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CLINICAL—ALIMENTARY TRACT

Colonoscopist Performance and Colorectal Cancer Risk After Adenoma Removal to Stratify Surveillance: Two Nationwide Observational Studies

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This article has an accompanying continuing medical education activity, also eligible for MOC credit, on page e19. Learning Objective: Upon completion of this CME activity successful learners will be able to identify limitations of the metrics used to evaluate colonoscopy performance and describe how current metrics relate to interval colorectal cancer.

See Covering the Cover synopsis on page 976; See editorial on page 1007.

BACKGROUND AND AIMS: Colonoscopy surveillance after adenoma removal is an increasing burden in many countries. Surveillance recommendations consider characteristics of removed adenomas, but not colonoscopist performance. We investigated the impact of colonoscopist performance on colorectal cancer risk after adenoma removal. **METHODS:** We compared colorectal cancer risk after removal of high-risk adenomas, low-risk adenomas, and after negative colonoscopy for all colonoscopies performed by colonoscopists with low vs high performance quality (adenoma detection rate <20% vs ≥20%) in the Polish screening program between 2000 and 2011, with follow-up until 2017. Findings were validated in the Austrian colonoscopy screening program. **RESULTS:** A total of 173,288 Polish colonoscopies were included in the study. Of 262 colonoscopists, 160 (61.1%) were low performers, and 102 (38.9%) were high performers; 11.1% of individuals had low-risk and 6.6% had high-risk adenomas removed at screening; 82.2% had no adenomas. During 10 years of follow-up, 443 colorectal cancers were diagnosed. For low-risk adenoma individuals, colorectal cancer incidence was 0.55% (95% confidence interval [CI] 0.40–0.75) with low-performing colonoscopists vs 0.22% (95% CI 0.14–0.34) with high-performing colonoscopists (hazard ratio [HR] 2.35; 95% CI 1.31–4.21; $P = .004$). For individuals with high-risk adenomas, colorectal cancer incidence was 1.14% (95% CI 0.87–1.48) with low-performing colonoscopists vs 0.43% (95% CI 0.27–0.69) with high-performing colonoscopists (HR 2.69; 95% CI 1.62–4.47; $P < .001$). After negative colonoscopy, colorectal cancer incidence was 0.30% (95% CI 0.27–0.34) for individuals examined by low-performing colonoscopists, vs 0.15% (95% CI 0.11–0.20) for high-performing (HR 2.10; 95% CI 1.52–2.91; $P < .001$). The observed trends were reproduced in the Austrian validation cohort. **CONCLUSIONS:** Our results suggest that endoscopist performance may be an important contributor in addition to polyp characteristics in determining colorectal cancer risk after colonoscopy screening.

Keywords: Colorectal Cancer Screening; Screening Colonoscopy; Cancer Prevention; Surveillance.

Colorectal cancer is the second leading cause of cancer death in the United States.[1] Colonoscopy screening is widely introduced to prevent colorectal cancer by removal of precancerous adenomas.[2,3]

Individuals with adenomas removed during colonoscopy are at higher risk for adenomas and cancer later in life. Thus, guidelines recommend colonoscopy surveillance every 5 to 10 years for individuals with low-risk adenomas (1 or 2 tubular adenomas <1 cm in diameter, or serrated adenomas <1 cm), and every 3 years for individuals with high-risk adenomas (≥1 cm in diameter, high-grade dysplasia, villous components, ≥3 adenomas, or serrated adenomas ≥1 cm or with dysplasia).[4,5] However, evidence for current surveillance guidelines is poor, especially for long-time follow-up.

Due to increasing screening activities, achieving surveillance after adenoma removal for all individuals is a challenge for health care systems around the world. In the

*Authors share co-first authorship; §Authors share co-senior authorship

Abbreviations used in this paper: ADR, adenoma detection rate; CI, confidence interval; HR, hazard ratio; ICD, International Classification of Diseases; IQR, interquartile range.

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WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Current surveillance recommendations are based solely on adenoma characteristics, whereas colonoscopist performance may also have a non-negligible effect on colorectal cancer after colonoscopy screening.

NEW FINDINGS

During 10 years of follow-up, individuals examined by low-performing colonoscopists had over 2-times higher risk of colorectal cancer than individuals examined by high-performing colonoscopists. Even patients with high-risk adenomas had a very low risk of interval cancer if a high-performing colonoscopist performed the screening.

LIMITATIONS

Lack of information on possible residual confounders and surveillance.

IMPACT

A combination of adenoma characteristics and colonoscopists performance should be considered for surveillance recommendations.

United States, more than 20% of all colonoscopies performed in individuals older than 55 years are for adenoma surveillance.[6] A randomized trial has started to investigate longer surveillance intervals than currently recommended, but results will not be available before another 10 years.[7]

Colonoscopist adenoma detection rate (ADR; the proportion of screening colonoscopies in which at least 1 adenoma is detected) is a valid measure for colonoscopy quality,[8,9] and has been introduced as a key quality indicator in screening guidelines.[10,11] A high ADR is associated with a low risk of colorectal cancer after colonoscopy (so-called interval cancer). Recent studies showed an association among ADR, adenoma characteristics, and post screening advanced neoplasia and colorectal cancer.[12,13] However, current surveillance guidelines do not take into account colonoscopist performance when determining surveillance intervals, and long-time follow-up data are lacking.

