along similar lines. He hopes that the government will order the industry to introduce drugs for diabetes and other common chronic diseases "in a limited-phase way" to allow for more uniform adverse-event reporting for a few years before widespread use, but he acknowledges that doing so would require changing the law.

In the view of the Pharmaceutical Research and Manufacturers of America (PhRMA), any such ban would be unconstitutional, said Scott Lassman, the organization's senior assistant general counsel. PhRMA's guidelines for voluntary actions by pharmaceutical companies, adopted in 2005, include recommendations that manufacturers educate doctors about products before advertising them to consumers and that they ask the FDA to review ads before they are aired, but these guidelines don't suggest how long companies should wait before advertising a new drug to prospective patients. Bristol-Myers Squibb has said it will wait at least 1 year, and Pfizer has said it will wait at least 6 months. Tracking by TNS Media Intelligence, a marketing information service, shows that companies are waiting an average of 15 months from the time a new drug is approved before advertising it directly to consumers.

Perhaps the best argument for revising the proposed laws regarding direct-to-consumer drug ads is that companies and regulators cannot ensure the accuracy of such ads during the early stages after drug approval, when a product's associated benefits and risks aren't fully understood.

In February, Novartis submitted a review to the FDA that pooled data from 29 clinical trials of Zelnorm (tegaserod), its drug for women with irritable bowel syndrome. The company's analysis showed that among patients treated with the drug, 0.1% had a heart attack, a stroke, or severe chest pain, and one patient died, whereas the rate among patients taking a placebo was 0.01%, and none died. Though the drug has been on the market for more than 4 years, the FDA withdrew it this past March because it didn't consider the drug's benefits sufficient to justify exposing patients to even low risks of a cardiac event. By that time, Zelnorm had become a popular treatment for irritable bowel syndrome despite having limited effectiveness. Why? Perhaps its success had something to do with its highly visible television ad campaign: attractive young women pulled up their shirts to reveal their bellies inscribed with the slogan "I feel better." Although the drug was only 5 to 10% more effective than placebo for women and was not shown to work at all for men, the belly-baring ad seems to have worked wonders: U.S. doctors wrote 2.1 million prescriptions for Zelnorm in 2005.

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Dr. Shuchman is a national correspondent for the *Journal*.

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FOCUS ON RESEARCH

Back Surgery — Who Needs It?

Richard A. Deyo, M.D., M.P.H.

Related articles, pages 2245 and 2257

Back surgery is not the final common pathway for everyone with persistent back pain. It offers specific therapy for specific anatomical derangements associated with specific complexes of symptoms. When surgery ranges beyond carefully defined situations, we can expect disappointed patients.

A generation ago, "back surgery" usually meant removing the offending portion of a herniated disk (Fig. 1). Times have changed, and both the indications and the surgical techniques have expanded enormously. Indeed, clinical science has struggled to keep pace with innovation, creating uncertainties about the efficacy and safety of some new surgical techniques. Patients and primary physicians now need a more sophisticated understanding of the diagnostic possibilities, treatment options, range of surgical techniques, and expected results.

