Annals of Internal Medicine ORIGINAL RESEARCH

Long-Term Colorectal Cancer Incidence and Mortality After a Single Negative Screening Colonoscopy

Nastazja Dagny Pilonis, MD; Marek Bugajski, MD, PhD; Paulina Wieszczy, MSc; Robert Franczyk, MD; Joanna Didkowska, PhD; Urszula Wojciechowska, PhD; Malgorzata Pisera, PhD; Maciej Rupinski, MD, PhD; Jaroslaw Regula, MD, PhD; and Michal Filip Kaminski, MD, PhD

Background: Current guidelines recommend a 10-year interval between screening colonoscopies, but evidence is limited.

Objective: To assess the long-term risk for colorectal cancer (CRC) and death from CRC after a high- and low-quality single negative screening colonoscopy.

Design: Observational study.

Setting: Polish Colonoscopy Screening Program.

Participants: Average-risk individuals aged 50 to 66 years who had a single negative colonoscopy (no neoplastic findings).

Measurements: Standardized incidence ratios (SIRs) and standardized mortality ratios (SMRs) of CRC after high- and low-quality single negative screening colonoscopy. High-quality colonoscopy included a complete examination, with adequate bowel preparation, performed by endoscopists with an adenoma detection rate of 20% or greater.

Results: Among 165 887 individuals followed for up to 17.4 years, CRC incidence (0.28 [95% CI, 0.25 to 0.30]) and mortality (0.19 [CI, 0.16 to 0.21]) were 72% and 81% lower, respectively, than in the general population. High-quality examination resulted in 2-fold lower CRC incidence (SIR, 0.16 [CI, 0.13 to 0.20]) and mortality (SMR, 0.10 [CI, 0.06 to 0.14]) than low-quality examination (SIR, 0.32 [CI, 0.29 to 0.35]; SMR, 0.22 [CI, 0.18 to 0.25]). In multivariable analysis, the hazard ratios for CRC incidence after high-quality versus low-quality colonoscopy were 0.55 (CI, 0.35 to 0.86) for 0 to 5 years, 0.54 (CI, 0.38 to 0.77) for 5.1 to 10 years, and 0.46 (CI, 0.25 to 0.86) for 10 to 17.4 years. Only after high-quality colonoscopy did the SIR and SMR for 10.1 to 17.4 years of follow-up not differ compared with earlier observation periods.

Limitation: The general population was used as the comparison group.

Conclusion: A single negative screening colonoscopy was associated with reduced CRC incidence and mortality for up to 17.4 years. Only high-quality colonoscopy yielded profound and stable reductions in CRC incidence and mortality throughout the entire follow-up.

Primary Funding Source: Polish Ministry of Health.

Ann Intern Med. 2020;173:81-91. doi:10.7326/M19-2477 **Annals.org**
For author, article, and disclosure information, see end of text.
This article was published at Annals.org on 26 May 2020.

In the average-risk population, current clinical practice guidelines recommend screening colonoscopies at 10-year intervals when results are negative (1–3). In 1997, this 10-year interval was endorsed based on indirect evidence, including the biological plausibility of the adenoma–carcinoma sequence and extrapolations from studies assessing colonoscopy sensitivity (4). However, the optimal screening interval after normal colonoscopy remains uncertain owing to the paucity of long-term data on the efficacy of colonoscopy.

The results of 3 studies indicate that the predictive benefit of a single negative colonoscopy may exceed 10 years (5–7); however, none was performed in a screening population. One study analyzed the efficacy of negative screening colonoscopy beyond 12 years of follow-up (8), but it was limited by the small number of individuals observed longer than 10 years and a high rate of repeat colonoscopy. Moreover, these studies did not assess baseline colonoscopy quality, and high-quality examination is a prerequisite for the recommended interval (9, 10).

The putative long-term efficacy of colonoscopy in the distal colorectum has been extrapolated from randomized trials of single flexible sigmoidoscopy, showing sustained reductions of colorectal cancer (CRC) incidence and mortality lasting at least 17 years (11–13). However, available data indicate that colonoscopy has little or no effect on the incidence of or mortality from cancer in the proximal colon (14, 15). One possible reason is the effect of baseline colonoscopy quality—in terms of adequate bowel preparation, cecal intubation, and adenoma detection rate (ADR)—which is more difficult to achieve in the proximal colon. No study has examined the effect of examination quality on long-term incidence and mortality of CRC in the proximal colon.

To address these evidence gaps, we performed a large cohort study to analyze long-term CRC incidence and mortality after a single high-quality or low-quality screening colonoscopy with negative results.

Methods

Study Design and Oversight

We analyzed long-term CRC incidence and mortality in a cohort of average-risk individuals (no family history of CRC) who had a single negative screening

See also:

Web-Only
Supplement

colonoscopy in the Polish Colonoscopy Screening Program (16). The cohort was followed by using linkage with the National Cancer Registry and population registries. Written informed consent was obtained from all screened individuals. The research proposal was reviewed by the local ethics committee and deemed exempt from oversight.

Polish Colonoscopy Screening Program and Study Population

In October 2000, a national CRC screening program was launched in Poland. Since then, primary screening colonoscopy has been offered to asymptomatic average-risk individuals aged 50 to 66 years, either in the opportunistic setting every 10 years or once in the individual's lifetime in a postal invitation–based program (introduced in 2014).

Our study cohort comprised individuals who had a single negative screening colonoscopy in the Polish Colonoscopy Screening Program between October 2000 and December 2011. All individuals had opportunistic screening colonoscopy—that is, participation was advised by general or family practitioners. After screening in the opportunistic setting, they were excluded from the invitation-based screening program and thus could not receive a second screening colonoscopy through the invitation-based program. Only participants who were still in the screening age range after 10 years could receive a second screening colonoscopy in the opportunistic setting.

To assess our cohort's exposure to further screening in the opportunistic setting, we analyzed the database and found that 2.4% had undergone a second screening colonoscopy. The screening program is entirely financed by the Polish Ministry of Health, independent of the general health care system, and screening colonoscopy outside of the screening program is not reimbursed by the public health sector. Analysis of medical registry records showed that private screening colonoscopies comprise less than 5% of screening colonoscopies in Poland. Overall, it is estimated that 8% of the Polish population undergoes screening colonoscopy.

"Negative colonoscopy" was defined as an examination not revealing any neoplastic lesion. Our analysis excluded individuals with a family history of CRC (at least 1 first-degree relative with CRC), hereditary CRC syndrome, screening in the past 10 years, screen-detected CRC, or CRC diagnosis within 6 months after index colonoscopy. To evaluate baseline colonoscopy quality, our analysis included only individuals examined by an endoscopist who performed 30 or more screening colonoscopies annually.

Assessment of Colonoscopy Quality

The Polish Colonoscopy Screening Program database includes integrated colonoscopy and histopathology results, with mandatory reporting of the following quality indicators: cecal intubation, bowel preparation adequacy, and the endoscopist's annual ADR. The records are verified annually for completeness by external auditors.

