Controversy over colonoscopy for colorectal cancer screening

Colonoscopy is widely considered the gold standard for large bowel investigations, allowing diagnosis and treatment to be undertaken; results from randomised trials of its use in colorectal cancer screening have been eagerly awaited. The findings from the first such trial—NordICC—were presented at UEG Week 2022 and published in the *New England Journal of Medicine*. In the trial, individuals aged 55–64 years in Poland, Norway, Sweden, and the Netherlands were randomly assigned to receive an invitation to have a single screening colonoscopy or to receive no such invitation (ie, receive usual care). Follow-up data were available for 84 585 participants. After a median follow-up of 10 years, the risk of colorectal cancer was lower in the invited group than in the usual care group in intention-to-screen analyses (0·98% *vs* 1·20%; risk ratio [RR] 0·82, 95% CI 0·70–0·93); the risk of colorectal cancer-related mortality in the invited group was not significantly lower than in the usual care group (0·28% *vs* 0·31%; 0·90, 0·64–1·16).

These headline findings sparked considerable debate. One *CNN* news piece described the results as a "meager benefit" and "disappointing", while #GITwitter was awash with heated discussion. The 18% reduction in the risk of colorectal cancer and the lack of a significant benefit in colorectal cancer-related mortality compare unfavourably with results of cohort studies of colonoscopy for colorectal cancer screening, which show reductions in the risk of incident colorectal cancers of 40–69% and of colorectal cancer-related death of 29–88%. But such comparisons are fraught with problems—eg, the unselected population in NordICC is likely to better reflect real-world populations invited to screening, and the findings of randomised trials are substantially less open to the effects of confounding and bias versus cohort studies. Further, several aspects of the trial demand a more nuanced interpretation.

One such aspect is that, of those invited to colonoscopy, only 42% underwent screening. In adjusted per-protocol analyses to estimate outcomes if all invited participants underwent screening, the risk of incident colorectal cancer at 10 years was reduced by 31% (RR 0·69, 95% CI 0·55–0·83) and for colorectal cancer-related death by 50% (0·50, 0·27–0·77). Thus, if completed, a colonoscopy is effective. The debate surrounding the trial's results has somewhat conflated the intervention being examined—ie, a population-level health policy to invite people for (and provide) screening colonoscopy—with colonoscopy as a patient-level intervention. The relatively low uptake of colonoscopy in NordICC—also noted in early data from the COLONPREV (uptake 24·6% with colonoscopy *vs* 34·2% with faecal immunochemical testing [FIT] every 2 years) and SCREESCO trials (35·1% *vs* 55·5% with two rounds of FIT)—highlights the issue of acceptability of an invasive colonoscopy as an initial screening modality. Preference for initial means of screening can vary—eg, by location, race and ethnicity, or socioeconomic status. Ensuring availability of non-invasive options (eg, FIT), with referral to colonoscopy for those with positive test results, may improve the performance of colorectal cancer screening programmes. Further research into population-specific preferences and methods to improve uptake are essential.

Also notable is the quality of the colonoscopies in NordICC. The adenoma detection rate (ADR), a key measure of colonoscopy quality, is inversely related to the risk of incident colorectal cancer and colorectal cancer-related death. ASGE/ACG guidelines for colonoscopy quality indicate that the performance target for ADR should be 25% or greater; this target was not met by 29% of endoscopists in NordICC. Caecal intubation benchmarks were also not met by all endoscopists. Thus cancers or their precursors could have remained undetected and untreated despite screening.

Finally, the effect of colonoscopy on the incidence of colorectal cancer and colorectal cancer-related deaths is likely to take time to become fully apparent. For instance, the incidence of colorectal cancer in the group invited to colonoscopy will have initially increased relative to the usual care group because of the detection of cancers that were not yet symptomatic; further, removal of polyps during colonoscopy will have altered subsequent risk of colorectal cancer. Maximum follow-up of participants in this report of NordICC was 10 years; a second analysis planned at 15 years is highly anticipated. Further insights into the role of colonoscopy in colorectal cancer screening will also be gleaned from the CONFIRM, COLONPREV, and SCREESCO trials, hopefully providing a clearer picture of colonoscopy's place among other options for colorectal cancer screening.

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For the **NordICC results** see *N Engl J Med* 2022; published online Oct 9. DOI:10.1056/NEJMoa2208375

For the ***CNN* news story** see https://edition.cnn.com/2022/10/09/health/colonoscopy-cancer-death-study/index.html

For more on **previous data on the effects of colonoscopy** see *Gastroenterology* 2020; **158:** 418–32

For more on the **COLONPREV trial** see *N Engl J Med* 2012; **366:** 697–706

For **initial results from SCREESCO** see **Articles** *Lancet Gastroenterol Hepatol* 2022; **7:** 513–21

For **guidelines on colonoscopy quality indicators** see *Gastrointest Endosc* 2015; **81:** 31–53

For **NordICC trial quality metrics** see *JAMA Intern Med* 2016; **176:** 894–902

For more on the **CONFIRM trial** see *Am J Gastroenterol* 2017; **112:** 1736–46