



## *In Case You Missed It* **Wait 7-10 Years for Repeat Colonoscopy If You Only Find 1-2 Small Adenomas... It's Not Too Long!**



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This summary reviews Click B, Pinsky PF, Hickey T, Doroudi M, Schoen, RE. Association of Colonoscopy Adenoma Findings with Long-Term Colorectal Cancer Incidence. JAMA 2018; 319(19): 2022-2031.

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### **STRUCTURED ABSTRACT**

**Question:** Is the long-term risk of colorectal cancer (CRC) different between individuals with 1-2 non-advanced (<10mm) adenomas vs no adenomas?

**Study Design:** Multi-center, prospective cohort from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Study. This study only examines PLCO patients randomized to receive flexible sigmoidoscopy and had a polyp or mass found and subsequently completed a colonoscopy.

**Setting:** Participants were recruited from 1993-2001 from 10 centers participating in PLCO.

**Patients:** Average-risk 55-74-year-olds who had a polyp or mass in the distal colon on flexible sigmoidoscopy, and then completed a follow up colonoscopy were included. Participants diagnosed with cancer at time of colonoscopy and those with no follow up time were excluded. Of the 15,935 participants included, 2,882 participants (18.1%) had an advanced adenoma, 5,068 participants (31.8%) had non-advanced adenomas, and 7,985 participants (50.1%) had no adenoma (i.e., hyperplastic polyp or no polyp found at colonoscopy). The median age was 64 (IQR: 61-68), 59.7% were men, 90.7% were White, and median follow up was 12.9 years (IQR: 9.8-15).

**Exposure:** Index colonoscopy with no adenoma, 1-2 non-advanced adenomas (< 10 mm) or advanced adenoma (adenoma ≥ 10 mm, with high-grade dysplasia or villous architecture).

**Outcomes:** Primary outcome was CRC incidence within 15 years of baseline colonoscopy. Secondary outcome was CRC mortality.

**Results:** Over a median 12.9 years of follow up, CRC incidence per 10,000-person years was 20.0, 9.1, and 7.5 in those with advanced adenomas, non-advanced adenomas, and no adenomas, respectively. Cumulative incidence of CRC over 15 years was 2.9%, 1.4%, and 1.2%, respectively, in those groups. Although those with advanced adenomas were significantly more likely to develop CRC (relative risk = 2.7; 95% CI: 1.9-3.7) compared to those with no adenoma, there was no significantly increased risk of CRC in those with non-advanced adenomas compared to those with no adenomas (RR = 1.2; 95% CI: 0.8-1.7) (Figure 1). The cumulative CRC incidence was similar between individuals with non-advanced adenomas and no adenomas at 5 years, 7 years, and 10 years from index colonoscopy (illustrated in Figure 2 of Click et al). The risk of CRC mortality was significantly increased in those with advanced adenomas (RR 2.6, 95% CI 1.2-5.7) compared to those with no adenomas. Again, those with non-advanced adenomas were not at increased risk of mortality compared to those with no adenomas (Figure 1).

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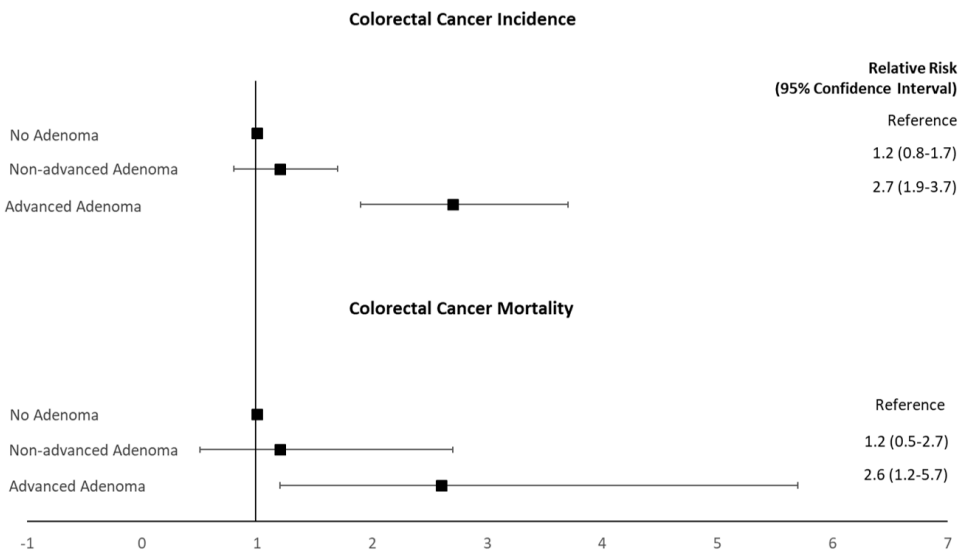


Figure 1. Relative Risk of CRC and CRC Mortality based on adenoma findings

## COMMENTARY

### *Why Is This Important?*

This research, along with 2 meta-analyses and European cohort studies, provide the foundation for the United States Multi-Society Task Force on Colorectal Cancer recommendation in 2020 to extend surveillance intervals to 7-10 years for average-risk individuals with 1-2 small or non-advanced adenomas on index screening colonoscopy.<sup>1</sup> The PLCO study was crucial because its large size (n = 15,935), prolonged follow-up (median 12.9 years), and comprehensive follow-up (93.8% compliance with annual study update on health) provided precise estimates of CRC incidence in the no adenoma and 1-2 small adenoma group.

### *Key Study Findings*

Patients diagnosed with 1-2 non-advanced adenomas have the same long-term risk of colorectal cancer and death from colorectal cancer as those with no adenomas (Figure 1). Those with advanced adenomas have a 2.7-fold increased risk of developing CRC and a 2.6-fold increased risk of dying from CRC.

### *Caution*

There was insufficient data to draw a conclusion about whether patients with three or more adenomas have an increased risk of CRC. This study was also conducted in an era before there was a strong commitment to colonoscopy quality (before split-dose bowel preparations, high-definition colonoscopes, adenoma detection monitoring, serrated lesion detection monitoring, endoscopic mucosal resection techniques). Most importantly, use of surveillance colonoscopy was only tracked for 21.9% of the study population, and surveillance colonoscopy was used more frequently in patients with 1-2 small adenomas (78.1%) vs individuals with no adenomas (69.9%). So, differences in use of surveillance colonoscopy could partly account for similarity of CRC incidence in these groups.

### *My Practice*

This high-quality study, along with other recent meta-analyses and European cohort studies cited in the 2020 USMSTF on CRC Screening Guideline, I strongly support extending surveillance intervals for those with 1-2 small

tubular adenomas. If a patient has undergone a high-quality colonoscopy (adequate bowel preparation, complete to cecum, high-adenoma detection rate provider, complete polyp resection), I recommend 7-year surveillance for those with 1-2 small adenomas and additional risk factors (male sex, smokers, metabolic syndrome/diabetes, obesity, > age 60) and 10-year surveillance for those without additional risk factors and under age 60.

### ***For Future Research***

Validation that 1-2 small adenomas truly confer low risk of future CRC through a prospective randomized controlled trial of different surveillance intervals is currently underway (the FORTE trial, NCT05080673). We also still need studies to assess long-term CRC risk in patients with three or more small tubular adenomas and studies in the contemporary era of high-quality colonoscopy to validate whether intensive surveillance of advanced adenomas is still warranted.

### **REFERENCE**

1. Gupta S, Lieberman D, Anderson JC, et al. Recommendations for Follow-Up After Colonoscopy and Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2020;158:1131-1153 e5.