Cecal intubation was defined as passage of the colonoscope tip to a point proximal to the ileocecal valve and complete visualization of the whole cecum and its landmarks (17). Bowel preparation adequacy was reported by using the Aronchick Scale (18). The endoscopist's annual ADR was defined as the proportion of screening colonoscopies with adenoma detection (19). Colonoscopies were categorized as high-quality if they met all of the following criteria: cecal intubation, adequate bowel preparation (very good, good, or sufficient), and endoscopist ADR of 20% or greater calculated on a yearly basis (the suggested quality threshold at the time of examination) (19).

Follow-up for CRC Incidence and Mortality

The study cohort was followed for CRC incidence and death by using the Polish Colonoscopy Screening Program database, the National Cancer Registry, and the Population Registry, which are interlinked by unique personal identification numbers. The Polish Colonoscopy Screening Program database is estimated as virtually 100% complete because reporting is mandatory for reimbursement. All cancers diagnosed in Poland must be reported to the National Cancer Registry, which is estimated as 94% complete (20). The date of cancer diagnosis and the date and cause of death were ascertained by using International Classification of Diseases, 10th edition (ICD-10), codes. The site of CRC was determined according to ICD-10 codes and was categorized as proximal (C18.0 to 18.5) or distal (C18.6, C18.7, C19, C20). Cases of unknown location (C18.9) were excluded from site-specific analysis.

Statistical Analysis

The study cohort was followed for CRC incidence and mortality after the date of index screening colonoscopy. For CRC incidence analysis, observation was completed at CRC diagnosis or censored at the time of death or end of follow-up (31 December 2017), whichever occurred first (**Supplement Table 1**, available at Annals.org). For CRC mortality analysis, observation was completed at CRC death, or censored at the time of non–CRC-related death or end of follow-up. For proximal CRC incidence and mortality, follow-up was additionally censored at time of distal CRC diagnosis. Individuals were stratified by sex for separate analysis of CRC risk and death in men and women. Person-years of follow-up were calculated for the total follow-up period and for 3 periods: 5 years or less, 5.1 to 10 years, and 10.1 or more years since colonoscopy. For analysis of the periods of 5.1 to 10 years and 10.1 or more years, we excluded all individuals with follow-up shorter than 5 and 10 years, respectively.

We calculated standardized incidence ratios (SIRs) and standardized mortality ratios (SMRs) as the number of observed CRCs and CRC deaths, respectively, in the cohort divided by the expected number of CRCs and CRC deaths that would occur in the general population, matched by sex, 5-year age group, and calendar year of follow-up (National Cancer Registry data) (**Supplement Table 2**, available at Annals.org). We calculated 95% CIs for SIRs and SMRs, assuming that event occur-

rence followed a Poisson distribution (21). If the observed number of events was less than 5, an exact method was used to calculate the CI; otherwise, a normal approximation was used. Between-subgroup differences in SIRs and SMRs were considered statistically significant if the 95% CIs did not overlap (22).

In sensitivity analysis, we compared the low-quality and high-quality groups by using Cox proportional hazard models adjusted for patient sex, age (<55, 55 to 59, or 60 to 66 years), type of health care facility (university hospital, public hospital, or private practice), endoscopist's specialty (gastroenterologist, surgeon, or internal medicine specialist), and average monthly gross salary in the region where screening colonoscopy was performed. Average monthly gross salary was calculated for each region (*powiat*) of Poland and year as a relative ratio to the national average and was divided into 3 groups (<95%, 95% to 104.9%, or ≥105%) (23). No variable selection algorithm was applied.

Cumulative incidence and mortality were estimated by using competing risks regression, following the model of Fine and Gray. The cumulative incidence rates were assessed by using values from the cumulative incidence estimate. Covariate values incorporated in the cumulative incidence curves were set to the average population. A failure event was defined as development of CRC for incidence or death from CRC for mortality, and a competing event was defined as death from another cause. The model estimates were adjusted for patient sex, age group (<40, 40 to 54, 55 to 59, or ≥60 years), health care facility, the endoscopist's specialty, and average monthly gross salary in the region where the screening colonoscopy was performed. We accounted for within-physician clustering by using clustered sandwich estimator of variance for both the Cox and the Fine and Gray models. We assumed an exchangeable correlation: That is, the SEs allow for intragroup correlation.

P values less than 0.05 were considered statistically significant. All analyses were performed by using Stata software, version 15.1, and R statistical software, version 3.4.1.

Role of Funding Source

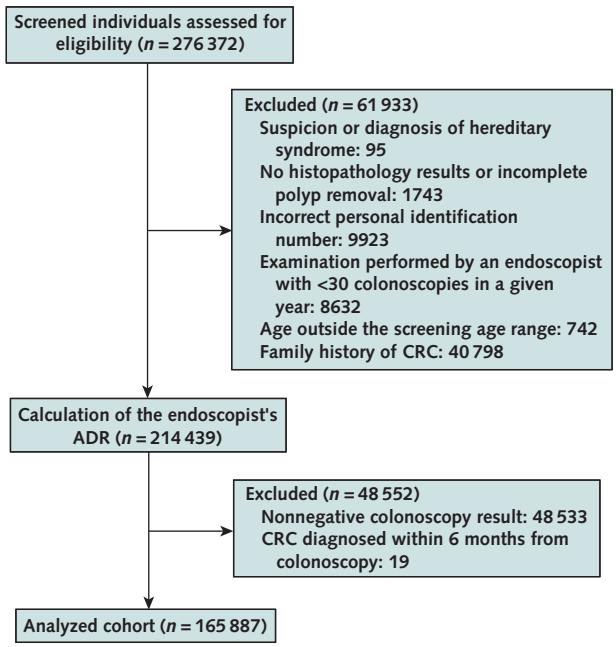
The study was supported by the Polish Ministry of Health, the Medical Center for Postgraduate Education in Warsaw (grant 5011091217/18), and the Polish Foundation of Gastroenterology. The funding sources had no role in the design, conduct, or reporting of the study.

RESULTS

Study Population

Among 276 372 individuals screened over the study period, 110 485 (40.0%) were excluded owing to nonnegative colonoscopy (48 533 [17.6%]), lack of histopathology results or incomplete polyp removal (1743 [0.6%]), suspicion or diagnosis of hereditary cancer syndrome (95 [<0.1%]), age outside of the screening age range (742 [0.3%]), incorrect personal identification number (9923 [3.6%]), examination by an endoscopist who performed fewer than 30 screening colonoscopies per year (8632 [3.1%]), or family history of CRC (40 798 [14.8%]). We also excluded 19 individuals who were diagnosed with CRC within 6 months after screening colonoscopy (**Figure 1**), of whom 12 were suspected to have CRC at baseline examination.

Figure 1. Study flow diagram.



ADR = adenoma detection rate; CRC = colorectal cancer.