We hypothesized that individuals with high-risk adenomas removed by colonoscopists with a low ADR may be at higher risk for colorectal cancer after 10 years, as compared with high-risk individuals examined by endoscopists with a high ADR. We took advantage of complete, high-quality data from the Polish National Colorectal Cancer Screening Program and compared the risk of colorectal cancer after colonoscopy screening for individuals with low- and high-risk adenomas and after negative colonoscopy according to colonoscopist ADRs. We validated our findings in an independent dataset from the Austrian colonoscopy screening program.

Methods

Polish Study Cohort

Since 2000, the Polish National Colorectal Cancer Screening Program offers colonoscopy screening every 10 years to inhabitants aged 50 to 66 years with no symptoms of colorectal cancer.[14,15] Individuals with a family history of colorectal cancer are eligible from 40 years. Between 2000 and 2011, the program had 132 screening centers. Surveillance colonoscopy after polyp removal is recommended according to the US guidelines.[16,17] Data from all screening colonoscopies are stored in a dedicated database, and all individuals are identified and followed using the Polish national individual identifier. The following information is registered in the screening database: sex, age, and family history of colorectal cancer of screening participants; intubation depth at screening colonoscopy; quality of bowel preparation; number, location, and characteristics of adenomas detected at screening (size, morphology, dysplasia grade); and completeness of removal.[14]

For this study, we analyzed data from the program for all individuals who underwent screening colonoscopy between January 1, 2000, and December 31, 2011, with follow-up through December 31, 2017. For calculation of the ADR, we excluded individuals with suspected or diagnosed hereditary colorectal cancer syndromes, lack of histopathology results, incomplete polyp removal, and those who underwent colonoscopy by colonoscopists with <100 examinations per year (Figure 1). For calculation of the risk for colorectal cancer after colonoscopy screening, we further excluded individuals with colorectal cancer detected at screening, with incomplete colonoscopies, and those with inadequate bowel preparation as defined on the Aronchick scale (poor or very poor).[18]

Endpoint Ascertainments

We used the Polish national individual identifier to link screening participants to the Polish Cancer and Population Registries, respectively, and retrieved dates of colorectal cancer diagnosis (histologically verified colorectal adenocarcinoma; International Classification of Diseases (ICD), 10th Revision codes C18.0–C20.0), and dates and causes of death. The Polish databases are close to 100% complete for our outcomes of interest.[19]

Colorectal cancer after screening was defined as colorectal adenocarcinoma diagnosed between 180 days and 10 years after screening colonoscopy. We also performed sensitivity analyses censoring individuals with low-risk adenomas after 5 years, and individuals with high-risk adenomas after 3 years.

We defined individuals with low-risk adenomas as those with 1 to 2 removed tubular adenomas <1 cm in size, and individuals with high-risk adenomas as those with removed adenomas ≥ 1 cm in size, with high-grade dysplasia, villous, or tubulovillous histology or ≥ 3 adenomas.[4]

We categorized all colonoscopists in the screening program into low performers and high performers, respectively, according to their individual annual ADR, as recently described.[8] Briefly, for each calendar year, ADRs for each colonoscopist were calculated (eg, for a colonoscopist who participated in the screening program for 5 years, 5 different ADR values were calculated).[8] Taking into account the adenoma prevalence during screening colonoscopy in Poland,[8] and the distribution of ADRs in our cohort (Table 1), we defined the threshold of low vs high performance at an ADR cutoff of 20% for our primary analyses. We also performed sensitivity analyses with an ADR threshold of 25% to be representative for other patient cohorts.[9]

Statistical Analyses

Individuals were classified as low-risk, high-risk, or no adenomas, according to their findings at screening colonoscopy. Quintiles of ADRs are shown in Table 1.

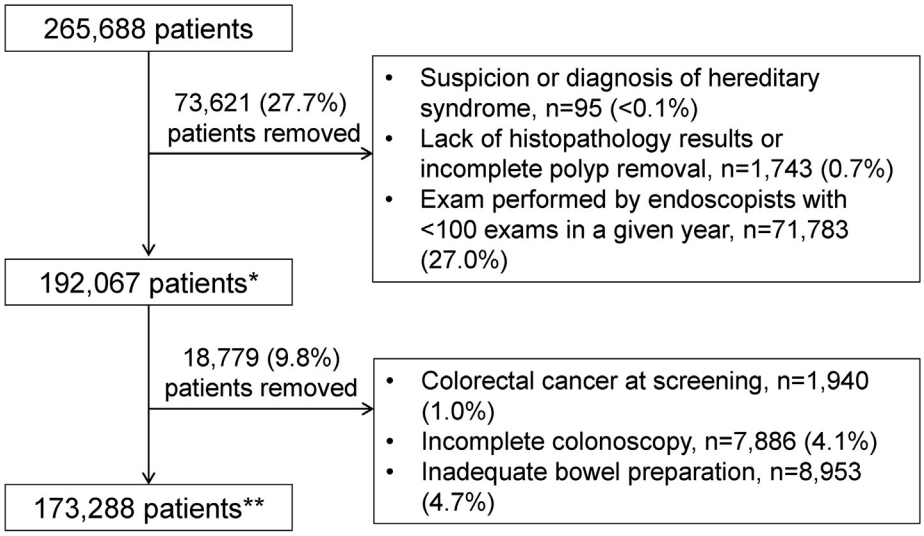

Figure 1. Study flow chart of the Polish colonoscopy screening cohort.

