Research Article

Cancer Epidemiology, Biomarkers & Prevention

Receipt of Colonoscopy Following Diagnosis of Advanced Adenomas: An Analysis within Integrated Healthcare Delivery Systems

Jessica Chubak[1,2], Dale McLerran[3], Yingye Zheng[3], Amit G. Singal[4,5], Douglas A. Corley[6], V. Paul Doria-Rose[7], Chyke A. Doubeni[8], Aruna Kamineni[1], Jennifer S. Haas[9], Ethan A. Halm[4,5], Celette Sugg Skinner[4], Ann G. Zauber[10], Karen J. Wernli[1], and Elisabeth F. Beaber[3] on behalf of the PROSPR consortium

Abstract

Background: To reduce colorectal cancer incidence and mortality, experts recommend surveillance colonoscopy 3 years after advanced adenoma removal. Little is known about adherence to that interval.

Methods: We describe patterns of and factors associated with subsequent colonoscopy among persons with ≥3 adenomas and/or ≥1 adenoma with villous/tubulovillous histology in four U.S. integrated healthcare delivery systems. We report Kaplan–Meier estimators of the cumulative percentage of patients undergoing colonoscopy 6 months to 3.5 years after an index colonoscopy with high-risk findings. Combining data from three healthcare systems, we used multivariable logistic regression with inverse probability of censoring weights to estimate ORs and 95% confidence intervals (CI) for associations between patient characteristics and receipt of subsequent colonoscopy.

Results: Among 6,909 persons with advanced adenomas, the percent receiving a subsequent colonoscopy 6 months to 3.5 years later ranged from 18.3% (95% CI: 11.7%–27.8%) to 59.5% (95% CI: 53.8%–65.2%) across healthcare systems. Differences remained significant in the multivariable model. Patients with ≥3 adenomas were more likely than those with 1 to 2 villous/tubulovillous adenomas to undergo subsequent colonoscopy. Subsequent colonoscopy was also more common for patients ages 60–74 and less common for patients ages 80 to 89 compared with those ages 50 to 54 years at their index colonoscopy. Sex, race/ethnicity, and comorbidity index score were generally not associated with subsequent colonoscopy receipt.

Conclusions: Colonoscopy within the recommended interval following advanced adenoma was underutilized and varied by healthcare system, age, and number of adenomas.

Impact: Strategies to improve adherence to surveillance colonoscopy following advanced adenomas are needed.

Introduction

To reduce colorectal cancer morbidity and mortality, the United States (U.S.) Multi-Society Task Force on Colorectal Cancer recommends 3-year surveillance colonoscopies for patients with high-risk adenomatous polyps, including 3 to 10 tubular adenomas, any tubular adenoma ≥10 mm, any adenoma with villous histology, any adenoma with high-grade dysplasia, sessile serrated polyps ≥10 mm or with dysplasia, or traditional serrated adenoma (1). Few published data exist about adherence to these guidelines. Several studies using Medicare data have reported 20% to 55% of patients with a polypectomy undergo procedures that can be used for surveillance (e.g., colonoscopy, flexible sigmoidoscopy) within 3 years (2–4); however, Medicare data do not have information on polyp histology, number, or size, and are thus unable to identify those with high-risk findings for whom a 3-year surveillance interval is recommended. A study in the Veterans Health Administration observed that slightly more than half of patients with high-risk adenomas did not receive a colonoscopy within the recommended interval (5). Follow-up of patients enrolled in two randomized controlled trials found that approximately one-third of patients with advanced adenomas received surveillance within 3 years (6, 7). It is unknown whether similar patterns are present in the general, nontrial population of U.S. patients. We thus undertook a cohort study to characterize patterns of and factors associated with colonoscopy receipt within approximately 3 years after diagnosis of such high-risk adenomas in four U.S. integrated healthcare delivery systems.

[1]Kaiser Permanente Washington Health Research Institute, Seattle, Washington. [2]Department of Epidemiology, School of Public Health, University of Washington, Seattle, Washington. [3]Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, Washington. [4]Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, Texas. [5]Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas. [6]Kaiser Permanente Northern California, Oakland, California. [7]Healthcare Delivery Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, Maryland. [8]Department of Family Medicine and Community Health, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania. [9]Division of General Internal Medicine, Brigham and Women's Hospital, Boston, Massachusetts. [10]Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, New York.

Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

Corresponding Author: Jessica Chubak, Kaiser Permanente Washington Health Research Institute, 1730 Minor Avenue, Suite 1600, Seattle, WA 98101. Phone: 206-287-2556; Fax: 206-287-2871; E-mail: jessica.chubak@kp.org

doi: 10.1158/1055-9965.EPI-18-0452

Materials and Methods

Study population

This study was conducted as part of the NCI-funded Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) consortium. The overall aim of PROSPR is to conduct multi-site, coordinated, transdisciplinary research to evaluate and improve cancer screening processes (8). The ten PROSPR Research Centers reflect the diversity of U.S. delivery system organizations. PROSPR colorectal cancer Research Centers include four different regional healthcare delivery systems. Study subjects were members of Kaiser Permanente Northern California (KPNC), Kaiser Permanente Southern California (KPSC), and Kaiser Permanente Washington (KPWA, which was Group Health at the time of the study), or had at least one primary care visit in the Parkland Health & Hospital System (Parkland), a safety-net system, on or after January 1, 2010 (9). Systems differed from one another in their screening and follow-up strategies and their organizational structures.