The stakes in providing such

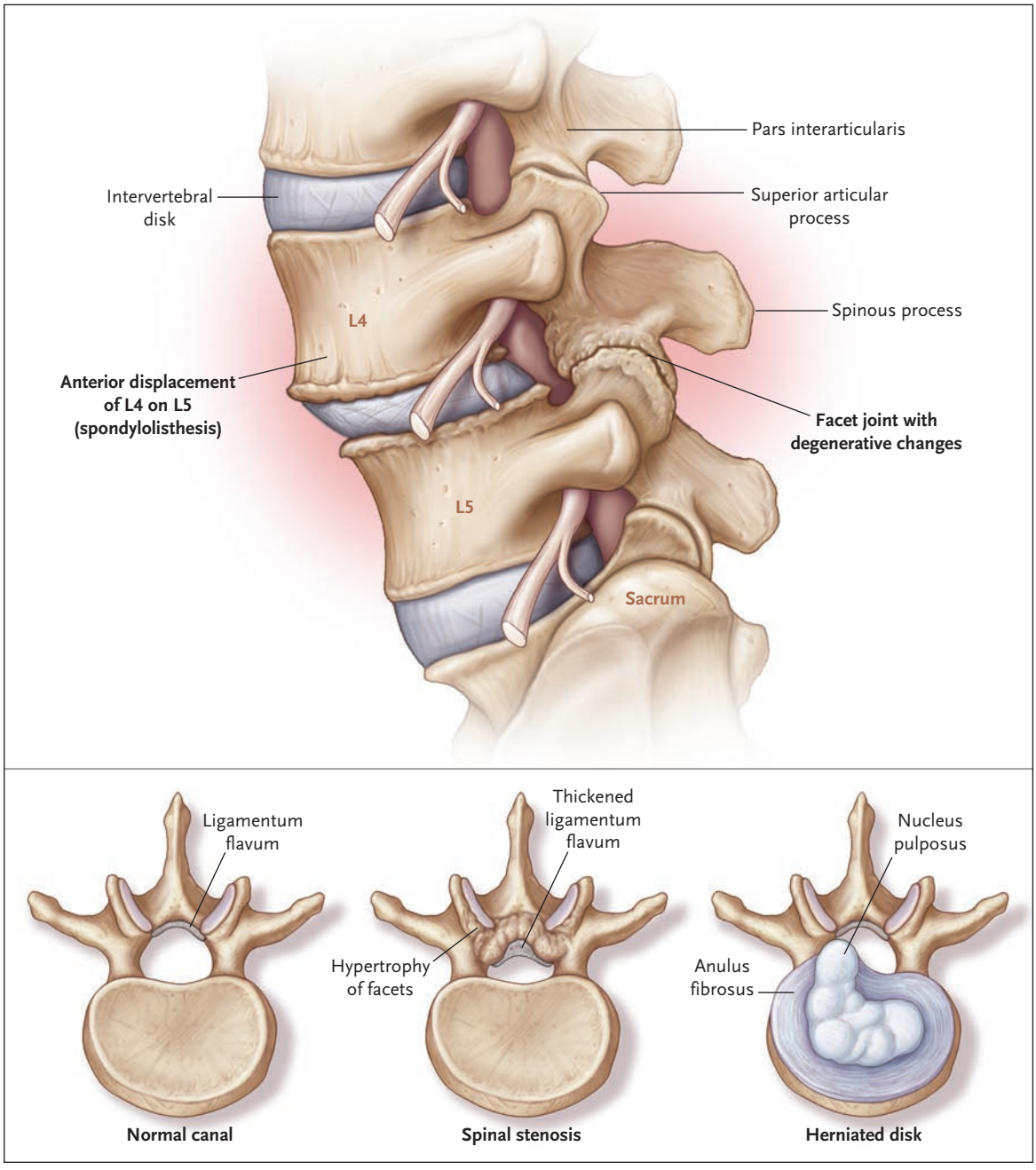

Figure 1. Common Pathoanatomical Conditions of the Lumbar Spine.

In the upper panel, a lateral view of the spine shows degenerative spondylolisthesis in the disk space between the L4 and L5 vertebrae, with degenerative changes in the disk and the facet joints. These changes have allowed forward displacement of the L4 vertebra on L5. This process may occur with or without spinal stenosis, as shown in a superior view of lumbar vertebrae in the lower panel, and may result in a narrowing of the spinal canal with compression of nerve roots. Also shown in the lower panel are changes that typically occur with a herniated disk.

an understanding are high. Despite assertions that surgery is only a last resort or is used more selectively than in the past, the rate of spine surgery has steadily increased in recent decades, even after adjustment for the aging of the population. Spinal fusion surgery, aimed at correcting structural problems or eliminating painful movement, accounted for more than $16 billion in hospital charges (excluding physicians' fees) for more than 300,000 operations in 2004. Among operating-