*This cohort was used to calculate annual adenoma detection rate for each colonoscopist.
**This cohort was used to calculate risk of interval cancer.

Table 1. Baseline Characteristics for Included Individuals and Their Colonoscopists in the Polish Colonoscopy Screening Program

Individual characteristics		
Age (*y*), mean (SD)	55.8 (5.5)	
Sex, n (%)		
Female	107,723 (62.2)	
Male	65,565 (37.8)	
1st degree relatives of CRC, n (%)		
No	138,919 (80.2)	
Yes	34,369 (19.8)	
Finding at screening colonoscopy, n (%)		
No adenoma	142,588 (82.2)	
Low-risk adenoma[a]	19,304 (11.1)	
High-risk adenoma[a]	11,306 (6.6)	
Colonoscopist characteristics	No. of endoscopists[b]	No. of colonoscopies
Yearly adenoma detection rate		
Quintile 1: <12.1%	89	34,519
Quintile 2: 12.1%–15.9%	105	35,498
Quintile 3: 16.0%–19.9%	109	38,236
Quintile 4: 20.0%–24.8%	109	33,721
Quintile 5: ≥24.9%	89	31,314

CRC, colorectal cancer; SD, standard deviation.
[a]Low-risk adenoma individuals: 1–2 removed tubular adenomas <1 cm in size. High-risk adenoma individuals: removed adenomas ≥1 cm in size, with high-grade dysplasia, villous or tubulovillous histology, ≥3 adenomas.[4]
[b]The sum of rows exceeds the total number of colonoscopists as 1 colonoscopist could be in different categories in different years.

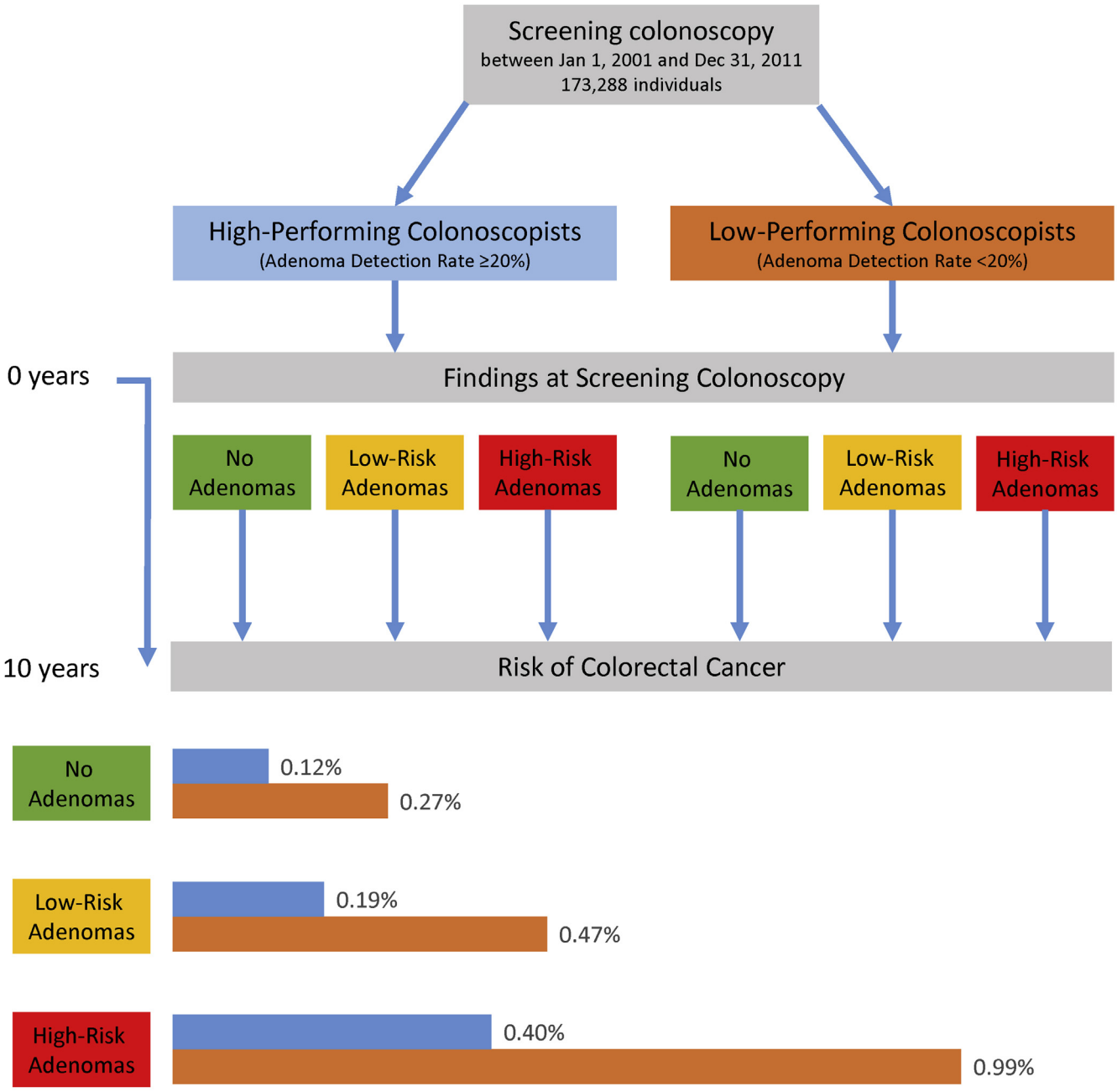

Figure 2. Kaplan-Meier cumulative 10-year risk of colorectal cancer after screening colonoscopy by colonoscopist adenoma detection rates and characteristics of removed adenomas.

