rescreening intervals.

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Colorectal cancer is the second leading cause of cancer-related deaths in the United States.¹ Screening reduces colorectal cancer incidence and mortality through the removal of precancerous adenomatous polyps (adenomas) and detection of cancers at an earlier, more treatable stage.²⁻¹⁶ Several screening options are available, including fecal testing, sigmoidoscopy, and colonoscopy^{2,3}; the latter is the most widely used test in the United States.¹⁷

Current guidelines recommend a 10-year rescreening interval after a negative colonoscopy result, defined as an examination with normal findings; this recommendation is supported by modest empirical data¹⁸ based primarily on estimates of the sensitivity of colonoscopy and the time it takes for a new adenoma to progress to cancer (ie, the adenoma-carcinoma sequence).¹⁹⁻²¹ However, colonoscopy quality as measured by physician adenoma detection rate varies widely and is associated with a higher risk of interval colorectal cancer.^{22,23} Also, colorectal cancer is a heterogeneous disease. For example, the serrated pathway of carcinogenesis may be associated with more rapid transition from precancer to invasive disease than the traditional adenoma-carcinoma sequence.¹⁸ These factors suggest the possibility that the 10-year rescreening interval may be too long. Conversely, long-term follow-up from sigmoidoscopy trials, a procedure that visualizes only the left colon, indicates that screening benefits may last for up to 17 years, suggesting the 10-year interval may be too short.²⁴⁻²⁸

Few studies have examined the long-term risk of colorectal cancer and related deaths after a negative colonoscopy result, and none have had sufficient power to evaluate cancer risks annually after examination compared with an unscreened population.²⁹⁻³³ Such information could provide greater certainty regarding the appropriate rescreening interval after a negative colonoscopy result for average-risk individuals.

To address this evidence gap, we examined the long-term risk of colorectal cancer and related deaths after a negative colonoscopy result in comparison with no screening in a large, community-based setting.

Methods

Study Design and Setting

A retrospective cohort study was conducted among health plan members of Kaiser Permanente Northern California (KPNC), an integrated health care delivery organization that serves approximately 4.0 million members in urban, suburban, and semirural regions throughout Northern California. The membership is diverse and similar in socioeconomic characteristics to the region's census demographics, including the proportions with commercial insurance, Medicare, and Medicaid.²³ The study was approved by the KPNC Institutional Review Board, which waived the requirement for individual informed consent.

Eligibility Criteria

The study population consisted of health plan members aged 50 to 75 years at any time in January 1, 1998, to December 31,

Key Points

Question What are the long-term risks of colorectal cancer and related deaths in average-risk patients after a colonoscopy with normal findings (negative colonoscopy results)?

Findings In this community-based study of 1 251 318 individuals, adjusted annual colorectal cancer risks were reduced by 46% to 95%, and related deaths by 29% to 96%, across more than 12 years of follow-up after negative colonoscopy results compared with average-risk individuals with no screening. Although reductions in risk were attenuated with increasing years of follow-up, there was a 46% lower risk of colorectal cancer and 88% lower risk of related deaths at the guideline-recommended 10-year rescreening interval.

Meaning A colonoscopy with normal findings in average-risk patients appears to be associated with a lower risk of colorectal cancer deaths and overall, proximal, distal, early-stage, and advanced-stage colorectal cancer for more than 12 years compared with no screening.

2015, who had 1 or more years of continuous health plan enrollment immediately before cohort entry, and were at average-risk for colorectal cancer. Average risk was defined as without a prior diagnosis of colorectal cancer, inflammatory bowel disease, familial polyposis syndromes, colonic adenomas, or colonic polyps; without a documented family history of colorectal cancer or prior colectomy; and no known history of prior colorectal cancer screening (ie, fecal testing, sigmoidoscopy, or colonoscopy).

