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Postpolypectomy Colonoscopy Surveillance Guidelines: Predictive Accuracy for Advanced Adenoma at 4 Years

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Background: Lack of confidence in postpolypectomy surveillance guidelines may be a factor in the observed low adherence rates among providers.

Objective: To assess the 2006 postpolypectomy colonoscopy surveillance guidelines, which recommend 3-year follow-up colonoscopy for individuals with high-risk adenomas (defined as ≥3 adenomas or any advanced adenomas) and 5- to 10-year follow-up for patients with 2 or fewer nonadvanced adenomas, who are considered to be at low risk.

Design: Analysis of prospective data from the Polyp Prevention Trial.

Setting: United States.

Participants: 1905 patients who had colorectal adenomas removed at baseline screening or diagnostic colonoscopy and completed the trial.

Measurements: Baseline adenoma characteristics, risk-stratified according to definitions used in the guidelines, were examined as predictors for advanced adenoma recurrence.

Results: 125 patients (6.6%) had advanced and 629 (33.0%) had nonadvanced adenoma recurrence; 1151 (60.4%) had no recurrence within 4 years of follow-up. The probability of advanced adenoma recurrence was 0.09 (95% CI, 0.07 to 0.11) among patients with high-risk adenomas at baseline and 0.05 (CI, 0.04 to 0.06) among those with low-risk adenomas at baseline. The relative risk for advanced adenoma recurrence for patients with high-risk adenomas versus those with low-risk adenomas at baseline was 1.68 (CI, 1.19 to 2.38) when advanced adenoma recurrence was compared with no advanced adenoma recurrence and 1.76 (CI, 1.26 to 2.46) when advanced adenoma recurrence was compared with no adenoma recurrence. The c-statistics for these 2 comparisons were 0.68 and 0.72, respectively.

Limitation: Participants were self-selected and had restrictions on the degree of obesity.

Conclusion: Although the risk for recurrence of advanced adenoma within 4 years is greater for patients with high-risk adenomas at baseline than for those with low-risk adenomas, the discrimination of this risk stratification scheme is relatively low.

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Clinical practice guidelines for postpolypectomy colonoscopy surveillance have been developed by different professional societies and updated as necessary on the basis of scientific evidence (1–4). However, surveys of gastrointestinal endoscopists (5) and primary care physicians (6, 7) have consistently shown a lack of adherence to surveillance guidelines, with repeated examinations being recommended at shorter intervals than the guidelines indicate. This suggests an overuse of surveillance colonoscopy, which already constitutes approximately 24% of procedures performed in the United States (8). Nonadherence may be due to a lack of knowledge of the guidelines, medical liability concerns, financial incentives, and differing recommendations by professional societies.

The U.S. Multi-Society Task Force on Colorectal Cancer and the American Cancer Society jointly developed and published a consensus update for postpolypectomy surveillance guidelines in 2006 to provide more consistency among guidelines (9). Patients were stratified as having high risk or low risk for subsequent development of advanced neoplasia on the basis of adenoma characteristics at baseline. The guidelines classify patients with 3 or more synchronous adenomas or any advanced adenomas (adenomas ≥1 cm in diameter or with a villous histology or high-grade dysplasia) as high risk. Individuals found to be at high risk at baseline are to have follow-up colonoscopy in 3 years, whereas those with fewer, nonadvanced, adenomatous polyps (low-risk patients) are to have repeated examination in 5 to 10 years. The guidelines recommend 10-year follow-up evaluation for average-risk individuals (those with no adenomatous polyps).

Lack of confidence in the postpolypectomy guidelines may be a common reason for nonadherence. According to Mysliwiec and colleagues (5), approximately 80% of surveyed endoscopists indicated that published evidence was very influential in their practice, but only half the respon-

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Context

Guidelines for surveillance colonoscopy after removing a colon polyp recommend more frequent surveillance after a high-risk finding at baseline (an advanced adenoma or ≥3 adenomas).

Contribution

The authors studied 1905 patients who had an adenoma at baseline colonoscopy and had follow-up colonoscopy at 1 year and 4 years. Overall, 6.6% had an advanced adenoma—considered to be high risk to become malignant—at 4 years. The advanced adenoma rates were 9% and 5% in patients with high-risk and low-risk adenomas at baseline colonoscopy, respectively.

Implication

The characteristics of an adenoma are not a reliable guide to the probability of recurrence of an advanced adenoma.