We included patients ages 50 to 89 years who received a colonoscopy between January 1, 2010, and December 31, 2010 (the "index" colonoscopy), at which $\geq$3 adenomas and/or $\geq$1 adenoma with villous/tubulovillous histology were found. Information needed to identify other high-risk findings such as large adenoma, high-grade dysplasia, serrated lesions, or serrated polyposis syndrome were not consistently available. However, at KPWA, data on adenoma size were available and patients with large adenomas ($\geq$1 cm) were included in a secondary analysis.

We excluded patients with any of the following within 6 months of their index colonoscopy: loss to follow-up (i.e., died; disenrolled from KPNC, KPSC, or KPWA; or reached age 65 at Parkland—at which point patients became eligible for Medicare and may have received care outside of Parkland), diagnosis of colorectal cancer, or receipt of another colonoscopy. We implemented this last restriction because colonoscopies performed within a short interval may have resulted from incomplete index exam or incomplete removal of polyp at the index colonoscopy.

Institutional review boards at study sites and the PROSPR Statistical Coordinating Center approved study procedures.

Exposures

Index colonoscopies were identified in electronic data sources via procedure codes at all sites (Supplementary Table S1). At Parkland, we also searched for "colonoscopy" in the EHR procedure description field when no code was present. Pathology results came from a variety of sources. KPNC and KPSC used electronic pathology databases with systematized nomenclature of medicine codes (https://www.snomed.org/) to identify histology (10) and the number of individual pathology containers with adenomas. At KPWA, results were obtained by natural language processing when electronic pathology reports were available or manually reviewed by medical abstractors otherwise. Compared with chart abstraction, specificities for $\geq$3 adenomas and villous/tubulovillous histology were both $\geq$98%. Sensitivity was 89%–100% for villous/tubulovillous histology and 50%–62% for $\geq$3 adenomas (depending on where the colonoscopy was performed). At Parkland, pathology results were manually reviewed by medical abstractors. In a 5% sample of reabstracted Parkland records, only 2.9% were inconsistent with respect to abstracted pathology.

We grouped index colonoscopy findings into the three finest mutually exclusive categories possible at all sites: 1 to 2 adenomas, with at least one having villous/tubulovillous histology; $\geq$3 adenomas without villous/tubulovillous histology; or $\geq$3 adenomas, with at least one having villous/tubulovillous histology.

Other exposures of interest included healthcare system, insurance type in 2010, sex, age at index colonoscopy, race/ethnicity, and Charlson comorbidity index score. Comorbidity was measured in the calendar year 2010 for Kaiser Permanente sites and for a 1-year period following PROSPR cohort entry in 2010 for Parkland patients.

Outcomes

Receipt of subsequent colonoscopy was ascertained in each site's electronic data sources (9) as described above until the earliest of the following: coverage disenrollment at KPNC, KPSC, and KPWA, aging out of the PROSPR study population (at age 90 years for KPNC, KPSC, and KPWA or age 65 years for Parkland), moving out of a cancer registry coverage area, colorectal cancer diagnosis, death, or administrative cutoff (end of data collection). Data were collected through December 31, 2013, at KPNC, KPSC, and KPWA, and September 30, 2014, for Parkland. Thus, end of data collection for administrative reasons occurred between 3.0 and 4.0 years after the index colonoscopy at KPNC, KPSC, and KPWA and between 3 years 9 months and 4.0 years at Parkland.

The main study outcome was receipt of a subsequent colonoscopy between 6 months and 3.5 years after the index colonoscopy date. We decided *a priori* to examine receipt of colonoscopy through 3.5 years to allow a 6-month "grace" period after it was due (at 3.0 years). In sensitivity analyses, we report on receipt of colonoscopy between 6 months and 3.0 years after the index colonoscopy.

Statistical analysis

We computed descriptive statistics for the cohort overall and by index colonoscopy findings and healthcare system. To account for censoring due to the factors described above (e.g., disenrollment from healthcare system, end of data collection), we used the Kaplan–Meier product limit estimator to obtain the cumulative percent along with 95% confidence intervals (CIs) of patients receiving colonoscopy with 6 months to 3.5 years after the advanced adenoma findings described above. Cumulative incidence curves were generated for each healthcare system.

We subsequently combined data across KPNC, KPSC, and KPWA and compared receipt of subsequent colonoscopy according to index colonoscopy findings, patient age at index colonoscopy, sex, race/ethnicity, insurance type, and Charlson comorbidity score using the log-rank test (11). *A priori*, we excluded Parkland patients in these pooled analyses because of differences in age ranges and insurance options as well as potential differences in predictors of surveillance in safety net settings. We used multivariable logistic regression to estimate odds ratios (ORs) and 95% CIs for receipt of colonoscopy between 6 months and 3.5 years after the index colonoscopy. Individuals who were censored between 6 months to 3.5 years (3.0 years for sensitivity analysis) were excluded from the logistic regression analyses because of missing data for the outcome of interest. To reduce potential bias of using only individuals with complete data, we used the inverse probability of censoring weighting method (12, 13) that is

commonly used for nonrandom missing data in binary outcomes derived from lifetime data. Briefly, a weighted logistic regression model was fit to individuals with complete data but their contribution to the estimation was inversely weighted by probability of model inclusion. The inclusion probability was calculated in the full cohort with a Cox regression model for time to censoring, with all exposure variables incorporated as predictor variables. Associations with Charlson comorbidity score varied with time based on Schoenfeld residual plots. Accordingly, we incorporated interactions between Charlson comorbidity score and time to censoring (modeled employing piece-wise linear and quadratic terms). Patients were then analyzed in a single weighted logistic regression model including healthcare system (KPNC, KPSC, KPWA), index finding (as described above), age at index colonoscopy (50–54, 55–59, 60–64, 65–69, 70–74, 75–79, and 80–89 years), sex, race/ethnicity (non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Hispanic, other, and missing), insurance (Medicare, commercial/private, other governmental), and Charlson score (0, 1, 2, 3+, unknown). We repeated the analysis using receipt of colonoscopy between 6 months and 3 years as the outcome. *Post hoc,* we considered but did not model outcomes at Parkland separately due to insufficient variation in findings at index colonoscopy (Supplementary Table S2).