Screening Exposure and Follow-up for Colorectal Cancer Outcomes

Colorectal screening status was examined as a time-varying exposure. Participants entered the cohort on the date they became eligible for screening and met the study eligibility criteria; they contributed person-time unscreened until they were either screened (by fecal test, sigmoidoscopy, or colonoscopy) or were censored (died, diagnosed with colorectal cancer, terminated health plan membership, or reached the end of the study interval [December 31, 2016]), whichever came first. If the screening test received was a negative colonoscopy result (an examination without biopsy or polypectomy and no colorectal cancer diagnosis at or within 6 months after the procedure), the participant contributed person-time in the negative colonoscopy results group until they were censored (died, diagnosed with colorectal cancer, terminated health plan membership, reached the end of the study interval, or received a subsequent colonoscopy or sigmoidoscopy, whichever came first). If an unscreened participant subsequently received a fecal test, sigmoidoscopy, or a positive colonoscopy, they stopped contributing unscreened person-time starting on the date of the test.

Colorectal cancer diagnosed 6 months or earlier after a screening test was attributed to the participant's screening exposure state immediately prior to the test. For example, colorectal cancer detected at or within 6 months after a screening test in a previously unscreened patient was counted as diagnosed while the person was contributing unscreened person-

time. If cancer was detected in an individual 6 months or more after a negative colonoscopy result, the case was counted as diagnosed while the individual was contributing person-time in the negative colonoscopy results group.

Deaths due to colorectal cancer as the primary cause were attributed to either the unscreened or negative colonoscopy results group if the cancer was diagnosed or the death occurred while the individual was contributing person-time unscreened or in the negative colonoscopy results group, respectively. Individuals were followed up for colorectal cancer deaths up to December 31, 2015, the latest date for which cause of death data were available.

Data Sources

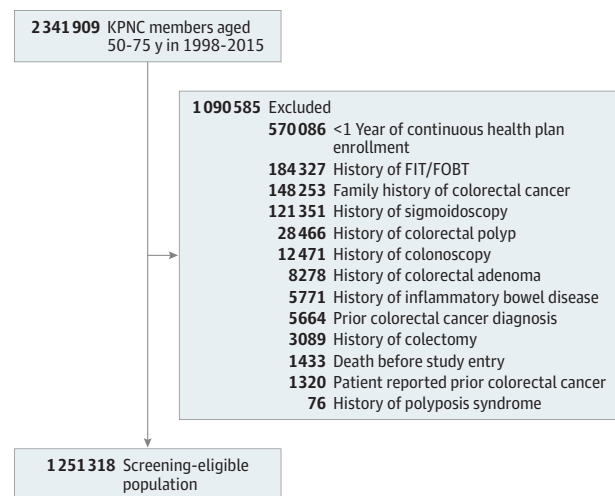
Data regarding colorectal cancer screening tests and diagnoses, demographics, and other covariates were obtained from a validated electronic laboratory, cancer registry, medical visit, demographic, and membership databases. Colorectal cancer mortality data were obtained from the KPNC mortality file, which is composed of data from the California Department of Vital Statistics, US Social Security Administration, and KPNC health care use data.

Endoscopic tests were identified using *Current Procedural Terminology* and *International Classification of Diseases, Ninth Revision (ICD-9)* codes. Validation studies have confirmed more than 99% capture of colonoscopy examinations, adenoma diagnoses and pathology classification, and cancers.²³ A validated algorithm that incorporated data from electronic consultation records, diagnostic codes from the ICD-9, and laboratory, pathologic, and radiologic tests was used to identify screening colonoscopies.³⁴ Family history of colorectal cancer was ascertained through ICD-9 codes and family history tables in the electronic medical records. Colorectal adenocarcinoma diagnoses and cancer stage were obtained from the KPNC cancer registry, which reports to the Surveillance, Epidemiology and End-Results (SEER) program. Early-stage colorectal cancer was defined using the American Joint Committee on Cancer staging system (stage I or II) or SEER summary staging (in situ, localized, or regional with direct extension only, according to the SEER Program Coding and Staging Manual 2013).³⁵ Advanced-stage colorectal cancer was defined using the American Joint Committee on Cancer staging system (stage III or IV) or SEER summary staging (regional or distant). Proximal cancers were those in the cecum, ascending colon, hepatic flexure, and transverse colon; distal cancers were those in the splenic flexure, descending colon, sigmoid colon, and rectum.

