

Colonoscopy vs Sigmoidoscopy: New Studies Fuel Ongoing Debate

By Charlie Schmidt

Mounting evidence shows that colorectal screening reduces cancer incidence and mortality, but scientists still disagree about the best way to look for risky polyps. Clinicians in the US favor colonoscopy, while European health systems rely far more on flexible sigmoidoscopy—a cheaper, less invasive method that can be performed without sedation, but that also reaches only into the distal or “left” side of the colon, while leaving the proximal or “right” side nearer to the large intestine un-monitored. According to Martin Brown, M.D., chief of the health services and economics branch at the National Cancer Institute (NCI), colonoscopy rates among those eligible for the procedure in the US (generally individuals aged 50 and over) climbed dramatically after Medicare began covering the procedure—from 19% in 2000 to 54.6% in 2010. Rates of flexible sigmoidoscopy (in combination with fecal occult blood testing, or FOBT) declined from 9.4% to 1.3% over the same time period.

New Data

Now a series of new studies are re-igniting debates over endoscopy in colorectal cancer screening. In the *New England Journal of Medicine* on May 21, Robert Schoen, M.D., from Pittsburgh Medical Center, and colleagues, reported results from the NCI’s Prostate, Lung, Colorectal, and Ovarian (PLCO) randomized clinical trial, showing that sigmoidoscopy reduced colon cancer incidence by 21% and mortality by 50%. These results confirmed findings from an earlier randomized clinical trial performed by a team led by Wendy Atkin, M.D., from Imperial College London, which was published in the *Lancet* on May 8, 2010. In that study sigmoidoscopy reduced cancer incidence by 36% and mortality by 50%. The UK team did not follow positive sigmoidoscopy findings with colonoscopy,

but the PLCO did, detecting right-sided polyps in some cases. But while right-sided colonoscopy screening in the PLCO trial was associated with significant reductions in cancer incidence, it had no effect on mortality.

Similarly, on June 11, Nancy Baxter, M.D., from St. Michaels College, University of Toronto, reported case-control findings in the *Journal of Clinical Oncology*, showing that colonoscopy significantly reduces cancer incidence and mortality, but only for tumors appearing on the colon’s left side (these data were reported as odds ratios, which can’t be compared to percent reductions from the PLCO on an apples-to-apples basis). Conducted on a US cohort, the findings confirmed earlier case-control results from a Canadian population that Baxter published in *Annals of Internal Medicine*, in 2009. That study also showed that colonoscopy limits deaths primarily from cancer developing in the left side of the colon.

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Given that right-sided colonoscopy has yet to show significant mortality reductions, some experts argue that sigmoidoscopy—despite its inability to reach farther into the colon—may be adequate in many cases. “While we try to understand and improve colonoscopy on the right side,

we should also consider that sigmoidoscopy may be sufficient and perhaps even preferable in combination with other tests, like high-sensitivity fecal immunochemical testing, said David Ransohoff, M.D., a professor of medicine and epidemiology at the University of North Carolina School of Medicine. Barnett Kramer, M.D., who directs the NCI’s Division of Cancer Prevention, echoes that conclusion. Moreover, because sigmoidoscopy is given at five-year intervals, Kramer adds, it might pick up intervening cancers that colonoscopy—given every ten years—could miss.

Other experts disagree. Schoen, for instance, counters that reductions in cancer incidence from right-sided colonoscopy



David Ransohoff, M.D.

screening reflect a clinical benefit, even if they aren’t accompanied by changes in mortality. “Would you rather not get colon cancer, even if you didn’t die from it?” he asked.

Why the Left-Right Discrepancy?

Jennifer Weiss, M.D., an assistant professor in the Department of Medicine at the University of Wisconsin, in Madison, says it’s likely that both the right and left sides of the colon are equally susceptible to cancer. However, scientists don’t know if a tumor’s location has a direct influence on mortality, she says, and studies investigating that question have produced conflicting results. Baxter’s research suggests that compared to its incidence in the general population, colorectal cancer develops more frequently in the right side after colonoscopy. What’s more, right- and left-sided lesions have significant biological differences. For instance, right-sided tumors are more

likely to express both the CpG island methylator phenotype, which is associated with higher risk, and also microsatellite instability, which reflects an accumulation of genetic damage from DNA repair defects. Right-sided lesions can also be harder to see; they're flatter than the raised polyps visualized more often in the left side of the colon, and they're also harder to remove. Finally, bowel preparation isn't as thorough in the right colon as it is in the left, and this further limits colonoscopy's resolution.

The US Preventative Services Task Force currently recommends three options for colorectal cancer screening: Annual FOBT, which checks for hidden blood in three consecutive stool samples; flexible sigmoidoscopy, every five years; or colonoscopy, every ten years.

In an editorial published last June, in the *New England Journal of Medicine*, John Inadomi, M.D., a gastroenterologist in the Department of Medicine at the University of Washington, Seattle, argued that eligible patients who decline colonoscopy for personal reasons should have ready access to these other options. Sigmoidoscopy

reduces cancer incidence and mortality “for the portion of the colon that it was designed to investigate,” and so it should therefore not be dismissed, he wrote. Furthermore, Inadomi points out that case-control data in support of colonoscopy (which costs \$1,000-\$1,500 in addition to fees for anesthesia and pathology analyses), are inferior to the randomized control data in support of sigmoidoscopy (which can be performed by nurses and other allied health professionals at a cost of \$200-\$300). Cost effective, evidence-based interventions will be favored should medical systems move from fee-for-service to bundled care payments, Inadomi predicted.

According to Christine Berg, M.D., chief of the early detection group in the NCI's Division of Cancer Prevention, colonoscopy was still emerging when PLCO started recruiting patients in 1993, and this explains why this enormous study used a screening method that has since gone out of favor in the US. Still, in Berg's view, colonoscopy has by now become the definitive test, although she admits that in the absence of a head-to-head comparison (not a worthwhile

endeavor, she says), it's impossible to know how much better it is than sigmoidoscopy. “We should acknowledge that colonoscopy is the superior approach and then we should go forward on improving it,” she says. “By that I mean improving the preparation and ability to find distal lesions and improving access to the procedure in the US.”

Ransohoff counters that 50% reductions in mortality from sigmoidoscopy—as confirmed by the US and UK trials—reflect a major screening benefit, even if it is smaller than the 90% mortality reduction with which colorectal endoscopy is erroneously associated. Moreover, Baxter adds that colonoscopy suffers from small but significant complications including bowel perforation and death in some cases. Speaking to colonoscopy alternatives, namely FOBT and sigmoidoscopy, she says “We assume that if we offer colonoscopy to everyone that they'll say ‘sign me up’ but that's not the case,” she says. “You might be better off having them sign up for a test that's less effective but that they're more willing to get.”

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