Comparative effectiveness:
“…comparing two (or more) treatments to determine which is most effective.”

“…the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care. The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels.”

A Cost Explosion
With healthcare costs rising to 17 percent of gross domestic product (GDP), Americans are deeply concerned about the relentless spiral of rising costs and insurance premiums. Assuming healthcare spending continues to rise at the historical average of 2.5 percent greater than GDP, by 2050 the highest income tax bracket would be 92 percent in order to finance federal spending.¹ Most health economists (81 percent) believe that new treatments and technologies (for example gender-specific implants, PEEK cages, intraspinous spacers) are responsible for the majority of the rise of health care costs.² If this belief holds true, then limiting the development, adoption and integration of new technologies to those that offer measurable benefit for reasonable cost is the key to curtailing healthcare spending. Federal reform efforts have supported “comparative effectiveness research (CER)” as a cornerstone to set healthcare spending priorities and thus control runaway costs.

The Policy Reaction
The American Recover and Reinvestment Act (ARRA) of 2009 allotted $1.1B for CER to compare “clinical outcomes, effectiveness, and appropriateness of items, services, and procedures.” The health reform law recently signed by President Obama creates the nonprofit Patient-Centered Outcomes Research Institute. The significant funding appropriation of $10 million for fiscal 2010, $50 million for fiscal 2011 and $150 million for fiscal 2012 ensures that data from CER will assume greater visibility and, most likely, increasingly influence decision-making.

A Few Definitions
The Congressional Budget Office defines CER as a “rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients. Such a study may compare similar treatments, such as competing drugs, or it may analyze very different approaches, such as surgery and drug therapy.” CER’s focus is on comparing clinical outcomes, and cost may or may not be factored into the review. Cost effectiveness analysis (CEA), on the other hand, attempts to establish value by comparing the costs and effects of different health interventions. Benefits are typically shown as an increase in life expectancy or, more commonly, as quality-adjusted life years (QALYs) to account for the effect of illness or treatment on a person’s quality as well and quantity of life.

A QALY is a combined estimate that reflects the value a person would place on improved health or the avoidance of side effects of treatment. The more cost effective a treatment, the more QALYs are gained per dollar cost.

Around the Globe
Other developed countries seeking to restrain healthcare costs have taken various steps to assess the comparative value of treatment options. Unlike the U.S., the majority of these countries also have fixed overall budgets for their national health systems, thus results of CER are used to determine coverage and payment for new technologies. Despite this major difference in
approach towards overall budgeting between the U.S. and most other nations, the approaches taken internationally may have important lessons for the increased U.S. efforts towards CER.

Perhaps the most prominent agency in the world that assesses comparative effectiveness is the National Institute for Health and Clinical Excellence (NICE), which was established in 1999 as part of the U.K.’s National Health Service (NHS). If NICE approves a drug, device or procedure, the NHS must cover it, but local health authorities make coverage decisions about treatments that NICE has not yet evaluated. To date, NICE has published appraisals of over 100 specific technologies and guidance on the use of about 250 procedures.

France, Germany, Australia and Canada have similar agencies that assess the cost effectiveness of new treatments and technologies, and prioritize national health spending.

Non-government-funded organizations have also become involved in CER. The best known may be the Cochrane Collaboration—a nonprofit that harnesses a network of volunteers who conduct systematic reviews of treatments. Since 1993, the Cochrane Collaboration has maintained an accessible database that now contains more than 4,500 reviews. Cochrane’s funding is private, and its established methodology is emulated by many conducting CER, including bodies in the U.S. that regularly draw upon Cochrane’s findings.

Comparative Effectiveness and Orthopaedics

There are signs that data from CER initiatives will exert growing influence on decision-making in orthopaedics. The Agency for Healthcare Research and Quality (AHRQ), the health research arm of the Department of Health and Human Services (HHS), recently put out a request for proposals to develop clinical registries for orthopaedic devices, drugs and procedures to conduct CER. Award recipients have not yet been announced.