Table 1 shows the characteristics of the 165 887 individuals in the study cohort, overall and according to examination quality. Screening colonoscopies in the analyzed cohort were performed by 505 different endoscopists. The number of procedures performed per endoscopist and the ADR distribution are shown in **Supplement Figures 1** and **2** (available at Annals.org). In the cohort, 113 513 individuals had low-quality colonoscopy and 52 374 had high-quality colonoscopy.

CRC Incidence and Mortality Rates

The study cohort was followed up to 17.4 years (median, 10.1 years). The distribution of follow-up time after low-quality and high-quality colonoscopy is shown in **Supplement Figure 3** (available at Annals.org). Over 1 680 765 person-years of follow-up, CRC was diagnosed in 489 individuals (cumulative incidence rate, 29.09 cases per 100 000 person-years [95% CI, 26.57 to 31.79]). Over 1 682 359 person-years of follow-up, 169 CRC-related deaths were identified (mortality rate, 10.05 deaths per 100 000 person-years [CI, 8.59 to 11.68]). **Table 2** shows CRC incidence and mortality rates after high-quality and low-quality single negative screening colonoscopy across the follow-up time. Cu-

Table 1. Characteristics of the Negative Screening Colonoscopy Cohort*

Characteristic	Overall (*N* = 165 887)	Low-Quality Colonoscopy (*n* = 113 513)	High-Quality Colonoscopy (*n* = 52 374)
Age, *y*			
Range	40–66	40–66	40–66
Mean (SD)	56.6 (4.6)	56.6 (4.7)	56.8 (4.4)
Age group, *n (%)*			
40–49 y	4466 (2.7)	3626 (3.2)	840 (1.6)
50–54 y	53 814 (32.4)	36 956 (32.6)	16 858 (32.2)
55–59 y	59 100 (35.6)	40 029 (35.3)	19 071 (36.4)
60–66 y	48 507 (29.2)	32 902 (29.0)	15 605 (29.8)
Sex, *n (%)*			
Male	57 489 (34.7)	39 763 (35.0)	17 726 (33.9)
Female	108 398 (65.3)	73 750 (65.0)	34 648 (66.2)
Cecal intubation, *n (%)*			
Yes	157 572 (95.0)	105 198 (92.7)	52 374 (100)
No	8315 (5.0)	8915 (7.3)	0
Bowel preparation, *n (%)*			
Very good, good, or sufficient	157 972 (94.6)	104 598 (92.2)	52 374 (100)
Poor or very poor	8915 (5.4)	8315 (7.9)	0
Endoscopist ADR, *n (%)*			
≥20%	57 899 (34.9)	5525 (4.9)	52 374 (100)
<20%	107 988 (65.1)	107 988 (95.1)	0

ADR = adenoma detection rate.
* Because of rounding, percentages may not total 100.

mulative incidence and mortality curves are presented in Supplement Figure 4 (available at Annals.org).

Standardized CRC Incidence and Mortality Rates During Follow-up

Compared with the general population, in our cohort, CRC incidence was lower by 72% (SIR, 0.28 [CI, 0.25 to 0.30]) and CRC mortality by 81% (SMR, 0.19 [CI, 0.16 to 0.21]). Beyond 10 years of follow-up, the SIR was 0.31 (CI, 0.24 to 0.37) and the SMR was 0.27 (CI, 0.19 to 0.34), showing reductions of CRC incidence and mortality similar to those observed for the period of 5.1 to 10 years (SIR, 0.30 [CI, 0.26 to 0.34] and SMR, 0.21 [CI, 0.17 to 0.26]).

Colonoscopy Quality and CRC Incidence and Mortality

Figure 2 shows the SIRs and SMRs of CRC after high- and low-quality single negative screening colonoscopy across follow-up. Overall, CRC incidence and mortality were significantly lower after high-quality colonoscopy than after low-quality examination. Notably, the reduced CRC incidence after high-quality colonoscopy remained stable throughout all study in-

Table 2. Incidence of and Mortality Rates From CRC per 100 000 Person-Years After High-Quality and Low-Quality Single Negative Screening Colonoscopy Across Follow-up

End Point	Time After Single Negative Screening Colonoscopy, by Colonoscopy Quality					
	0–5.0 Years			5.1–10.0 Years		
	Overall	Low-Quality	High-Quality	Overall	Low-Quality	High-Quality
CRC incidence						
Individuals, *n*	165 887	113 513	52 374	163 476	111 861	51 615
Person-years at risk	824 499	564 238	260 261	658 962	470 232	188 731
Cases of CRC, *n*	163	131	32	232	193	39
Expected cases of CRC, *n*	679	464	215	780	559	221
Incidence rate (95% CI)	19.77 (16.73–22.80)	23.22 (19.24–27.19)	12.30 (8.04–16.56)	35.21 (30.68–39.74)	41.04 (35.25–46.83)	20.66 (14.18–27.15)
SIR (95% CI)	0.24 (0.20–0.28)	0.28 (0.23–0.33)	0.15 (0.10–0.20)	0.30 (0.26–0.34)	0.35 (0.30–0.39)	0.18 (0.12–0.23)
CRC mortality						
Individuals, *n*	165 887	113 513	52 374	163 601	111 961	51 640
Person-years at risk	824 771	564 465	260 306	197 805	161 974	35 832
Cases of CRC, *n*	35	28	7	87	74	13
Expected cases of CRC, *n*	325	222	103	406	291	114
Mortality rate (95% CI)	4.24 (2.84–5.65)	4.96 (3.12–6.80)	2.69 (0.70–4.68)	13.19 (10.42–15.96)	15.71 (12.13–19.29)	6.88 (3.14–10.62)
SMR (95% CI)	0.11 (0.07–0.14)	0.13 (0.08–0.17)	0.07 (0.02–0.12)	0.21 (0.17–0.26)	0.25 (0.20–0.31)	0.11 (0.05–0.18)

CRC = colorectal cancer; SIR = standardized incidence ratio; SMR = standardized mortality ratio.

tervals (≤5 years, 5.1 to 10 years, and >10 years after index colonoscopy). Mortality from CRC after high-quality colonoscopy was significantly lower 5.1 to 10 years after examination. The cumulative incidence rates of CRC after 15 years were 0.30% and 0.56% after a single high- and low-quality negative screening colonoscopy, respectively. In addition, in multivariate analysis, the risk for CRC was significantly lower among individuals who had high-quality colonoscopy than those who had low-quality colonoscopy. Hazard ratios for CRC after high-quality colonoscopy remained stable throughout the entire follow-up (Table 3).

We also assessed how ADR cutoff points of 15%, 25%, and 30% influence CRC incidence and mortality. Overall, there was no substantial difference in the obtained SIRs and SMRs compared with the 20% ADR reference used in our study (Supplement Table 3, available at Annals.org).