In an exploratory analysis among KPWA patients, we estimated ORs and 95% CIs for those with adenomas ≥1 cm who were not otherwise included in our main analysis (i.e., no villous/tubulovillous features and <3 adenomas total). On the basis of guidelines, this group would also be expected to return for surveillance colonoscopy at 3 years.

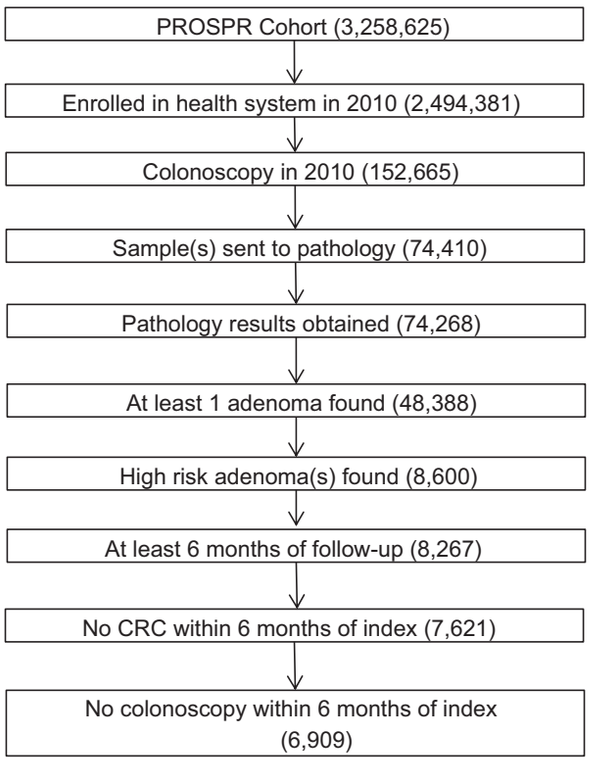

Figure 1.
Study population: PROSPR colorectal cohort members with an index colonoscopy with high-risk findings in 2010. CRC, Colorectal cancer.

Results

Study population

From 3,258,625 people in the PROSPR cohort, we identified 6,909 eligible patients based on their colonoscopy findings (Fig. 1). Characteristics of subjects overall and by high-risk index colonoscopy findings are presented in Table 1. Patients were predominantly male (59.7%) and non-Hispanic white (60.6% among nonmissing), and from KPNC (49.0%) or KPSC (43.6%). Age was relatively evenly distributed across 5-year age groups from 50 to 54 through 65 to 69 years and steadily declined in size thereafter. Mean age was 64.1 years (SD = 8.9 years). In this population of patients with high-risk findings, 60.6% of patients had 1 to 2 villous/tubulovillous adenomas; 30.9% had ≥3 adenomas without villous/tubulovillous features; and 8.4% had ≥3 adenomas with at least one villous/tubulovillous adenoma. Supplementary Table S2 shows characteristics by healthcare system. Having ≥3 adenomas with no villous features was much more common at Parkland (Supplementary Table S2).

Cumulative incidence of subsequent colonoscopy

The median follow-up time was 3.41 years [interquartile range (IQR): 3.12–3.70 years] among the 6,909 patients in this study. Among individuals without an observed subsequent colonoscopy, the median follow-up time was 3.30 years (IQR: 3.04–3.64 years). By 3.5 years after the index colonoscopy, approximately one quarter of patients (24.5%) had been administratively censored and a small percentage had aged out (0.7%), moved away (<0.1%), died (3.8%), disenrolled (9.2%), or been diagnosed with colorectal cancer (<0.1%) without first being observed to have a colonoscopy. Taking censoring into account, we saw wide variation across healthcare systems in the percentage of people who received a subsequent colonoscopy within 6 months to 3.5 years of their index colonoscopy: 18.3% (95% CI: 11.7%–27.8%) at Parkland, 47.0% (95% CI: 45.0%–49.1%) at KPSC, 48.1% (95% CI: 46.1%–50.1%) at KPNC, and 59.5% (95% CI: 53.8%–65.2%) at KPWA (Table 2).

Site-specific differences in colonoscopy rates were significant ($P < 0.0001$; Fig. 2). Cumulative incidence curves showed similar patterns across sites, most notably the sharp increase at approximately 3 years. The percentage of patients receiving colonoscopy did not plateau during the follow-up period; rather the rate of colonoscopy remained high 3.5 to 4 years after the index colonoscopy (Fig. 2) with only a suggestion of decline.

We stratified incidence curves by patient characteristics at KPNC, KPSC, and KPWA (Fig. 3). Time to subsequent colonoscopy differed by index colonoscopy findings (Fig. 3A, $P < 0.0001$). Patients with ≥3 adenomas with some villous/tubulovillous histology at index had higher rates of colonoscopy and received colonoscopy sooner than other groups, except at KPWA (Table 2). Age at index was also associated with time to subsequent colonoscopy (Fig. 3B; $P < 0.0001$); patients ages 80 to 89 years at their index exam were least likely to receive a subsequent colonoscopy. Cumulative incidence curves did not vary much by patient characteristics with exception for patients with missing Charlson score, missing race/ethnicity, and Medicaid/other governmental insurance (Supplementary Fig. S1).