The Institute of Medicine (IOM) was tasked with establishing national priorities for use of CER funds from the stimulus bill. The IOM set out a list of 100 priority areas for research. Included in the list were recommendations to:

- Establish a prospective registry to compare the effectiveness of treatment strategies for low back pain without neurological deficit or spinal deformity.
- Compare the effectiveness of treatment strategies (e.g., artificial cervical discs, spinal fusion, pharmacologic treatment with physical therapy) for cervical disc and neck pain.

Specific awards for CER targeting these areas in orthopaedics have not yet been made public, and not all CER projects on the priorities list will be funded.

Overseas, Australian, Sweden and the U.K. have prominent joint arthroplasty registries. Annual reports from these registries compare outcomes for all implants used in each country. All three have also begun collecting patient outcomes necessary for health economic analyses. Comparative data from these registries have already begun to influence regulatory decisions in the U.S. For example, data from the Australian registry showing poor results from DePuy Orthopaedics’ ASR hip prosthesis has been influential in spurring the company to communicate with U.S. surgeons about problems associated with the implant. In Australia, the registry data has prompted removal of the ASR from the market.

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While the U.S. is the world’s largest user of orthopaedic devices, efforts to set up similar registries have, for the most part, failed. Thus there is little U.S. data against which to balance these comparative reports from overseas. The national joint registry recently established by the AAOS holds promise, although it will be years before significant data mature.
Touching on the Void

Signs suggest that the steady growth and profits enjoyed by the orthopaedic implant sector over the past few decades are under threat in this time of increasing price pressures. Traditionally, many of the high-cost procedures such as hip and knee replacements were concentrated in older patients who were on Medicare. Now, over 45 percent of hip replacements are performed on patients under the age of 65. With procedure rates rising 15 percent per year and with a shift in utilization to younger patients, purchasers, payors and policymakers are questioning the need for so many procedures.

The relatively high profit margins for orthopaedic devices are also coming under scrutiny. A recent New York Times article pointed out operating profit margins of 23 to 30 percent for major orthopaedic manufacturers, and called these devices “an inviting target” for Medicare cost control efforts.

Disclosures and litigation about questionable consulting arrangements and growing concern about additional benefits created by expensive new technologies coming to market invite questions about transparency and value. Articles raise issues about appropriateness and safety, such as Richard Deyo’s recent analysis of mounting complication rates associated with the fifteen-fold increase in complex spinal fusions over five years in Medicare patients.

*Published results were found not to be reproducible by registry data, and were often skewed by inclusion of the implant inventor’s cases.*

Payors and policymakers are pinning their hopes on CER to fill in some of these recently exposed uncertainties regarding safety, quality and cost of orthopaedic procedures. However, decisive comparative analysis relies on robust data that are simply not available in the published literature. The outcomes that matter to these stakeholders are patient outcomes (i.e. level of function before and after the procedure), complications, revision rates and costs. There are no means to collect patient outcome and cost data systematically in the U.S. because there is little registry data, and the majority of published studies are small and lack the general patient health status measures required for complete CER. The only information on revision rates relates to overall numbers of procedures and is not available by implant type. Work presented at the European Federation of National Associations of Orthopaedics and Traumatology (EFORT) Congress last year documented that arthroplasty registries contained more realistic performance data on revisions than did the published orthopaedic literature. Published results were found not to be reproducible by registry data, and were often skewed by inclusion of the implant inventor’s cases. In some instances, the inventor’s revision rates were five times lower than the other clinicians in the study and up to ten times lower than rates reported in registries.

In such countries as Sweden, national registries provide reliable estimates for both patient outcomes and costs. Kaplan-Meier survival curves document revision rates over time for each implant. Quality of life measures have consistently shown an excellent cost-effectiveness ratio of $3,000 per QALY. Because patient populations, utilization rates and costs differ between the U.S. and Sweden, it is difficult to extrapolate this value to the U.S. population. Even when CEA results are available, what society is willing to pay for a QALY is a matter of debate. In the U.K., treatments costing more than $50,000 per QALY are generally not approved. In the U.S., the threshold is felt to be higher – perhaps up to $100,000 per QALY.