Our primary analyses were the comparisons of interval cancer risk for low-risk, high-risk, and no adenoma individuals who were examined by low- vs high-performing endoscopists (ADR of <20% as compared with ≥20%), respectively after 10 years of follow-up. These analyses comprised the following 3 comparisons:

- low-risk adenoma individuals examined by low- vs high-performing colonoscopists
- high-risk adenoma individuals examined by low- vs high-performing colonoscopists
- no adenoma individuals examined by low- vs high-performing colonoscopists (Figure 2)

For each comparison, the rates of interval cancer were derived as the number of colorectal cancers per 100,000 person-years of risk over the years of follow-up for the Polish cohort and Austrian cohort, respectively. The corresponding hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using Cox proportional hazard models with sandwich estimator of variance to allow for intra-colonoscopist correlation. Forward stepwise regression at a 0.1 significance level was used for variable selection. Variables tested for inclusion were individuals' age (40–49, 50–54, 55–59, 60–66 years), sex, and family history of colorectal cancer (1 or more first-degree relatives with colorectal cancer, vs none). All tests were 2-sided and .05 significance level was used. All analyses were performed using Stata software, version 15.1 (StataCorp, College Station, TX).

All screened individuals were followed from the date of screening colonoscopy to the date of colorectal cancer diagnosis and were censored at the time of death, after 10 years of follow-up, or the end of the observation period (whichever occurred first).

In sensitivity analyses for follow-up time after screening, we censored individuals with low-risk adenoma after 5 years, individuals with high-risk adenoma after 3 years, and individuals without adenomas after 10 years.

Validation Cohort

As a validation cohort, we used a screening cohort from Austria. The Austrian screening program offers colonoscopy screening to average-risk inhabitants starting at the age of 50 years, and for individuals 30 to 49 years with a family history of colorectal cancer or expressed fear of cancer.[20] Surveillance or new screening is recommended after 10 years for low-risk and negative colonoscopy and after 3 years for high-risk adenomas, respectively.[4] The program has had a quality assurance program since 2007, in which approximately 50% of screening centers participate.[20,21] The current study cohort comprises all screening colonoscopies performed between January 2008 and March 2015 at the centers participating in the quality assurance program. Available data included individual's characteristics (age and sex), intubation depth, and colonoscopy findings (number, size, location, and histopathology of the most advanced lesion).[20,21] For endpoint ascertainment, hospital admission and discard diagnoses for colorectal cancer (ICD-9 and ICD-10 codes C18–21 and ICD-9 codes 153, 154, respectively) until March 31, 2015, were retrieved from the Main Association of Statutory Insurance Companies in Austria. The database does not include information on family history of colorectal cancer. All screened individuals were followed from the date of screening colonoscopy and censored at the end of follow-up or surveillance colonoscopy (whichever occurred first). For calculation of ADR, colonscopists with <30 examinations per year were excluded. All other analyses and categorizations followed the main study cohort from Poland.

Institutional Review Board Approval

In Poland, in accordance with policy institutions, this observational study of routinely collected data from the Polish screening programs did not require review by an institutional review board. The use of the Austrian patient data was approved by the ethics committee of the Medical University of Vienna (EK1323/2015).

Results

Polish Cohort

A total of 173,288 individuals underwent screening colonoscopy and were included (Figure 1). Table 1 shows baseline characteristics of the included individuals and the performance distribution of the 262 participating colonoscopists.

After a median follow-up of and censoring after 10 years (IQR 7.85–10 years) and 1,545,629 person-years of follow-up, 443 interval colorectal cancers were diagnosed. Median time to cancer diagnosis was 5.9 years (IQR 4.0–7.9 years).

The median colonoscopist ADR was 17.9% (IQR 13.1%–23.5%); 108,253 individuals (62.5%) were examined by low-performing colonoscopists, and 65,035 (37.5%) were examined by high-performing colonoscopists. Of the individuals, 11.2% were classified as low-risk, 6.5% as high-risk, and 82.3% had no adenomas at screening colonoscopy.

For low-risk individuals, cumulative 10-year colorectal cancer incidence was 0.55% (95% CI 0.40–0.75) for those examined by low-performing colonoscopists vs 0.22% (95% CI 0.14–0.34) for those examined by high-performing colonoscopists (HR 2.35; 95% CI 1.31–4.21; $P = .004$). For individuals with high-risk adenomas, colorectal cancer incidence was 1.14% (95% CI 0.87–1.48) for those examined by low-performing colonoscopists vs 0.43% (95% CI 0.27–0.69) for those examined by high-performing colonoscopists (HR 2.69; 95% CI 1.62–4.47; $P < .001$). For individuals with no adenomas, colorectal cancer incidence was 0.30% (95% CI 0.27–0.34) when examined by low-performing colonoscopists vs 0.15% (95% CI 0.11–0.20) for high-performing colonoscopists (HR 2.10; 95% CI 1.52–2.91; $P < .001$) (Figure 2, Table 2, Supplementary Table 1).