Incidence of and Mortality From CRC According to Sex

The incidence of and mortality rates from CRC per 100 000 person-years were 30.9 cases (CI, 26.53 to 35.79 cases) and 9.88 deaths (CI, 7.49 to 12.81 cases) in men and 28.15 cases (CI, 25.11 to 31.46 cases) and 10.13 deaths (CI, 8.34 to 12.19 cases) in women. Table 4 shows the numbers of CRC cases and deaths and the SIRs and SMRs of CRC in women and men, according to examination quality and time from colonoscopy. Overall, SIRs and SMRs significantly differed between men and women, but this difference was not observed after high-quality examination. In both men and women, the reduced CRC incidence after colonoscopy remained stable for all studied intervals (≤5 years, 5.1 to 10 years, and >10 years after index colonoscopy). For CRC mortality, stable reduction was observed only for men, whereas in women this was observed only after high-quality examination.

Proximal CRC Incidence and Mortality

Table 5 shows the number of proximal and distal CRC cases and SIRs and SMRs of proximal and distal CRC according to examination quality and time from colonoscopy. Proximal CRC incidence was reduced by 73% after high-quality screening (SIR, 0.27 [CI, 0.17 to 0.36]), whereas this reduction was significantly lower after low-quality screening (SIR, 0.55 [CI, 0.47 to 0.64]). Notably, proximal SMR was significantly reduced after high-quality colonoscopy (SMR, 0.50 [CI, 0.19 to 0.81]) but not after low-quality examination (SMR, 0.92 [CI, 0.67 to 1.18]).

DISCUSSION

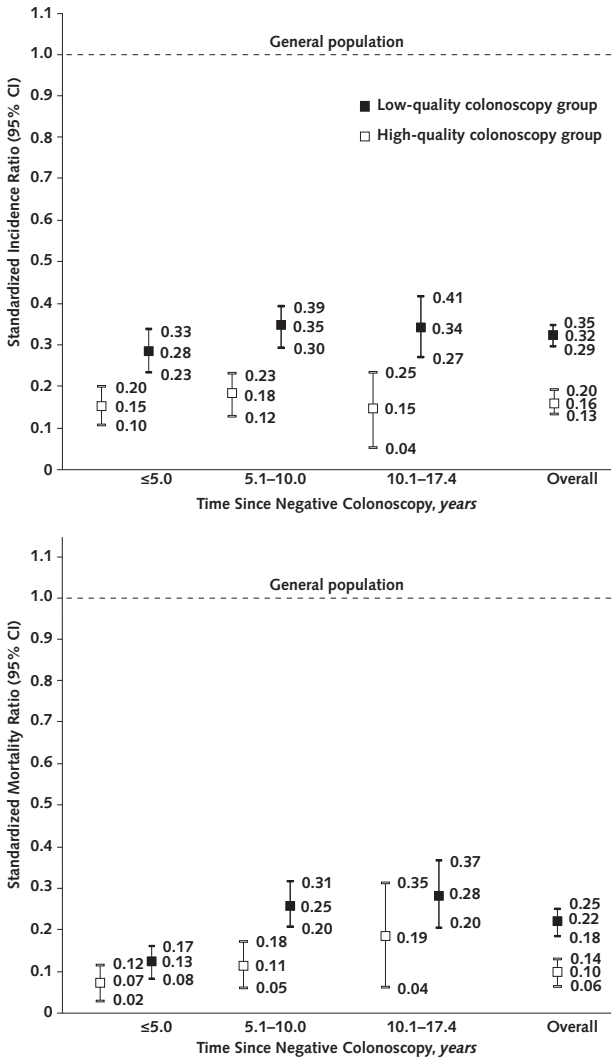
The results of this large population-based study demonstrated that persons with a single screening colonoscopy with a negative result had significantly reduced CRC incidence and mortality over the following 17.4 years. The reduction rates for the period beyond the currently recommended 10-year interval (10 to 17.4 years) did not significantly differ from those in the earlier observation periods. This was mainly driven by long-lasting reductions in CRC incidence and mortality (by 84% and 90%, respectively) after high-quality screening colonoscopies. High quality was key for the profound long-term efficacy of screening colonoscopy in the proximal colon, and among women. These findings are of paramount importance, because previous reports have questioned the efficacy of colonoscopy in the proximal colon (6, 7, 15, 24) and of screening sigmoidoscopy in women (25).

The currently recommended 10-year screening colonoscopy intervals were selected on the basis of limited evidence regarding the durability of its effectiveness (4). Recent reports have suggested that colonoscopy effectiveness may extend beyond the recommended 10 years, although they have been limited by short follow-up

Table 2–Continued

Time After Single Negative Screening Colonoscopy, by Colonoscopy Quality					
10.1-17.4 Years			Entire Follow-up Period		
Overall	Low-Quality	High-Quality	Overall	Low-Quality	High-Quality
86 365	67 525	18 840	165 887	113 513	52 374
197 304	161 526	35 778	1 680 765	1 195 996	484 770
94	86	8	489	410	79
308	253	55	1766	1276	491
47.64 (38.01-57.27)	53.24 (41.99-64.49)	22.36 (6.87-37.85)	29.09 (26.52-31.67)	34.28 (30.96-37.60)	16.30 (12.70-19.89)
0.31 (0.24-0.37)	0.34 (0.27-0.41)	0.15 (0.04-0.25)	0.28 (0.25-0.30)	0.32 (0.29-0.35)	0.16 (0.13-0.20)
86 536	67 671	18 865	165 887	113 513	52 374
659 783	470 905	188 878	1 682 359	1 197 344	485 015
47	41	6	169	143	26
176	144	32	906	657	249
23.76 (16.97-30.55)	25.31 (17.56-33.06)	16.74 (3.35-30.14)	10.05 (8.53-11.56)	11.94 (9.99-13.90)	5.36 (3.30-7.42)
0.27 (0.19-0.34)	0.28 (0.20-0.37)	0.19 (0.04-0.35)	0.19 (0.16-0.21)	0.22 (0.18-0.25)	0.10 (0.06-0.14)

Figure 2. Standardized incidence ratios and standardized mortality ratios during follow-up after a single negative high-quality or low-quality screening colonoscopy.



(6, 8), small screening cohorts (7, 8), mixed or nonscreening populations (6, 7, 15), case–control design (15, 24), high rates of repeated colonoscopies (7, 8), and lack of information on baseline examination quality (6–8, 15, 24). In a cohort of patients after adenoma removal, the reduction in CRC mortality was similar during the first 10 years of follow-up and afterward (26). Subsequent case–control and cohort studies have also demonstrated low yields of large polyps (27) or advanced neoplasia (28) within the 10-year surveillance periods after negative screening colonoscopy, and low additional benefit of repeated colonoscopy at 10 years (29). Our present results are in line with these previous studies and extend the evidence to the screening population, far beyond the recommended 10-year interval, and using relevant end points of CRC incidence and mortality. Recent analyses suggest that 20-year or 15-year intervals between screening colonoscopies may have the same cost-effectiveness as the 10-year interval (30, 31). Moreover, the cumulative incidence rates of CRC in the study cohort after 15 years were 0.30% and 0.56% for an individual after single high- and low-quality negative screening colonoscopy, respectively. This 15-year CRC risk is substantially lower than the 3% threshold used to recommend screening in the recent guidelines (32).