Statistical Analysis

Descriptive statistics were used to evaluate the demographic and clinical characteristics of cohort members, overall at cohort entry and for the 2 exposure groups at the midpoint of the study. Overall, site-specific (proximal and distal) and stage-specific (early-stage and advanced-stage) colorectal cancer incidence and overall colorectal cancer mortality rates were age-standardized using single years to the 2000 US census population and stratified by follow-up time (6 months to ≤ 1 year, annually for years 2 through 12, and >12 years for colo-

Figure 1. Flow Diagram for Selection of Screening-Eligible Cohort



FIT, fecal immunochemical testing; FOBT, fecal occult blood testing; and KPNC, Kaiser Permanente Northern California.

rectal cancer incidence; and ≤ 1 year, annually for years 2 through 12, and >12 years for colorectal cancer mortality). Because the negative colonoscopy results group excluded those with a diagnosis of colorectal cancer 6 or less months after the index examination, we excluded the first 6 months after the negative colonoscopy result or cohort entry for the unscreened group from calculations of person-years in the age-adjusted incidence rate analysis.

The 95% CIs for incidence and mortality rates were calculated based on a Poisson distribution using the inverted γ function. Multivariable Cox proportional hazards regression models were used to calculate hazard ratios (HRs) and 95% CIs for colorectal cancer and related mortality by exposure group as a time-varying exposure to account for changes over follow-up. The unscreened group served as the referent group. All Cox proportional hazards regression models were adjusted for age (birth year), sex, race/ethnicity, Charlson comorbidity index score, and body mass index. A sensitivity analysis was performed that eliminated follow-up colonoscopies with a screening indication. All statistical tests were 2-sided, and a P value $<.05$ was considered statistically significant. SAS software, version 9.3 (SAS Institute Inc) was used for all statistical analyses.

Results

Demographic Characteristics

After exclusions, there were 1 251 318 average-risk screening-eligible study participants who contributed 9 339 345 person-years of follow-up (Figure 1). Among 1 251 318 individuals contributing person-time unscreened, 5743 colorectal cancer cases were diagnosed during 4 639 809 person-years of follow-up, including 1821 proximal cancers (31.7%) and 2588 advanced-stage cancers (45.1%). Among 99 166 participants who subsequently contributed 417 987 person-years in the negative co-

Table. Characteristics of Screening-Eligible Cohort Members Overall and at Study Midpoint

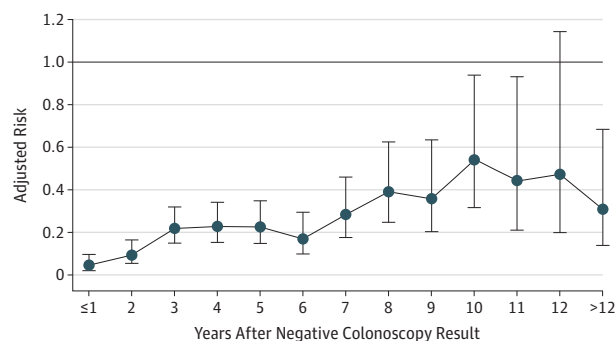
Characteristic	No. (%)		
	Overall Cohort	Unscreened	Negative Colonoscopy Result ^a
Participants	1 251 318 (100)	259 373 (100)	17 253 (100)
Total follow-up, y ^b			
Mean	7.5	11.6	13.7
Median (IQR)	6.0 (2.4-11.6)	11.5 (8.3-15.4)	13.7 (10.8-17.8)
Age, y	Entry	Midpoint	Midpoint
Mean (SD)	55.6 (7.0)	60.7	66.1
Median (IQR)	52.0 (50.0-60.0)	58.2 (53.3-66.1)	65.1 (58.9-73.0)
50-59	924 174 (73.9)	149 611 (57.7)	5145 (29.8)
60-69	246 249 (19.7)	61 499 (23.7)	6214 (36.0)
70-75	80 895 (6.5)	23 805 (9.2)	2927 (17.0)
Sex			
Male	613 692 (49.0)	122 024 (47.0)	7056 (40.9)
Female	637 481 (50.9)	137 325 (52.9)	10 195 (59.1)
Race/ethnicity			
White	708 955 (56.7)	154 761 (59.7)	11 787 (68.3)
Hispanic	144 079 (11.5)	32 128 (12.4)	1975 (11.4)
Black	77 351 (6.2)	16 547 (6.4)	1123 (6.5)
Asian/Pacific Islander	155 013 (12.4)	31 770 (12.2)	2014 (11.7)
Other, unknown	165 920 (13.3)	24 167 (9.3)	354 (2.1)
Charlson comorbidity index score			
0	895 979 (71.6)	192 354 (74.2)	10 992 (63.7)
1	228 412 (18.3)	45 542 (17.6)	3975 (23.0)
2	72 562 (5.8)	13 924 (5.4)	1412 (8.2)
≥3	54 365 (4.3)	7553 (2.9)	874 (5.1)
BMI			
<25	513 639 (41.0)	78 008 (30.1)	5377 (31.2)
25-29	380 097 (30.4)	89 481 (34.5)	6495 (37.6)
≥30	357 582 (28.6)	91 884 (35.4)	5381 (31.2)
Missing	234 986 (18.8)	13 428 (5.2)	59 (0.3)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range.

