Gastroenterology 2018;155:1059–1068

Number of Adenomas Removed and Colorectal Cancers Prevented in Randomized Trials of Flexible Sigmoidoscopy Screening

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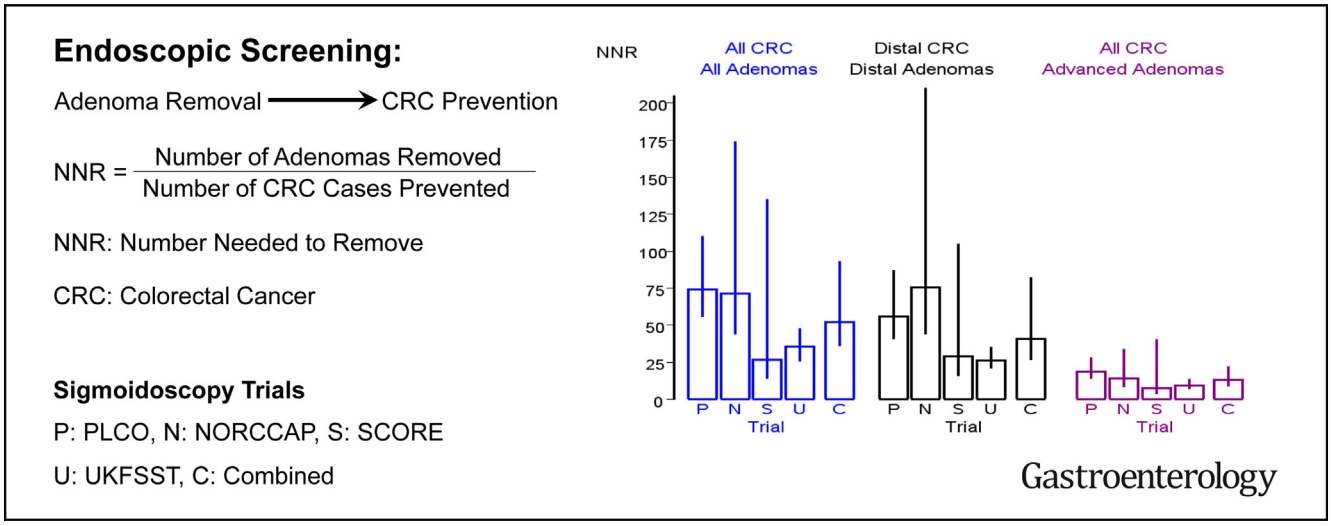

BACKGROUND & AIMS: Screening for colorectal cancer (CRC) with sigmoidoscopy reduces CRC incidence by detecting and removing adenomas. The number needed to screen is a measure of screening efficiency, but is not directly associated with adenoma removal. We propose the following 2 new metrics for quantifying the relationship between adenoma removal and CRC prevented: number of adenomas needed to remove (NNR) and adenoma dwell time avoided (DTA). **METHODS:** We collected data from 4 randomized trials of sigmoidoscopy screening (1 in the United States and 3 in Europe) to assess NNR and DTA. For each trial, NNR was computed as the number of adenomas removed from subjects in the intervention group, divided by the number of CRCs prevented. DTA was computed similarly but taking into account the timing of adenoma removal. Combined results across trials were assessed using standard meta-analytic techniques. **RESULTS:** The estimated NNR for the PLCO (Prostate, Lung, Colorectal and Ovarian) trial was 74 (95% confidence interval [CI], 56–110), for the NORCCAP (Norwegian Colorectal Cancer Prevention) trial was 71 (95% CI, 44–174), for the SCORE (Screening for Colon Rectum) trial was 27 (95% CI, 14–135), and for the UKFSST (UK Flexible Sigmoidoscopy Screening Trial) was 36 (95% CI, 28–52). The combined estimate (meta-analysis) of NNR was 52 (95% CI, 36–93) assuming heterogeneity (P for heterogeneity = .014). DTA estimates among trials ranged from 278 to 730 years, with a combined estimate of 500 (95% CI, 344–833) years assuming heterogeneity (P for heterogeneity = .035), or 2 CRC cases prevented per 1000 adenoma dwell years avoided. The combined estimates of NNR and DTA restricted to advanced adenomas were 13 (95% CI, 9–22) and 122 (95% CI, 90–190) years, respectively. **CONCLUSIONS:** We collected data from 4 randomized trials of sigmoidoscopy screening for CRC to develop metrics of endoscopic efficiency, NNR and DTA, which are directly linked to adenoma detection and removal. They can be used to compare screening among endoscopic modalities and to more precisely measure adenoma to carcinoma transition rates.

Keywords: Efficiency of Screening; Early Detection; Colon Cancer; Tumor.

WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Screening for colorectal cancer (CRC) with sigmoidoscopy reduces CRC incidence by removing adenomas.