To our knowledge, ours is the first study to include baseline examination quality in the analysis of long-term risk for CRC and mortality after negative colonoscopy. Our analyses are key for understanding the effect of examination quality on CRC risk beyond 10 years, colonoscopy effectiveness in the proximal colon, and the difference in risk between women and men. The SIRs and SMRs at more than 10 years after high-quality colonoscopy were not significantly different from those in earlier observation periods. In contrast, with low-quality examination, SMRs became significantly higher after the first 5 years of observation. The SIRs were 2-fold higher after low-quality examinations than after high-quality examinations in each of the 3 observation periods. These findings suggest that up to 17.4 years after negative colonoscopy, many cases of CRC arise from lesions missed at baseline examination rather than from newly developed lesions. Similarly, previous results suggest that more than 50% of postcolonoscopy cases of CRC arise from missed lesions (33). Although zero risk cannot be proven, it seems that subsequent screening at 10 years would add little to the more than 80% reduction in CRC risk, and the very low 15-year CRC risk of 0.24%, after high-quality baseline examination. Each component of high-quality examination—cecal intubation, adequate bowel preparation, and ADR of 20% or greater—contributed to the observed colonoscopy efficacy, with ADR (34, 35) being most important (**Supplement Table 4**, available at Annals.org). Of note, use of ADR cutoffs of 15% to 30% did not substantially change our main findings.

Compared with low-quality negative screening colonoscopy, high-quality examination was associated with a 2-fold greater reduction in the risk for proximal colon cancer throughout the 17.4-year follow-up. Furthermore, only high-quality negative screening colonoscopy yielded a significant reduction in proximal CRC mortality. These findings may explain previous results showing that risk reduction did not extend beyond 7 years after baseline examination of unspecified quality (6). Moreover, other reports demonstrate that colonoscopies performed before the quality assurance era had little or no effect on proximal CRC incidence and death (7, 15, 24). Colonoscopy quality indicators—cecal intubation rate, adequate bowel preparation, and the endoscopist's ADR (9, 36)—are particularly important for efficacy in the proximal colon. Naturally, if the cecum is not reached, proximal colon assessment is incomplete. Moreover, an inadequate

preparation is more likely in the proximal colon, potentially hampering its visualization. Proximal colon lesions are flatter and are often located on the proximal side of folds, requiring a skilled endoscopist to detect them (37). Finally, some proximal precursor lesions (for example, sessile serrated polyps) are very subtle and indistinct, such that endoscopists require specific knowledge to recognize and differentiate them from surrounding healthy mucosa (38). In our study cohort, we cannot prove that high-quality colonoscopy was associated with better detection of sessile serrated polyps, but other studies have shown that high ADR is correlated with detection of sessile serrated polyps (39). Our results suggest that high-quality colonoscopy provides long-lasting reductions in distal and proximal CRC incidence and mortality, but the magnitude of effect may still be lower for the proximal colon.

Examination quality particularly affected CRC incidence and mortality in women. After high-quality colonoscopy, the incidence and mortality reduction rates in women were similar to those in men and were stable across the entire follow-up. After low-quality colonoscopy, incidence rates in women were significantly higher than the rates observed in men throughout the follow-up. This was also seen for mortality rates during 5.1 to 10 years after examination. This indicates that high-quality examination is crucial for ensuring the higher effectiveness of screening colonoscopy over sigmoidoscopy, because the latter reportedly has little or no effect on CRC incidence and mortality in women (25) and for proximal colon cancer (40).

Our study has limitations. First, comparison of CRC incidence and mortality between our cohort and the general population was limited by the inability to adjust for differences in risk factors other than age and sex. Furthermore, this comparison allowed quantification of the predictive but not protective effects of screening, because negative screening colonoscopy does not include therapeutic intervention; rather, it ascertains that an individual is free of neoplasia at that time. However, our aims were to analyze CRC incidence and mortality within and beyond the currently recommended 10-year interval, and their relation with baseline examination quality. For this purpose, comparison of our cohort with the general population seems sufficient. To assess the roles of other potential confounders, we performed multivariable analyses with the calculated risks for CRC and death adjusted for age, sex, examination quality, annual income (to approximate socioeconomic status), facility type, and endoscopist's training level. Participant income played a significant confounding role and was probably associated with other unmeasured but well-established CRC risk factors, such as diet, body mass index, and physical activity. Al-

Table 3. Hazard Ratios for CRC and Death From CRC*

Variable	CRC Incidence		CRC Mortality	
	Hazard Ratio (95% CI)	*P* Value	Hazard Ratio (95% CI)	*P* Value
High- vs. low-quality				
0–5 y of follow-up	0.55 (0.35–0.86)	0.009	0.55 (0.22–1.37)	>0.2
5–10 y of follow-up	0.54 (0.38–0.77)	0.001	0.47 (0.25–0.88)	0.018
>10 y of follow-up	0.46 (0.25–0.86)	0.016	0.74 (0.33–1.63)	>0.2
Individual's sex				
Female (reference)	1		1	
Male	1.08 (0.90–1.29)	>0.2	0.95 (0.69–1.32)	>0.2
Individual's age				
<55 y (reference)	1		1	
55–59 y	1.31 (1.02–1.70)	0.035	1.11 (0.69–1.79)	>0.2
60–66 y	2.39 (1.88–3.03)	<0.001	3.29 (2.27–4.77)	<0.001
Type of health care facility				
University hospital (reference)	1		1	
Public hospital	1.24 (0.95–1.62)	0.116	1.17 (0.77–1.79)	>0.2
Private practice	1.19 (0.92–1.56)	0.189	1.42 (0.94–2.15)	0.097
Endoscopist's specialty				
Gastroenterologist (reference)	1		1	
Surgeon	1.14 (0.95–1.38)	0.159	1.24 (0.92–1.67)	0.153
Internal medicine specialist	0.97 (0.68–1.39)	>0.2	0.83 (0.43–1.59)	>0.2
Average monthly gross salary†				
<95% (reference)	1		1	
95%–104.9%	0.71 (0.58–0.88)	0.002	0.60 (0.40–0.89)	0.011
≥105%	0.70 (0.55–0.90)	0.005	0.61 (0.42–0.90)	0.011

CRC = colorectal cancer.
* Multivariable Cox model.
† With respect to the national average (Poland = 100%).