^a Defined as an examination with normal findings.

^b Total follow-up refers to the total time (in years) from cohort entry to final censoring. For the unscreened and negative colonoscopy results groups at the study midpoint (July 1, 2007), the total follow-up is the total time from cohort entry to final censoring among those who were in the unscreened and negative colonoscopy results groups, respectively, at the study midpoint.

Figure 2. Adjusted Risk of Colorectal Cancer Incidence by Time Interval After a Negative Colonoscopy Result



Hazard ratios were obtained by time-varying multivariable Cox proportional hazards models and adjusted for age, sex, race/ethnicity, Charlson comorbidity index score, body mass index, and screening level exposure status prior to negative colonoscopy result (defined as an examination with normal findings). Error bars indicate 95% CIs.

olonoscopy results group, 184 colorectal cancer cases were diagnosed, including 94 proximal cancers (51.1%) and 91 advanced-stage cancers (49.5%). At cohort entry, for the overall

cohort, the mean (SD) age was 55.6 (7.0) years, 50.9% were men, and the median length of follow-up from cohort entry was 6.0 years (interquartile range, 2.4-11.6 years) (Table). Characteristics of the 2 exposure groups at the study midpoint are shown in the Table.

Colorectal Cancer Incidence and Mortality Rates

Among the unscreened cohort, colorectal cancer incidence rates increased with follow-up time from 62.9 per 100 000 person-years (95% CI, 55.7-70.0) in year 1, to 224.8 per 100 000 person-years (95% CI, 202.5-247.0) at more than 12 years (Figure 2, eTable 1 in the Supplement). Related mortality rates increased from 10.5 per 100 000 person-years (95% CI, 8.2-12.8) in year 1 to 192.0 per 100 000 person-years (95% CI, 169.7-214.3) at more than 12 years (Figure 3, eTable 2 in the Supplement).

In the negative colonoscopy results group, incidence rates increased from 16.6 per 100 000 person-years (95% CI, 6.7-26.6) in year 1 to a high of 133.2 per 100 000 person-years (95% CI, 70.9-227.8) in year 10. Related mortality rates increased from 6.8 per 100 000 person-years (95% CI, 0.8-12.7) in year 1 to a high of 92.2 per 100 000 person-years (95% CI, 19.0-165.4) in year 12 (Figure 3). Incidence rates by site and stage

followed a pattern similar to overall rates, generally increasing gradually with increasing follow-up time (Figure 4; eTable 3 in the Supplement).