Table 1. Characteristics of patients with a high-risk finding on a colonoscopy in 2010 at KPNC, KPSC, KPWA, and Parkland ($N = 6{,}909$)

Characteristics	*n* (%)
Healthcare system	
Kaiser Permanente Northern California	3,387 (49.0)
Kaiser Permanente Southern California	3,010 (43.6)
Kaiser Permanente Washington	401 (5.8)
Parkland Health and Hospital System	111 (1.6)
Index colonoscopy findings	
1–2 adenomas with ≥1 villous/tubulovillous adenoma	4,189 (60.6)
≥3 adenomas, no villous/tubulovillous adenomas	2,137 (30.9)
≥3 adenomas with ≥1 villous/tubulovillous adenoma	583 (8.4)
Sex	
Male	4,122 (59.7)
Female	2,787 (40.3)
Age at index colonoscopy (years)	
50–54	1,190 (17.2)
55–59	1,172 (17.0)
60–64	1,337 (19.4)
65–69	1,211 (17.5)
70–74	1,049 (15.2)
75–79	605 (8.8)
80–89	345 (5.0)
Race/ethnicity	
Non-Hispanic white	4,064 (60.6)
Non-Hispanic black	725 (10.8)
Non-Hispanic Asian	640 (9.5)
American Indian/Alaska Native	14 (0.2)
Pacific Islander	24 (0.4)
Other	3 (0.0)
Multiple	77 (1.1)
Hispanic	1,163 (17.3)
Missing	199
Insurance (2010)	
Medicaid	72 (1.0)
Medicare	3,295 (47.7)
Commercial/private	3,463 (50.1)
Other governmental	7 (0.1)
Uninsured	72 (1.0)
Charlson comorbidity index score (2010)[a]	
0	3,070 (46.9)
1	1,306 (20.0)
2	828 (12.6)
3+	1,342 (20.5)
Missing	363

[a]2010 for Kaiser Permanente patients; for one year following PROSPR cohort entry in 2010 for Parkland patients.

Primary analysis

Multivariable weighted logistic model results generally confirmed findings from the cumulative incidence curves (Table 3). Compared with patients with 1 or 2 adenomas with villous features, having ≥3 adenomas was associated with higher odds of colonoscopy 6 months to 3.5 years after the index colonoscopy for patients with no villous/tubulovillous features [OR = 1.29 (95% CI: 1.16–1.44)] and for patients with some villous/tubulovillous features [OR = 1.43 (95% CI: 1.19–1.71)] at their index colonoscopy. In addition, subsequent colonoscopy was more common for patients ages 60 to 74 years and less common for patients ages 80 to 89 years compared with the reference age group of individuals ages 50 to 54 years. Compared with KPNC, the odds of subsequent colonoscopy were higher at KPWA and slightly lower at KPSC. Having an unknown Charlson score was also associated with increased odds of subsequent colonoscopy. Sex and insurance were not associated with receipt of subsequent colonoscopy. Compared with non-Hispanic white patients, Hispanic patients had higher rates of colonoscopy and patients with missing race/ethnicity had lower rates. Supplementary Table S3 shows model results for KPNC, KPSC, and KPWA separately. Results from KPNC and KPSC were generally similar to one another but appeared to differ from KPWA with respect to index colonoscopy findings and race/ethnicity.

Secondary analyses

When we truncated follow-up at 3.0 years, the percent of patients who received a colonoscopy ranged from 10.2% (95% CI: 5.6%–18.2%) to 30.9% (95% CI: 26.3%–36.0%) across sites. Multivariable model results were generally similar to the primary findings (Supplementary Table S4).

At KPWA, using the data available for adenoma size, we identified an additional 156 patients not included in the main analysis who had at least 1 large adenoma but <3 adenomas total and no villous histology. Among these patients, 48.2% completed a colonoscopy between 6 months and 3.5 years.

Discussion

In this population-based study in four U.S. healthcare systems, the likelihood of receiving a subsequent colonoscopy within 6 months to 3.5 years after ≥3 adenomas or any adenomas with villous features differed by healthcare system, ranging from 18.3% to 59.5% across systems. The safety net system in our study had a substantially lower rate of subsequent colonoscopy compared with the other sites, likely related to differences in resources and patient populations. Although statistically significantly different, the percent of patients with a subsequent colonoscopy at KPNC and KPSC was similar (48.1% and 47.0%, respectively). The percent at KPWA (which was Group Health at the time of the study) was higher. Differences across sites might have been due to residual confounding by patient-level factors or unmeasured organizational-level differences related to patient outreach, surveillance protocols, medical center capacity, or ease of scheduling. Most importantly, we observed at all sites that a substantial percentage of persons with high-risk adenomas did not receive a subsequent colonoscopy during the guideline-recommended interval.

As expected, the rate of colonoscopy increased at around 3 years, when patients would have been due for a surveillance colonoscopy. Overall adherence to surveillance recommendations could have been related to factors such as outreach efforts and ease of scheduling. KPNC, KPSC, KPWA had, at some medical centers, recall lists for patients recommended to have a follow-up testing. In the systems we studied, primary care providers received results of the index colonoscopy and the surveillance interval recommendations. However, none of the healthcare systems had centralized, systematic surveillance efforts in place at the time of the study for contacting all patients, which might explain why the overall percent receiving a colonoscopy was not higher.