Table 4. SIRs and SMRs of CRC, Stratified by Sex*

End Point	Time After Single Negative Screening Colonoscopy, by Colonoscopy Quality					
	0–5.0 Years			5.1–10.0 Years		
	Overall	Low-Quality	High-Quality	Overall	Low-Quality	High-Quality
Women						
CRC cases						
Observed, *n*	107	87	20	143	120	23
Expected, *n*	357	242	115	398	283	116
SIR (95% CI)	0.30 (0.24–0.36)	0.36 (0.28–0.44)	0.17 (0.10–0.25)	0.36 (0.30–0.42)	0.42 (0.35–0.50)	0.20 (0.12–0.28)
CRC deaths						
Observed, *n*	21	17	4	61	53	8
Expected, *n*	163	111	53	198	140	57
SMR (95% CI)	0.13 (0.07–0.18)	0.15 (0.08–0.23)	0.08 (0.02–0.19)	0.31 (0.23–0.39)	0.38 (0.28–0.48)	0.14 (0.04–0.24)
Men						
CRC cases						
Observed, *n*	56	44	12	89	73	16
Expected, *n*	321	222	99	382	276	105
SIR (95% CI)	0.17 (0.13–0.22)	0.20 (0.14–0.26)	0.12 (0.05–0.19)	0.23 (0.18–0.28)	0.26 (0.20–0.33)	0.15 (0.08–0.23)
CRC deaths						
Observed, *n*	14	11	3	26	21	5
Expected, *n*	161	111	50	208	151	57
SMR (95% CI)	0.09 (0.04–0.13)	0.10 (0.04–0.16)	0.06 (0.01–0.18)	0.12 (0.08–0.17)	0.14 (0.08–0.20)	0.09 (0.01–0.16)

CRC = colorectal cancer; SIR = standardized incidence ratio; SMR = standardized mortality ratio.
* All SIRs and SMRs with nonoverlapping 95% CIs are considered significantly different.

though these risk factors could have resulted in a lower overall risk for CRC incidence and death (healthy volunteer bias), they should have a limited effect on the stability of the protective effect of colonoscopy, which was the main focus of this study. In addition, our comparison with the general population, of which some proportion (~10%) was actually exposed to screening, indicates that the results are not biased in favor of screening colonoscopy.

Second, the data on CRC diagnoses and deaths were derived from the National Cancer Registry, which is 90% complete (20). Registration completeness remained relatively stable over the follow-up, and it is assumed not to influence our study results. In addition, the follow-up time was slightly shorter for persons who had high-quality colonoscopy than those who had low-quality colonoscopy. This is a nat-

Table 5. SIRs and SMRs of CRC, Stratified by Tumor Site*

End Point	Time After Single Negative Screening Colonoscopy, by Colonoscopy Quality					
	0–5.0 Years			5.1–10.0 Years		
	Overall	Low-Quality	High-Quality	Overall	Low-Quality	High-Quality
Proximal CRC cases						
Observed, *n*	51	43	8	107	88	19
Expected, *n*	140	95	45	183	130	53
SIR (95% CI)	0.36 (0.26–0.46)	0.45 (0.32–0.59)	0.18 (0.05–0.30)	0.58 (0.47–0.70)	0.68 (0.54–0.82)	0.36 (0.20–0.52)
Distal CRC cases						
Observed, *n*	91	70	21	93	78	15
Expected, *n*	459	314	145	514	369	146
SIR (95% CI)	0.20 (0.16–0.24)	0.22 (0.17–0.28)	0.14 (0.08–0.21)	0.18 (0.14–0.22)	0.21 (0.16–0.26)	0.10 (0.05–0.15)
Deaths from proximal CRC						
Observed, *n*	12	11	1	32	26	6
Expected, *n*	23	15	8	34	24	10
SMR (95% CI)	0.52 (0.23–0.82)	0.73 (0.30–1.17)	0.12 (0.00–0.70)	0.94 (0.62–1.27)	1.08 (0.67–1.50)	0.60 (0.12–1.08)
Deaths from distal CRC						
Observed, *n*	10	6	4	37	34	3
Expected, *n*	171	114	56	246	175	71
SMR (95% CI)	0.06 (0.02–0.09)	0.05 (0.01–0.09)	0.07 (0.02–0.18)	0.15 (0.10–0.20)	0.19 (0.13–0.26)	0.04 (0.01–0.12)

CRC = colorectal cancer; SIR = standardized incidence ratio; SMR = standardized mortality ratio.
* The analysis excluded 86 CRCs (14.3%) coded without a specified tumor site. All SIRs and SMRs with nonoverlapping 95% CIs are considered significantly different.

Table 4–Continued

Time After Single Negative Screening Colonoscopy, by Colonoscopy Quality					
10.1–17.4 Years			Entire Follow-up		
Overall	Low-Quality	High-Quality	Overall	Low-Quality	High-Quality
61	56	5	311	263	48
156	126	30	912	651	261
0.39 (0.29–0.49)	0.44 (0.33–0.56)	0.17 (0.02–0.31)	0.34 (0.30–0.38)	0.40 (0.36–0.45)	0.18 (0.13–0.24)
30	26	4	112	96	16
85	69	16	446	319	126
0.35 (0.23–0.48)	0.38 (0.23–0.58)	0.25 (0.07–0.64)	0.25 (0.20–0.30)	0.30 (0.24–0.36)	0.13 (0.06–0.19)
33	30	3	178	147	31
152	127	25	855	625	230
0.22 (0.14–0.29)	0.24 (0.15–0.32)	0.12 (0.02–0.35)	0.21 (0.18–0.24)	0.24 (0.20–0.27)	0.13 (0.09–0.18)
17	15	2	57	47	10
90	76	15	460	338	122
0.19 (0.10–0.28)	0.20 (0.10–0.30)	0.13 (0.02–0.48)	0.12 (0.09–0.16)	0.14 (0.10–0.18)	0.08 (0.03–0.13)

ural consequence of improving colonoscopy quality over the study inclusion period (41).

Finally, we could not assess whether the study individuals had repeat examination outside of the Polish Colonoscopy Screening Program. We estimate that this rate is low, because screening colonoscopy is not reimbursed in the public health care system outside of the Polish Colonoscopy Screening Program, and screening colonoscopy through the private health care system is uncommon. There is no reason to believe that this introduced bias, because the analyzed groups should not differ in National Cancer Registry completeness or access to private health services.

In summary, we found that a single negative screening colonoscopy was associated with reduced CRC incidence and mortality over up to 17.4 years of follow-up. Only high-quality colonoscopy provided a profound and stable reduction in both CRC incidence and mortality throughout follow-up. These results suggest that the currently recommended 10-year interval

Table 5–Continued

Time After Single Negative Screening Colonoscopy, by Colonoscopy Quality					
10.1–17.4 Years			Entire Follow-up		
Overall	Low-Quality	High-Quality	Overall	Low-Quality	High-Quality
33	30	3	191	161	30
80	66	15	403	291	112
0.41 (0.27–0.55)	0.45 (0.29–0.62)	0.20 (0.04–0.58)	0.47 (0.41–0.54)	0.55 (0.47–0.64)	0.27 (0.17–0.36)
47	42	5	231	190	41
198	163	35	1171	845	326
0.24 (0.17–0.31)	0.26 (0.18–0.34)	0.14 (0.02–0.27)	0.20 (0.17–0.22)	0.22 (0.19–0.26)	0.13 (0.09–0.16)
15	12	3	59	49	10
16	14	3	74	53	20
0.94 (0.46–1.41)	0.86 (0.37–1.34)	1.00 (0.21–2.92)	0.80 (0.59–1.00)	0.92 (0.67–1.18)	0.50 (0.19–0.81)
24	21	3	71	61	10
111	91	20	527	380	147
0.22 (0.13–0.30)	0.23 (0.13–0.33)	0.15 (0.03–0.44)	0.13 (0.10–0.17)	0.16 (0.12–0.20)	0.07 (0.03–0.11)

for screening colonoscopy is safe and could potentially be extended, provided that quality metrics are universally assessed and the baseline examination meets recommended standards.

