Medicare Payment Advisory Commission and the Center for Medicare and Medicaid Innovation created by the ACA, will need to be negotiated. Although multiple entities pursuing the same tasks could stumble over each other, there are also real opportunities for synergy. In particular, shared staffing between the IPAB and the innovation center could strengthen both.

The legislative requirement that the IPAB submit annual proposals will encourage recommendations for short-term payment fixes rather than long-term changes that might in fact bend the cost curve. If the IPAB is to be truly effective, it must consider not just cuts in provider payments but also changes in how providers are paid, or perhaps even in consumer incentives. Although the statute prohibits reduction in "payment rates" for hospitals before 2020, it does not prohibit the IPAB from recommending changes in payment methods, which might have longer-term effects on cost. But the necessity of making year-to-year cuts will probably focus the IPAB's attention on short-term cuts in Medicare Advantage plans, which are already slated for deep cuts under the ACA, or on prescription drug prices.

The IPAB's success will also depend on Congress's reactions to its recommendations. A three-fifths Senate vote will be needed to override payment cuts, but Congress could increase Medicare funding through independent legislation. The fact that legislators regularly evade the sustainable growth rate has been cited as proof that Congress cannot cut Medicare costs. On the other hand, Congress left in place the vast majority of the Medicare-savings provisions in the 1990, 1993, 1997, and 2005 budget reconciliation acts.[5] And our current fiscal crisis may sharpen lawmakers' resolve to cut spending.

Another major question is whether it is possible to cut Medicare's provider payments as long as private payers' rates remain unconstrained. If the gap between private and Medicare rates continues to grow, health care providers may well abandon Medicare. And the IPAB can make only nonbinding recommendations to Congress regarding private payments. In the long run, Congress may not be able to cap Medicare expenditures without addressing private expenditures as well. If the IPAB opens the door to rate setting for all payers, it may well be the most revolutionary innovation of the ACA.

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Identifying and Eliminating the Roadblocks to Comparative-Effectiveness Research

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Patient-advocacy and health policy groups have hailed comparative-effectiveness research (CER) as a means of reducing health care costs without compromising the quality of care. The federal commitment of $1.1 billion under the American Recovery and Reinvestment Act (ARRA) ensures that the scientific community will undertake considerable amounts of such research. Yet major federal policy changes and innovative measures were required before one CER study, "Comparison of Age-Related Macular Degeneration [AMD] Treatments Trials (CATT)," could even be launched. Our experience with CATT highlights important roadblocks and dramatic changes needed in federal infrastructure for CER to be conducted efficiently.

In July 2005, clinical trial results established the efficacy of ranibizumab (Lucentis) for the

treatment of neovascular (or "wet") AMD, the leading cause of severe vision loss in the United States.[1,2] While awaiting approval from the Food and Drug Administration (FDA), ophthalmologists began using intravitreal bevacizumab (Avastin), off label, to treat neovascular AMD because of its structural similarity to ranibizumab, its availability, and its low cost.[3] Bevacizumab was rapidly adopted as first-line therapy because of its apparent effectiveness. The need for a head-to-head trial comparing ranibizumab and bevacizumab became obvious, and in June 2006, the National Eye Institute (NEI) approved funding for CATT. When ranibizumab was approved by the FDA on June 30, 2006, and its cost became known, the significance of the trial took on an added dimension. Some 95% of patients with neovascular AMD are Medicare beneficiaries, and at $2,000 for a monthly dose, ranibizumab would cost the Centers for Medicare and Medicaid Services (CMS) $1 billion to $3 billion per year, whereas bevacizumab, at $50 a dose, would cost the agency less than $100 million.

Who pays for drugs in a clinical trial in which there is no pharmaceutical company sponsor or partner will be a central question for most CER trials. In CATT, the NEI grant covered the $1 million cost for the purchase, repackaging, and distribution of bevacizumab. Because ranibizumab was FDA-approved and covered by Medicare, we assumed that its $25 million cost would be covered: an executive memorandum signed by President Bill Clinton in 2000 had established that Medicare must cover routine care for patients in clinical trials. Yet the CMS determined that the existing Medicare Clinical Trial Policy did not permit payment for drugs that were being compared in a clinical trial. Efforts to change this policy culminated in the Revised Medicare Clinical Trial Policy of July 2007, which explicitly extended coverage to drugs under investigation if they were normally covered outside of the trial.