Patients 80 years and older at their index colonoscopy were less likely than younger patients to complete a subsequent colonoscopy. Our study could not examine reasons for not receiving a subsequent colonoscopy; however, it seems plausible that the association with age may be related to concerns regarding increased risk of adverse events and decreased potential benefits with colonoscopy as people age (14). Completion of colonoscopy was also greater among patients with ≥3 adenomas compared

Table 2. Cumulative incidence of colonoscopy between 6 months and 3.5 years after index colonoscopy with high-risk findings, by healthcare system and index colonoscopy findings

Healthcare system	Index colonoscopy findings	Percent who received subsequent colonoscopy (95% CI)
KPNC	1–2 adenomas with ≥1 villous/tubulovillous adenoma	45.7 (43.3–48.3)
	≥3 adenomas, no villous/tubulovillous adenomas	50.4 (46.7–54.2)
	≥3 adenomas with ≥1 villous/tubulovillous adenoma	56.3 (50.1–62.6)
	All	48.1 (46.1–50.1)
KPSC	1–2 adenomas with ≥1 villous/tubulovillous adenoma	43.8 (41.2–46.5)
	≥3 adenomas, no villous/tubulovillous adenomas	51.7 (47.9–55.5)
	≥3 adenomas with ≥1 villous/tubulovillous adenoma	54.5 (47.8–61.6)
	All	47.0 (45.0–49.1)
KPWA	1–2 adenomas with ≥1 villous/tubulovillous adenoma	61.2 (53.7–68.7)
	≥3 adenomas, no villous/tubulovillous adenomas	57.9 (48.8–67.2)
	≥3 adenomas with ≥1 villous/tubulovillous adenoma	49.3 (25.1–79.7)
	All	59.5 (53.8–65.2)
Parkland	1–2 adenomas with ≥1 villous/tubulovillous adenoma	46.7 (13.7–93.2)
	≥3 adenomas, no villous/tubulovillous adenomas	16.8 (10.4–26.3)
	≥3 adenomas with ≥1 villous/tubulovillous adenoma	—
	All	18.3 (11.7–27.8)

with 1 to 2 adenomas with villous/tubulovillous features. We did not find evidence of an association between age, race/ethnicity, or sex and subsequent colonoscopy receipt, with the exception of a slightly higher percent among Hispanic patients in the combined Kaiser Permanente analysis and lower percent for Hispanic patients and non-Hispanic black patients at KPWA.

Comparison to prior studies

To our knowledge, this is the first multisystem analysis outside of clinical trials of receipt of subsequent colonoscopy among patients with high-risk findings. Two studies have looked at receipt of surveillance colonoscopy in randomized controlled trial participants (6, 7). Schoen and colleagues examined surveillance colonoscopy use among participants in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (7), comparing participants with advanced adenomas (≥1 cm, villous/tubulovillous histology, or high grade/severe dysplasia), nonadvanced adenomas, and no adenomas. Among the 1,342 participants with advanced adenomas, 30.7% received a surveillance colonoscopy within 3 years compared with 19.5% of the 117 patients with ≥3 nonadvanced adenomas ($N = 117$). As in our study, there was a substantial uptick in colonoscopy between 3 and 4 years: by 4 years, 50.2% of patients with advanced adenoma in the Schoen and colleagues study had received a subsequent colonoscopy. Patients with advanced adenoma who were younger (55–69 years) and had a first-degree family history of colorectal cancer were more likely to undergo surveillance with 7 years than those who were older (70–74 years) or had no family history.

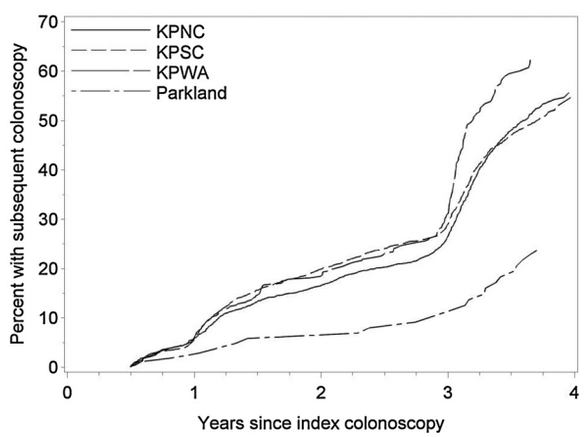

Figure 2.
Time from index colonoscopy to subsequent colonoscopy, by healthcare system.

Laiyemo and colleagues studied surveillance colonoscopy in Polyp Prevention Trial participants who completed the trial and had an end-of-trial colonoscopy (6). Approximately one-third (36.3%) of participants with high-risk adenomas (≥3, ≥1 cm, villous histology, severe or high-grade dysplasia) at the end of the trial had a colonoscopy within 3 years, with the percent increasing to 69.2% in 6 years.