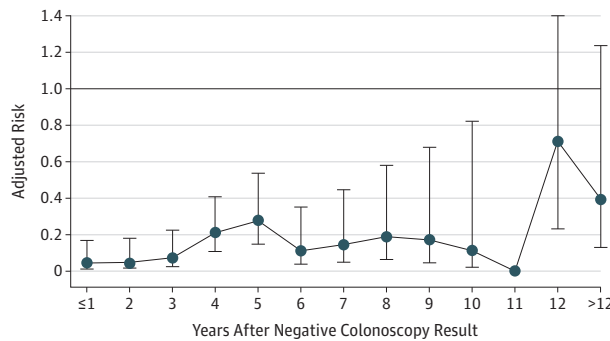
Covariate-Adjusted Risks of Colorectal Cancer and Related Deaths

Compared with the unscreened group, the covariate-adjusted risks of colorectal cancer were reduced by 46% to 95%

across more than 12 years of follow-up in the negative colonoscopy results group, with annual rates all statistically significant with the exception of year 12 when the 95% CI included the null. Hazard ratios ranged from 0.05 (95% CI, 0.02-0.10) at 1 year or less to 0.54 (95% CI, 0.31-0.94) at year 10—the guideline-recommended rescreening interval (Figure 2). There was also a 22% to 87% lower adjusted risk of proximal colorectal cancer, and a 50% to 99% lower risk of distal cancer, across follow-up years in the negative colonoscopy results group, although the 95% CIs included the null after year 7 for proximal cancers and after year 9 for distal cancers (Figure 4). Similarly, there was a 31% to 95% reduced risk of early-stage colorectal cancer, and a 59% to 96% lower risk of advanced-stage colorectal cancer across follow-up in the negative colonoscopy results group, although the 95% CIs included the null after year 9 for early-stage cancers and after year 11 for advanced-stage cancers (Figure 4; eTable 3 in the Supplement). The rate of repeat endoscopic procedures, primarily screening examinations, increased at year 10, consistent with the recommended 10-year rescreening interval (eTable 4 in the Supplement). In a sensitivity analysis during which colonoscopies that had a screening indication were dropped, compared with the unscreened group, the year 10 HR was lower by 47% (HR, 0.53; 95% CI, 0.30-0.93), compared with 46% reported for the main analysis, as noted above.

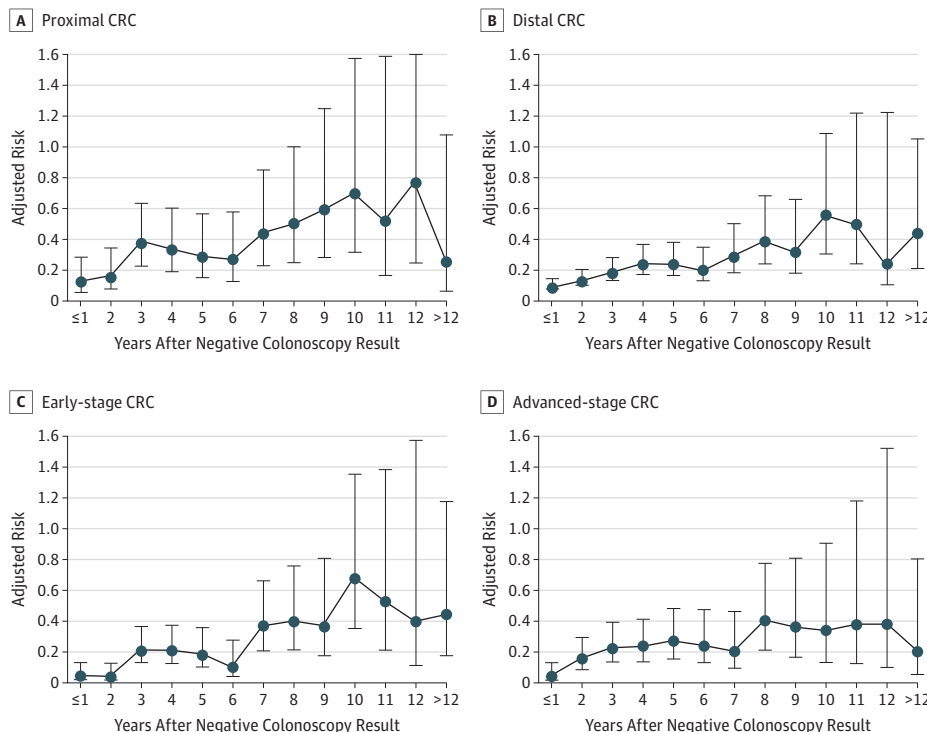
Compared with the unscreened group, the covariate-adjusted risks of colorectal cancer mortality were reduced by 29% to 96% across follow-up in the negative colonoscopy results group, with all annual rates statistically significant, with