Low performance and high-risk adenomas were significantly associated with interval cancers 10 years after screening colonoscopy. However, the interaction term in the multivariable model was not significant (interaction between ADR $\geq$20 and low-risk adenomas $P = .81$, and between ADR $\geq$20 and high-risk adenomas $P = .44$, respectively, data not shown). For individuals with no adenomas, the cancer risk after 10 years was twice as high if examined by low-performing colonoscopists compared with high-performing colonoscopists (Table 1).

Sensitivity analyses with censoring individuals at the time of recommended surveillance, and with different thresholds for low- and high-performing colonoscopists, confirmed both the group of individuals with high-risk adenomas examined by low performers as those at highest risk for interval cancers, and the increased risk for interval cancers for patients with a negative colonoscopy examined by a low performer compared with a high performer. The difference was smaller when the observation period was censored at time of recommended surveillance (Supplementary Tables 2 and 3). Colorectal cancer incidence rates per 100,000 person-years are summarized in Supplementary Table 4, and gave similar results.

Validation Cohort

A total of 137,169 individuals underwent screening colonoscopy and were included. The median follow-up was 3.1 years (IQR 1.7–5 years), and 465,464.21 person-years of follow-up. A total of 103 interval colorectal cancers were diagnosed during follow-up. Supplementary Table 5 shows performance distribution of the 242 participating endoscopists.

For individuals with low-risk adenomas, colorectal cancer risk per 100,000 person-years was 2.51 for those examined by low-performing colonoscopists vs 1.14 for those examined by high-performing colonoscopists (HR 2.11; 95% CI 0.61–7.28; $P = .238$). For individuals with

Table 2. Absolute 10-Year Risk of CRC After Screening Colonoscopy in Different Adenoma Risk Groups (No Adenoma, Low-Risk Adenoma, High-Risk Adenoma), Stratified by ADR of Colonoscopists (ADR <20% vs ADR ≥20%)

	ADR <20%			ADR ≥20%				
Risk group	No. of CRC cases/no. of Individuals	CRC risk,[a] % (95% CI)	CRC risk per 100,000 prs-y (95% CI)	No. of CRC cases/no. of individuals	CRC risk,[a] % (95% CI)	CRC risk per 100,000 prs-y (95% CI)	HR[b] (95% CI)	*P* value
No adenoma	250/94,097	0.30 (0.27–0.34)	29.05 (25.56–32.88)	57/48,491	0.15 (0.11–0.20)	13.68 (10.36–17.72)	2.10 (1.52–2.91)	<.001
Low-risk adenoma	39/8380	0.55 (0.40–0.75)	52.14 (37.08–71.27)	21/11,014	0.22 (0.14–0.34)	22.38 (13.86–34.21)	2.35 (1.31–4.21)	.004
High-risk adenoma	57/5776	1.14 (0.87–1.48)	109.02 (82.58–141.22)	19/5,530	0.43 (0.27–0.69)	40.11 (24.15–62.64)	2.69 (1.62–4.47)	<.001

CRC, colorectal cancer; prs-y, person years.
[a]Ten-year cumulative risk from Kaplan-Meier method.
[b]ADR <20% vs ADR ≥20%. Using stepwise regression hazard ratio for no adenoma and low-risk adenoma groups were adjusted for age group and family history of CRC. High-risk adenoma group was adjusted only for age group.

high-risk adenomas, colorectal cancer incidence was 9.77 for those examined by low-performing colonoscopists vs 4.31 for those examined by high-performing colonoscopists (HR 2.16; 95% CI 0.92–5.08; $P = .079$). For individuals with no adenomas, colorectal cancer incidence was 2.51 when examined by low-performing colonoscopists vs 1.49 for high-performing colonoscopists (HR 1.65; 95% CI 1.03–2.64; $P = .038$).

Absolute colorectal cancer risk and colorectal cancer rates per 100,000 person-years for different ADR thresholds and censoring at different time points are shown in Supplementary Tables 6A and 6B. The results show similar trends as those of the Polish cohort.

Conclusions

Current surveillance recommendations after screening colonoscopy are based on characteristics of removed adenomas, and do not take into account performance quality of colonoscopists. Our study of a 10-year follow-up after screening colonoscopy indicates that surveillance should be informed by performance quality of colonoscopists and characteristics of removed adenomas.

Intriguingly, even individuals with high-risk adenomas at screening have a very low risk of interval cancer after screening, provided that a high-performing colonoscopist performed their screening. This finding challenges current surveillance guidelines and questions the need of frequent surveillance for this group. Conversely, if a low-performing colonoscopist performed their screening, the 10-year cumulative colorectal cancer risk was significantly higher (more than 1%). These individuals may benefit from increased surveillance.

It is well known that ADR is correlated with interval colorectal cancer after colonoscopy.[8,9] ADR is therefore established as an important quality indicator for screening colonoscopy, and its reporting is recommended in current guidelines. This study is introducing the next step of improving quality indicators in screening colonoscopy, as it links polyp status of individuals to colonoscopist performance with a long-time follow-up of 10 years, to be applied in surveillance recommendations for individuals after screening.