Several studies using Medicare data have looked at colonoscopy following polypectomy (2–4). Cooper and colleagues examined receipt of colonoscopy within 1, 3, and 5 years of an index colonoscopy with any polypectomy (all polyp types) in 2001 to 2004 among Medicare beneficiaries aged ≥70 (3). One quarter received a colonoscopy within 3 years. Factors associated with not receiving subsequent colonoscopy within 5 years in a multivariable model included female sex, older age, and later index procedure years. Black race, higher risk of colorectal cancer, receipt of prior colonoscopy, and people in southern regions of the U.S. were more likely to receive subsequent colonoscopy. They did not observe associations with comorbidity, income, education, or physician specialty. In another study of Medicare beneficiaries (age ≥65 years) with polypectomy in 1994, Amonaker and colleagues found that approximately one-half underwent colonoscopy within 3 years; rates were significantly higher among men than women and in younger than older patients (2). Lansdorp–Vogelaar studied surveillance (primarily colonoscopy, though they did not have indication) among Medicare beneficiaries age ≥66 years who had a colonoscopy with polypectomy in 1998–1999, 2000–2001, or 2002–2003 (4). The percentage receiving a subsequent colonoscopy within 3 years ranged from 20% (2002–2003 cohort) to 31.5% (1998–1999 cohort). By 5 years, 58% and

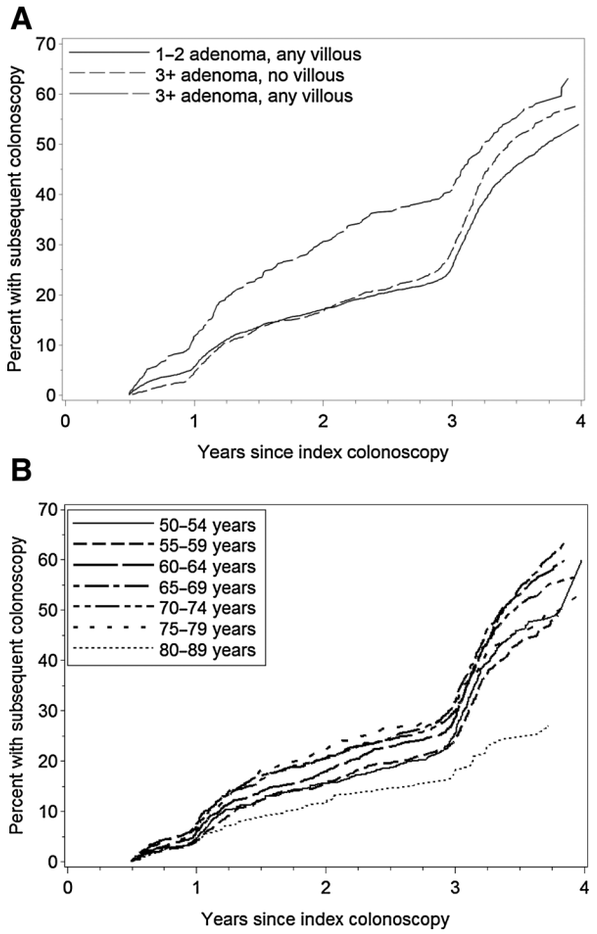

Figure 3.
Time from index colonoscopy to subsequent colonoscopy by index colonoscopy findings (**A**) and age at index colonoscopy at KPNC, KPSC, and KPWA (**B**).

45% of the 2002–2003 and 1998–1999 cohorts, respectively, had undergone colonoscopy. Female sex, older age, comorbidity, and later years of index exam were associated with not completing a colonoscopy within 5 years. Race and rural/urban status were not associated with colonoscopy receipt. A key limitation of studies with Medicare data is the lack of information on the characteristics of polyps (i.e., histology, number, and size), and thus could not assess whether the surveillance intervals were concordant with guideline-recommendations. The study populations likely included patients with low-risk adenoma or even no adenoma for whom a 3-year- or 5-year surveillance interval may not been appropriate.

A Veterans Health Administration study reported on receipt of colonoscopy following high-risk findings ($N = 128$), which were defined as $\geq$3 adenomas or at least 1 adenoma $\geq$10 mm or with high-grade dysplasia (5). Villous features were not included in the definition of high-risk adenomas. The authors reported that within 4 years and 2 months of the index colonoscopy, more than half (54.1%) of the cohort had yet to undergo a subsequent colonoscopy. None of the factors they examined was associated with underuse of colonoscopy.

Several small, single-institution studies have looked at predictors of surveillance colonoscopy (15, 16). In one of these, Murphy and colleagues examined risk factors for underuse of surveillance colonoscopy, conducting telephone surveys with 100 people with a prior adenoma (not necessarily an advanced adenoma) who did not complete their surveillance colonoscopy and 104 patients who did (16). The study, which was not limited to 3-year surveillance exams, found perceived barriers (e.g., cost, insurance coverage) and social deprivation were associated with lower completion of colonoscopy, whereas cancer worry and perceived benefits were associated with higher colonoscopy completion. Comorbidity was not related to receipt of surveillance colonoscopy. Braschi and colleagues studied 103 patients with either 1 advanced adenoma, cancer, or $\geq$3 adenomas of any type (15); only 21% received a colonoscopy within 3 years, and this was not related to patient sex, race/ethnicity, or insurance status. However, patients who had at least one primary care provider visit within a year of their surveillance due date were more likely to receive a colonoscopy.

Study strengths and limitations

A major strength of our study was the availability of pathology data that enabled us to identify a population of patients with advanced adenomas at the index colonoscopy. Thus, we could restrict our analysis to patients known to be due for surveillance colonoscopy within 3 years. Another strength of our study was the large sample size and diversity of patient populations and healthcare systems we studied.

However, our study had some limitations. Not all patients with high-risk findings were included because data on adenoma size, high-grade dysplasia, and presence of sessile serrated polyps were not available at all sites and because the NLP algorithm used to identify KPWA patients with $\geq$3 adenomas had only moderate sensitivity. Findings from KPWA did not suggest major differences in colonoscopy rates in patients with large adenomas, <3 adenomas total, and no villous/tubulovillous histology compared with patients included in the main analysis. We were also unable to study patients with serrated polyposis syndrome, for whom guidelines recommend a 1-year surveillance interval. It is worth noting that site-specific Kaplan–Meier curves appear to show accelerated colonoscopy rates between 12 and 18 months post-index, suggesting that our sample either included some patients due for follow-up at 1-year or who returned for symptom evaluation. Given that the percentage receiving a colonoscopy did not plateau between 3.5 to 4.0 years, it would be valuable to understand colonoscopy receipt over a longer follow-up period.