But there were other roadblocks to be overcome. The estimated 15% of Medicare beneficiaries who do not have supplemental insurance are responsible for a 20% copayment for drugs. If drugs being compared in a trial cost different amounts, copayments will also differ. Such increased costs may lead patients who are assigned to receive the more expensive drug to refuse treatment as their bills accumulate or to switch to the less expensive drug, thereby eroding the integrity of the study design.

In CATT, the differential is large, with copayments as high as $5,000 per year for ranibizumab versus $100 per year for bevacizumab. With half the patients assigned to bevacizumab, charges to Medicare for CATT patients would be $25 million less than they would be if all patients were treated with ranibizumab. However, the CMS had no authority to waive the $1 million in copayments for participants who had no supplemental insurance, even though the agency stood to save $24 million. Ordinarily, National Institutes of Health (NIH) grant funds cannot be used to cover the costs of usual patient care or expenses that would be incurred outside of a study. Fortunately, the NIH Grants Policy Statement does outline exceptional circumstances and guiding principles for cases in which special reimbursement procedures can be adopted to meet a unique need. This flexibility allowed the NEI to allocate grant funds to cover the residual copayments for the study drug after the supplemental insurance companies had been billed.

Still, other roadblocks remained. In most trials, the identity of the study drugs is masked by having a centralized facility procure, package, and distribute the drugs to participating centers. When drugs are obtained commercially and billing is performed by the local centers, masking becomes more difficult. How do you bill for a drug when its identity is unknown? How do patients remain unaware of their treatment assignment when their insurance company's "explanation of benefits" identifies the drug being injected? How do you prevent supplemental insurers from identifying the drug on their statements? Who makes the initial investment to purchase the drugs? CMS staff members spent a year working with the study leaders to develop a Medicare Demonstration Project to address such billing and masking problems. In May 2007, this project was approved by the CMS, but 2 months later, with no explanation, the Office of the General Counsel of the Department of Health and Human Services refused to approve it, and it could not be executed.

The investigators elected to proceed with an alternative but cumbersome masking system that has proven robust. Ideally, CMS dollars would have been used to pay for the full cost of the drugs, thus averting all billing and co-

payment issues. The CMS indicated that, aside from demonstration projects, it had no authority to modify standard billing procedures and that only "an act of Congress" could authorize such flexibility. CATT leadership therefore proposed the initial language for an amendment to the Medicare Improvements for Patients and Providers Act of 2008, granting authority to the secretary of health and human services to develop alternative payment mechanisms for NIH-sponsored trials if they are needed to enhance the trials' scientific integrity. The bill was passed on July 15, 2008. Still, to our knowledge, there is no defined CMS process for initiating discussion of such alternative payment mechanisms.

The goal of providing study drugs to CATT patients at no out-of-pocket expense was achieved. The cost of ranibizumab is billed to Medicare, and 80% of it is covered under the Revised Medicare Clinical Trial Policy. The remaining cost is paid by insurance companies for patients with supplemental policies and by the NEI for those without such policies. Although the Medicare Act of 2008 came too late to benefit CATT directly, our goal was to prevent similar delays from occurring in future CER trials.

CATT enrollment began in February 2008, and our enrollment goal of 1200 patients was achieved in December 2009. The roadblocks delayed study initiation by more than a year, while another 200,000 patients and their doctors had to make decisions without important information about relative efficacy and safety. Once enrollment was initiated, it was undoubtedly slowed by a cobbled-together drug-payment system.

Despite our efforts, there is still insufficient infrastructure for the implementation of federally sponsored CER trials. Not only is there no established pathway for navigating issues of payment and masking for clinical trials involving Medicare beneficiaries, but trials focused on conditions that affect patients of all ages face the more daunting task of coordinating these logistics with hundreds of insurance plans. We believe that the Federal Coordinating Council for Comparative Effectiveness Research[4] must address these issues, and the insurance industry should be called on to facilitate CER trials. A comprehensive federal policy that would cover all drug-related costs and avert the need to rely on current billing and payment mechanisms would greatly simplify the planning and execution of CER trials. Without such a policy, it is difficult to imagine that the $1.1 billion of ARRA funding for CER will be used effectively.

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