Higher interval cancer rates for low-performing colonoscopists can be explained by 3 possible reasons. First, a lesion is missed and develops into colorectal cancer. Second, patients' risk of future neoplasia is not correctly classified because adenomas are missed by low-performing endoscopists. Third, patients undergoing colonoscopy by high-performing endoscopists undergo more surveillance colonoscopies. Even if findings at the first colonoscopy are unrelated to future risk of colorectal cancer, patients with polyps at the first colonoscopy may have a lower risk of colorectal cancer because of more frequent subsequent colonoscopies. Patients who had a colonoscopy performed by a high-performing endoscopist will have more subsequent colonoscopies performed than those performed by a low-performing endoscopist. Our results indicate that adding endoscopists' performance to

surveillance recommendations based on colonoscopy findings would help to identify those who would benefit most from surveillance. Our results may have important consequences for clinical practice. As indicated, colonoscopist screening ADR is important to define future cancer risk. Individuals with high-risk adenomas removed at screening by low-performing endoscopists are at highest risk (1% over 10 years). These individuals may be offered enhanced surveillance. However, they comprise only 3.2% of our screening cohort. All other groups had a 10-year interval cancer risk of less than 0.6%, challenging the intensity of current surveillance strategies. These findings are in line with previous studies questioning the need for surveillance after 10 or 15 years.[22,23] By reallocating resources to individuals with the highest risk, we believe that the total amount of surveillance colonoscopies can be reduced dramatically without patient harm.

The observed trends were consistent with different ADR cutoffs, and different follow-up times after screening and could be reproduced in an independent screening colonoscopy cohort from Austria including 137,169 colonoscopies, although with a shorter follow-up and thus fewer events. For the main analyses, we used an ADR cutoff of 20% because this was the quality standard during data collection, and it reflects the population adenoma prevalence pattern in Poland as well as in Austria.[21,24] For other populations with higher detection rates and adenoma prevalence, other thresholds may be applied.

Our main analyses are absolute risks expressed as 10-year cumulative risk of colorectal cancer. We also present colorectal cancer rates per 100,000 person-years, as the follow-up time in validation cohort is less than 10 years. As displayed, the 2 measures provide comparable results.

Strengths of the present study include the large size, long follow-up after screening, completeness of the data and an independent validation cohort. Previous studies on the impact of adenoma characteristics respectively ADR on interval cancers were based on heterogeneous colonoscopy cohort,[23,25] had shorter follow-up,[12,13] a smaller patient cohort,[13] or lack assessment of performance quality.[25,26] Limitations include the nature of register-based studies, and the lack of possible residual confounders, such as body mass index, smoking, and tobacco use. Moreover, our data set included very few serrated lesions (1% in the Polish cohort, 1% in the Austrian cohort) and thus cannot be applied to this polyp entity. The follow-up of the Austrian validation cohort is shorter, and thus, the results are more uncertain than the main cohort. Twenty-seven percent of individuals were excluded from the study because the colonoscopist did not complete >100 examinations per year. Nevertheless, to provide high-quality data, a large number of colonoscopies is important for a robust estimation of ADR. Finally, there was a predominance of women in the main study cohort with a relatively low ADR. However, the main findings could be reproduced in the validation cohort with a more balanced gender profile and the differences in interval cancer incidences could already be observed using an ADR cutoff of 20%.

In conclusion, our study proposes a new rationale for surveillance recommendations after screening colonoscopy with the combination of adenoma characteristics and colonoscopist performance based on long-time follow-up evidence.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2020.10.009.

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Supplementary Table 1. Interval CRC After Screening Colonoscopy in Different Adenoma Risk Groups (No Adenoma, Low-Risk Adenoma, High-Risk Adenoma) Stratified by ADR of Colonoscopists (ADR <20% vs ADR ≥20%)

No-adenoma group	HR	95% CI	*P*
ADR ≥20% (vs ADR<20%)	2.10	1.52–2.91	<.001
Age 50–54 (ref. 40–49)	1.55	0.88–2.73	.126
Age 55–59 (ref. 40–49)	1.88	1.11–3.21	.020
Age 60–66 (ref. 40–49)	3.65	2.11–6.33	<.001
1st degree family history (vs none)	1.32	0.98–1.78	.069
Low-risk adenoma			
ADR≥20% (vs ADR<20%)	2.35	1.31–4.21	.004
Age 50–54 (ref. 40–49)	2.47	0.64–9.60	.191
Age 55–59 (ref. 40–49)	2.64	0.57–12.22	.214
Age 60–66 (ref. 40–49)	5.43	1.27–23.23	.023
1st degree family history (vs none)	1.80	0.99–3.27	.053
High-risk adenoma			
ADR ≥20% (vs ADR<20%)	2.69	1.62–4.47	<.001
Age 50–54 (ref. 40–49)	0.97	0.25–3.83	.967
Age 55–59 (ref. 40–49)	1.87	0.58–6.07	.298
Age 60–66 (ref. 40–49)	2.27	0.70–7.32	.170

NOTE. Observation period censored after 10 years. Using stepwise regression HRs for proximal CRC in no adenoma and high-risk adenoma groups were adjusted for age group and in low-risk adenoma group HR was not adjusted. HRs for distal CRC were adjusted for age group in no-adenoma group, age group and family history in low-risk group and sex in high-risk group
CRC, colorectal cancer.