There may be some patients who, for clinical reasons, such as comorbidity, were recommended *not* to undergo a subsequent colonoscopy despite having advanced adenomas on their index colonoscopy. Thus, not returning a colonoscopy within 3.5 years may have been clinically appropriate for a small percentage of cases. Our data did not permit us to evaluate this question.

We did not have data on colonoscopy indication, so it is possible that some of the colonoscopies we observed were for diagnostic purpose (i.e., symptom evaluation) rather than routine surveillance. This limits our ability to assess whether patients came back for colonoscopy "too early" since evaluation of symptoms via colonoscopy may be clinically appropriate. However, missing data on indication does not limit our ability to determine the extent to which patients remained in need of surveillance after

Table 3. Association between healthcare system, patient characteristics, and receipt of colonoscopy 6 months to 3.5 years after high-risk findings, KPNC, KPSC, and KPWA

	Percentage with subsequent colonoscopy	OR (95% CI)
Index colonoscopy findings		
1–2 adenomas with ≥1 villous/tubulovillous adenoma	45.7 (44.0–47.5)	1.00 (Reference)
≥3 adenomas, no villous/tubulovillous adenomas	51.4 (48.9–54.0)	1.29 (1.16–1.44)
≥3 adenomas with ≥1 villous/tubulovillous adenoma	55.3 (50.8–60.0)	1.43 (1.19–1.71)
Health system		
KPNC	48.1 (46.1–50.1)	1.00 (Reference)
KPSC	47.0 (45.0–49.1)	0.89 (0.80–0.99)
KPWA	59.5 (53.8–65.2)	1.41 (1.14–1.74)
Age at index colonoscopy (years)		
50–54	45.9 (42.6–49.4)	1.00 (Reference)
55–59	43.5 (40.1–47.1)	0.93 (0.78–1.11)
60–64	53.1 (49.8–56.4)	1.27 (1.08–1.49)
65–69	54.5 (51.2–57.8)	1.58 (1.25–2.00)
70–74	51.2 (47.8–54.6)	1.28 (1.00–1.63)
75–79	45.6 (41.3–50.1)	1.08 (0.82–1.41)
80–89	24.2 (19.4–29.9)	0.36 (0.26–0.50)
Sex		
Male	48.5 (46.7–50.3)	1.00 (Reference)
Female	47.9 (45.8–50.2)	1.02 (0.92–1.13)
Race/ethnicity		
Non-Hispanic white	47.4 (45.7–49.3)	1.00 (Reference)
Non-Hispanic black	50.3 (45.9–54.8)	1.17 (0.99–1.39)
Non-Hispanic Asian	51.2 (46.7–55.9)	1.11 (0.94–1.32)
Hispanic	49.3 (46.0–52.8)	1.16 (1.01–1.34)
Other[a]	49.4 (39.8–60.0)	0.87 (0.61–1.26)
Missing	39.6 (31.4–49.0)	0.46 (0.34–0.63)
Insurance		
Medicare	48.7 (46.8–50.7)	1.00 (Reference)
Commercial/private	48.0 (46.1–50.1)	1.06 (0.87–1.28)
Medicaid and other governmental	39.1 (25.6–56.6)	1.20 (0.60–2.39)
Charlson comorbidity index score		
0	47.6 (45.5–49.7)	1.00 (Reference)
1	48.8 (45.7–52.0)	1.12 (0.98–1.28)
2	49.0 (45.1–53.1)	1.04 (0.89–1.22)
3+	47.1 (44.0–50.3)	1.04 (0.90–1.20)
Unknown	55.9 (48.4–63.8)	1.76 (1.37–2.26)

[a]Other includes American Indian/Alaska Native, Pacific Islander, and multiple races.

the recommended interval, as any subsequent colonoscopy—regardless of indication—may "count" for the purpose of compliance with surveillance guideline.

Finally, although our study was large and population-based, it is important to note that patients were from integrated healthcare delivery systems. Thus, the findings from this study may not generalize to other settings and to patients not affiliated with a healthcare system. Furthermore, we did not have a large enough sample at Parkland to examine factors in a multivariable model. Of note, almost all patients from Parkland in this analysis were classified as having ≥3 adenomas without villous features likely due to differences in how polyps were processed and interpreted.

Implications

The fact that a large proportion of patients with ≥3 adenomas or any adenoma with villous/tubulovillous features did not receive a subsequent colonoscopy within 3.5 years—even in healthcare systems with some procedures to support colonoscopy surveillance after high-risk adenomas—suggests a need for additional evidence-based interventions to improve adherence to surveillance guidelines. Although we did not observe many associations between patient characteristics and receipt of subsequent colonoscopy, we recommend that future studies assessing the effectiveness of interventions to increase surveillance colonoscopy utilization evaluate intervention effectiveness in patient subgroups to try to ensure benefits and harms are equitable and health disparities are minimized.

Disclosure of Potential Conflicts of Interest

A.G. Singal is a consultant/advisory board member for Exact Sciences. No potential conflicts of interest were declared by the other authors.

Disclaimer

C.A. Doubeni is a member of the U.S. Preventive Services Task Force (USPSTF). This article does not necessarily represent the views and policies of the USPSTF.

