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Utilization and Yield of Surveillance Colonoscopy in the Continued Follow-Up Study of the Polyp Prevention Trial

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Abstract

Background and Aims—Prospective information on use and yield of surveillance colonoscopy is limited. We examined utilization and yield of surveillance colonoscopy among participants in the Polyp Prevention Trial (PPT) after the 4-year dietary intervention trial ended.

Methods—A cohort of 1,297 participants was followed. We calculated the cumulative probability of post-trial colonoscopy and investigated the yield and predictive factors for adenoma and advanced adenoma recurrence over a mean follow-up time of 5.9 years.

Results—Seven-hundred and seventy-four subjects (59.7%) had a repeat colonoscopy. Among 431 subjects with low-risk adenomas (1-2 non-advanced adenomas) at baseline and no adenoma recurrence at the end of the PPT (lowest-risk category), 30.3% underwent a repeat colonoscopy within 4 years. Among 55 subjects who had high-risk adenomas (advanced adenoma and/or ≥3 non-advanced adenomas) at baseline and again at the end of the PPT (highest-risk category), 41.3% had a colonoscopy within 3 years and 63.5% had an examination within 5 years. The cumulative yield of advanced adenoma through 6 years was 3.6% for the lowest-risk category, 38.9% for the highest-risk category, and ranged from 6.6% to 13.8% for intermediate-risk categories. An advanced

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adenoma at the colonoscopy at the end of the PPT was significantly associated with an advanced adenoma recurrence during surveillance (HR=6.2; 95% CI: 2.5-15.4).

Conclusions—Surveillance colonoscopy was over-utilized for low-risk subjects and under-utilized for high-risk subjects. Advanced adenoma yield corresponded with the adenoma risk category. Resource consumption can be better managed by aligning utilization with the risk of adenoma recurrence.

Keywords

Colonoscopy utilization; polypectomy; surveillance; colorectal adenoma

Introduction

Colonoscopy with polypectomy significantly reduces colorectal cancer (CRC) incidence.[1, 2] However, individuals with adenomas who have undergone polypectomy remain at risk for adenoma recurrence with a cumulative recurrence rate of approximately 36-52% at 3-4 years [3] underscoring the need for continued surveillance. Patients are recommended to undergo follow up colonoscopy in 3 years if they have had high-risk adenomas (HRA) defined as 3 or more synchronous adenomas or an advanced adenoma (size ≥1 cm in diameter, villous histology or high grade dysplasia); those with low-risk adenomas (LRA) defined as 1 or 2 non-advanced adenomas should wait for at least 5 years before undergoing repeat examinations and those without adenomas should undergo repeat examinations in 10 years.[4] The findings at the last colonoscopy determine the interval for repeat colonoscopy.[5]

Surveillance colonoscopy for individuals with previously diagnosed colonic neoplasia consumes considerable endoscopic resources, constituting approximately 24% of colonoscopies performed in both academic and non-academic settings in the United States,[6] and may contribute to longer waiting periods for screening procedures.[7] Mysliwiec *et al*[8] and Boolchand *et al*[9] have reported in surveys of endoscopy providers and primary care physicians that physicians tend to recommend surveillance in excess of guidelines. However, these observations were based on provider self report of hypothetical case scenarios.

We evaluated a cohort of subjects who participated in the Polyp Prevention Trial (PPT), a randomized controlled trial evaluating the effect of a comprehensive dietary modification on colorectal adenoma recurrence.[10] After the trial ended, subjects were invited to participate in the Polyp Prevention Trial – Continued Follow-up Study (PPT-CFS), a passive post-trial follow-up while under the care of their personal health care providers. The follow-up included two assessments of diet by means of mailed food frequency questionnaires and obtaining all subsequent colonoscopy, operative and pathology reports.

The primary aim of the PPT-CFS was to evaluate adenoma recurrence in the intervention and control arms of the PPT for at least four years after completion of the original trial. As recently reported, there was no difference in adenoma recurrence rates between the intervention and control arms even though the differences in the dietary patterns accomplished during the active PPT persisted.[11]

The objective of this study was to examine colonoscopy utilization among the PPT participants after completion of the trial, and to assess the yield of finding neoplastic lesions from colonoscopy evaluations of the subjects spanning a period of approximately 10 years: 4 years during the PPT and 6 years during the PPT-CFS.