—The Editors

dents indicated that practice guidelines were very influential. This response highlights a perceived disconnect between published evidence and postpolypectomy guidelines. In another survey, 17% to 21% of gastroenterologists knew the guidelines but disregarded them, opting for earlier surveillance colonoscopy (10). Merritt and colleagues (11) reported that clinical practice guidelines are often fast-tracked without an adequate evaluation of their effectiveness. Therefore, validating guidelines may increase physicians' confidence and improve adherence. Our study is a step in that direction.

We sought to assess the utility of the risk-based stratification recommended by the current guidelines, using data from the dietary PPT (Polyp Prevention Trial). We measured the ability of adenoma characteristics at baseline (as defined in the 2006 consensus update on postpolypectomy surveillance guidelines) to predict subsequent advanced adenoma recurrence within 4 years.

METHODS

The Polyp Prevention Trial

The rationale, design, and results of the PPT are published elsewhere (12–14). In brief, the PPT was a 4-year, multicenter, randomized, controlled trial involving 2079 patients age 35 years or older who had at least 1 histologically confirmed adenoma removed during a screening or diagnostic colonoscopy within 6 months of random assignment. A total of 1663 patients reported a single reason for colonoscopy, whereas 416 had 2 or more reasons for the examination (12). Overall, approximately 9% had colonoscopy because of family history of polyps or cancer (screening), 22% for routine polyp surveillance, and 69% for diagnostic studies. The PPT sought to determine whether a low-fat, high-fiber diet affected the rate of colorectal adenoma recurrence. Patients were randomly assigned to adopt a low-fat, high-fiber diet with increased intake of fruits and vegetables or their usual diet (control). Exclusion criteria included a history of surgical resection of adenomatous polyps, bowel resection, colorectal carcinoma, the polyposis syndrome, or inflammatory bowel disease; use of lipid-lowering drugs; and body weight greater than 150% of ideal. The PPT was approved by the institutional review boards of the National Cancer Institute and each of the 8 participating clinical centers. All patients gave written informed consent. Our analysis is based on 1905 patients who completed the trial by having end point colonoscopy. The trial took place from 1991 to 1998. We included all patients in the trial because the dietary intervention had no effect on adenoma recurrence (14).

Exposure and Outcome Assessment

At baseline and at every annual follow-up visit, the investigators used direct interview to obtain information on each patient's demographic characteristics, health-related lifestyle, diet, and use of medication and dietary supplements. The patients had a clearing colonoscopy approximately 1 year after random assignment (1-year colonoscopy) to remove any lesion that the baseline colonoscopy missed. Patients were followed for approximately 4 years after random assignment and had a surveillance colonoscopy at the end of follow-up (4-year colonoscopy). We defined any histologically confirmed adenoma detected on colonoscopy after the 1-year colonoscopy as recurrent. For the 137 patients who did not have 1-year colonoscopy, we defined any histologically confirmed adenomatous polyps occurring at least 2 years after randomization as recurrent. We used the endoscopists' colonoscopy reports as the source for size, number, and location of polyps. Histology and degree of atypia were confirmed by 2 trial pathologists who were masked to the randomization. We defined adenomas removed from the rectosigmoid to the splenic flexure as distal and those removed from the transverse colon to cecum as proximal.

Statistical Analysis

We examined adenoma characteristics at baseline as predictors of advanced adenoma recurrence for up to 3 years after clearance colonoscopy as our primary analysis, similar to that of van Stolk and colleagues (15). We repeated our analyses after including adenomas found during clearance colonoscopy, as well as the recurrent adenomas defined above, even though the National Polyp Study (16) has reported that surveillance colonoscopy at 3 years was as effective as follow-up colonoscopy at both 1 and 3 years.

We used SAS software (SAS Institute, Cary, North Carolina) for all analyses. We compared the baseline characteristics by using the *t* test and chi-square tests for continuous and categorical variables, respectively. We used log-binomial modeling (a binary regression model in which the probability of a recurrence is parameterized on the log scale) to assess baseline adenoma characteristics, as defined

by the guidelines, as predictors of advanced adenomas through 4-year colonoscopy. This modeling method expresses association in terms of relative risks and 95% CIs. When the model did not converge, which is known to occur with log-binomial modeling, we used the SAS nonlinear programming procedure to find the maximum likelihood estimates (17). We used a Wald test to test whether the relative risks were equal to 1. We included age, sex, body mass index, nonsteroidal anti-inflammatory drug use, location of adenomas, and family history of colorectal cancer in the multivariable models. We calculated the probability of advanced adenoma recurrence as a function of baseline adenoma characteristics; this is mathematically equivalent to the positive predictive value associated with the baseline characteristics. We used the c-statistic (equivalent to the area under the receiver-operating characteristic curve) to measure discrimination (the ability of the predictive model to distinguish between patients with and those without the outcome of interest) (18, 19). The c-statistic is 0.5 if a prediction is no better than random and 1.0 for a perfectly predictive model.

