Physicians’ primary responsibility has always been to provide the best care for their individual patients, but the proliferation of modern tests and treatments has complicated their task. With so many options, it is often hard during an office visit to know whether to order a test and what to do with the results. And the ever-rising cost of health care makes patient management even more complicated because physicians must also choose wisely and not waste societal resources.1 Although the plight of the physician is not as fraught as Hamlet’s, modern physicians do have difficult decisions about optimal selection of tests and treatments.

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Whether or not to order a test is a question that cuts across diseases and specialties. Tests provide information that might be important or might be irrelevant, depending on the clinical context. In caring for an individual patient, the question is whether the information from the test might change a clinical decision. In their classic analysis of whether to test or not in choosing a treatment, Pauker and Kassirer2 showed that when patients have a high chance of benefitting from treatment, the optimal strategy is simply to treat without doing a test, whereas for patients with a low chance of benefitting from treatment, the optimal strategy is to neither test nor treat. However, for patients in whom the chance of benefitting from treatment is intermediate, the optimal strategy is to obtain a test and use the results to choose to treat or not. The precise range of this intermediate probability sweet spot for testing depends on the benefits, harms, and costs of the disease, the treatment, and the test. This conceptual framework can be applied to many clinical decisions about whether to order a test and helps to answer the question of when the information a test provides will improve outcomes at a reasonable cost.

Use of Statins in Prevention

The value of statins in preventing adverse coronary heart disease (CHD) outcomes has been demonstrated repeatedly by many randomized clinical trials in a variety of populations. For patients with clinically evident CHD, the value of statins in secondary prevention is well proven and is highly effective. No further tests are required to decide whether to recommend statins for secondary prevention—treat all is the optimal strategy.

In primary prevention of CHD, however, selection of patients for statin treatment is more complicated because their risk of developing CHD varies so widely, and the expected benefits of treatment are much less and occur further in the future. In primary prevention, testing to refine CHD risk estimates might improve clinical decision making and treatment recommendations. American College of Cardiology/American Heart Association guidelines published in 20103 found good evidence that measurement of coronary calcium by cardiac computed tomography could improve CHD risk prediction, even after traditional cardiac risk factors have been taken into account. Coronary calcium scoring was given a class IIa recommendation for patients at intermediate risk of CHD—a 10-year risk of 10% to 20%, a class IIB recommendation for lower risk patients (6%–10%), and a class III recommendation for persons at lowest risk of CHD.4 These recommendations were based on epidemiological studies, not on a formal cost-effectiveness analysis.

In this issue, Pletcher et al4 report a sophisticated analysis of the effectiveness and cost-effectiveness of measuring coronary calcium to guide statin therapy in the setting of primary prevention. They follow the framework established by Pauker and Kassirer2 and model the choice among 3 strategies: (1) treat with statins without testing, (2) test and treat with statins if the coronary calcium score is elevated, or (3) neither treat with statins nor test. They project the likely outcomes of these 3 strategies for a range of patients who might be considered for primary prevention, but for simplicity they focus on a hypothetical cohort of women, aged 55 years, with an elevated cholesterol level and a 10-year CHD risk of 7.5%. Because their simulation model can be adjusted to accommodate different assumptions, they modeled the clinical outcomes of these 3 strategies under a set of favorable statin assumptions (low-cost statins that have no effect on quality of life) and a set of less favorable statin assumptions (high-cost statins that slightly decrease quality of life).

Their model provides some interesting insights into use of testing to select statin treatment. One point is that the total cost of each strategy is key and includes the cost of a coronary calcium scan, the cost of statin treatment, and the ultimate cost of treating CHD. In the test strategy, the upfront cost of coronary calcium testing ($225 per patient) will be offset by treating fewer patients with statins, with a break-even point after ≈1.2 years for low-cost statins and after just 1.5 months for high-cost statins. The eventual costs of CHD treatment, however, dwarf the costs of testing and statins, so preventing CHD might save more money. Over a lifetime, they project that if statin costs are low, a hypothetical 55-year-old woman with high cholesterol would have essentially the same total health-care costs in all 3 strategies, so the treat all strategy is optimal.
because it prevents more CHD events at the same overall cost. The first insight is that if statins are cheap and have no adverse effects, there is no reason to get an expensive test to decide whether to use them.

The optimal strategy is less obvious, however, under the less favorable statin assumptions—higher cost statins that have a small negative effect on quality of life. In this scenario, the optimal strategy is to test with a coronary calcium scan and then identify and treat the higher risk women, because then only the women most likely to benefit would be exposed to the adverse effects and higher statin costs. The second insight from the model of Pletcher et al4 is that when the treatment is more costly and less well tolerated, testing to target therapy becomes the best strategy.

One of the advantages of using a simulation model such as this is that all the key assumptions can be varied to check whether the optimal decision will change. In an earlier study of using high sensitivity C-reactive protein testing to guide statin treatment,5 my colleagues and I found that the optimal strategy was exquisitely sensitive to any reduction in quality of life by statins: reductions of just 1% to 2% were enough to make test and treat a better strategy than treat all. The model of Pletcher et al4 similarly shows that testing for coronary calcium becomes the optimal strategy if statins reduce quality of life by as little as 1% to 2%, even when statins are inexpensive. The insight from these models is that among low-risk patients, even small decrements in quality of life during years of treatment can offset the small benefits in disease prevention that will occur in the distant future. There are surprisingly few reliable data on the quality of life among low-risk individuals prescribed statins, but anecdotally quite a few individuals experience annoying side effects. Doing a test to refine CHD risk estimates seems to be the optimal strategy when patients are reluctant to take a statin because of minor adverse effects.

**Newer Guidelines**

The new American College of Cardiology/American Heart Association clinical guidelines for primary prevention of CHD substantially lowered the risk threshold for initiating statin treatment.6 One might ask whether these new, lower risk thresholds to initiate treatment make use of testing to guide statin treatment obsolete. I don’t think so, because the new guidelines have not changed the fundamentals of this decision: many healthy individuals are at such low risk of developing CHD that they should not be prescribed a statin for primary prevention. So, there will always be a boundary between individuals with high enough risk to warrant treatment and individuals with a risk low enough that statin treatment is not warranted. Whenever there is a treatment threshold, patients near that boundary might benefit from testing to guide choice of treatment. The analysis by Pletcher et al4 anticipated the new guidelines and actually support the lower risk threshold to initiate statin treatment. Even with new guidelines, there are intermediate-risk patients for whom physicians still need to ask the fundamental question of whether to test or not to test.

**Disclosures**

None.

**References**

To Test or Not to Test, That Is the Question
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