



Do Not Extend Interval Between CRC Screening Colonoscopies from 10 to 15 Years: Perils of Administrative Databases



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This summary reviews Liang Q, Mukama T, Sundquist K, et al. Longer interval between first colonoscopy with negative findings for colorectal cancer and repeat colonoscopy. JAMA Oncol 2024 May 2:e240827.

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STRUCTURED ABSTRACT

Question: After a negative colonoscopy, is the risk of colorectal cancer (CRC) reduced for longer than 10 years compared to controls who don't get colonoscopy?

Design: Retrospective case-control study using nationwide health and administrative databases.

Setting: Sweden.

Patients: Cases were individuals aged 45-69 years old who underwent their first colonoscopy for any indication between 1990-2016 and had no adenomas found during colonoscopy. For each case, up to 18 controls matched for sex, birth year, and baseline age (i.e., follow-up starting at same age when matched case underwent colonoscopy) were identified from Swedish healthcare registries and followed from 1990-2018. Exclusion criteria included family history of CRC and presence of inflammatory bowel disease.

Interventions/Exposure: Colonoscopy with no adenomas or CRC found (i.e.,

negative colonoscopy). Initial indication for colonoscopy was not recorded. Since there was only limited CRC screening with biennial fecal occult blood tests in Sweden starting in 2008, most colonoscopies were likely performed for diagnostic purposes. Data on quality of colonoscopy, including quality of bowel preparation, cecal intubation, and adenoma detection rates (ADR), were not available.

Outcome: CRC incidence and CRC-specific mortality.

Data Analysis: Standardized incidence ratios and standardized mortality ratios after adjustment for multiple potential confounders, including birth year, sex, baseline age at time of colonoscopy, geographic location, and socio-economic status.

Funding: Publication states that funding was obtained by co-investigators Q Liang, K Sundquist, J Sundquist, and M Fallah, but does not state source of funding. Q Liang received grant support from the China Scholarship Council.

Results: The study cohort included 110,074 individuals with negative colonoscopy and 1,981,332 matched controls who did not have colonoscopy recorded in Swedish health databases. Study population was 59% female with median age interquartile range (IQR) of 59 years old (52-64). During up to 29 years of follow-up, CRC occurred in 0.44% of individuals with negative colonoscopy and in 1.1% of individuals without colonoscopy. For CRC-specific mortality, rates were 0.10% and 0.28%, respectively.

At year 15 after negative colonoscopy, the standardized incidence ratio for CRC was 0.72 (95% confidence interval [CI] 0.54-0.94) and standardized mortality ratio for CRC-specific mortality was 0.55 (95% CI 0.29-0.94). At Year 15, the 10-year cumulative risks of CRC and CRC-specific death in the exposed group (negative colonoscopy) were 72% and 55% of the 10-year cumulative risks in the control group, respectively.

Furthermore, the difference in 5-year cumulative incidence rates of CRC between individuals who had a second screening at year 10 negative for CRC (2.9/1,000 individuals) and those who did not have a second screening (5.3/1,000 individuals), showed that 2.4 CRC cases per 1,000 individuals could be missed by extending the screening to 15 years.

COMMENTARY

Why Is This Important?

We're summarizing this study because it was publicized extensively in gastroenterology news services and the lay me-

dia. The media emphasized the authors' provocative conclusion that the interval between colonoscopies could be extended to 15 years. This conclusion seems

overly optimistic given study design limitations (see **Caution** section). As discussed in prior summaries,¹⁻² the methodology of these epidemiologic reports is frequently flawed and usually does not produce conclusions that should change patient care. Instead, these studies are most helpful as hypothesis-generating exercises and may serve as the foundation for design of prospective studies. Unfortunately, it can be confusing for patients and physicians when this type of study is publicized.

Nevertheless, there is growing data that the intervals after negative screening colonoscopies could be extended beyond 10 years.³⁻⁴ Prospectively collected data from Germany indicates that only 5%-6% of individuals have advanced adenomas found on repeat screening colonoscopy performed 10 years after a negative screening colonoscopy and that the incidence remains low for several more years.³ A recent Canadian population-based cohort study⁴ found individuals with a negative colonoscopy were less likely to develop CRC compared to similar controls who didn't get colonoscopy, even if the colonoscopy was performed more than 15 years ago. These findings most likely reflect that individuals with no adenomas found on screening colonoscopy are less than average-risk for developing CRC. Whether due to genetic or environmental factors, individuals with negative colonoscopies seem less likely to develop adenomas than the average individual.

Key Study Findings

At Year 15, the 10-year cumulative risks of CRC and CRC-specific death in the exposed group (negative colonoscopy) were 72% and 55% of the 10-year cumulative risks in the control group, respectively.

Caution

The indication for colonoscopy was not recorded and most individuals probably underwent colonoscopy as a diagnostic test instead of for average-risk CRC screening. More importantly, it's likely that the quality of colonoscopy was sub-optimal. Although no data was recorded about key colonoscopy quality indicators, including cecal intubation rates, frequency of adequate bowel preparation, or adenoma detection rates, data from the NordiCC randomized controlled trial⁵ reported an ADR of only 14.4% among Swedish endoscopists in the context of a clinical trial from 2009-2014. Therefore, it's likely that the ADR was poor among the "negative colonoscopy" patients in this study, and the protective effect of colonoscopy would be minimized. In fact, when looking at the unadjusted rates of CRC in the cases and controls, colonoscopy appears to have reduced the risk of CRC by only about 60%.

My Practice

For the reasons outlined above, these data won't change my current practice. After a normal screening colonoscopy, I'll continue to recommend repeat

screening colonoscopy in 10 years, which is consistent with current US clinical practice guidelines. It's worth remembering that the 10-year interval after a negative screening colonoscopy is based largely on our understanding of the adenoma-carcinoma sequence. This stepwise progression of accumulating multiple genetic mutations in the colon is quite slow and estimated to take at least 10 years.⁶ If individuals with a negative screening colonoscopy are truly less than average risk for developing adenomas, then we may be able to extend the interval between colonoscopies. However, we need more and better data first. Until we have that data and until guideline recommendations change, I'll continue to educate my patients to come back in 10 years after a negative screening colonoscopy.

For Future Research

Ongoing prospective studies will clarify the risk of extending the interval after normal screening colonoscopies from 10 to 15 years.

Conflict of Interest

Dr. Schoenfeld reports no relevant conflicts of interest.

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