Comparison Groups for Analyses

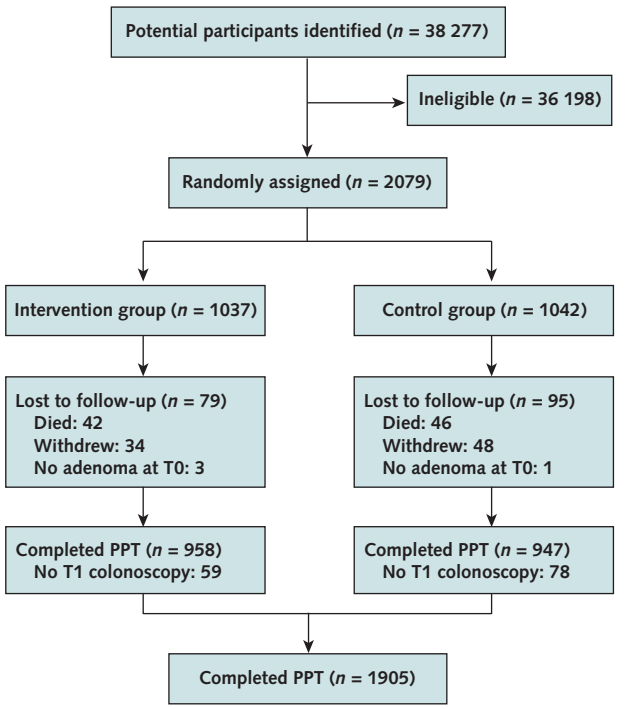
For all analyses of outcome, we compared recurrence of advanced adenomas versus no recurrence of advanced adenomas and versus no adenoma recurrence. We stratified baseline adenomas by size (≥1 cm vs. <1 cm in diameter), number (≤2 vs. ≥3 adenomas, and 1, 2, or ≥3 adenomas), degree of atypia (presence or absence of high-grade dysplasia), histology (villous or tubulovillous vs. no villous characteristics), advanced versus nonadvanced, and high-risk versus low-risk at baseline.

We evaluated baseline adenoma location as distal only, proximal only, both proximal and distal, and unspecified. We excluded 41 patients from analyses involving adenoma location because the location could not be determined. Because we were interested in whether the presence of any proximal adenoma is associated with advanced adenoma recurrence, we analyzed baseline adenoma location by comparing any proximal adenoma (proximal only and both) with distal only. In another analysis of the risk associated with adenoma location, we included only patients with baseline low-risk adenomas (1 or 2 nonadvanced adenomas) and categorized them as having 1 distal, 1 proximal, 2 distal, or 2 adenomas (with at least 1 proximal adenoma).

Role of the Funding Source

The study was funded by the Intramural Research Program of the Center for Cancer Research and Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health; and the Division of Cancer Prevention, National Cancer Institute, National Institutes of Health. The funding source had a role in the design and reporting of the study and in the decision to submit the manuscript for publication and approved the final version of the manuscript.

Figure. **Study flow diagram for the Polyp Prevention Trial (*PPT*).**



One hundred seventy-four patients did not complete the trial. Four patients were excluded late (no baseline adenoma), 88 died before the end of the trial (from causes unrelated to the trial), and 82 withdrew (72 did not have follow-up colonoscopy, 9 declined to participate, and 1 withdrew because of ill health).

RESULTS

Baseline Characteristics

Of the 2079 patients randomly assigned in the PPT, only 1905 (91.6%) completed the trial (**Figure**). The patients who did not complete the trial were older and more likely to have a history of smoking (**Appendix Table**, available at www.annals.org). **Table 1** shows selected baseline characteristics of patients who completed the PPT. Individuals with high-risk adenomas at baseline were slightly older and less likely to take nonsteroidal anti-inflammatory drugs. Of the patients who completed the PPT, 715 (37.5%) had advanced adenomas at baseline (**Table 2**); 282 (14.8%) had ≥3 adenomas and 142 (7.4%) had ≥3 adenomas of which at least 1 was advanced. At baseline, 855 patients (44.9%) had high-risk (advanced or ≥3) adenomas. A total of 1218 patients (63.9%) had 1 adenoma. One thousand thirty patients (54.1%) had only distal adenomas, and 504 (26.5%) had only proximal adenomas.