From The Maria Sklodowska-Curie National Research Institute of Oncology and Medical Center for Postgraduate Education, Warsaw, Poland (N.D.P., M.B., P.W., M.R., J.R.); The Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland (R.F., M.P.); National Cancer Registry of Poland, The Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland (J.D., U.W.); and The Maria Sklodowska-Curie National Research Institute of Oncology and Medical Center for Postgraduate Education, Warsaw, Poland, and Institute of Health and Society, University of Oslo, Oslo, Norway (M.F.K.).

Financial Support: By the Polish Ministry of Health, the Medical Center for Postgraduate Education in Warsaw (grant 5011091217/18), and the Polish Foundation of Gastroenterology.

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M19-2477.

Reproducible Research Statement: *Study protocol and statistical code:* Available from Dr. Pilonis (e-mail, nastazja@gmail.com). *Data set:* Not available.

Corresponding Author: Nastazja Dagny Pilonis, MD, Department of Gastroenterology, The Maria Sklodowska-Curie National Research Institute of Oncology, Roentgen Street 5, 02-781 Warsaw, Poland; e-mail, nastazja@gmail.com.

Current author addresses and author contributions are available at Annals.org.

References

1. **Wolf AMD, Fontham ETH, Church TR, et al.** Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. CA Cancer J Clin. 2018;68:250-281. [PMID: 29846947] doi:10.3322/caac.21457
2. **Rex DK, Boland CR, Dominitz JA, et al.** Colorectal cancer screening: recommendations for physicians and patients from the U.S. Multi-Society Task Force on Colorectal Cancer. Gastroenterology. 2017;153:307-323. [PMID: 28600072] doi:10.1053/j.gastro.2017.05.013
3. **von Karsa L, Patnick J, Segnan N, et al; European Colorectal Cancer Screening Guidelines Working Group.** European guidelines for quality assurance in colorectal cancer screening and diagnosis: overview and introduction to the full supplement publication. Endoscopy. 2013;45:51-9. [PMID: 23212726] doi:10.1055/s-0032-1325997
4. **Winawer SJ, Fletcher RH, Miller L, et al.** Colorectal cancer screening: clinical guidelines and rationale. Gastroenterology. 1997;112:594-642. [PMID: 9024315]
5. **Brenner H, Chang-Claude J, Seiler CM, et al.** Does a negative screening colonoscopy ever need to be repeated? Gut. 2006;55:1145-50. [PMID: 16469791]
6. **Lakoff J, Paszat LF, Saskin R, et al.** Risk of developing proximal versus distal colorectal cancer after a negative colonoscopy: a population-based study. Clin Gastroenterol Hepatol. 2008;6:1117-21; quiz 1064. [PMID: 18691942] doi:10.1016/j.cgh.2008.05.016
7. **Nishihara R, Wu K, Lochhead P, et al.** Long-term colorectal-cancer incidence and mortality after lower endoscopy. N Engl J Med. 2013;369:1095-105. [PMID: 24047059] doi:10.1056/NEJMoa1301969
8. **Lee JK, Jensen CD, Levin TR, et al.** Long-term risk of colorectal cancer and related deaths after a colonoscopy with normal findings. JAMA Intern Med. 2019;179:153-160. [PMID: 30556824] doi:10.1001/jamainternmed.2018.5565
9. **Rex DK, Schoenfeld PS, Cohen J, et al.** Quality indicators for colonoscopy. Am J Gastroenterol. 2015;110:72-90. [PMID: 25448873] doi:10.1038/ajg.2014.385
10. **Kaminski MF, Regula J, Kraszewska E, et al.** Quality indicators for colonoscopy and the risk of interval cancer. N Engl J Med. 2010;362:1795-803. [PMID: 20463339] doi:10.1056/NEJMoa0907667
11. **Atkin W, Wooldrage K, Parkin DM, et al.** Long term effects of once-only flexible sigmoidoscopy screening after 17 years of follow-up: the UK Flexible Sigmoidoscopy Screening randomised controlled trial. Lancet. 2017;389:1299-1311. [PMID: 28236467] doi:10.1016/S0140-6736(17)30396-3
12. **Segnan N, Armaroli P, Bonelli L, et al; SCORE Working Group.** Once-only sigmoidoscopy in colorectal cancer screening: follow-up findings of the Italian Randomized Controlled Trial–SCORE. J Natl Cancer Inst. 2011;103:1310-22. [PMID: 21852264] doi:10.1093/jnci/djr284
13. **Holme Ø, Løberg M, Kalager M, et al.** Effect of flexible sigmoidoscopy screening on colorectal cancer incidence and mortality: a randomized clinical trial. JAMA. 2014;312:606-15. [PMID: 25117129] doi:10.1001/jama.2014.8266
14. **Baxter NN, Warren JL, Barrett MJ, et al.** 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. [PMID: 22689809] doi:10.1200/JCO.2011.40.4772
15. **Brenner H, Chang-Claude J, Seiler CM, et al.** Protection from colorectal cancer after colonoscopy: a population-based, case-control study. Ann Intern Med. 2011;154:22-30. [PMID: 21200035] doi:10.7326/0003-4819-154-1-201101040-00004
16. **Regula J, Rupinski M, Kraszewska E, et al.** Colonoscopy in colorectal-cancer screening for detection of advanced neoplasia. N Engl J Med. 2006;355:1863-72. [PMID: 17079760]
17. **Lieberman D, Nadel M, Smith RA, et al.** Standardized colonoscopy reporting and data system: report of the Quality Assurance Task Group of the National Colorectal Cancer Roundtable. Gastrointest Endosc. 2007;65:757-66. [PMID: 17466195]
18. **Aronchick CA, Lipshutz WH, Wright SH, et al.** Validation of an instrument to assess colon cleansing [Abstract]. Am J Gastroenterol. 1999;94:2667.
19. **Rex DK, Petrini JL, Baron TH, et al; ASGE/ACG Taskforce on Quality in Endoscopy.** Quality indicators for colonoscopy. Am J Gastroenterol. 2006;101:873-85. [PMID: 16635231]
20. **Didkowska J, Wojciechowska U.** Cancer in Poland in 2013. Warsaw: National Cancer Registry of Poland, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology; 2015.
21. **Ederer F, Mantel N.** Confidence limits on the ratio of two Poisson variables. Am J Epidemiol. 1974;100:165-7. [PMID: 4412586]
22. **Breslow NE, Day NE.** The design and analysis of cohort studies. In: Statistical Methods in Cancer Research. Lyon, France: International Agency for Research on Cancer, World Health Organization; 1987.
23. Statistics Poland. 2019. Accessed at https://bdl.stat.gov.pl/BDL/start on 6 November 2019.
24. **Baxter NN, Goldwasser MA, Paszat LF, et al.** Association of colonoscopy and death from colorectal cancer. Ann Intern Med. 2009;150:1-8. [PMID: 19075198]
25. **Holme Ø, Løberg M, Kalager M, et al; NORCCAP Study Group.** Long-term effectiveness of sigmoidoscopy screening on colorectal cancer incidence and mortality in women and men: a randomized trial. Ann Intern Med. 2018;168:775-782. [PMID: 29710125] doi:10.7326/M17-1441
26. **Zauber AG, Winawer SJ, O'Brien MJ, et al.** Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths.

