Speaking for the Evidence: Colonoscopy vs Computed Tomographic Colonography

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At a recent National Institutes of Health State-of-the-Science Conference on “Enhancing the Use and Quality of Colorectal Cancer Screening,” the final discussion period was dominated by an animated debate between optical colonoscopists and computed tomographic (CT) colonographers about the relative merits of their respective screening tests (optical colonoscopy and CT colonography). A similar exchange between gastroenterology and radiology specialty societies occurred in strongly worded letters to the White House after President Obama had CT colonography for colorectal cancer screening during his annual physical examination. Gastroenterologists claimed that optical colonoscopy is the “gold standard” test; radiologists claimed that Medicare unfairly excludes reimbursement for CT colonography as a screening test (1).

Although high-quality evidence is absolutely necessary for making optimal health-care decisions (whether for individuals or for populations), it is a curious fact that evidence does not speak for itself. To get the meaning from evidence, judgment is required at several points (2,3). The primary evidence disagreement between gastroenterologists and radiologists seems to be how to weigh the benefits and harms of the two screening tests, an issue that others disagree about as well.

Two national guideline groups have reached different conclusions about whether CT colonography should be added to the list of “approved” colorectal cancer screening tests and thus covered by Medicare. In 2008, the US Preventive Services Task Force (USPSTF) added colonoscopy to its list of recommended colorectal cancer screening tests but found the evidence for CT colonography “insufficient” to weigh the benefits and harms (4). (Full disclosure: I was a member of the USPSTF when this recommendation was made.) In that same year, however, in a joint guideline, the Multi-Society Task Force, the American Cancer Society, and the American College of Radiology did add CT colonography to its list of recommended colorectal cancer screening tests (5).

In this issue of the Journal, Knudsen et al. (6) make an important contribution to the discussion with their cost-effectiveness study of CT colonography screening for people aged 65–80 years. This study is well done by a group of careful evidence-based investigators who are part of the National Cancer Institute–supported Cancer Intervention and Surveillance Modeling Network (CISNET) consortium.

To help us decide whether Medicare should add CT colonography to its list of reimbursed colorectal cancer screening tests, the CISNET group considered how much CT colonography would need to cost (the “threshold cost”) for it to be as efficient (in terms of costs and effectiveness) as the currently reimbursed screening tests. With their best assumptions about the effectiveness of CT colonography and the natural history of colorectal cancer, the authors report that the threshold cost for CT colonography would need to be quite low: between $108 and $205 per scan. At $488 per scan (a cost that might be expected based on other CT costs), CT colonography is not a “good buy” compared with other screening tests. However, if adding CT colonography substantially increased adherence to colorectal cancer screening within the general population, then CT colonography would be a good buy at the higher threshold cost. Although underuse of colorectal cancer screening is a general problem (7), we do not have convincing evidence that adding the option of CT colonography would indeed increase the percentage of the population being screened.

How should we interpret this new study and should it persuade Medicare to reimburse for CT colonography screening (assuming either the cost of CT colonography can be lowered or future research finds that CT colonography substantially increases population adherence to screening)?

Although not “new” evidence in itself, a cost-effectiveness analysis extends previous evidence into the future, allows us to integrate various parts of strategies (eg, effectiveness, adherence, and complications), considers the effects of the strategy over time, allows us to gain insight into the factors that matter most to cost-effectiveness, and adds the critically important factor of cost. It should help us by providing a quantitative way of combining benefits and harms for each strategy, making it easier to compare one strategy with another. In this case, it should help the differing groups resolve their disagreements about colorectal cancer screening tests.

But cost-effectiveness analyses do not speak for themselves; we have to consider their limitations, as were well discussed by the authors of this analysis. First, cost-effectiveness analyses are built on assumptions about two fundamental issues: 1) the natural history of the disease and 2) the multiple effects of the strategy. If evidence about natural history or the effects of the strategy is incomplete or flawed to an important degree, no cost-effectiveness analysis can rescue us. Second, even if we have reasonable evidence on natural history and strategy effects, it may be difficult to quantify the benefits and harms into a single metric.