Recurrent Adenomas

During follow-up, 1151 patients (60.4%) had no adenoma recurrence, 125 (6.6%) had advanced adenoma, and 629 (33.0%) had nonadvanced adenoma at follow-up. Patients with adenoma recurrence were older and predominantly male (data not shown).

Table 1. **Selected Baseline Characteristics of Participants in the Polyp Prevention Trial**

Characteristic	All Participants (n = 1905)	High-Risk Adenomas at Baseline (n = 855)	Low-Risk Adenomas at Baseline (n = 1050)	*P* Value*
Mean age (SD), *y*	61.1 (9.9)	61.5 (9.6)	60.7 (10.0)	0.051
Men, *n (%)*	1228 (64.5)	563 (65.8)	665 (63.3)	0.25
Drug use, *n (%)*				
Nonsteroidal anti-inflammatory drugs	640 (33.6)	265 (31.0)	375 (35.7)	0.030
Aspirin	438 (23.0)	186 (21.8)	252 (24.0)	0.25
Alcohol use, *n (%)*	1103 (57.9)	491 (57.4)	612 (58.3)	0.71
Positive family history of colorectal cancer, *n (%)*	511 (26.8)	222 (26.0)	289 (27.5)	0.44
Body mass index, *n (%)*†				
<25 kg/m^2	498 (26.1)	215 (25.1)	283 (26.9)	–
25–29 kg/m^2	898 (47.1)	412 (48.2)	486 (46.3)	0.53
30–38.8 kg/m^2	509 (26.7)	228 (26.7)	281 (26.8)	–
Smoking status, *n (%)*				
Never	741 (38.9)	323 (37.8)	418 (39.8)	–
Former	911 (47.8)	409 (47.8)	502 (47.8)	0.38
Current	253 (13.3)	123 (14.4)	130 (12.4)	–
Race, *n (%)*				
White	1706 (89.5)	759 (88.8)	947 (90.2)	–
Black	154 (8.1)	73 (8.5)	81 (7.7)	0.55
Other‡	45 (2.4)	23 (2.7)	22 (2.1)	–

* For comparison between participants with high-risk versus those with low-risk adenomas at baseline.
† An exclusion criterion for the Polyp Prevention Trial was body weight more than 150% of ideal.
‡ Includes Hispanic, Indian/Native American, and Asian/Pacific Islander ethnicity.

Prediction of Advanced Adenoma Recurrence

The probability of advanced adenoma recurrence was 0.09 (95% CI, 0.07 to 0.11) among patients with baseline high-risk adenoma and 0.05 (CI, 0.04 to 0.06) among those with baseline low-risk adenoma, as defined by current guidelines. The recurrence rates were similar for both definitions of high-risk adenoma: 0.09 (CI, 0.07 to 0.11) among those with baseline advanced adenomas and 0.10 (CI, 0.07 to 0.14) among those with 3 or more adenomas at baseline (**Table 2**). In analyses with 1 baseline adenoma characteristic in each regression model (**Table 2**), the presence of 1 or more advanced adenomas, size 1 cm or greater, high-grade dysplasia, and villous histology were each associated with advanced adenoma recurrence regardless of the comparison group, whereas the presence of 3 or more adenomas was a risk factor only when the comparison group was no adenoma recurrence. However, the predictive ability of the log-binomial models with these baseline adenoma characteristics is relatively low. The c-statistics for the models ranged from 0.67 to 0.73. A c-statistic of 0.7 is considered to have limited discriminatory ability, whereas a c-statistic greater than 0.8 has discrimination thought to be adequate for real clinical utility (20).

In multivariable analyses that included all individual baseline adenoma characteristics in the model, only villous histology and proximal location were independent predictors of advanced adenoma recurrence in the primary analysis, which used only the 4-year colonoscopy data (**Table 3**). The c-statistics for the multivariable models were 0.71 and 0.74. The results were similar when we included 1-year colonoscopy as well as 4-year colonoscopy results in our analysis, except that polyp size of 1 cm or greater became a significant risk factor for advanced adenoma recurrence when no advanced adenoma recurrence was used as the reference group (relative risk, 1.56 [CI, 1.13 to 2.14]) but not when no adenoma recurrence was the comparison category (relative risk, 1.25 [CI, 0.92 to 1.69]). The c-statistics for the multivariable models were 0.69 when advanced adenoma was compared with nonadvanced adenoma recurrence and 0.73 when advanced adenoma was compared with no adenoma recurrence.

