Many new colorectal cancer screening technologies have emerged since the publication of the first randomized trials of Hemoccult II fecal occult blood testing (FOBT) in the early 1990s (1), which complicates the task of forming clinical policy for colorectal cancer screening. As a coherent body of evidence about these tests gradually emerges, several organizations have issued practice guidelines for colorectal cancer screening. This editorial contrasts the processes and recommendations of 2 prominent organizations.

In developing guidelines, each organization must set the rules: whom to include on the panel, who should recuse themselves for conflict of interest, what evidence to examine, how to evaluate the evidence, and how to translate it into recommendations. Because of the rapid emergence of new technologies, guideline panels cannot realistically rely on the gold standard for evidence on screening for cancer: randomized trials that use death from cancer as the end point.

In the absence of randomized trials, guideline-making organizations have often relied on the judgment of experts who review the available data and apply criteria (in some cases explicit; in others, implicit) to estimate the benefits and harms of screening strategies. Some organizations have used systematic evidence reviews and formal modeling of benefits, harms, and cost. Some convene a panel of experts in the clinical topic. Others use clinicians who are experts in evaluating evidence and ask clinical experts to review their conclusions. Recently issued colorectal cancer guidelines allow us to see these different approaches in action.

This issue includes the most recent U.S. Preventive Services Task Force (USPSTF) guidelines (2), an updated focused systematic review of key questions (3), and a decision analysis to help compare different testing strategies and decide on the age at which to start and stop screening (4). The USPSTF guidelines appear several months after the American Cancer Society—U.S. Multi-Society Task Force (ACS-MSTF) guidelines, commissioned by the American Cancer Society and issued jointly by professional societies representing gastroenterology and radiology (5). The USPSTF and ACS-MSTF approached their task quite differently, and their recommendations reflect these differences.

In keeping with its standard practice (6, 7), the USPSTF commissioned a systematic review of several key questions (3). This systematic review reached several conclusions. First, newer tests for occult blood (such as Hemoccult SENSA) detect more neoplasms than Hemoccult II, but with lower specificity. Second, immunochemical tests for occult blood detect as many cases of cancer as the newer guaiac tests and are somewhat more specific. Third, first-generation stool DNA tests are not substantially better than tests for fecal blood. Fourth, computed tomographic (CT) colonography in experienced hands is much more sensitive than tests for occult blood and about as specific, but it involves exposure to radiation and often requires colonoscopy to biopsy lesions. Computed tomographic colonography also detects extracolonic findings that often trigger a diagnostic search that sometimes identifies important disease. Finally, colonoscopy is not perfectly accurate—it misses some cases of cancer and large polyps—and has higher rates of serious harm than other strategies.

In its deliberations, the USPSTF also had the results of USPSTF-commissioned microsimulation decision models performed by researchers affiliated with the National Cancer Institute—supported Cancer Intervention and Surveillance Modeling Network collaborative (4). These analyses used state-of-the-art modeling techniques, informed by best estimates of the key model inputs, to compare the benefits and harms of screening strategies that differed in the starting age, stopping age, and testing interval. The modelers presented estimates of health benefit and harm (the latter measured by deaths from perforating the colon during procedures) by using life-years gained or lost; they used the number of colonoscopies required to produce these health effects as their measure of efficiency.

The USPSTF use of modeling is a step in the right direction, but the models reflect some surprising choices. They did not quality-adjust their estimates of benefits and harms. Their measure of effort (colonoscopies required) did not account for patient time invested in screening or the institutional costs of achieving high levels of adherence. They did not use the worldwide standard measure of efficiency—cost per quality-adjusted life-year—so policymakers cannot compare the efficiency of colorectal cancer screening with that of other health care interventions. Finally, the modelers did not evaluate some new, controversial screening strategies (such as CT colonography or stool DNA testing).

The models found that annual or biennial Hemoccult II used alone or flexible sigmoidoscopy used alone every 5 years was less effective than 3 other strategies that the models found to be roughly equivalent: colonoscopy alone every 10 years, annual high-sensitivity FOBT alone (which requires the fewest colonoscopies), or the combination of sigmoidoscopy every 5 years and high-sensitivity stool testing conducted at the midpoint between sigmoidoscopic examinations. These results are consistent with those of previous cost-effectiveness analyses (8).

Of note, the USPSTF also addressed when to stop screening. According to their models, screening beyond age 75 years added little benefit relative to the additional number of colonoscopies required. The USPSTF recommended against routine colorectal cancer screening from age 75 to
85 years, except in special circumstances, and recommended against routine screening after age 85 years under any circumstances. This topic—when to stop screening—is a growing area of preventive services research. The basic principle is that people should avoid screening tests when they are unlikely to survive long enough to benefit from early detection—or when the risk for adverse effects begins to increase disproportionately. In randomized trials of FOBT screening in mostly middle-aged volunteers, it took 5 years before screened patients had a clearly lower mortality rate from colorectal cancer than control participants. Thus, it makes sense to stop screening for colorectal cancer if a person’s life expectancy is less than 5 years, either because of advanced age or comorbid conditions. These conclusions also emerge from empirical work (9).