Methods

Study population

The details of the rationale, design, and results of the PPT have been described in previous publications.[10, 12, 13] In brief, the PPT was a 4-year multicenter, randomized, controlled trial to assess the effect of a low-fat, high-fiber, fruit and vegetable diet on the risk of recurrence of colorectal adenomas. The study involved 2,079 subjects who were recruited and randomized between June 1991 and January 1994. Participants were 35 years and older and had one or more histologically confirmed adenomatous polyps removed within 6 months before study entry. The subjects had no previous history of surgical resection of adenomatous polyps, bowel resection, colorectal carcinoma, polyposis syndrome, or inflammatory bowel disease. The participants also weighed no more than 150% of their ideal body weight and were not on any lipid-lowering medications. The clinical trial was approved by the Institutional Review Boards of the National Cancer Institute, and each of the eight participating clinical centers (Kaiser Foundation Research Institute, California; University of Pittsburgh, Pennsylvania; Wake Forest University, North Carolina; State University of New York (SUNY) at Buffalo, New York; Memorial Sloan Kettering Cancer Center, New York; University of Utah School of Medicine, Utah; Edward Hines Jr. VA Hospital, Illinois; and Walter Reed Army Medical Center, Washington DC). All subjects gave written informed consent.

A total of 2,079 subjects were randomized, but only 1,905 (91.6%) completed the 4-year PPT by undergoing the trial endpoint colonoscopy. The trial did not demonstrate an effect of the dietary intervention on the risk of adenoma recurrence.[10] After the trial was completed, letters of invitation were sent to the PPT participants for enrollment in a post-trial observation “continued follow-up study” (CFS) that did not involve visitation to a clinical center. Subjects indicated their willingness to participate by returning postcards. A total of 1,297 participants agreed to participate in the continued follow-up study. Unlike during the PPT when colonoscopic examinations were scheduled according to the protocol of the dietary intervention trial, the subjects in the CFS were left to the usual care of their primary care physicians and endoscopists. These physicians performed and should have been aware of the results of the endoscopy performed during the PPT. They were also the ones who arranged any testing that occurred during the PPT-CFS. The PPT-CFS follow-up began in 1995 and ended in 2004.

Exposure and outcome assessment

In the main PPT trial protocol, the trial investigators coordinated the dietary intervention program at the clinical centers, but the colonoscopies were performed by the participants' usual endoscopist. The participants underwent colonoscopy one year after randomization (T1) to ensure the removal of any possible missed lesions from the qualifying (T0) examination and were followed for a total of approximately four years after randomization. Then, they underwent repeat colonoscopy (T4) to determine whether they had a recurrent adenoma. Subjects underwent a mean of 3.1 colonoscopies during the PPT. During the PPT-CFS, health and lifestyle questionnaires provided information on the participants' demography, hospitalizations, and colonoscopy utilization. All colonoscopy and pathology reports as well as all hospitalizations and death certificates were collected. For this study, we defined an adenoma as recurrent if found at any colonoscopy performed after the T4 colonoscopy which determined the endpoint of the PPT. The endoscopists' colonoscopy reports provided information on size, multiplicity, and location of polyps. Histology and degree of atypia were extracted from the pathologists' reports.

Statistical analyses

We defined the start of follow-up as the date of the last PPT colonoscopy while the end of follow-up was the last contact date. Subjects were censored if they did not have colonoscopy

by the last day of contact. We compared the baseline characteristics of subjects who agreed to participate in PPT-CFS to those who declined using the Wilcoxon rank-sum test and chi-square to compare means and proportions of exposure variables.