The CISNET analysis provides examples of the problems of uncertainty and difficulty in quantification. An example for CT colonography is the issue of extracolonic findings. Studies of CT colonography have found that extracolonic findings occur in 40%–98% of people (8–13). As many as 24% of people who have a single CT colonography have further diagnostic workup or...
treatment based on an extracolonic finding (8), a percentage that could be higher in community settings. Although the probability of at least one extracolonic finding in an individual undergoing multiple rounds of screening over 25 years must be substantially higher than these estimates, we really do not know how high it is. CT colonography amounts to a screening program for other cancers—lung, adrenal, kidney, pancreas, and liver—much in the way of whole-body CT scans. The USPSTF does not recommend screening for any of these cancers. Because the effects of the incidental findings from this “semi” whole-body screening on the quality and length of people’s lives are not known, the authors were not able to include them in this analysis. But that does not mean that decision makers should assume there are no negative effects.

An example of uncertainty about harms of optical colonoscopy is the effect of the current optical colonoscopy policy of removing every polyp regardless of size. CT colonography does not detect small polyps (eg, those 5 mm or smaller) very well (11); removing any polyp increases the risk of optical colonoscopy complications (14,15). If these small polyps are an important cause of colorectal cancer mortality, and waiting until the next screening round is not effective in preventing these deaths, then optical colonoscopy would provide more benefit than CT colonography. But if these polyps are not important contributors to colorectal cancer mortality, or if waiting until the next screening round is as effective as detecting them when they are small, then polyps are being removed unnecessarily by optical colonoscopy—a form of “over-treatment”—subjecting many people to an increased risk of optical colonoscopy complications and subjecting all of us to increased cost. The microsimulation models used by CISNET accounted for the costs of these potentially unnecessary polypectomies but were unable to quantify the effect of their complications on quality of life. Again, decision makers would do well to consider this issue, regardless of the problems for cost-effectiveness analyses.

Despite the problems of uncertain evidence and difficulties in quantifying harms, the CISNET investigators have made an important contribution. But there may be additional ways to assist decision makers. The USPSTF often uses another approach—the outcomes table—to help weigh benefits and harms (2,3). This approach is an accounting of the various specific benefits and harms of decision options for a hypothetical general population. As an example, I have constructed a “back-of-the-envelope” outcomes table for optical colonoscopy and CT colonography (Supplementary Table, available online). Although the outcomes table does not crunch benefits and harms into a single metric (such as “quality-adjusted life-years”), it does provide decision makers with an explicit list of the frequency of various benefits and harms to be weighed and balanced. Like cost-effectiveness analyses, outcomes tables are limited by the available evidence; however, they are more transparent than “single-metric” cost-effectiveness analyses and allow trade-offs between benefits and harms to be clearly understood and even individualized.

Outcomes tables can be improved—beyond my crude, back-of-the-envelope example—by the use of the same models that provide the basis for cost-effectiveness analyses. What is important about these tables is their explicit listing of the benefits and harms (often given, but not emphasized in cost-effectiveness analyses), and their detailing of the evidence on which the numbers in each cell are based. As is evident in my CT colonography–optical colonoscopy outcomes table, there are multiple gaps in the evidence concerning the benefits and harms of CT colonography and optical colonoscopy, leading to an impressive degree of uncertainty. But outcomes tables also have their drawbacks: they do not easily deal with time and they do not allow quantitative comparisons between strategies for different outcomes, both of which are advantages of cost-effectiveness analysis. Outcomes tables and cost-effectiveness analyses should not be competing approaches; each provides information complementary to the other. It would be ideal for decision makers to have both.

Given the outcomes table (note that the numbers in the online table are rough, rather than precise, estimates, and I invite others to help me improve it) and the CISNET analysis, if I were to vote again today on whether to include CT colonography on the list of recommended colorectal cancer screening tests, I would still vote that the evidence is insufficient and thus would not recommend it. (Disclosure: I am no longer a member of the USPSTF.) Although there remain multiple uncertainties (eg, does CT colonography increase adherence to screening? what about the variation in CT colonography done in the community?), an important concern is the potential harm of the many extracolonic findings from CT colonography.

But the CT colonography discussion—and recent research (16,17) about the uncertain benefits of optical colonoscopy for right-sided colorectal cancer—has also raised important questions about optical colonoscopy. The harms and cost of this procedure make it a questionable primary screening test.

Perhaps neither gastroenterologists nor radiologists are unbiased enough to speak for this evidence. There are important uncertainties, and even with modeling and our best guesses, the trade-offs between benefits and harms are not obvious. Wouldn’t it be interesting if we ended up, a few years from now, with neither CT colonography nor optical colonoscopy as the primary screening test but rather an improved fecal test as our “gold standard”? 

References


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