Exploratory Analyses of Predictors of Recurrence

Patients with proximal adenomas at baseline were less likely than patients with only distal adenomas at baseline to have large (≥1 cm) adenomas at baseline (25.8% vs. 37.7%; $P < 0.001$), villous histology (16.4% vs. 23.8%; $P < 0.001$), high-grade dysplasia (5.7% vs. 9.5%; $P = 0.002$), and advanced adenoma (32.0% vs. 43.3%; $P < 0.001$). Proximal adenomas at baseline were associated with advanced adenoma recurrence during follow-up in all models. We subsequently evaluated the effect of proximal location on advanced adenoma recurrence among patients with low-risk adenomas (1 or 2 nonadvanced adenomas) at

baseline. The presence of 2 adenomas with at least 1 in the proximal colon was significantly associated with an increased risk for advanced adenoma recurrence (relative risk, 2.62 [CI, 1.29 to 5.29]) compared with 1 distal adenoma (**Table 4**). The c-statistics for all predictive models in our analyses ranged from 0.64 to 0.74.

DISCUSSION

In our study, only the villous histology component of the definition of an advanced adenoma was an independent predictor at baseline of recurrent advanced adenomas within 4 years. Adenoma size, high-grade dysplasia, and presence of 3 or more synchronous nonadvanced adenomas were not independent risk factors. Overall, we found the current postpolypectomy guidelines to have limited predictability for advanced adenoma recurrence within 4 years, even when individual baseline adenoma characteristics were statistically significant risk factors.

In addition, patients with 2 nonadvanced adenomas were at increased risk for advanced adenomas if they had any proximal adenoma. The current postpolypectomy guidelines do not make any surveillance recommendations based on adenoma location at baseline. However, when we incorporated adenoma location into the definition of baseline high-risk adenoma, the probability of advanced adenoma recurrence with this new high-risk definition was

Table 2. **Association of Adenoma Characteristics at Baseline with Advanced Adenoma Recurrence in 4 Years**

Characteristic at Baseline Colonoscopy	Findings at 4-Year Colonoscopy			Probability of Advanced Adenoma Recurrence if Baseline Finding Is Present (95% CI)	Relative Risk (95% CI)*	
	Advanced Adenoma	Nonadvanced Adenoma	No Adenoma		Advanced Adenoma Recurrence vs. Nonadvanced Adenoma Recurrence	Advanced Adenoma Recurrence vs. No Adenoma Recurrence
All participants (*n* = 1905)	125	629	1151	0.06 (0.05–0.08)	–	–
Risk status						
Low-risk adenoma (*n* = 1050)	51	343	656	0.05 (0.04–0.06)	1.0 (reference)	1.0 (reference)
High-risk adenoma (*n* = 855)	74	286	495	0.09 (0.07–0.10)	1.68 (1.19–2.38)	1.76 (1.26–2.46)
Adenoma stage†						
Nonadvanced (*n* = 1190)	60	415	715	0.05 (0.04–0.06)	1.0 (reference)	1.0 (reference)
Advanced (*n* = 715)	65	214	436	0.09 (0.07–0.11)	1.94 (1.38–2.73)	1.83 (1.32–2.54)
Adenoma histology						
Nonvillous (*n* = 1521)	78	518	925	0.05 (0.04–0.06)	1.0 (reference)	1.0 (reference)
Villous (*n* = 384)	47	111	226	0.12 (0.09–0.16)	2.43 (1.72–3.42)	2.24 (1.62–3.11)
Adenoma size‡						
<1 cm (*n* = 1204)	67	420	717	0.06 (0.04–0.07)	1.0 (reference)	1.0 (reference)
≥1 cm (*n* = 560)	44	167	349	0.08 (0.06–0.10)	1.57 (1.09–2.27)	1.46 (1.03–2.08)
Degree of atypia§						
No high-grade dysplasia (*n* = 1752)	109	579	1064	0.06 (0.05–0.07)	1.0 (reference)	1.0 (reference)
High-grade dysplasia (*n* = 145)	15	47	83	0.10 (0.06–0.16)	1.73 (1.04–2.86)	1.81 (1.11–2.94)
Adenoma location‖						
Distal only (*n* = 1030)	49	295	686	0.05 (0.04–0.06)	1.0 (reference)	1.0 (reference)
Any proximal (*n* = 834)	73	316	445	0.09 (0.07–0.11)	1.58 (1.11–2.25)	1.84 (1.31–2.59)
Number of adenomas¶						
Comparison 1						
≤2 (*n* = 1623)	97	487	1039	0.06 (0.05–0.07)	1.0 (reference)	1.0 (reference)
≥3 (*n* = 282)	28	142	112	0.10 (0.07–0.14)	1.17 (0.76–1.79)	1.64 (1.10–2.43)
Comparison 2						
1 (*n* = 1218)	66	341	811	0.05 (0.04–0.07)	1.0 (reference)	1.0 (reference)
2 (*n* = 405)	31	146	228	0.08 (0.05–0.10)	1.26 (0.83–1.91)	1.38 (0.92–2.06)
≥3 (*n* = 282)	28	142	112	0.10 (0.07–0.14)	1.27 (0.80–2.01)	1.84 (1.20–2.81)