NEW FINDINGS

The NNRs estimated from four sigmoidoscopy screening trials varied from 27 to 74. The combined meta-analysis estimate of NNRs over the four trials was 52 (95% CI: 36-93).

LIMITATIONS

These NNR estimates were derived from sigmoidoscopy trials where most adenomas removed were from the distal colorectum; therefore, NNRs for colonoscopy screening may differ.

IMPACT

The new NNR metric can help inform patients, caregivers, and policy makers of the benefits and burden of adenoma removal in relation to colorectal cancer prevention.

In randomized trials of cancer screening, the number needed to screen (NNS) to prevent 1 death from the cancer of interest is a widely used metric to assess the efficiency of screening.[1] This metric has been developed for early detection cancer screening tests, such as mammography and prostate-specific antigen, tests designed to detect cancers at an early, curable stage, but not to prevent incident cancer.

In contrast, endoscopic screening for colorectal cancer (CRC) reduces cancer incidence by identifying and removing adenomatous polyps (adenomas).[2–7] The effect of screening on cancer incidence may be of even greater importance than the effect of early detection of cancer in reducing CRC mortality.[8] In CRC screening, the NNS to prevent 1 CRC is computed as the number of subjects screened (or intended to screen), divided by the number of CRCs prevented. However, the NNS is dependent on several factors that may differ across screening settings—the incidence rate of CRC in the underlying population, the screening compliance rate, and the quality of endoscopy. Further, the NNS does not directly connect the specific intervention that prevents CRC, namely adenoma removal, to the outcome of reduced CRC incidence. Therefore, a metric that is more closely associated with adenoma removal may be more suitable in assessing the efficiency of colorectal cancer screening in preventing CRC.

Efficiency is affected by the burden of adenoma removal. While the concepts of overdiagnosis and overtreatment are widely accepted with respect to prostate and breast cancer, these concepts are less commonly applied to precancerous lesions, such as adenomas, because treatment of adenomas is easier, cheaper, and has less adverse effects than treatment of invasive cancer.[9] However, the high prevalence of adenomas at screening, the increasing focus on achieving high adenoma detection rates during colonoscopy, and the fact that adenoma diagnosis leads to recommendations for increased testing through follow-up surveillance colonoscopy, mandates a closer study of the relationship between number of adenomas removed and number of cancers prevented. Furthermore, because there are many-fold greater numbers of adenomas than cancers, the impact on efficiency of their removal is still substantial.

To evaluate screening efficiency and link adenoma removal quantitatively to CRC prevention, we propose 2 new metrics. The first is the mean number of adenomas needed to be removed to prevent 1 incident CRC, termed the *number needed to remove* (NNR). Additionally, to account for the timing of adenoma removal in relation to the risk for CRC over time, the second metric is the total adenoma dwell time needed to avoid (by adenoma removal) to prevent 1 cancer, termed *dwell time avoided* (DTA), where dwell time is the time an adenoma resides in the colorectum. We apply these metrics to data from 4 large-scale randomized sigmoidoscopy screening trials, all of which showed significant reductions in CRC incidence in the intervention compared to control arms.

Methods

Trial Designs and Findings

The current study includes 4 randomized sigmoidoscopy screening trials, the PLCO (Prostate, Lung, Colorectal and Ovarian) trial from the United States, the NORCCAP (Norwegian Colorectal Cancer Prevention) trial, the SCORE (Screening for Colon Rectum) trial from Italy, and the UKFSST (UK Flexible Sigmoidoscopy Screening Trial).[4–7] Table 1 shows the trial designs, including algorithms for referral to colonoscopy after screening, and the CRC incidence findings. PLCO had 2 scheduled screens, whereas the others were all trials of one-time (baseline) sigmoidoscopy. In NORCCAP, half of the intervention arm was scheduled to also receive once-only screening with a fecal immunochemical test at the time of the sigmoidoscopy. The trials had different criteria, based on the findings at screening sigmoidoscopy, for referral to colonoscopy (Table 1). Follow-up colonoscopy to the sigmoidoscopy screen was performed within a few weeks of the screen for UKFSST, NORCCAP, and SCORE; for PLCO, it was generally performed within 4 months of the screen. Surveillance colonoscopies after diagnosis of adenomas were scheduled according to national guidelines (NORCCAP, SCORE, and UKFSST) or community practice (PLCO).

Median follow-up ranged from 10.5 to 11.9 years.[4–7] All trials found significant reductions in CRC incidence, with intent-to-treat risk ratios (RR) all within a narrow range (0.77–0.82).[4–7] All trials also showed significant reductions in the

Abbreviations used in this paper: **CRC, colorectal cancer; DTA, dwell time avoided; NNR, number needed to remove; NNS, number needed to screen; RR, risk ratio.**

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0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2018.06.040