We defined adenoma characteristics according to the risk stratification scheme of the postpolypectomy surveillance guidelines.[4] We defined high-risk adenomas as the presence of three or more synchronous adenomas and/or by the presence of an advanced adenoma (defined as an adenoma ≥ 1cm, with villous histology or with high-grade or severe dysplasia). We analyzed incident colorectal cancers as advanced adenomas. We defined low-risk adenomas as 1 – 2 non-advanced adenomas. We considered the findings at T0 and T1 as baseline lesions and classified subjects into one of two mutually exclusive categories, LRA or HRA, based on the most advanced finding. If a subject had an advanced adenoma or ≥3 synchronous adenomas at either T0 or T1, the subject was categorized as a HRA. We classified subjects by findings at the end of PPT (T4 colonoscopy) into HRA recurrence, LRA recurrence, and those without adenoma recurrence. Therefore, participants with HRA at both baseline (T0/T1) and at the end of the PPT (T4) constitute the highest risk category; those with LRA at baseline (T0/T1) and no adenoma recurrence at the end of the PPT (T4) constitute the lowest risk category and all the other subjects were at intermediate risks for advanced adenoma recurrence.

Using the Kaplan-Meier method, we computed the cumulative probability of the first occurrence of colonoscopy to assess the effect of the findings at baseline and at the last PPT colonoscopy examination on subsequent utilization. We defined a year of follow-up as 365 days from the date of last PPT examination. To accommodate colonoscopy scheduling challenges for both patients and their healthcare providers, for overutilization we focused on procedures performed at least one year before the recommended time. We used Cox proportional hazards regression models to identify predictive factors for colonoscopy utilization. We also examined the yield of adenoma detection during the PPT-CFS and used logistic regression models to assess factors associated with adenoma recurrence. All reported P-values correspond to two-sided tests. We used Statistical Analysis Systems (SAS) software version 8 (SAS Institute Inc, Cary, NC) for all analyses.

Results

Of 1,297 subjects who agreed to participate in the PPT-CFS, 869 (67%) were males and the mean age at the start of the PPT-CFS was 65.3 years. When compared to those who declined to participate, those who agreed to participate were more likely male, more highly educated, and more likely to have a family history of colorectal cancer in a first degree relative, but there was no age difference between the two groups. The participants in PPT-CFS also had more colonoscopic examinations during PPT (Table 1). The mean length of follow-up in the PPT-CFS was 5.9 years.

PPT-CFS colonoscopy use

A total of seven hundred and seventy four participants (59.7%) had at least one colonoscopy during follow-up. More than one indication for colonoscopy was listed for some patients. On an aggregate, the indications for colonoscopy were personal history of polyps/routine post-polyp surveillance (88%), family history of colorectal cancer (14%), bleeding/anemia (10%), and change in bowel habits (7%). Among 431 subjects who had 1-2 non-advanced adenomas at baseline and did not have an adenoma recurrence at the end of PPT, 30.3% underwent repeat colonoscopy within 4 years (guidelines in place in 1997[14] and 2003 [5] recommend waiting for at least 5 years for follow-up) (Table 2). In contrast, among the participants who had a HRA at baseline and at the end of PPT (n=55) (guidelines recommend follow up in 3 years), 41.3% and 57.5% had a repeat colonoscopy within 3 years and 4 years, respectively.

When analyzed based on the end of PPT (T4) findings only (irrespective of baseline adenoma characteristics) the cumulative probability of first colonoscopy was 17.6% in 3 years and 63.9% in 6 years among those without any adenoma at the end of PPT (n=853) and 36.3% in 3 years and 69.2% in 6 years among all subjects with HRA at the end of PPT (n=93). Among subjects with 1-2 non-advanced adenomas at the end of PPT (n=351), 51.2% had repeat colonoscopy within the recommended 5 years (Table 2).

Among subjects with at least 5 years of follow up (n=1133), participants who were in the highest risk category were more likely to have multiple colonoscopies when compared to those in the lowest risk category (18% versus 4.3%). Overall, multiple colonoscopic examinations were more likely to be performed among subjects with HRA at the last PPT examination irrespective of the baseline adenoma findings (data not shown).

In the multivariable proportional hazard model predicting colonoscopy utilization, participants who completed the PPT within 1997-1999 calendar years compared to those who completed PPT before 1997, were more likely to undergo repeat colonoscopy during follow-up. Family history of colorectal cancer, and the presence of an advanced adenoma or ≥3 non-advanced adenomas at the last PPT examination were also positively associated with colonoscopy use during the PPT-CFS. Subjects who were older than 65 years of age were less likely to undergo a repeat colonoscopy (HR 0.86, 95% CI: 0.74-0.99) (Table 3).