* Multivariable adjustment for baseline age, sex, body mass index, nonsteroidal anti-inflammatory drug use, adenoma location, and family history of colorectal cancer.
† 142 (19.9%) participants with advanced adenomas at baseline and 140 (11.8%) without advanced adenomas at baseline had ≥3 adenomas ($P < 0.001$), and 142 (50.4%) participants with ≥3 adenomas at baseline and 573 (35.3%) with ≤2 adenomas at baseline had advanced adenomas ($P < 0.001$). Among participants with nonadvanced adenomas at baseline ($n = 1190$), 140 had ≥3 adenomas at baseline and 1050 had ≤2 adenomas at baseline. The probability of advanced adenoma recurrence was 0.06 (95% CI, 0.03–0.12) for participants with ≥3 adenomas at baseline and 0.05 (CI, 0.04–0.06) for participants with ≤2 adenomas at baseline. Relative risks for advanced adenoma recurrence were 0.82 (CI, 0.39–1.71) for distinguishing advanced vs. nonadvanced adenoma recurrence and 1.17 (CI, 0.58–2.33) for distinguishing advanced vs. no adenoma recurrence.
‡ Information on size was missing for 141 participants.
§ Information on high-grade dysplasia was missing for 8 participants.
‖ Information on location of adenoma was missing for 41 participants.
¶ Regardless of adenoma histologic characteristics or size.

Table 3. **Multivariable Model for Advanced Adenoma Recurrence with All Adenoma Characteristics in the Same Model**

Baseline Factor	Relative Risk (95% CI) at 4-Year Colonscopy*	
	Advanced Adenoma Recurrence vs. Nonadvanced Adenoma Recurrence	Advanced Adenoma Recurrence vs. No Adenoma Recurrence
Age (per 1-year increase)	1.04 (1.02–1.06)	1.05 (1.03–1.07)
Male sex	1.22 (0.81–1.84)	1.34 (0.90–2.01)
Nonsteroidal anti-inflammatory drug use	0.55 (0.35–0.86)	0.56 (0.36–0.86)
Positive family history of colorectal cancer	1.22 (0.81–1.83)	1.31 (0.88–1.95)
Body mass index†		
<25 kg/m^2	1.0 (reference)	1.0 (reference)
25–29 kg/m^2	0.99 (0.61–1.62)	1.10 (0.69–1.77)
30–38.8 kg/m^2	1.58 (0.95–2.60)	1.69 (1.04–2.75)
Any proximal disease vs. distal disease only	1.90 (1.27–2.85)	2.00 (1.36–2.92)
Villous/tubulovillous component vs. no villous component	2.38 (1.56–3.64)	2.25 (1.49–3.39)
Presence of high-grade dysplasia	1.11 (0.62–1.97)	1.11 (0.64–1.90)
Size ≥1 cm vs. <1 cm	1.06 (0.69–1.61)	0.93 (0.61–1.41)
≥3 adenomas vs. ≤2 adenomas	0.98 (0.62–1.55)	1.46 (0.96–2.22)
c-Statistic‡	0.71	0.74

* Multivariable adjustment for baseline age, sex, body mass index categories, nonsteroidal anti-inflammatory drug use, family history of colorectal cancer, and adenoma characteristics at baseline (location, size, high-grade dysplasia, and villous component).
† An exclusion criterion for the Polyp Prevention Trial was body weight more than 150% of ideal.
‡ The c-statistic is the area under the receiver-operating characteristic curve constructed from the relative risk model. It assesses the ability of baseline adenoma, demographic characteristics, and nonsteroidal anti-inflammatory drug use to predict advanced adenoma recurrence. It can be interpreted as the probability of a randomly selected patient with an advanced adenoma recurrence having a higher predicted probability than a randomly selected patient without an advanced adenoma recurrence. A c-statistic of 1.0 implies perfect predictability; a value of 0.5 implies predictability equivalent to that of flipping a coin.