Figure 3. Adjusted Risk of Colorectal Cancer Mortality by Time Interval After a Negative Colonoscopy Result



Hazard ratios were obtained by time-varying multivariable Cox proportional hazards models and adjusted for age, sex, race/ethnicity, Charlson comorbidity index score, body mass index, and screening level exposure status prior to negative colonoscopy result (defined as an examination with normal findings). Error bars indicate 95% CIs.

Figure 4. Adjusted Risks of Colorectal Cancer by Time Interval After a Negative Colonoscopy Result: Site- and Stage-Specific Analyses



Adjusted risks for proximal (A), distal (B), early-stage (C), and advanced-stage (D) colorectal cancer. Hazard ratios were obtained by time-varying multivariable Cox proportional hazards models and adjusted for age, sex, race/ethnicity, Charlson comorbidity index score, body mass index, and screening level exposure status prior to negative colonoscopy result (defined as an examination with normal findings). Error bars indicate 95% CIs.

the exception of year 12 and greater than 12 years for which the 95% CIs included the null (Figure 3). Hazard ratios ranged from 0.04 (95% CI, 0.01-0.17) at 1 year or less to 0.71 (95% CI, 0.23-2.22) at year 12. The risk at year 10, the guideline-recommended rescreening interval, remained significantly reduced by 88% (HR, 0.12; 95% CI, 0.02-0.82).

Discussion

Among individuals at average risk for colorectal cancer in this large, community-based setting, compared with those who were unscreened, those who had a negative colonoscopy result had a reduced risk of colorectal cancer and related deaths throughout the more than 12-year follow-up period, and although reductions in risk were attenuated with increasing years of follow-up, there was a 46% lower risk of colorectal cancer and 88% lower risk of related deaths at the current guideline-recommended 10-year rescreening interval. In separate analyses, reduced risks of colorectal cancer were observed by colon site and cancer stage, although 95% CIs were wider and included the null in the later years.

The present study expands knowledge regarding risks of colorectal cancer and related deaths following a negative colonoscopy result by providing annual incidence and mortality rates for more than 12 years following a negative colonoscopy result and for those unscreened from the same background population. To our knowledge, no prior studies have evaluated colorectal cancer mortality, and studies evaluating colorectal cancer risk after a negative colonoscopy result have mostly pooled the time intervals after examination (eg, 5-10 years, 7-10 years) making it difficult to determine the optimal timing for rescreening.²⁹⁻³³ Only 1 study evaluated risk estimates annually since the negative colonoscopy result, and significant incidence reductions up to 14 years were reported.³⁰ However, the study had several limitations, including the use of the general local population as a comparison group, which limited the ability to adjust for differences in important clinical characteristics; lack of censoring at the time of subsequent colonoscopies as additional endoscopy-related interventions (eg, polypectomy) could have altered the amount of time required for cancer to develop after an initial negative colonoscopy result; and the high percentage of cancer cases without a specific location (nearly 30%), which affected site-specific risk estimates.

In another observational study, a paradoxical decrease in risk over pooled time intervals after examination was reported; the risk of colorectal cancer 5.1 to 10.0 years after a negative colonoscopy result (standardized incidence ratio: 0.28; 95% CI, 0.09-0.65) was approximately half that of the risk 1.1 to 2.0 years or 2.1 to 5.0 years after colonoscopy (0.59; 95% CI, 0.48-0.72 and 0.55; 95% CI, 0.41-0.73, respectively).²⁹ Other studies, including a pooled cohort of nurses and other health care professionals, reported sustained reductions in risk, but only within pooled time intervals (7.1-10.0 years and 5.1-10.0 years, respectively) given insufficient power for annual incidence estimates.^{32,33} The present study had a true unscreened control group from the same background popula-

tion and evaluated annual risks for colorectal cancer and related mortality for more than 12 years after a negative colonoscopy result.

