

implemented. The FDA is committed to pursuing these answers with the medical and scientific communities and will take the steps necessary to ensure that the benefits of anesthetic use in children continue to outweigh any potential risks.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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## How CER Could Pay for Itself — Insights from Vertebral Fracture Treatments

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The pain and disability caused by osteoporotic vertebral fractures have long motivated the search for effective therapy. Two procedures designed to restore vertebral body height and function have been widely adopted: percutaneous vertebroplasty, in which cement is injected into the vertebral body to support the fractured bone; and kyphoplasty, a variant of vertebroplasty in which a balloon is inserted and inflated in a collapsed vertebral body, restoring the bone's height before the cement injection. Initial studies suggested that these procedures were superior to conventional symptomatic treatment. But when later studies cast doubt on those favorable findings, health care funding agencies sought to curb their use. The story of these procedures offers a glimpse of the ways in which comparative-effectiveness research (CER) may influence medical practice and health care expenditures.

Early studies of these procedures were neither randomized

nor blinded, and because the symptoms of compression fractures often abated over time, the lack of adequate controls made it impossible to know whether improvements that followed treatment would have occurred even without surgery. Furthermore, neither procedure was risk-free; reported complications included compression fractures, cement leakage, pulmonary complications, paraplegia, and death.<sup>1</sup> In a scenario that's likely to be repeated frequently as CER gains greater acceptance and support, randomized trials eventually followed the observational studies that had fostered the initial enthusiasm.<sup>2</sup> If the full consequences of that research are not yet fully apparent, their potential importance is. Were the results of better-designed studies translated into practice, the reduction in U.S. health care expenditures would be considerable.

CER treats effectiveness as a balance of benefits and harms; when the risks associated with a procedure outweigh its clinical

benefits, it is appropriate and ethical to limit its use. Both the clinical need and the desire to avoid wasteful expenditures were part of the rationale for subjecting these procedures to comparative studies. Furthermore, consensus that these procedures were promising but unproven led several countries to make them available on an interim-coverage basis. These arrangements, in effect from 2006 through 2010, allowed the procedures to be performed in everyday practice while further evidence was generated.

Trials conducted during that period suggested that kyphoplasty did not improve outcomes. The studies of vertebroplasty produced varying results, but the highest-quality trials cast doubt on the benefit and raised additional safety concerns. In a randomized but non-blinded trial by Kallmes et al.,<sup>3</sup> patients who underwent vertebroplasty and controls had similar reductions in disability and pain scores, with a trend toward a higher rate of clinically meaningful improvement in pain

Vertebroplasty and Kyphoplasty Volumes and Costs in the United States, with Potential Savings from Decreased Use*						
Payer (Data Source)	Procedure	Total Estimated No. of Procedures (% Accounted for by Specified Payer)	Mean Cost per Procedure	Aggregate Costs in 2008	Annual Savings with a 50% Decrease in Utilization	Annual Savings with an 80% Decrease in Utilization
<i>dollars</i>						
Medicare (NIS)	Vertebroplasty	11,253 (82.2)	11,411	128,407,983	64,203,992	102,726,386
	Kyphoplasty	19,397 (82.7)	14,336	278,075,392	139,037,696	222,460,314
Medicare (SASD)	Vertebroplasty	6,260 (77.7)	4,451	27,863,260	13,931,630	22,290,608
	Kyphoplasty	11,684 (76.2)	7,328	85,620,352	42,810,176	68,496,282
Medicare total (NIS + SASD)	Vertebroplasty	17,513 (80.5)	—	156,271,243	78,135,622	125,016,994
	Kyphoplasty	31,081 (80.1)	—	363,695,744	181,847,872	290,956,595
Private insurance (NIS)	Vertebroplasty	1,522 (11.1)	14,514	22,090,308	11,045,154	17,672,246
	Kyphoplasty	2,992 (12.8)	11,968	35,808,256	17,904,128	28,646,604
Private insurance (SASD)	Vertebroplasty	1,341 (16.6)	4,865	6,523,965	3,261,983	5,219,172
	Kyphoplasty	2,913 (18.9)	9,945	28,969,785	14,484,893	23,175,828
Private insurance total (NIS + SASD)	Vertebroplasty	2,863 (13.2)	—	28,614,273	14,307,137	22,891,418
	Kyphoplasty	5,905 (15.2)	—	64,778,041	32,389,021	51,822,433
<b>Combined total of principal procedures</b>	—	57,362 (94.8)	—	613,359,301	306,679,652	490,687,440
Medicare, secondary procedure (NIS)	Vertebroplasty	3,024	11,411	34,506,864	17,253,432	27,605,491
	Kyphoplasty	14,932	14,336	214,065,152	107,032,576	171,252,122
Private insurance, secondary procedure (NIS)	Vertebroplasty	653	14,514	9,477,642	4,738,821	7,582,114
	Kyphoplasty	2,979	11,968	35,652,672	17,826,336	28,522,138
<b>Grand Total, Principal + Secondary</b>	—	78,950	—	907,061,631	453,530,817	725,649,305

\* Data are from the 2008 Nationwide Inpatient Sample (NIS) and the State Ambulatory Surgery Databases (SASD) of the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality (AHRQ).<sup>5</sup> Complete SASD data were analyzed and provided by Claudia Steiner of AHRQ. Primary procedures not paid for by Medicare or private insurance were provided to patients with Medicaid or no insurance. The estimates of budget impact are conservative, in part because we used costs (as reported to the Centers for Medicare and Medicaid Services) instead of charges or actual payments, and in part because the SASD covers only 28 states. We conservatively estimate that 17,000 (80%) of the NIS procedures coded as secondary were actually the major procedure performed; SASD coded fewer than 3000 procedures as secondary, and these have been excluded from the analysis.