Supplementary Table 2. Interval CRC After Screening Colonoscopy in Different Adenoma Risk Groups (No Adenoma, Low-Risk Adenoma, High-Risk Adenoma) Stratified by ADR of Colonoscopists (ADR <25% vs ADR ≥25%)

No-adenoma group	HR	95% CI	*P*
ADR ≥25% (vs ADR <25%)	2.01	1.25–3.25	.004
Age 50–54 (ref. 40–49)	1.51	0.86–2.66	.152
Age 55–59 (ref. 40–49)	1.83	1.08–3.11	.025
Age 60–66 (ref. 40–49)	3.54	2.05–6.12	<.001
1st degree family history (vs none)	1.31	0.97–1.77	.074
Low-risk adenoma			
ADR ≥25% (vs ADR <25%)	2.95	1.41–6.16	.004
Age 50–54 (ref. 40–49)	2.49	0.65–9.55	.184
Age 55–59 (ref. 40–49)	2.64	0.57–12.19	.212
Age 60–66 (ref. 40–49)	5.45	1.27–23.29	.022
1st degree family history (vs none)	1.81	1.01–3.26	.047
High-risk adenoma			
ADR ≥25% (vs ADR <25%)	2.05	1.13–3.74	.019
Age 50–54 (ref. 40–49)	0.94	0.24–3.67	.925
Age 55–59 (ref. 40–49)	1.79	0.55–5.82	.329
Age 60–66 (ref. 40–49)	2.18	0.67–7.04	.193

NOTE. Observation period censored after 10 years. Using stepwise regression HRs for CRC in no-adenoma and low-risk adenoma groups were adjusted for age group and family history of CRC, and in high-risk adenoma group was adjusted for age group only.
CRC, colorectal cancer.

Supplementary Table 3. Interval CRC After Screening Colonoscopy in Different Adenoma Risk Groups (No Adenoma, Low-Risk Adenoma, High-Risk Adenoma) Stratified by ADR of Colonoscopists (ADR <20% vs ADR ≥20% and ADR <25% vs ADR ≥25%)

Cutoff 20%			
No-adenoma group	HR	95% CI	P
ADR ≥20% (vs ADR <20%)	2.10	1.52–2.91	<.001
Age 50–54 (ref. 40–49)	1.55	0.88–2.73	.126
Age 55–59 (ref. 40–49)	1.88	1.11–3.21	.020
Age 60–66 (ref. 40–49)	3.65	2.11–6.33	<.001
1st degree family history (vs none)	1.32	0.98–1.78	.069
Low-risk adenoma			
ADR ≥20% (vs ADR <20%)	1.23	0.56–2.70	.615
Age 55–59 (ref. 40–54)	0.81	0.25–2.63	.724
Age 60–66 (ref. 40–54)	2.39	0.96–5.92	.060
High-risk adenoma			
ADR ≥20% (vs ADR<20%)	4.14	1.16–14.82	.029
Cutoff 25%			
No-adenoma group			
ADR ≥25% (vs ADR<25%)	2.01	1.25–3.25	.004
Age 50–54 (ref. 40–49)	1.51	0.86–2.66	.152
Age 55–59 (ref. 40–49)	1.83	1.08–3.11	.025
Age 60–66 (ref. 40–49)	3.54	2.05–6.12	<.001
1st degree family history (vs none)	1.31	0.97–1.77	.074
Low-risk adenoma			
ADR ≥25% (vs ADR<25%)	1.88	0.72–4.93	.198
Age 55–59 (ref. 40–54)	0.81	0.25–2.65	.732
Age 60–66 (ref. 40–54)	2.41	0.97–5.98	.059
High-risk adenoma			
ADR≥25% (vs ADR<25%)	2.54	0.58–11.10	.215

NOTE. Observation period censored at time of recommended surveillance (3 or 5 years). Using stepwise regression HR for CRC in no adenoma was adjusted for age group and family history of CRC, in low-risk group was adjusted for age group, and in high-risk adenoma group was not adjusted.
CRC, colorectal cancer.

Supplementary Table 4. CRC Rates per 100,000 Person Years of Follow-up for Low-Risk Individuals, High-Risk Individuals, and After Negative Colonoscopies, Respectively, Stratified by Endoscopist ADRs (Thresholds of Low vs High Performance at 20% and 25%, Respectively)

Censoring after 10 years						
	ADR <20%			ADR ≥20%		
Risk group	CRC cases	Person-years	Rate per 100,000 person-years (95% CI)	CRC cases	Person-years	Rate per 100,000 p-years (95% CI)
No adenoma	250	860,686	29.05 (25.56–32.88)	57	416,678	13.68 (10.36–17.72)
Low-risk adenoma	39	74,794	52.14 (37.08–71.27)	21	93,820	22.38 (13.86–34.21)
High-risk adenoma	57	52,286	109.02 (82.58–141.22)	19	47,365	40.11 (24.15–62.64)

Censoring after 10 years						
	ADR <25%			ADR ≥25%		
Risk group	CRC cases	Person-years	Rate per 100,000 person-years (95% CI)	CRC cases	Person-years	Rate per 100,000 p-years (95% CI)
No adenoma	283	1,090,287	25.96 (23.02–29.16)	24	187,077	12.83 (8.22–19.09)
Low-risk adenoma	52	116,466	44.65 (33.35–58.55)	8	52,148	15.34 (6.62–30.23)
High-risk adenoma	65	73,932	87.92 (67.86–112.05)	11	25,719	42.77 (21.35–76.51)