PPT-CFS adenoma yield

Adenoma yield was assessed in 774 subjects who underwent colonoscopy in PPT-CFS. Regardless of baseline findings, participants with adenoma recurrence at the end of PPT (n=272) compared to those without a recurrence at the end of PPT (n=502), have a higher yield of any adenoma (45.6% versus 24.5%, P<0.001) and advanced adenoma (9.9% versus 3.8%, P<0.001) recurrence at first colonoscopy during the PPT-CFS (Table 4). Among subjects with 1-2 non-advanced adenomas at baseline and no recurrence at the end of PPT (n=250), the lowest-risk category, the yield of an advanced adenoma in the first post-trial colonoscopy through 6 years was 2.8%. The overall yield of advanced adenoma was 3.6% when all colonoscopy examinations were included. However, among subjects with HRA at baseline and at the end of PPT (n=36), the highest-risk category, the yield of advanced adenoma through 6 years at first post-trial colonoscopy was 30.6% and the overall yield of advanced adenoma was 38.9% when all colonoscopy examinations were included (Table 4). Adenoma yield was similar for colonoscopy performed < 4 years versus ≥ 4 years after the last PPT evaluations (details not shown).

In a multivariable logistic model, men were more likely to have an adenoma recurrence at the first PPT-CFS colonoscopy compared to women and those with advanced adenoma at the last PPT colonoscopy were more likely to have any adenoma and advanced adenoma recurrence compared to those without adenoma at the end of the PPT (Table 5).

Discussion

Our study evaluated surveillance colonoscopy use and yield in a community-based setting. We found apparent over utilization of surveillance colonoscopy among low-risk and under utilization among high-risk subjects in relation to practice guidelines [4, 5, 14]. Regarding yield of adenoma and advanced adenoma during surveillance, we found that yields corresponded to the risk stratification inherent to current post-polypectomy surveillance guidelines, such that subjects with low risk adenomas had lower yields of recurrent adenoma and advanced adenoma, and higher risk subjects with baseline advanced adenomas had higher yields of recurrent adenoma and advanced adenoma.[4]

Among those who had low-risk adenomas (1-2 non advanced adenomas) at baseline and did not have any adenoma at the end of PPT, the lowest -risk category in this cohort, 30% had a follow-up colonoscopy examination within four years. Under guidelines in place during PPT and PPT-CFS [5, 14] and under current guidelines [4], subjects with 1-2 tubular adenomas are recommended to wait for at least 5 years before undergoing a repeat colonoscopy. A repeat exam within 4 years in this group would be considered over utilization, since the minimum timing for a repeat examination would be 5 years, having never manifested an advanced lesion.

In contrast, only 36% of those who had an HRA (advanced adenoma and/or ≥3 non-advanced adenomas) at the end of the PPT had a surveillance examination within 3 years, and only 65% had a repeat examination within 5 years, demonstrating that a significant proportion of high-risk subjects do not obtain timely surveillance. It is noteworthy that the post-polypectomy guidelines published during the PPT and the PPT-CFS in 1997 [14] and 2003 [5] consistently recommend a 3-year follow-up examination for subjects with advanced adenomas.

In our study, participants with a family history of colorectal cancer (CRC) were more likely to have a surveillance colonoscopy during the PPT-CFS (HR 1.3, 95%CI: 1.1 – 1.5), but a family history was not significantly associated with either adenoma or advanced adenoma recurrence. This increased utilization may be due to an increased perceived risk of CRC and a low threshold for surveillance on the part of providers, or could be due to subjects' concerns and requests for evaluation. The current post-polypectomy guideline is based primarily on adenoma findings. [4] Further studies of the impact of family history of CRC on the yield of surveillance are needed.

