

## Colonoscopy Remains The Best Method To Prevent Colon Cancer

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The recently published European study examining colonoscopy in Sweden, Poland, Norway, and the Netherlands, “Effect of Colonoscopy Screening on Risks of Colorectal Cancer and Related Death” in the New England Journal of Medicine calls into question the effectiveness of colonoscopy screening.<sup>1</sup> The findings of the Nordic-European Initiative on Colorectal Cancer (NordICC) trial by Dr Bretthauer, et al, casts doubt on the benefits of colonoscopy in preventing colorectal cancer (CRC), which is a leading cause of cancer deaths in the U.S. The results as presented, misrepresent the true impact of colonoscopy as a screening modality and could have a detrimental impact on colon cancer screening as a whole.

The NordICC study reported outcomes of patients in a randomized trial in which one third of patients appropriate for colorectal cancer screening were invited to undergo a one-time colonoscopy, while the other two thirds were randomized to usual care. The paper reports a primary intention-to-treat analysis, and demonstrates a modest decrease in colorectal cancer incidence (18% risk reduction) in those randomized to screening, as well as no statistically significant decrease in CRC mortality. The popular media has seized on these data to cast doubt on the value of colonoscopy in cancer prevention of CRC.<sup>2</sup>

Contrary to reporting, data from the trial strongly endorses the utility of colonoscopy as a preventive measure against colorectal cancer. The single most important and under-reported aspect of this trial is that only 42% of patients who were invited for a colonoscopy completed the procedure. Among patients who actually completed a colonoscopy, there was a strong protective effect against cancer, with a 31% decrease in colorectal cancer incidence as well as a 50% reduction in mortality compared to the population that did not complete a colonoscopy. These data are consistent with prior studies and reinforce that a colonoscopy is effective if it is completed. In prior studies, screening colonoscopy has been associated with a 40 to 69% decrease in the incidence of colorectal cancer. Additionally, studies have shown up to an 88% decrease in the risk of death from colorectal cancer.<sup>3</sup>

When evaluating the study and interpreting results, we must also take into account differences in the patient populations. Historic evidence demonstrates the incidence of colon cancer in Nordic countries is less than seen in the U.S. population. This data could certainly lead to a lower detection rate and thereby not be applicable to a U.S. population. In the NordICC group, the incidence reduction of colon cancer was three times higher in Norway than Poland, suggesting the groups were not equally matched in the arms of the trial.

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<sup>1</sup>Bretthauer M, Løberg M, Wieszczy P, et al. Effect of Colonoscopy Screening on Risks of Colorectal Cancer and Related Death, New Engl J Med, 2022 Oct 9. doi:10.1056/NEJMoa2208375

<sup>2</sup><https://www.cnn.com/2022/10/10/health/colonoscopy-study-q-and-a-wellness/index.html>

<sup>3</sup> Ladabaum U, Dominitz JA, Kahi C, Schoen RE. Strategies for colorectal cancer screening. Gastroenterology 2020;158:418-432.

Additionally, there is evidence that a substantial proportion of the colonoscopies done in this study were of sub-standard quality. A validated benchmark used to assess colonoscopy quality in the U.S. is the adenoma detection rate. Adenoma detection rate is the proportion of screening colonoscopies in which one or more adenomas is detected. Guidelines have suggested an adenoma detection rate of >25% by the endoscopist is the minimum acceptable to document quality of procedures.<sup>4</sup> In the NordICC study, nearly 30% of the endoscopists who were included in the study did not meet the adenoma threshold of 25% that is used as an established quality indicator for U.S. providers.

Finally, both the timeline of the benefit of colonoscopy, as well as its use as a serial exam are not adequately measured in this study. The benefits of removal of a polyp might not be evident in prevention of cancer death for a decade or more after the procedure. We often perform serial colonoscopies, not just one, when a patient has been demonstrated to be predisposed to polyp formation. Neither of these factors would be evident given the current trial's design.

Occam's razor is an often used problem solving technique in medical practice. The principle suggests that in a setting where competing theories or explanations exist, the simplest explanation is preferred and often valid. We should refer back to Occam to analyze the wide breadth of data that we have before us. The correct conclusion from the presented data is that colonoscopy reduces the incidence and the mortality of colorectal cancer. Do we have enough evidence to abandon colonoscopy for colon cancer prevention based on this trial? The answer is a strong no! While the NordICC trial findings raise interesting questions, unfortunately the study methodology and results leave much to be desired. The study certainly does not provide rationale for any patient to delay or forego colonoscopy for the screening of colon cancer.

The main take-home lesson from this study is that a screening test is unable to prevent cancer when it is not used. The tragedy of this trial was that 58% of those who were offered screening declined, condemning the trial to poor outcomes. As even the authors have noted, in this study with up to a 50% reduction in mortality risk, colonoscopy is a critical tool in preventing colon cancer. Here is the simple message that our society should continue to carry to our patients: screening colonoscopy prevents cancers and saves lives.

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<sup>4</sup> Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. *Gastrointest Endosc* 2015;81:31-53.