Authors' Contributions

Conception and design: J. Chubak, A.G. Singal, D.A. Corley, V.P. Doria-Rose, C.A. Doubeni, J.S. Haas, E.A. Halm, C.S. Skinner, E.F. Beaber

Development of methodology: J. Chubak, D.A. Corley, V.P. Doria-Rose, C.A. Doubeni, E.F. Beaber

Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): J. Chubak, A.G. Singal, C.A. Doubeni, A. Kamineni, E.A. Halm, C.S. Skinner, K.J. Wernli

Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): J. Chubak, D. McLerran, Y. Zheng, D.A. Corley, V.P. Doria-Rose, C.A. Doubeni, A. Kamineni, A.G. Zauber, E.F. Beaber
Writing, review, and/or revision of the manuscript: J. Chubak, D. McLerran, Y. Zheng, A.G. Singal, D.A. Corley, V.P. Doria-Rose, C.A. Doubeni, A. Kamineni, J.S. Haas, E.A. Halm, C.S. Skinner, A.G. Zauber, K.J. Wernli, E.F. Beaber
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): J. Chubak, D. McLerran
Study supervision: J. Chubak, D.A. Corley, C.S. Skinner, E.F. Beaber

Acknowledgments

This work was funded by NCI at the NIH (grant no. U54CA163261, to J. Chubak, A. Kamineni, and K.J. Wernli; U54CA163262, to D.A. Corley, C.A. Doubeni, and A.G. Zauber; U54CA163308, to A.G. Singal, E.A. Halm, and C.S. Skinner; U01CA163304, to D. McLerran, Y. Zheng, and E.F. Beaber; and U54CA163307, to J.S. Haas).

The authors thank the participating PROSPR Research Centers for the data they have provided for this study. A list of the PROSPR investigators and contributing research staff is provided at: https://healthcaredelivery.cancer.gov/prospr/acknowledgements.html. We also thank Cameron Haas for assisting with reviewing the literature for this manuscript.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received April 24, 2018; revised July 6, 2018; accepted September 4, 2018; published first November 20, 2018.

References

1. Lieberman DA, Rex DK, Winawer SJ, Giardiello FM, Johnson DA, Levin TR, et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2012;143:844–57.
2. Amonkar MM, Hunt TL, Zhou Z, Jin X. Surveillance patterns and polyp recurrence following diagnosis and excision of colorectal polyps in a Medicare population. Cancer Epidemiol Biomarkers Prev 2005;14:417–21.
3. Cooper GS, Kou TD, Barnholtz Sloan JS, Koroukian SM, Schluchter MD. Use of colonoscopy for polyp surveillance in medicare beneficiaries. Cancer 2013;119:1800–7.
4. Lansdorp-Vogelaar I, Fedewa S, Lin CC, Virgo KS, Jemal A. Utilization of surveillance after polypectomy in the medicare population–a cohort study. PLoS One 2014;9:e110937.
5. Murphy CC, Sandler RS, Grubber JM, Johnson MR, Fisher DA. Underuse and overuse of colonoscopy for repeat screening and surveillance in the Veterans Health Administration. Clin Gastroenterol Hepatol 2016;14:436–44.
6. Laiyemo AO, Pinsky PF, Marcus PM, Lanza E, Cross AJ, Schatzkin A, et al. Utilization and yield of surveillance colonoscopy in the continued follow-up study of the polyp prevention trial. Clin Gastroenterol Hepatol 2009;7:562–7.
7. Schoen RE, Pinsky PF, Weissfeld JL, Yokochi LA, Reding DJ, Hayes RB, et al. Utilization of surveillance colonoscopy in community practice. Gastroenterology 2010;138:73–81.
8. Beaber EF, Kim JJ, Schapira MM, Tosteson AN, Zauber AG, Geiger AM, et al. Unifying screening processes within the PROSPR consortium: a conceptual model for breast, cervical, and colorectal cancer screening. J Natl Cancer Inst 2015;107:djv120.
9. Tiro JA, Kamineni A, Levin TR, Zheng Y, Schottinger JS, Rutter CM, et al. The CRC screening process in community settings: a conceptual model for the Population-based Research Optimizing Screening through Personalized Regimens Consortium. Cancer Epidemiol Biomarkers Prev 2014;23:1147–58.
10. Corley DA, Jensen CD, Marks AR, Zhao WK, Lee JK, Doubeni CA, et al. Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med 2014;370:1298–306.
11. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457–81.
12. Horvitz DG, Thompson DJ. A generalization of sampling without replacement from a finite universe. J Am Stat Assoc 1952;47:663–85.
13. Klein JP, Van Houwelingen HC, Ibrahim J, Scheike T, editors. Handbook on survival analysis. Boca Raton, FL: CRC Press; 2016.
14. Lin JS, Piper MA, Perdue LA, Rutter CM, Webber EM, O'Connor E, et al. Screening for colorectal cancer: updated evidence report and systematic review for the U.S. Preventative Services Task Force. JAMA 2016;315:2576–94.
15. Braschi C, Pelto DJ, Hennelly MO, Lee KK, Shah B, Montgomery GH, et al. Patient-, provider-, and system-level factors in low adherence to surveillance colonoscopy guidelines: implications for future interventions. J Gastrointest Cancer 2014;45:500–3.
16. Murphy CC, Lewis CL, Golin CE, Sandler RS. Underuse of surveillance colonoscopy in patients at increased risk of colorectal cancer. Am J Gastroenterol 2015;110:633–41.