

tients with varying risk characteristics and coexisting conditions but for women, members of minority groups, and others who have historically been underrepresented in clinical trials. Current CER efforts aim to ensure that much more useful data will be collected and that better methods will be developed for understanding differences in effectiveness among different patient groups.

As CER guides individual patient care, it will also guide and promote innovation. In some cases, federal support of the research will reduce the development costs of new medical technologies. Emerging CER methods promise to be more rapid, relevant, and efficient. Furthermore, the development of explicit standards for CER methodology will help to clarify which forms of evidence are sufficiently informative for health care decision makers — an advance that will be particularly important for the most novel personalized approaches, such as the creation of monoclonal antibodies directed against a cancer in a specific patient. Such exciting prospects do not obviate the need for evaluation; they change the kind of evaluation that is needed. CER may well re-

quire innovative approaches to clinical trials — such as adaptive, pragmatic, or other novel trial designs. Individualized therapies might be evaluated through the random assignment of patients to tailored therapy or a conventional alternative; such an approach would neither disadvantage the personalized therapy nor presume its superiority.

The deepest concern about CER is that it will be misused, which is why some legislators seek to prohibit information on comparative effectiveness from influencing coverage policy and payment decisions. But surely these decisions will not be improved by discouraging the use of the most relevant and valid information about what works and in whom. CER is not a panacea, but it is a key to individualized care and innovation, not a threat. An initiative to advance our knowledge about the effectiveness of clinical strategies can hasten the day when personalized medicine transforms health care.

Dr. Garber and Dr. Tunis report serving on the Institute of Medicine (IOM) Committee on Priorities for Comparative Effectiveness Research. Dr. Garber reports receiving lecture fees from De Novo Ventures, Express Scripts, and Covidien and consulting fees from McKinsey and Co. and Perlegen, a genomics company. Dr. Tunis also reports serving as director of the Center for Medi-

cal Technology Policy, which receives unrestricted funding from a number of foundations, government grants, as well as health plans and life sciences companies. No other potential conflict of interest relevant to this article was reported.

The views expressed in this article are those of the authors and do not necessarily represent those of the IOM, the IOM Committee on Priorities for Comparative Effectiveness Research, the Department of Veterans Affairs, or Stanford University.

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Debate about Funding Comparative-Effectiveness Research

Jerry Avorn, M.D.

The proposal to include \$1.1 billion for comparative-effectiveness research (CER) in the federal stimulus package encountered a vigorous and well-coordinated backlash. The campaign to gut this funding ultimately failed, but the debate it engendered and the resonance of the opposition's arguments in both lay and policy

circles reveal much about the issues that will surround such research and its application in the coming years.

The contested provisions were designed to support studies comparing the efficacy and safety (and, by extension, the cost-effectiveness) of alternative ways of addressing common clinical prob-

lems. Interventions to be evaluated will include pharmaceuticals, devices, procedures, and diagnostic approaches, such as imaging studies. This research will fill important information gaps facing clinicians, patients, and payers concerning what works best. Currently, the Food and Drug Administration (FDA) often approves new

medications on the basis of modest-sized studies involving patients with relatively few coexisting conditions who are followed for brief periods. Sometimes the only efficacy requirement is a demonstration that a new product works better than placebo in improving a surrogate outcome measure, such as a laboratory-test result, rather than achievement of an actual clinical benefit. The bar is set even lower for medical devices such as pacemakers and implantable defibrillators, which may only have to be shown to be similar to previously approved products or simply not to be dangerous. For new surgical procedures or imaging studies, there may be almost no evidentiary bar at all.

Vigorous marketing of the costliest new approaches fills this informational vacuum, encouraging the widespread use of goods or services that may be no better, less safe, or more costly than usual care — or all of the above. Of course, many new interventions clearly are better in one or more of these domains, but we have no systematic way of collecting or disseminating such information. It is these lacunae that the funding for comparative-effectiveness studies was designed to help fill. At 1/20 of 1% of our \$2 trillion annual health care expenditure, the CER funding amounts to a fraction of what any corporation would spend to find out whether it was getting its money's worth from its purchases. It represents one of the best investments we can make to edge the health care system away from the fiscal catastrophe it faces, since such studies will help to reduce spending on poorer clinical decisions and to spare resources for expenditures that will help patients most (and most affordably). This research is a public good, like

highways and clean air. The private sector is no more likely to identify badly mispriced or potentially toxic treatments than it was to spot badly mispriced or potentially toxic products of the banking industry.

What's the objection? After all, scientific medicine has always been based on conducting well-designed research to determine what works. The problem is that comparative studies will be threatening to makers and sellers of costly goods and services that offer no benefit over existing alternatives. But advocating ignorance is not a winning political strategy, so the foes of CER have found spokespeople to make their case in moral and policy arguments, by warning — astonishingly — that such knowledge will inexorably degrade the quality and accessibility of health care.