In contrast to the defined methods of the USPSTF, the ACS-MSTF guideline writers adopted 2 clinical perspectives to guide their process and recommendations. First, the goal of screening should be to prevent colorectal cancer; detecting polyps should therefore be the principal consideration in designing screening programs. As such, the panel recommended giving first priority to structural examinations—endoscopic inspection or imaging. It recommended noninvasive stool tests only when patients had poor access to structural tests or were reluctant to have them. Secondly, accuracy at a single point in time should be the principal criterion for recommending a test, rather than accuracy of repeated testing over time (so-called “program sensitivity”). In adopting the second principle, the ACS-MSTF cited concern about poor long-term adherence to annual stool testing.

These perspectives led the ACS-MSTF to place considerable weight on 1 characteristic (single-application sensitivity for cancer >50%), thus making other considerations (frequency of testing, adverse effects, and costs) relatively less important. The ACS-MSTF panel did not use decision modeling or a systematic review to reach its recommendations, nor did it grade the strength of the evidence or formally rate the strength of each recommendation. It did identify recommendations that it based solely on clinical judgment.

A comparison of the USPSTF and ACS-MSTF recommendations (Table) provides insight into these agencies’ decision criteria. The ACS-MSTF recommended against Hemoccult II, on the basis of its low sensitivity at a single point in time. The USPSTF did not recommend against Hemoccult II or sigmoidoscopy alone, despite their relatively low estimated benefit. The ACS-MSTF did not recommend against use of sigmoidoscopy alone, perhaps because it met the ACS-MSTF criterion for single-application sensitivity.

The ACS-MSTF recommended CT colonography because of its good accuracy for larger polyps and cancer. The USPSTF withheld a recommendation on CT colonography because it could not estimate the benefit–harm ratio, citing insufficient evidence about the potential harms of extracolonic findings and radiation exposure. Other modeling studies suggest that CT colonography is effective if it is accurate for large polyps at a reasonable cost. These analyses lacked good estimates of the risk for radiation exposure and the effect of extracolonic findings (10, 11). The ACS-MSTF also felt that evidence was sufficient to recommend stool DNA testing (based on a single-application sensitivity for colorectal cancer >50%), whereas the USPSTF, citing insufficient evidence, did not make any recommendation. A previous modeling study found stool DNA testing every 5 years to be less effective and more costly than either colonoscopy or annual FOBT screening (12).

What do these differing processes and recommendations tell us about the current state of the art in making guidelines? First, the consistent application of defined methods for gathering, interpreting, and rating evidence promotes transparency and internal consistency. Second, modeling is useful because it integrates different types of evidence to estimate the net benefit of different screening strategies. However, to be most informative, modeling must evaluate all of the relevant strategies and their costs. Third, guideline makers must decide on a process for using modeling results and follow it consistently. Finally, recommendations should be specific about starting and stopping ages, testing intervals, and follow-up. In short, we think the public is best served by a relatively structured, comprehen-

### Table. A Comparison of Colorectal Cancer Screening Recommendations

<table>
<thead>
<tr>
<th>Strategy</th>
<th>ACS-MSTF (5)</th>
<th>USPSTF (2)</th>
<th>USPSTF Modeling Findings (4)</th>
<th>Other Modeling Studies (8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoccult II annually</td>
<td>No</td>
<td>Yes</td>
<td>Suboptimal</td>
<td>Mixed</td>
</tr>
<tr>
<td>High-sensitivity Hemoccult or fecal immunochemical test annually</td>
<td>Yes</td>
<td>Yes</td>
<td>Suboptimal</td>
<td>Suboptimal</td>
</tr>
<tr>
<td>Flexible sigmoidoscopy alone every 5 years</td>
<td>Yes</td>
<td>Yes</td>
<td>Suboptimal</td>
<td>Suboptimal</td>
</tr>
<tr>
<td>Computed tomographic colonography every 5 years</td>
<td>Yes</td>
<td>Insufficient evidence</td>
<td>Not evaluated</td>
<td>Yes (10, 11)</td>
</tr>
<tr>
<td>Colonoscopy every 10 years</td>
<td>Yes*</td>
<td>Yes</td>
<td>Insufficient evidence*</td>
<td>Suboptimal (12)</td>
</tr>
<tr>
<td>Stool DNA testing every 5 years</td>
<td>Yes</td>
<td>Yes</td>
<td>Suboptimal</td>
<td>Suboptimal</td>
</tr>
</tbody>
</table>


* Interval not stated.
hensive, transparent approach in which the entire body of evidence drives the recommendations.

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