0.09 (CI, 0.07 to 0.11), compared with 0.04 (CI, 0.03 to 0.06) for the new low-risk category. The relative risk estimates were 2.02 (CI, 1.38 to 2.96) and 2.12 (CI, 1.46 to 3.07), but the c-statistic for the multivariable models remained only 0.68 and 0.71 for distinguishing recurrence of advanced adenomas versus no recurrence of advanced adenomas and no adenoma recurrence, respectively. Therefore, inclusion of another baseline adenoma characteristic associated with a statistically significant relative risk for recurrence did not materially improve the limited predictability that we observed in the current guidelines' risk stratification scheme.

We evaluated the diagnostic accuracy of the multivariable risk models (which incorporated baseline adenoma and demographic variables) for predicting advanced adenoma recurrence, thereby assessing the utility of the current postpolypectomy guidelines. Our study suggests that statistically significant risk factors—both adenoma features and demographic and lifestyle characteristics—do not necessarily translate into clinically useful predictive guidelines. If other studies confirm our findings, a review of the postpolypectomy guidelines to improve their ability to predict recurrence of important colorectal lesions may be warranted.

Table 4. **Effect of Location of Advanced Adenoma Recurrence among Participants with 1 or 2 Low-Risk Adenomas at Baseline***

Baseline Colonoscopy			Findings at 4-Year Colonoscopy			Probability (95% CI) of Advanced Adenoma Recurrence if Baseline Finding Is Present	Relative Risk (95% CI)†	
Number of Adenomas	Location	Participants, *n*	Recurrent Advanced Adenomas	Recurrent Nonadvanced Adenomas	No Recurrent Adenoma		Advanced Adenoma Recurrence vs. Nonadvanced Adenoma Recurrence‡	Advanced Adenoma Recurrence vs. No Adenoma Recurrence‡
1	Distal	483	15	145	323	0.03 (0.02–0.05)	1.0 (reference)	1.0 (reference)
1	Proximal	302	18	90	194	0.06 (0.04–0.09)	1.64 (0.84–3.20)	1.69 (0.87–3.27)
2	Distal	81	2	34	45	0.02 (0.00–0.09)	0.72 (0.17–3.09)	0.95 (0.22–3.99)
2	≥1 proximal	152	14	63	75	0.09 (0.05–0.15)	2.62 (1.29–5.29)	3.16 (1.60–6.26)

* For 1018 of 1050 participants; 32 participants with missing information on location were excluded.
† Multivariable adjustment for baseline age, sex, body mass index categories, nonsteroidal anti-inflammatory drug use, and family history of colorectal cancer.
‡ The c-statistic was 0.71 for advanced adenoma recurrence vs. nonadvanced adenoma recurrence and 0.74 for advanced adenoma recurrence vs. no adenoma recurrence. The c-statistic is the area under the receiver-operating characteristic curve constructed from the relative risk model. It assesses the ability of baseline adenoma, demographic characteristics, and nonsteroidal anti-inflammatory drug use to predict advanced adenoma recurrence. It can be interpreted as the probability of a randomly selected patient with an advanced adenoma recurrence having a higher predicted probability than a randomly selected patient without an advanced adenoma recurrence. A c-statistic of 1.0 implies perfect predictability; a value of 0.5 implies predictability equivalent to that of flipping a coin.

Many of our findings confirm those from other studies. The 39.6% overall rate of adenoma recurrence in our study was similar to that in previous reports, which ranged from 35% to 48.6% at 3 to 4 years (15, 16, 21–25). Unlike previous investigations (16, 26, 27), we did not find multiple adenomas at baseline to be a risk factor for subsequent advanced adenomas; however, similar to other studies (28, 29), we did find that an advanced adenoma at baseline was a risk factor—albeit one with limited predictability.