N Engl J Med. 2012;366:687-96. [PMID: 22356322] doi:10.1056/NEJMoa1100370
27. **Lieberman DA, Holub JL, Morris CD, et al.** Low rate of large polyps (>9 mm) within 10 years after an adequate baseline colonoscopy with no polyps. Gastroenterology. 2014;147:343-50. [PMID: 24768680] doi:10.1053/j.gastro.2014.04.020
28. **Ponugoti PL, Rex DK.** Yield of a second screening colonoscopy 10 years after an initial negative examination in average-risk individuals. Gastrointest Endosc. 2017;85:221-224. [PMID: 27222282] doi:10.1016/j.gie.2016.05.024
29. **Murthy SK, Dubé C, Rostom A, et al.** Risk of colorectal cancer after a negative colonoscopy in low-to-moderate risk individuals: impact of a 10-year colonoscopy. Endoscopy. 2017;49:1229-1236. [PMID: 28915524] doi:10.1055/s-0043-117402
30. **Zauber AG, Lansdorp-Vogelaar I, Knudsen AB, et al.** Evaluating test strategies for colorectal cancer screening: a decision analysis for the U.S. Preventive Services Task Force. Ann Intern Med. 2008;149:659-69. [PMID: 18838717]
31. **Knudsen AB, Zauber AG, Rutter CM, et al.** Estimation of benefits, burden, and harms of colorectal cancer screening strategies: modeling study for the US preventive services task force. JAMA. 2016;315:2595-609. [PMID: 27305518] doi:10.1001/jama.2016.6828
32. **Helsingen LM, Vandvik PO, Jodal HC, et al.** Colorectal cancer screening with faecal immunochemical testing, sigmoidoscopy or colonoscopy: a clinical practice guideline. BMJ. 2019;367:l5515. [PMID: 31578196] doi:10.1136/bmj.l5515
33. **Robertson DJ, Lieberman DA, Winawer SJ, et al.** Colorectal cancers soon after colonoscopy: a pooled multicohort analysis. Gut. 2014;63:949-56. [PMID: 23793224] doi:10.1136/gutjnl-2012-303796
34. **Kaminski MF, Regula J, Kraszewska E, et al.** Quality indicators for colonoscopy and the risk of interval cancer. N Engl J Med. 2010;362:1795-803. [PMID: 20463339] doi:10.1056/NEJMoa0907667
35. **Corley DA, Jensen CD, Marks AR, et al.** Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med. 2014;370:1298-306. [PMID: 24693890] doi:10.1056/NEJMoa1309086
36. **Kaminski MF, Thomas-Gibson S, Bugajski M, et al.** Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy. 2017;49:378-397. [PMID: 28268235] doi:10.1055/s-0043-103411
37. **Rondagh EJ, Bouwens MW, Riedl RG, et al.** Endoscopic appearance of proximal colorectal neoplasms and potential implications for colonoscopy in cancer prevention. Gastrointest Endosc. 2012;75:1218-25. [PMID: 22482917] doi:10.1016/j.gie.2012.02.010
38. **IJspeert JE, Bastiaansen BA, van Leerdam ME, et al; Dutch Workgroup serrAted polypS & Polyposis (WASP).** Development and validation of the WASP classification system for optical diagnosis of adenomas, hyperplastic polyps and sessile serrated adenomas/polyps. Gut. 2016;65:963-70. [PMID: 25753029] doi:10.1136/gutjnl-2014-308411
39. **Kahi CJ, Li X, Eckert GJ, et al.** High colonoscopic prevalence of proximal colon serrated polyps in average-risk men and women. GastrointestEndosc.2012;75:515-20.[PMID:22018551]doi:10.1016/j.gie.2011.08.021
40. **Brenner H, Stock C, Hoffmeister M.** Effect of screening sigmoidoscopy and screening colonoscopy on colorectal cancer incidence and mortality: systematic review and meta-analysis of randomised controlled trials and observational studies. BMJ. 2014;348:g2467. [PMID: 24922745] doi:10.1136/bmj.g2467
41. **Kaminski MF, Wieszczy P, Rupinski M, et al.** Increased rate of adenoma detection associates with reduced risk of colorectal cancer and death. Gastroenterology. 2017;153:98-105. [PMID: 28428142] doi:10.1053/j.gastro.2017.04.006

Current Author Addresses: Drs. Pilonis, Bugajski, Franczyk, Rupinski, and Regula: Department of Gastroenterology, The Maria Sklodowska-Curie National Research Institute of Oncology, Roentgen Street 5, 02-781 Warsaw, Poland.
Drs. Wieszczy, Pisera, and Kaminski: Department of Gastroenterology, Hepatology and Oncology, Medical Center for Postgraduate Education, The Maria Sklodowska-Curie National Research Institute of Oncology, Roentgen Street 5, 02-781 Warsaw, Poland.
Drs. Didkowska and Wojciechowska: National Cancer Registry of Poland, The Maria Sklodowska-Curie National Research Institute of Oncology, Wawelska Street 15B, 02-034 Warsaw, Poland.

Author Contributions: Conception and design: N.D. Pilonis, M. Bugajski, P. Wieszczy, M.F. Kaminski.
Analysis and interpretation of the data: N.D. Pilonis, M. Bugajski, P. Wieszczy, R. Franczyk, M. Rupinski, J. Regula, M.F. Kaminski.
Drafting of the article: N.D. Pilonis, R. Franczyk, M. Rupinski, J. Regula.
Critical revision for important intellectual content: N.D. Pilonis, M. Bugajski, P. Wieszczy, J. Didkowska, U. Wojciechowska, M.F. Kaminski, J. Regula,
Final approval of the article: N.D. Pilonis, M. Bugajski, P. Wieszczy, R. Franczyk, J. Didkowska, U. Wojciechowska, M. Pisera, M. Rupinski, J. Regula, M.F. Kaminski.
Provision of study materials or patients: M. Rupinski, M.F. Kaminski.
Statistical expertise: P. Wieszczy.
Obtaining of funding: M.F. Kaminski.
Administrative, technical, or logistic support: M. Rupinski, J. Regula.
Collection and assembly of data: N.D. Pilonis, R. Franczyk, J. Didkowska, U. Wojciechowska, M. Rupinski, J. Regula, M.F. Kaminski.