Censoring on surveillance						
	ADR <20%			ADR ≥20%		
Risk group	CRC cases	Person-years	Rate per 100,000 person-years (95% CI)	CRC cases	Person-years	Rate per 100,000 p-years (95% CI)
No adenoma	250	860,686	29.05 (25.56–32.88)	57	416,678	13.68 (10.36–17.72)
Low-risk adenoma	12	41,605	28.84 (14.9–50.38)	13	54,696	23.77 (12.66–40.64)
High-risk adenoma	13	17,251	75.36 (40.13–128.83)	3	16,501	18.18 (3.75–53.12)

Censoring on surveillance						
	ADR <25%			ADR ≥25%		
Risk group	CRC cases	Person-years	Rate per 100,000 p-years (95% CI)	CRC cases	Person-years	Rate per 100,000 p-years (95% CI)
No adenoma	283	109,0287	25.96 (23.02–29.16)	24	187,077	12.83 (8.22–19.09)
Low-risk adenoma	20	65,743	30.42 (18.58–46.98)	5	30,557	16.36 (5.31–38.18)
High-risk adenoma	14	24,759	56.55 (30.92–94.85)	2	8992	22.24 (2.69–80.32)

NOTE. Observation period censored after 10 years, and at recommended surveillance, respectively.
CRC, colorectal cancer.

Supplementary Table 5. Austrian Validation Cohort: ADR of Participating Endoscopists

Colonoscopist ADR, %	No. of colonoscopies
Quintile 1: <15.2	27,797
Quintile 2: 15.2–19.3	28,840
Quintile 3: 19.3–23.2	26,549
Quintile 4: 23.2–28.9	27,446
Quintile 5: ≥28.9	26,537

Supplementary Table 6A. Validation Cohort: CRC Risk per 100,000 Person-Years for Low-Risk Adenoma Individuals, High-Risk Adenoma Individuals, and After Negative Colonoscopy, Stratified by Endoscopist Performance (ADR Cutoff 20% and 25%, Respectively)

	ADR <20%			ADR ≥20%				
Risk group	Number of individuals	CRC, n	CRC rate per 100,000 person-years	Number of individuals	CRC cases	CRC rate per 100,000 person-years	HR[a] (95% CI)	*P* value
No adenoma	50,197	43	2.513	56,882	29	1.489	1.65 (1.03–2.64)	.038
Low-risk adenoma	5606	5	2.512	12,961	5	1.138	2.11 (0.61–7.28)	.238
High-risk adenoma	3158	10	9.770	8365	11	4.313	2.16 (0.92–5.08)	.079
	ADR <20%			ADR ≥20%				
Risk group	Number of individuals	CRC, n	CRC rate per 100,000 person-years	Number of individuals	CRC cases	CRC rate per 100,000 person-years	HR[a] (95% CI)	*P* value
No adenoma	74,259	63	2.448	32,820	9	0.829	2.92 (1.45–5.87)	.003
Low-risk adenoma	9909	8	2.253	8658	2	0.706	3.11 (0.66–14.63)	.152
High-risk adenoma	5699	15	8.100	5824	6	3.484	2.24 (0.87–5.77)	.095

NOTE. Observation period censored at the end of follow-up period, or at the actual date of surveillance colonoscopy, respectively.
CRC, colorectal cancer.
[a]Low performers vs high performers, adjusted for age and sex of individuals, not accounted for within-physician clustering and possible correlations between the same individual with multiple examinations.

Supplementary Table 6B. Validation Cohort: CRC Risk per 100,000 Person Years for Low-Risk Adenoma Individuals, High-Risk Adenoma Individuals, and After Negative Colonoscopy, Stratified by Endoscopists' Performance (ADR Cutoff 20% and 25%, Respectively)

	ADR <20%			ADR ≥20%				
Risk group	Number of individuals	CRC cases	CRC risk per 100,000 person-years	Number of individuals	CRC cases	CRC risk per 100,000 person-years	HR[a] (95% CI)	*P* value
No adenoma	50,197	43	2.513	56,882	29	1.489	1.64 (1.02–2.63)	.040
Low-risk adenoma	5606	3	1.507	12,961	5	1.230	1.25 (0.30–5.24)	.758
High-risk adenoma	3158	5	6.893	8365	8	4.325	1.53 (0.50–4.67)	.458
	ADR <20%			ADR ≥20%				
Risk group	Number of individuals	CRC cases	CRC risk per 100,000 person-years	Number of individuals	CRC cases	CRC risk per 100,000 person-years	HR[a] (95% CI)	*P* value
No adenoma	74,259	63	2.448	32,820	9	0.829	2.92 (1.45–5.87)	.003
Low-risk adenoma	9909	6	1.690	8658	2	0.757	2.35 (0.48–11.65)	.295
High-risk adenoma	5699	9	6.921	5824	4	3.318	2.17 (0.67–7.04)	.198

NOTE. Observation period censored at the end of follow-up period or at recommended time of surveillance (3 years for high-risk adenoma, 5 years for low-risk adenomas). Total number of person years: 450,786.35. Total number of events: 93.
CRC, colorectal cancer.
[a]Low performer vs high performer, adjusted for age and sex of individuals, not accounted for within-physician clustering and possible correlations between the same individual with multiple examinations