A special feature of this investigation is the opportunity to assess the effect of cumulative load of prior adenoma findings on the yield of surveillance. In the PPT-CFS, there was a strong gradient in advanced adenoma yield based on the cumulative load of advanced adenoma findings during prior colonoscopies. The yield of advanced adenoma at the first post-trial colonoscopy ranges from 2.8% for the lowest risk category (1-2 tubular adenomas at T0/T1, no adenoma at T4) to 30.6% for the highest risk category (high risk adenoma at T0/T1 and at T4), while the intermediate risk categories have adenoma yields of 4.7 – 8.9%. The impact of a previous high risk adenoma is demonstrated when examining the impact of an advanced adenoma as opposed to low risk adenomas at baseline in subjects who had low risk adenomas at the end of PPT (T4 examination). Among subjects who had low-risk adenomas at the end of the PPT those that had a high-risk adenoma at baseline had an 8.9% probability of an advanced adenoma recurrence at the first post-trial colonoscopy compared to only 4.7% for subjects who had low-risk adenomas at baseline (Table 4).

We also observed a lesser, but important gradient of advanced adenoma yield based on the findings at the last PPT colonoscopy. At the first post-trial colonoscopy, the advanced adenoma yield was 3.8% for no adenoma, versus 6.8% for low-risk adenoma, and 20.0% for the high-risk adenoma groups. Including all the PPT-CFS colonoscopies, the advanced adenoma yields were 5.2%, 9.2% and 27.7% in the no adenoma, low-risk adenoma, and high-risk adenoma groups, respectively. This gradient mirrors the surveillance colonoscopy results among subjects in the Veteran Affairs colonoscopy screening trial, with an advanced adenoma yield at 5.5 years of approximately 2.4%, 6.1%, and 16% among subjects with no adenoma, low-risk adenoma, and advanced adenoma at baseline.[15]

A high-risk adenoma at the initial PPT colonoscopy examination was associated with advanced adenoma yield during the first PPT-CFS colonoscopy (HR 2.4, 95%CI: 1.2 – 4.6), but not as much so as an advanced adenoma at the most recent examination (HR 6.2, 95%CI: 2.5 – 15.4) underscoring the need to take all advanced adenoma findings into consideration for surveillance recommendations, but also suggestive that more recent findings may require additional emphasis.

A major strength of this study is that we evaluated utilization and yield of colonoscopy in a relatively large, geographically dispersed cohort of patients. We observed them prospectively in a real world setting, with follow-up care determined by their healthcare providers. These practitioners performed all the PPT-associated colonoscopies, were potentially aware of all previous findings, and were the ultimate determinant of surveillance utilization during the PPT-CFS. Many factors may influence surveillance utilization, including physician preference and patient request. Participants in the PPT-CFS may have been more likely to undergo subsequent surveillance, having had a greater frequency of a family history of CRC, more education, and having undergone more colonoscopy during the main PPT trial. Regardless, physicians are responsible and empowered to serve as the gatekeeper for colonoscopy utilization. It is up to them to align risk and utilization.

Our estimates of surveillance colonoscopy use could be an underestimate of what transpires in the general population, as 97% of the participants in this cohort had three colonoscopy exams within four years as part of the PPT trial. As a result, after participation in the PPT, surveillance colonoscopy utilization may have been less than what usually occurs. Alternatively, PPT participants were self-selected, more educated, and may be more health conscious and eager to undergo colonoscopy than comparable members of the general population. Regarding yield of surveillance colonoscopy, subjects with >150% of ideal body weight were not eligible for the PPT, which restricted the degree of obesity in participants. Obesity has been associated with colorectal adenomas.[16, 17] Hence, the yield of adenoma may be lower than would be expected in the general population. Also, a small number of procedures were performed for diagnostic purposes such as bleeding, change in bowel habits or anemia, but we are unable to estimate the impact of these symptoms on utilization or yield.

In conclusion, our study suggests an overuse of surveillance colonoscopy among low-risk subjects with a corresponding low yield of advanced adenomas. Underutilization was observed among high-risk subjects. Adenoma yield at surveillance corresponded to adenoma risk category. Resource consumption by surveillance colonoscopy can be better managed by aligning utilization with the risk of adenoma recurrence.