The magnitude of risk reduction for colorectal cancer incidence after negative colonoscopy results was greater in the distal than proximal colon, a pattern consistent with prior studies.^{30,33,36} Potential explanations include incomplete examinations and inadequate bowel cleansing of the right colon; difficulty identifying right colon polyps, which tend to be flatter, and sessile serrated adenomas, which are more difficult to see^{18,37-39}; and differences in proximal vs distal polyp biology, leading to different rates of neoplastic progression.^{40,41} For example, microsatellite instability, CpG island methylation, and mucinous histologic characteristics are more frequently seen in proximal than distal lesions, and may influence tumorigenesis.^{40,41}

Our study has policy implications on the timing of rescreening after a negative colonoscopy result. The current guideline-recommended 10-year rescreening interval is not based on a predetermined risk threshold, and while we observed a reduced risk of colorectal cancer and related deaths throughout the more than 12-year follow-up period, an examination of absolute risk (incidence) could provide another justification for the timing for rescreening. For example, if the incidence rate exceeded a predefined threshold, such as the rate among individuals aged 50 to 54 years (59.3 cases per 100 000 person-years according to SEER),⁴² the age for routine initiation of screening and then rescreening at 7 years after a negative colonoscopy result (69.1 cases per 100 000 person-years) could be justified. Additional research is needed to evaluate the costs and benefits of earlier vs later rescreening, optimal rescreening tests following a negative colonoscopy result (eg, another colonoscopy vs annual fecal immunochemical testing), and whether the benefits of rescreening vary between subgroups.

Strengths and Limitations

Strengths of the study include overall, site-specific, and stage-specific cancer risk estimates, and mortality risk estimates by year after a negative colonoscopy result from a large, community-based, average-risk population. The cohort study design avoided or reduced the chance of some of the biases inherent to case-control studies, including selection and recall biases. Screening-test exposures were captured comprehensively via electronic health records. The use of a validated cancer registry enabled accurate and comprehensive detection of colorectal cancers and related deaths. Cancer incidence and mortality rates in the negative colonoscopy results group were compared with unscreened controls from the same background population. To our knowledge, the large sample size enabled evaluation of the overall colorectal cancer risk with higher precision than previous studies.

Study limitations include the possibility of residual confounding inherent to observational studies, including the possibility that differential distribution of unmeasured confounders (eg, red meat intake, smoking) or incompletely measured confounders (eg, family history of colorectal cancer) may have contributed to risk differences between the unscreened and negative colonoscopy results groups. Information on colonoscopy quality measurements, such as extent of examination and bowel

preparation quality, was not available; however, this is unlikely to be a confounder as a prior study with this population reported high rates of colonoscopy completion (98%) and adequate bowel preparation (92%).³⁴ Excluding patients with incomplete examinations would likely only strengthen our findings of the reduced risk of colorectal cancer after a negative colonoscopy result.

The exclusion of colorectal cancers diagnosed within 6 months after a negative colonoscopy result would have overestimated the risk benefit associated with a negative colonoscopy result if these cancers were missed at the index colonoscopy. Overdiagnosis bias stemming from the guideline-recommended 10-year rescreening interval is possible, although in a sensitivity analysis, removal of patients with screening colonoscopies did not significantly affect the HR estimates.

Conclusions

In average-risk, screening-eligible patients, compared with no screening, a negative colonoscopy result was associated with a lower risk of colorectal cancer deaths and overall, proximal, distal, early-stage, and advanced-stage colorectal cancer for more than 12 years after examination. At the guideline-recommended 10-year rescreening interval after a negative colonoscopy result, risks of colorectal cancer and related deaths were 46% and 88% lower, respectively. Our findings can inform guideline recommendations for rescreening and future studies to evaluate the costs and benefits of earlier vs later rescreening intervals.

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