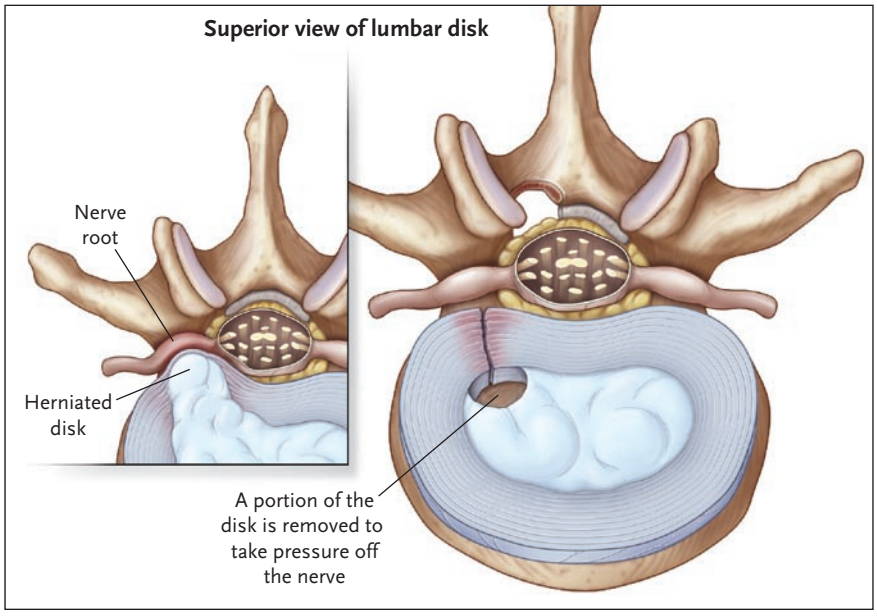

Figure 2. Conventional Diskectomy.

The protruding segment of the disk that is causing nerve-root compression is excised. The remainder of the disk is usually left undisturbed.

room procedures, only coronary bypass surgery, tracheostomy, cesarean delivery, and knee replacement resulted in higher aggregate charges. Laminectomy and excision of intervertebral disks, aimed at decompressing nerve roots, added another $5 billion in hospital fees and another 242,000 inpatient procedures.[1] These figures do not include the lumbar diskectomies performed on an outpatient basis, which now account for at least 25% of such procedures.[2] Are the benefits worth the growing costs and the risks?

Two articles in this issue of the *Journal* help to define more clearly the type of patient who benefits from lumbar surgery. The study by Peul et al. (pages 2245–2256) — a randomized, controlled trial of early diskectomy (Fig. 2), as compared with nonsurgical therapy or delayed surgical therapy — bolsters the case that surgery is effective for patients with sciatica owing to herniated disks. Investigators studied patients with sciatica who had not had sufficient improvement after 6 to 12 weeks of nonsurgical treatment. Excluding patients with briefer episodes was important, because even without surgery, sciatica improves within 3 months in 75% of patients.[3]

Even among patients with persistent sciatica, recovery was likely whether or not surgery was performed. Studies involving repeated imaging show that most herniated disks shrink over time. But surgery accelerates the pace of recovery, and for some patients, faster recovery may be worth the risks.

After a year, recovery was about the same with surgery as with nonsurgical care, though almost 40% of patients who were initially assigned to the nonsurgical group later underwent surgery. A similar convergence of results after 2 to 4 years was apparent in earlier randomized, controlled trials. Thus, for patients with persistent sciatica, there seems to be a reasonable choice between surgical and nonsurgical treatment, which may be influenced by aversion to surgical risks, the severity of symptoms, and willingness to wait for spontaneous healing. Since patients who underwent surgery months after entering the study did as well as those who had surgery within 2 weeks, there does not seem to be a therapeutic window that closes quickly.

The study by Weinstein et al. (pages 2257–2270) addresses a very different condition, degenerative spondylolisthesis with associated spinal stenosis. In this condition, vertebral misalignment involving the displacement of one vertebra on another owing to degenerative changes in the facet joints causes both back and leg pain. Unintended crossovers between the surgical and nonsurgical groups in this study were so extensive that the authors highlight an analysis according to treatment received rather than an intention-to-treat analysis. They combined these as-treated results with similar results from an observational cohort study, essentially creating a single large cohort study showing that surgery offers a significant advantage over nonsurgical therapy. An adjustment for potentially confounding factors is reassuring, even though randomized, controlled trials have sometimes contradicted results from even well-designed cohort studies. Thus, caution is in order. Because of both measured and unmeasured differences between the treatment groups, the observational analysis may overestimate the benefit of surgery. Because of the many crossovers, the intention-to-treat analysis may show a "diluted" effect that underestimates the benefit of surgery. The true magnitude of the surgical advan-