Tsunami Warning

The upcoming wave of CER in orthopaedics will underscore the lack of robust data on which to base these comparative analyses, and will create hurdles for orthopaedic manufacturers. In the absence of data supporting a technology’s efficacy, safety and cost effectiveness payors may respond in the following ways:

- They may rely on claims data to assess outcomes following a procedure. Claims data, in addition to being imprecise, is also lacking in the patient outcomes that measure the health and quality-of-life improvements resulting from surgery. Using claims data as a surrogate for clinical studies will allow only for estimating the costs, but not many of the benefits of treatment.
- Payors may extrapolate data from overseas to U.S. patients. Because patient populations, techniques and surgical indications may vary, ex-U.S. data may not be a reliable surrogate. For example, patients in Europe typically wait longer for joint arthroplasty, thereby attaining perhaps a different level of functional improvement post-procedure.
- In the absence of data showing clear clinical benefit, reimbursement and coverage for a procedure or technology may be denied or restricted. Even established procedures that are expensive and/or increasing dramatically in volume, such as spinal fusion, may be impacted.

Any of these three scenarios could drown the prospects of a company caught unprepared for this wave of change.

The push towards CER will also affect different sectors within orthopaedics differently. Joint replacement has well-established data showing cost effectiveness for these procedures. Total joint replacement also does not appear on the list of top CER targets in the IOM’s list. Thus, the impact of CER on total joints will be limited and may occur later, say in three to five years rather than in the immediate future. The implants most likely to be affected are newer, more expensive implants, such as gender-specific knees that do not have accumulated data quantifying the value obtained for their higher cost.
CER may be more troublesome for the spine sector, wherein cost effectiveness is not clear even for established techniques. The fact that treatment for spinal conditions has surfaced as an early topic for new CER means that in the next two to three years, comparative reviews are likely to emerge. These reviews will serve to underscore the lack of data on cost effectiveness of spinal procedures and nudge payors to scenario #3 above: restriction of coverage and reimbursement.

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Riding the Wave

It is clear that the cost benefit calculation for bringing new technologies to market is already changing. The combination of price pressures, CER and a tighter regulatory climate has provided disincentives for the development of “me-too” drugs and devices.

Successful companies will have to devote more resources upfront and bring to market only those products that offer superior benefit at acceptable increases in costs or that are more cost effective than current therapeutic options.

There are several ways in which companies can adapt to the new climate, with strategies to harness rather than be swamped by the CER wave:

- **STAY ALERT** to changes in health policy. Visit the AHRQ and IOM websites (www.ahrq.gov and www.iom.edu) to keep abreast of new research and proposals in orthopaedics. Read the annual reports put out by the Australian, Swedish and U.K. joint registries if you are in the joint replacement space. Take advantage of the educational programs in healthcare policy and outcomes research now offered at many orthopaedic meetings and trade conferences, such as AAOS and OMTEC.

- **IDENTIFY GAPS** in the evidence on yours and on your competitors’ products. Do a thorough evidence review to understand the questions that might be raised in any technology assessments involving your product or procedure and the benchmarks that must be met for cost effectiveness.

- **DEFINE** your target population. Your technology may not be cost effective for all patients, but it may be the best treatment for select subgroups. Yes, ideally you would like your indication to be as broad as possible, but limited coverage and reimbursement is better than none. Also, if you start with a narrow indication, you may be able to expand later as the technology matures and as the learning curve flattens out, possibly improving your safety and efficacy profile and lowering costs.

- **GATHER DATA** early to assess your technology’s cost effectiveness and to plug the evidence gaps identified above. Use consultants to help determine study endpoints. Think of data as an insurance policy against the potential impact of CER. Collecting data is relatively inexpensive compared with R&D costs. In the era of CER, data will change from “nice to have” to “need to have.” Data takes time to mature, so start collecting it now in order for it to be available in two to five years when you need it.

If you know that your technology adds value by providing measurable benefits at reasonable additional cost, then understanding and measuring your comparative advantages are the best ways to ensure that your company rises with the coming tide.
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Strata is a medical informatics company that offers software solutions to collect, analyze and disseminate evidence about established and emerging technologies. Strata has over 12 years of experience with patient data registries and decision support tools. Strata has now launched HealthLink, a web networking portal for patients that both provides evidence-based information and collects health outcome data.

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REFERENCES
5 www.ncbi.nlm.nih.gov/pubmed/18383407