Sigmoidoscopy may reduce the incidence and mortality of colorectal cancer (CRC) in two ways. The first is by direct detection of distal (left-sided) early-stage CRC and removal of precancerous adenomatous polyps. The second takes advantage of the association between distal neoplastic findings and advanced neoplasia in the proximal colon. Several studies have shown a synchronous relationship between distal neoplastic findings and advanced proximal neoplasia (APN), in which the risk (or prevalence) of APN increases as the extent of distal neoplasia increases (1–4).

Between 2009 and 2012, four trials of screening sigmoidoscopy were published (5–8), three of which reported outcomes of one-time sigmoidoscopy compared with usual care (5–7). Table 1 shows descriptive data and main results of the three trials. The trials are similar in the age range of invited and screened subjects, in intervention and control groups, and in the primary end points (CRC incidence and mortality). In all four trials, the effect of sigmoidoscopy on overall CRC mortality was due to its effect on distal CRC. Despite their similarities, the trials differ somewhat in their main findings. The differences in cancer outcomes may be due to differences in the underlying populations’ risk profiles, in persons who were willing to participate and who were randomly assigned, in their adherence to the trial, and in follow-up duration (and the shorter duration for the Norwegian Colorectal Cancer Prevention Trial (NORCCAP) trial likely accounts for the lack of effect of screening on CRC incidence). These factors are beyond the control of study investigators and providers. Another reason for the differences in outcomes—one that is controllable—is the intervention itself: how well sigmoidoscopy was performed, and perhaps most important, the sigmoidoscopic findings that led to further evaluation with colonoscopy. Among the three trials, the proportion of patients referred for colonoscopy after sigmoidoscopy ranged from 4% in the Screening for Colon REctum (SCORE) trial to 18% in the NORCCAP trial (Table 1).

As countries and large health-care systems consider moving from trial evidence about the efficacy of sigmoidoscopy to its implementation, it is important to understand the effect of the varying referral rates for colonoscopy on CRC-specific outcomes in terms of detection of advanced neoplasia and the required effort and resources. In addition to understanding these parameters for implementation, they may be used for modeling and comparing the effectiveness and cost-effectiveness of sigmoidoscopy to other CRC screening strategies. In this issue of the Journal, the article by Castells and colleagues (9) quantifies the trade-off between detection of advanced neoplasia (CRC and advanced adenomatous polyps) and diagnostic efficiency.

To explore this trade-off, the investigators utilized baseline data from the Grupo Cooperativo para el Cribado del Cancer Colorectal en Espana (COLONPREV) trial of screening colonoscopy vs biennial fecal immunochemical testing (FIT) (10) to compare the three sets of criteria for colonoscopy referral. The criteria sets were compared in asymptomatic persons aged 50–69 years who were either randomly assigned to the colonoscopy arm of the trial or who were randomly assigned to and eligible for the FIT arm but requested a screening colonoscopy instead. The end points for comparison were 1) detection rate for any advanced neoplasia; 2) test characteristics for APN; and 3) number needed to screen to detect one person with APN. All estimates were based on simulation of sigmoidoscopy from colonoscopic findings. Two definitions of distal were considered—one with and one without the descending colon. Test characteristics were measured in age- and sex-specific subgroups. Distal findings were explored as predictors of APN (9).

Colonoscopy referral would have occurred for 6.2% of the study population using the UK criteria, 12.0% using the SCORE criteria, and 17.9% using the NORCCAP criteria. NORCCAP criteria were most sensitive for APN whereas UK criteria were most specific and efficient. Colonoscopy detected any advanced neoplasia in 520 of 5059 (10.3%) individuals, whereas detection with the three sets of criteria ranged from 6.3% for the UK criteria to 7.0% for NORCCAP, which is 61% to 68% of all advanced neoplasia. Colonoscopy identified APN in 255 (5.0%) persons. Sensitivity of the referral criteria for APN ranged from 22% for the UK criteria to 37% for NORCCAP. Among persons referred, the
number needed to screen with colonoscopy to detect one person with APN was six for the U.K. criteria, eight for SCORE, and 10 for NORCCAP. Including the descending colon with the distal colon improved APN sensitivity by absolute amounts of 2% to 4% overall, by 5% to 8% for men aged 50–59 years, and by 8% to 9% for women aged 60–69 years. A large (≥10 mm) distal adenoma was the strongest independent predictor of APN.

The study by Castells and colleagues very nicely quantifies the trade-offs among the three sets of colonoscopy referral criteria between the proportion of advanced neoplasia detected and efficiency/resource utilization. These data may be used to inform countries and health-care systems about what to expect in terms of yield, efficiency, and resource allocation—information that may also be useful for comparing different CRC screening strategies. Reproducing the study findings in other large screening colonoscopy cohorts would strengthen these results, particularly for the age- and sex-specific subgroup analyses, and would determine the robustness of each set of referral criteria in different populations.

The large screening colonoscopy datasets from Germany (11), Poland (12), and Austria (13) would be especially informative for these analyses.

One-time sigmoidoscopy detects most advanced colonic neoplasia; however, it is clear that using distal colonic findings alone in sigmoidoscopy screening—regardless of which criteria are used for colonoscopy referral—will miss most APN. Unfortunately, a breakdown is not provided of how much of the missed APN was advanced adenomas vs proximal CRC. Nevertheless, the high proportion of missed APN highlights the need for a way to quantify and stratify risk for advanced neoplasia among “average-risk” persons prior to consideration of any CRC screening. Effective risk stratification would help identify patient subgroups in which sigmoidoscopy would be particularly efficacious; it might also identify subgroups for which other screening tests may be warranted, either in addition to sigmoidoscopy (eg, FIT) or in lieu of it (eg, colonoscopy). Such a system has the potential to make CRC screening more efficient and could help increase the uptake of CRC screening to levels comparable to breast and cervical cancer screening.

**References**

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