As the stimulus bill was being debated in January and February, the opposition to CER found its voice in commentators who claimed that these studies will inevitably lead to government domination of the doctor-patient relationship, "cookbook medicine," and rationing. Certainly, important issues do arise in trying to translate CER findings into specific decisions regarding patient care and reimbursement, but much of the attack relied on overt mischaracterizations of the legislation's content. Scott Gottlieb, a deputy FDA commissioner in the last administration, stated that the Congressional Budget Office had determined that CER "won't actually save much money"¹ — a contention he based on an article that said precisely the opposite.² "The risk," he said, "is that the conclusions will be flawed and still used to restrict coverage decisions, especially by Medicare." Nothing in the legislation, how-

ever, provided for payment restrictions based on CER findings.

In calmer times, fiscal conservatives might have been expected to support a plan to generate information about treatment benefits, risks, and costs so that physicians, consumers, and payers could use this knowledge in making purchasing decisions. But these are not normal times. On January 23, Representative Tom Price (R-GA), a physician, sent out an "alert" through the Republican Study Committee, falsely warning that the CER legislation would create "a permanent government rationing board prescribing care instead of doctors and patients." The true intent of the CER provision, Price warned, was "to enable the government to ration care" (emphases in original). "Every policy and standard will be decided by this board and would be the law of the land for every doctor, drug company, hospital, and health insurance plan."

Parallel arguments appeared in a letter sent January 26 to several influential members of Congress, cosigned by more than 60 advocacy groups, and again in a January 29 editorial in the *Wall Street Journal*. In an op-ed by columnist George Will that appeared in the *Washington Post* the same day, CER had morphed from a form of research into an imaginary new federal body with broad powers. Will named the agency "the CER" and claimed that with such a system, "Congress could restrict the tax exclusion for private health insurance to 'insurance that complies with the Board's recommendation.' The CER," he went on, "which would dramatically advance government control — and rationing — of health care, should be thoroughly debated, not stealthily created in the name of 'stimulus.'"³ In fact, unaffordability

rations care far more than comparative studies ever could.

The assault took on a more Orwellian tone 10 days later when Betsy McCaughey, a former lieutenant governor of New York, linked funding for CER with the stimulus bill's provisions supporting the use of electronic medical records. She warned that the inclusion of both initiatives was designed to enable electronic monitoring of individual patient-care decisions by the federal government and punishment of clinicians who fail to comply with imminent rationing guidelines.⁴ The radio talk-show host Rush Limbaugh then disseminated this message to millions of listeners, warning that once the stimulus bill "computerizes everybody's health record," a new federal bureaucracy "will monitor treatments to make sure your doctor is doing what the federal government deems appropriate."⁵

This avalanche of nonfacts did not succeed in derailing the stimulus bill or its CER funding. Although these commentaries painted caricatures of new federal powers that were not in the bill, they were a shot across the bow of the entire CER enterprise. As the debate continues, we are likely to see more diatribes designed to further an ideological or commer-

cial agenda. But CER also raises important issues that warrant the continuing attention of thoughtful clinicians and policymakers. For instance, although such research may well determine the first-line approach most likely to benefit a typical patient, what is the best way to individualize treatment for "outlier" patients for whom that approach turns out not to be the best strategy? For some medications, pharmacogenetics may give us an evidence-based way to identify these patients prospectively, but that science is not ready to be applied to most therapeutic decisions. Moreover, cost-effectiveness is a concept laden with difficult ethical and methodologic issues that we cannot dismiss simply on the basis of an appeal to utilitarianism. What is the moral responsibility of the physician to care for a patient for whom the best therapy may not meet conventional standards of cost-effectiveness? These aspects of the debate will need to continue as we begin to implement CER with this vital new funding.

Fortunately, Congress did not let warnings of a dystopian scientific police state undercut the nation's need to learn what works best in medicine. Given the quality and cost crises we face, preserving ignorance would have been

a poor strategy for improving the effectiveness, safety, and affordability of health care. Although CER dodged a barrage of well-coordinated bullets this time, the debate is bound to continue. To engage in it responsibly, we must stay focused on the methodologic, practical, and ethical issues we will face in the new era of CER, while avoiding the disinformation and distractions that seek to equate generating new knowledge with denial of care.

No potential conflict of interest relevant to this article was reported.

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The Neglected Purpose of Comparative-Effectiveness Research

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On February 17, 2009, President Barack Obama signed into law an initiative providing \$1.1 billion to support research on the comparative effectiveness of drugs, medical devices, surgical procedures, and other treat-

ments for various conditions. This comparative-effectiveness research (CER) initiative has generated considerable controversy. Industry and free-market advocates have expressed concerns about the role of cost-effectiveness analyses within

CER and subsequent governmental intrusion into doctor-patient decisions.

Despite such controversy, the broad consensus is that although the amount of funding the federal government provides for re-