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Abbreviations in this paper

CFS
Continued Follow-up Study

CI
Confidence interval

HR
Hazard ratio

HRA
High-risk adenomas

LRA
Low-risk adenomas

OR
Odds ratio

PPT
Polyp Prevention Trial

Table 1

Comparison of selected characteristics between the Polyp Prevention Trial-Continued Follow-up Study (PPT-CFS) participants and non-participants

Characteristics	Completed PPT (N = 1,905)		
	In CFS (n = 1297)	Not in CFS (n = 608)	P value
Male	67%	59%	0.001
Mean age at start of follow-up (SD)	65.3 (9.6)	65.9 (10.2)	0.19
White, Non Hispanic	90%	89%	0.31
Education: High school or higher	78%	68%	<0.001
Family history of colorectal cancer	28.4%	23.5%	0.03
No. of Colonoscopy During PPT			
Mean number	3.26	3.14	0.02
2	3%	9%	
3	71%	68%	
4	21%	18%	
5+	5%	5%	
Mean length (years) of follow-up in PPT-CFS after last PPT exam (10^{th}, 90^{th} percentile)	5.9 (3.8,7.7)	Not applicable	
Year of last PPT (T4) examination			
1993-1994	0.5%	3%	<0.001
1995	13%	19%	
1996	29%	32%	
1997	46%	37%	
1998	11%	9%	
Adenomas during the PPT			
Advanced adenoma at baseline	38%	36%	0.30
HRA at baseline	45%	44%	0.44
Any adenoma at last PPT examination	34%	32%	0.25
Advanced adenoma at last PPT examination	4.4%	2.6%	0.06
HRA at last PPT examination	7.2%	7.7%	0.66
Advanced adenoma at any PPT examination	44%	39%	0.06
HRA at any PPT examination	53%	51%	0.38

Advanced Adenoma = size ≥ 10 mm, villous histology, or high grade dysplasia HRA = advanced adenoma or ≥ 3 synchronous adenomas

Table 2

Cumulative percent probability (Kaplan-Meier analysis) of first colonoscopy by the PPT findings among 1,297 subjects in the PPT-CFS

Adenoma findings at T0*/ T1†	Adenoma findings at T4‡	Number of subjects	Recommended follow-up time	Cumulative rate of first PPT-CFS colonoscopy by year of follow-up**				
				Year 2	Year 3	Year 4	Year 5	Year 6
LRA§	No adenoma	431	≥ 5 years	4.5	17.6	30.3	49.8	62.9
	LRA	177	≥ 5 years	7.5	23.8	40.0	53.7	66.2
	HRA	38	3 years	18.4	29.2	55.1	67.4	69.1
HRA¶	No adenoma	422	Uncertain	5.9	17.7	31.5	49.8	64.9
	LRA	174	Uncertain	10.2	26.5	39.4	48.8	59.4
	HRA	55	3 years	24.2	41.3	57.5	63.5	71.1
ALL //	No adenoma	853	Uncertain	5.2	17.6	30.9	49.8	63.9
	LRA	351	Uncertain	8.8	25.2	39.7	51.2	62.6
	HRA	93	Uncertain	21.8	36.3	55.9	65.2	69.2

*T0 = Baseline/qualifying colonoscopy (< 6 months prior to randomization)

†T1 = Colonoscopy performed approximately one year after randomization

‡T4 = Colonoscopy performed approximately four years after randomization (end of the PPT)

§LRA = Low risk adenomas (1 – 2 non-advanced adenomas)

¶HRA = High risk adenomas (either advanced adenoma or ≥ 3 synchronous adenomas)

//Findings at T4 irrespective of T0/T1 adenoma characteristics

**Year of follow-up is ≤ number of years from the date of last PPT examination (e.g., a colonoscopy at Year 2 occurred within 365 days*2 from the last PPT colonoscopy)

Table 3

Multivariable proportional hazards model predicting colonoscopy utilization

Factor	Hazard Ratio (95% CI)†
Age > 65	0.86 (0.74-0.99)
Male	1.0 (0.8-1.1)
Year 1997-1999 (of last PPT) versus before 1997	1.2 (1.0-1.4)
Family history of colorectal cancer (Yes versus No)	1.3 (1.1-1.5)
More than high school education versus high school education or less	1.14 (0.95-1.40)
HRA¶ at T0/T1 vs LRA§ at T0/T1	1.0 (0.9-1.2)
No adenoma at last PPT	1.0 (reference)
Advanced adenoma at last PPT ‡	1.45 (1.04-2.00)
≥ 3 non-advanced adenomas at last PPT ‡	1.7 (1.2-2.6)
1-2 non-advanced adenomas at last PPT ‡	1.10 (0.95-1.30)

