Editor’s Perspective

Medicine Should Be More Like Missouri
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Missouri is the “Show Me” State. Although the origins of the term are uncertain, it seems that it might have been etched into the national consciousness during a speech by U.S. Congressman Willard Duncan Vandiver. In an 1899 speech he stated, “I come from a state that raises corn and cotton and cockleburs and Democrats, and frothy eloquence neither convinces nor satisfies me. I am from Missouri. You have got to show me.”

The “Show Me” spirit is sometimes lacking in the field of Medicine, where we seem intent on integrating new tests and procedures before they are thoroughly vetted. Although we bemoan the slow adoption of effective treatments, we often prematurely adopt unproven strategies. Our quality measures are focused on underuse—the missed opportunity to provide a strongly indicated test or treatment. National registries, often industry-sponsored, also are commonly oriented toward addressing undertreatment, further fueling a national preoccupation on having not done enough rather than on having done too much.

It is true that this emphasis on undertreatment has improved quality of care. In the mid-1990s, for example, only about half of the patients nationally, and in several states only about one-third, who were ideal candidates for β-blocker therapy after having survived an acute myocardial infarction were prescribed the medication. Ideal candidates were identified by careful chart reviews that determined a group with no documented absolute or relative contraindications. This pattern of care was described almost 15 years after clinical trials provided evidence of the benefit. Moreover, those who were treated had better survival, concordant with what would be expected based on the trials. Studies that revealed similarly stark patterns for the prescription of aspirin and angiotensin converting-enzyme inhibitors led to quality measures that tracked undertreatment, public reporting that disseminated the information, quality initiatives that sought to address the problem and, ultimately, improvements in care.

We have not, however, responded with equal enthusiasm to the issue of overuse, the application of strategies that have not yet proved their worth. There are many practices in which the “frothy eloquence” of advocates has replaced the hard evidence that should be necessary to justify widespread adoption. In their embrace of yet-to-be-proven drugs and technologies, early adopters—both physicians and patients who embrace the new—are betting that new is better. The bet can occasionally be prescient, but it can also be foolhardy.

Ultimately, our studies about quality of care need to address areas of overuse and premature adoption to the same degree that we are currently addressing issues of underuse and delayed adoption. We should not presume that strategies are effective because they have face validity. The medical literature is strewn with studies based on subsequently discredited strategies that seemed at the time so obviously beneficial that some might have even questioned the need for a study.

The recent example of ezetimibe, a novel agent for cholesterol lowering that was approved based on its ability to modify lipid levels, highlights this practice pattern. Although prior agents that favorably affected this risk factor had failed to improve patient outcomes, the Food and Drug Administration did not require the company to provide evidence that it reduced risk. An intense marketing campaign created a blockbuster product with more than $5 billion in annual sales. The remarkable adoption of a new drug with a novel mechanism occurred simultaneously with an ongoing trial to determine the safety and effectiveness of the drug.

A recent close call demonstrates the potential hazard of exuberant adoption of new drugs that lack strong evidence supporting their use. Torcetrapib, a cholesterol ester transfer protein inhibitor, had remarkably favorable effects on lipid levels, raising high-density lipoprotein and lowering low-density lipoprotein. Pfizer, the developer of the drug, chose to initiate a clinical trial before Food and Drug Administration approval, the results of which showed a 58% increase in the risk of death in patients treated with torcetrapib compared with those treated with atorvastatin. How surprising was the finding? Only days before the trial was halted, the Chief Executive Officer of Pfizer had announced that torcetrapib would be one of the most important compounds of our generation. If that trial had not been conducted and torcetrapib had been approved solely on its lipid effects, there is little doubt that a massive marketing campaign would have quickly catalyzed it to blockbuster status. Such adoption, perhaps even exceeding that which accompanied ezetimibe, would have caused many deaths. It is uncertain whether the risks would have ever been revealed.

Premature adoption can also take a toll on society. With increases in the costs of medical care attaining unsustainable levels, strategies that incur costs without benefits are produc-
ing harm. If ezetimibe is not shown to be better than less expensive alternatives—or is worse—the billions spent on the drug will have been wasted. Until the trial is completed, any cost expenditure on the part of providers would be made simply on a hunch. The trial is conducted by many of the leaders in cardiovascular medicine, under the auspices of Harvard and Duke. The existence of the trial speaks to the uncertainty about the benefit of the drug because it would be unethical to conduct the trial if we were certain that the drug was effective.

The constant need to make decisions under conditions of uncertainty is one of medicine’s biggest challenges. We rarely know with great confidence the precise balance of benefit and risk that is associated with a particular test or treatment. In facing daily decisions, patients and their physicians must choose despite the limitations of the evidence. In the marketplace of medicine, do we assume benefit until we are shown otherwise?

Given the stakes, perhaps we ought to take a skeptical stance on new and expensive technologies before recommending their adoption into widespread use. The only exception might be for life-threatening or severely disabling conditions for which no alternatives exist. Even in these circumstances, it would be preferable to use the strategy in ways that can produce a greater understanding of its effectiveness.

In Circulation: Cardiovascular Quality and Outcomes, we have published articles that focus attention on the overuse of clinical strategies. We published two studies from the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluations) trial that put the results of the main trial in perspective. The COURAGE investigators sought to determine whether percutaneous coronary intervention would improve outcomes in patients with coronary artery disease who were optimally treated. They found that the interventional strategy did not reduce the risk of death, myocardial infarction, or other major cardiovascular events. In a cost-effectiveness analysis published in Circulation: Cardiovascular Quality and Outcomes, the authors reported that “the added cost of [percutaneous coronary intervention] was approximately $10,000, without significant gain in life-years or quality-adjusted life-years.”12 In the current issue, we extend the insights from COURAGE with information about consistency of the results across patients irrespective of the extent of coronary disease. The findings further strengthen the conclusion that percutaneous coronary intervention can be safely deferred in these patients. The adoption of a COURAGE approach to patient care could have substantial cost savings without a decrement in patient outcomes. The findings also raise a question about how many patients have undergone percutaneous coronary intervention with the expectation of benefits that were not borne out by the trial.

In another study in our journal that addressed overuse, Garcia and colleagues examined the common practice of providing coronary revascularization for patients with significant coronary artery disease who are scheduled for major vascular surgery. They had already shown that the Coronary Artery Revascularization Prophylaxis (CARP) trial revealed no long-term survival benefit with a strategy of preoperative coronary artery revascularization before elective vascular surgery. Questions had been raised, however, about the highest-risk patients. Their further examination of the trial failed to find a benefit of revascularization even in the highest-risk subsets. The trial again raised the question of how many patients had been treated with the presumption of benefit that the trial could not demonstrate.

Such studies seem to be sending the message that it may be wise to adopt a bit more of the Missouri approach when considering new tests and treatments. We do not want to be laggards in adopting strategies that provide clear benefit. On the other hand, perhaps we should insist on a “Show Me” mindset when it comes to those strategies in which the net benefit is yet unproven. As a journal, we will continue to seek articles on both sides, paying careful attention to overuse and waste as well as underuse and missed opportunities.

Disclosures

None.

References


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