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EDITORIAL

New American College of Physicians Guidance on Colorectal Cancer Screening: Less Is More

A wide variety of screening tests are available for colorectal cancer screening, ranging from inexpensive, noninvasive, but frequently repeated fecal testing for occult blood over long-lasting but invasive and burdensome colonoscopy and sigmoidoscopy to new but expensive fecal DNA markers and other emerging tests. Although the various choices and substantial potential for innovation make colorectal cancer screening an exciting field, they also present a challenge for guideline makers who are tasked with providing up-to-date and evidence-based recommendations for clinical practice.

In a new guidance statement, the American College of Physicians (ACP) provides an update of its colorectal cancer screening recommendations (1). Although the new ACP guidance is based on the same data as recent guidelines from the U.S. Preventive Services Task Force (USPSTF) (2) and American Cancer Society (3), they differ in 3 important ways:

1. ACP does not recommend colorectal cancer screening for persons aged 45 to 49 years.
2. ACP does not recommend fecal DNA or computed tomography colonography screening.
3. ACP recommends fecal testing for occult blood only every other year, not yearly as in the other guidelines.

The ACP developed these updated recommendations after conducting a thorough evaluation of the evidence review and decision analyses commissioned by USPSTF in 2021. When formulating its recommendations, ACP emphasized the importance of clinical and empirical data in the context of absolute disease prevalence, rather than relying solely on disease modeling. In addition, unlike the guidelines of USPSTF and the American Cancer Society, the ACP guidance statements took cost into consideration. The ACP panel also paid attention to the risks and burden for patients and societal issues, such as equality, with the different screening tests. All this may explain the differences in recommendations between the ACP guidance and the other guidelines. The new recommendations, surprising as they may be for some, may turn the tide toward more dispassionate, evidence-based assessment of absolute benefits and harms of colorectal cancer screening.

The ACP discourages screening for asymptomatic average-risk persons younger than 50 years. The reasoning includes a lack of evidence on clinically relevant absolute benefits as compared with the expected harms of screening in this age group. It may seem intuitive to expect similar relative screening benefits and harms for younger persons compared with older persons. However, considering the much lower disease risk, a much larger number of younger persons will need to be screened to prevent 1 case of cancer. Consequently, ACP cautions that absolute screening benefits may not outweigh the harms in this age group. We agree (4).

The ACP voices concern about reliance on microsimulation disease modeling as the basis for screening recommendations in the other U.S. screening guidelines (2, 3). It points out unrealistic assumptions made in the modeling process, such as 100% participation and equal effects across age groups, which may have contributed to an exaggerated interpretation of screening net benefits, leading to recommendations for too much screening for too many people. By recommending against screening for younger persons and advocating for longer test intervals for fecal testing for occult blood for all age groups, the ACP takes a step toward a screening approach that involves less testing without compromising net benefits.

The new ACP guidance does not recommend stool testing with DNA markers (1). The only DNA stool test currently approved is Cologuard by Exact Sciences. It was initially recommended by USPSTF in 2016 and reaffirmed in the 2021 USPSTF guideline update. The ACP clarifies that it does not endorse fecal DNA stool testing because no comparative clinical trial data that show its effectiveness on colorectal cancer incidence or mortality against standard fecal immunochemical tests are available. Considering that the average fecal immunochemical test costs $3 to $4 versus $680 for Cologuard, this is a reasonable argument, especially when the recommended fecal immunochemical test interval is 2 years rather than 1 year (5). New approaches, such as fecal RNA testing and blood-based molecular testing, are expected to enter the market in the future and will add to the already long list of options for colorectal cancer screening (6, 7). The new ACP guidance document raises the bar for evidence of effectiveness required for these new tests to be considered in future guideline recommendations.

Although the new ACP statement is at odds with USPSTF and American Cancer Society guidance in important ways and will spark debate in the United States, it is more in line with international guidelines (8, 9). One such guideline argues along the same lines as ACP in that the small absolute benefit of screening for persons younger than 50 years may not outweigh its risks (8). That guideline introduces a risk threshold for colorectal cancer screening and proposes that persons with a 15-year risk for colorectal cancer below 3% may not benefit from any current colorectal cancer screening test, given their harms and burdens. The concept of using personalized disease risk as a basis for screening has not yet found its way into ACP or other U.S. screening guidelines, but such a personalized risk measure may be a more effective alternative to suboptimal surrogates, such as age, race, and ethnicity. As the ACP panel points out, race and ethnicity are more social constructs than biological risk factors and should be used with caution for clinical practice recommendations (1).

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The updated guidance statement from ACP advocates for reserving screening recommendations for tests and patient populations associated with favorable high-quality benefit–harm assessments. It shifts away from the more-testing-to-more-people approach in other U.S. guidelines. One aspect that may have deserved more attention is the advantage of colonoscopy and sigmoidoscopy screening in *preventing* colorectal cancer by removal of polyps, contrasting with fecal tests that primarily aim at *detecting* cancer at an early stage. If they work as expected, colonoscopy and sigmoidoscopy can reduce the risk for colorectal cancer, whereas the other tests can prevent persons from dying of cancer but not from developing cancer in the first place. This distinction of preventive versus early detection screening deserves emphasis in shared decision-making conversations to help patients choose the right screening option based on their preferences and needs.

Michael Bretthauer, MD, PhD
Clinical Effectiveness Research Group, University of Oslo, Oslo, Norway

Yu-Xiao Yang, MD
Department of Medicine, University of Pennsylvania, Perelman School of Medicine, Philadelphia, Pennsylvania

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Corresponding Author: Michael Bretthauer, MD, PhD, Clinical Effectiveness Research Group, University of Oslo, Postbox 1089 Blindern, 0318 Oslo, Norway; e-mail, michael.bretthauer@medisin.uio.no.

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