(30% decrease from baseline) in the vertebroplasty group that neared statistical significance (64% vs. 48%,  $P=0.06$ ). In a randomized, blinded trial by Buchbinder et al.,<sup>4</sup> vertebroplasty did not have a statistically significant advantage over placebo in any measured outcome over 6 months, although pain diminished in both groups.

These studies illustrate the difficulty of inferring the effects of

treatments for a condition with a variable time course, particularly when its manifestations are strongly influenced by placebo effects. But the studies at best cast doubt on the magnitude of any benefits from these procedures and at worst established their ineffectiveness. The findings led U.S. and other payers to revisit their interim funding decisions. To improve safety and quality and to respond to pres-

ures for fiscal responsibility and efficiency in health care, payers are deciding to limit or withdraw coverage for these procedures. In late 2010, the Blue Cross Blue Shield Association's Medical Advisory Panel confirmed its decision that neither procedure met its criteria for established effectiveness, and in Canada, the Ontario Health Technology Advisory Committee ruled that vertebroplasty should not be considered

the standard treatment for osteoporotic vertebral fractures.

Any CER agenda strives for improved safety and quality of care. By identifying relative ineffectiveness, CER may also improve the health care system by freeing up resources to be used for safer and more effective forms of care. Savings from limiting the use of care whose effectiveness is unproven can be substantial,

Centered Outcomes Research Institute, created by the Affordable Care Act (ACA), is fully operational, its budget is expected to reach \$500 million annually, or just two thirds of the potential savings each year from diminished use of just two apparently ineffective procedures.

The savings might be reduced if patients who don't receive one of these procedures end up being

date information about subgroups that were not studied in a trial. But the limitations of conventional observational studies for a condition with fluctuating symptoms and whose main manifestation is pain apply here: without double blinding and closely matched controls, it will be surpassingly difficult to distinguish the effects of the intervention from the natural history of the condition. Thus, without randomized trials, ineffective and costly treatments with risks and complications would continue to be administered largely because the alternative treatments are disappointing. If nothing else, well-designed studies demonstrating ineffectiveness can help redirect research toward the development of alternatives.

Of course, savings will be derived from CER only if practice changes. In the United States, it's unclear whether these studies are powerful enough to overturn coverage decisions or cut utilization of established procedures. The status quo plays a large role in determining the burden of proof for interventions: if a procedure has spread widely, large, well-designed studies must show that it's clearly ineffective or harmful before payers and providers will abandon it; for a new procedure, the assumption is that effectiveness has not been established, so good studies demonstrating effectiveness are required for its adoption. Increasingly, funding agencies and policymakers aim to subject established practices to greater scrutiny, since often interventions adopted without strong evidence are later found to be ineffective or not as effective as initially thought.

ACA features such as bundled

***Without randomized trials, ineffective and costly treatments with risks and complications would continue to be administered largely because the alternative treatments are disappointing.***

whether the intervention is new or has already been disseminated. According to our analyses of data from the Healthcare Cost and Utilization Project,<sup>5</sup> in 2008 the cost of kyphoplasty and vertebroplasty was approximately \$1 billion. The table shows the estimated savings in the United States, by insurance type, under alternative assumptions about reductions in utilization. A 50% reduction in utilization would deliver annual savings of \$450 million; an 80% reduction would save about \$725 million annually. Since these figures are based on costs rather than charges or payments, they are highly conservative. And although these figures appear small relative to U.S. health care expenditures, the procedures are not among the most common. Furthermore, savings are large in relation to the \$1.1 billion that Congress allocated to CER in the 2009 American Recovery and Reinvestment Act. When the Patient-

treated more aggressively with other forms of care. For example, patients who do not undergo vertebroplasty might receive more pain medications or physical therapy than patients who undergo the procedure. However, such offsets in savings would be substantial only if the procedures greatly diminish symptoms for an extended period. Furthermore, the cost-savings estimates don't take into account expenditures for the treatment of adverse effects of the procedures.

CER won't always yield definitive conclusions about a therapy's effectiveness; individual patients might benefit despite disappointing results in randomized trials. But the adoption of a procedure in routine practice, if not part of a well-designed study, probably won't reveal the characteristics of the patients likely to benefit. If observational studies are well designed and build on clinically detailed data, they can often eluci-

payments, shared savings programs, and outcomes-based payments offer mechanisms for stimulating the adoption of practices that are supported by CER and the abandonment of practices that CER calls into question. The benefits for patients are large, as are the potential savings. Support for CER, reinforced by appropriate payment changes, is likely to represent a very good investment for the federal government and U.S. taxpayers.

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