† Age, sex, calendar year, education, family history of colorectal cancer and adenoma characteristics in model

§ LRA = Low-risk adenomas (1 – 2 non-advanced adenomas)

¶ HRA = Advanced adenoma or ≥ 3 synchronous adenomas

‡ Versus no adenoma at last PPT

Table 4

Adenoma yield by the PPT findings among 774 subjects who underwent PPT-CFS colonoscopy

			First PPT-CFS colonoscopy			All PPT-CFS colonoscopy		
Adenoma findings at T0*/T1†	**Adenoma findings at T4‡**	**N**	**Mean time in years to 1st exam (SD)**	**% with any Adenoma**	**% with Advanced Adenoma****	**Mean time in years to last exam (SD)**	**% with any Adenoma**	**% with Advanced Adenoma**
LRA§	No adenoma	250	4.1 (1.4)	23.2	2.8	4.7 (1.3)	26.0	3.6
	LRA	106	3.9 (1.4)	40.6	4.7	4.5 (1.4)	46.2	6.6
	HRA	29	3.5 (1.7)	58.6	6.9	4.7 (1.3)	65.5	13.8
HRA¶	No adenoma	252	4.1 (1.3)	25.8	4.8	4.7 (1.3)	30.6	6.8
	LRA	101	3.6 (1.5)	39.6	8.9	4.8 (1.3)	43.6	11.9
	HRA	36	2.9 (1.5)	66.7	30.6	4.4 (1.6)	75.0	38.9
ALL//	No adenoma	502	4.1 (1.3)	24.5	3.8	4.7 (1.3)	28.3	5.2
	Any adenoma	272	3.6 (1.5)	45.6	9.9	4.6 (1.4)	51.1	13.6
	LRA	207	3.8 (1.5)	40.1	6.8	4.6 (1.4)	44.9	9.2
	HRA	65	3.1 (1.6)	63.1	20.0	4.5 (1.5)	70.8	27.7

*T0 = Baseline/qualifying colonoscopy (< 6 months prior to randomization)

†T1 = Colonoscopy performed approximately one year after randomization

‡T4 = Colonoscopy performed four year after randomization (end of the PPT)

§LRA = Low-risk adenomas (1 – 2 non-advanced adenomas)

¶HRA = Advanced adenoma or ≥ 3 synchronous adenomas

//Findings at T4 irrespective of T0/T1 adenoma characteristics

**Advanced Adenoma = size ≥ 10 mm, villous histology, or high grade dysplasia or incident colorectal cancers

Table 5

Multivariable logistic model for factors associated with adenoma recurrence at the first PPT-CFS colonoscopy

Factor	Any Adenoma OR (95% CI)	Advanced Adenoma OR (95% CI)
Male	1.7 (1.2-2.4)	2.0 (0.9-4.6)
Age > 65 years	1.3 (0.96-1.8)	1.3 (0.7-2.5)
Family History of colorectal cancer	1.1 (0.8-1.5)	1.0 (0.5-2.0)
Time > 4 years versus time ≤ 4 years after the PPT	1.1 (0.8-1.5)	0.8 (0.4-1.6)
HRA at T0/T1 vs LRA at T0/T1[¶]	1.1 (0.8-1.5)	2.4 (1.2-4.6)
No adenoma at the end of the PPT	1.0	1.0
1-2 non-advanced adenomas at the end of the PPT	2.0 (1.4-2.8)	1.7 (0.8-3.5)
≥3 non-advanced adenomas at the end of the PPT	4.8 (2.1-11.3)	3.1 (0.9-10.6)
Advanced adenomas at the end of the PPT	4.2 (2.1-8.5)	6.2 (2.5-15.4)

[¶] T0 = Baseline/qualifying colonoscopy (< 6 months prior to randomization)

T1 = Colonoscopy performed approximately one year after randomization

HRA = Advanced adenoma or ≥ 3 synchronous adenomas

LRA = Low-risk adenomas (1 – 2 non-advanced adenomas)