In a recent study by Lieberman and colleagues (30), 895 patients with neoplasia detected on screening colonoscopy and 298 neoplasia-free control participants from a Veterans Affairs population were followed for approximately 5.5 years and had repeated colonoscopy during this period. After adjustment for age and family history of colorectal cancer, the investigators found that adenoma size of 1 cm or greater, villous adenoma, and high-grade dysplasia were associated with an increased risk for advanced adenoma recurrence compared with participants without adenomas at baseline. For most baseline adenoma characteristics, Lieberman and colleagues (30) reported slightly higher probabilities of advanced adenoma recurrence than we found: 1 or 2 adenomas regardless of histology, 6.5% versus 6.0%; adenoma size of 1 cm or greater, 15.5% versus 7.9%; villous adenoma, 16.1% versus 12.2%; and high-grade dysplasia, 17.4% versus 10.3%. The exception was 1 or 2 nonadvanced adenomas at baseline, for which we and Lieberman and colleagues found a similar probability (4.9% vs. 4.6%, respectively). On the basis of high-risk adenoma characteristics, the probability of advanced adenoma recurrence in Lieberman and colleagues' sample ranged from 0.12 to 0.17 through 5.5 years of follow-up; this range is similar to ours (0.08 to 0.12).

Although the PPT was a dietary intervention trial, it provided an opportunity to investigate baseline factors associated with adenoma recurrence in a large population. Studying the PPT population contributed several potential strengths. The PPT is a large, randomized, controlled trial in which all patients had at least 1 baseline adenoma removed during colonoscopy; trial pathologists were used; information on candidate risk factors was prospectively gathered; and all patients had planned colonoscopic assessment for recurrence after 4 years of follow-up.

However, our study also has limitations. Participants in the PPT were self-selected and may have been healthier than similar members of the general population (the healthy volunteer effect). First, because the PPT studied a specific dietary pattern, the investigators excluded patients who needed to follow a strict dietary regimen, such as diabetics, and those with cholesterol levels high enough to require medication. Second, the design of the PPT excluded people who weighed more than 150% of their ideal body weight. This exclusion affects the generalizability of our results, because obesity may be associated with an increased risk for adenoma recurrence (31). Finally, the PPT population had clearing colonoscopies approximately 1 year after random assignment to remove missed lesions from qualifying colonoscopy; adenoma recurrence in our study may therefore be lower than that in usual practice.

The focus of colonoscopy guidelines should be to identify individuals at the highest risk and target them for surveillance, similar to the risk prediction recommendations for cardiovascular disease (32). Our study suggests that the adenoma-based risk stratification used in the current postpolypectomy surveillance guidelines have limited predictability for advanced adenoma recurrence. Misclassification of high-risk patients as low-risk may lead to missing potentially preventable colorectal cancer, and misclassification of low-risk patients as high-risk may impose further burden on our limited endoscopic resources. To achieve the overarching goals of practice guidelines—widespread adoption of recent clinical advances, improvement in quality of care through reduction in inappropriate practice pattern variation, and promotion of health care cost-effectiveness (11, 33, 34)—we need to improve the predictive ability of the guidelines' recommendations.

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Appendix Table. **Comparison of the Polyp Prevention Trial Participants: Completers versus Noncompleters**

Baseline Characteristic	Completers (n = 1905)	Noncompleters (n = 174)	P Value
Mean age (SD), *y*	61.1 (9.9)	65.8 (10.3)	<0.001
Men, *n (%)*	1228 (64.5)	123 (70.7)	0.099
Drug use, *n (%)*			
Nonsteroidal anti-inflammatory drugs	640 (33.6)	61 (35.1)	0.70
Aspirin	438 (23.0)	46 (26.4)	0.30
Alcohol use, *n (%)*	1103 (57.9)	101 (58.1)	0.97
Positive family history of colorectal cancer, *n (%)*	511 (26.8)	36 (20.7)	0.079
Body mass index, *n (%)**			
<25 kg/m^2	498 (26.1)	52 (29.9)	–
25–29 kg/m^2	898 (47.1)	66 (37.9)	0.064
30–38.8 kg/m^2	509 (26.7)	56 (32.2)	–
Smoking status, *n (%)*			
Never	741 (38.9)	49 (28.2)	–
Former	911 (47.8)	97 (55.8)	0.020
Current	253 (13.3)	28 (16.1)	–
Race, *n (%)*			
White	1706 (89.5)	155 (89.1)	–
Black	154 (8.1)	17 (9.8)	0.45
Other†	45 (2.4)	2 (1.2)	–

* An exclusion criterion for the Polyp Prevention Trial was body weight more than 150% of ideal.
† Includes Hispanic, Indian/Native American, and Asian/Pacific Islander ethnicity.