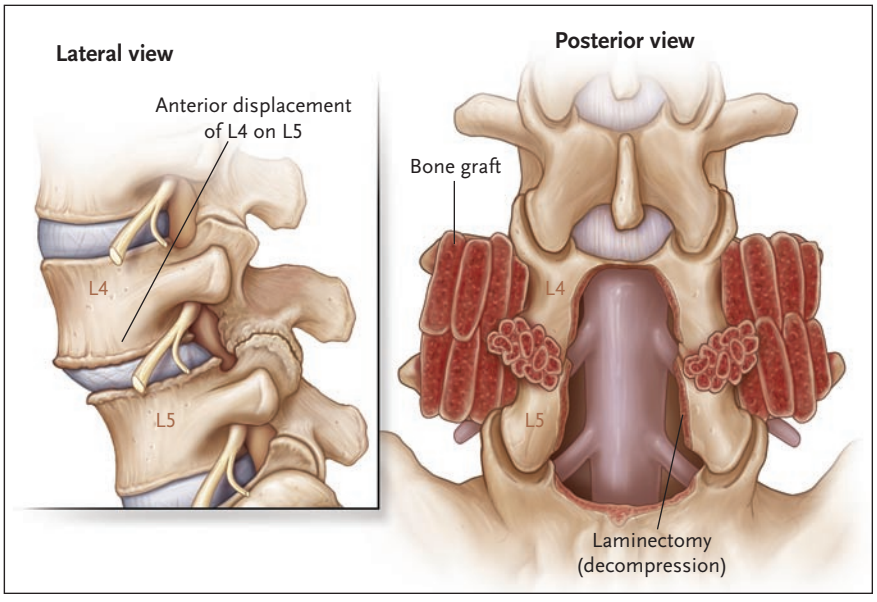

Figure 3. Lumbar Spinal Fusion.

A typical spinal fusion procedure involves placement of bone-graft material between the transverse processes of adjacent vertebrae and between the posterior elements of the vertebrae. The bone-graft material may be autologous, typically obtained from the iliac crest through a separate incision, or an allograft, using prepared bone products from cadaveric sources. This figure does not show any surgical implants, but screws, plates, and "fusion cages" (hollow, fenestrated cylinders packed with bone and placed between the vertebral bodies) are sometimes used to affix adjacent vertebrae in addition to bone grafting. In the case of spondylolisthesis, the surgeon will first decompress the nerves and may try either to reduce the magnitude of slip or to fuse the vertebrae in their current positions.

tage probably lies somewhere between the two estimates.

Since about 95% of surgical patients in this study underwent a spinal fusion procedure (Fig. 3), it was essentially a trial of fusion for spondylolisthesis. The results are consistent with trials comparing fusion with decompression alone for spondylolisthesis. The study further solidifies the basis for performing spinal fusion in patients with persistent leg pain, spondylolisthesis, and associated spinal stenosis. The findings are also consistent with those of a previous trial of surgery for isthmic spondylolisthesis, a condition in which a fatigue fracture of the pars interarticularis causes the vertebral slip.

Patients in this spondylolisthesis trial tended to have improvement with nonsurgical therapy but to a smaller degree than the authors observed in their previous trial of surgery for herniated disks. Previous studies of nonsurgical treatment for spinal stenosis similarly suggest a low rate of improvement, in contrast to studies in patients with herniated disks. The less favorable prognosis of spinal stenosis may be an important factor for patients considering surgery.

In the two trials presented here, both back pain and leg pain were ameliorated by surgery, but leg pain resolved more quickly and fully than back pain. Thus, benefits are likely to be greatest for nerve-root–associated symptoms.

Degenerative spondylolisthesis with stenosis is primarily a condition of older adults rather than of younger patients, who typically have herniated disks with sciatica. In addition, fusion surgery is more invasive than diskectomy, with a higher complication rate. Surgical complication rates increase substantially after 80 years of age, which changes the risk–benefit equation — a problem that has yet to be addressed directly by researchers.

Another uncertainty concerns the relative merits of instrumented versus noninstrumented fusion. In the study by Weinstein et al., surgeons used pedicle screws in most fusions. Previous trials have suggested a small advantage of instrumentation in promoting solid bony fusion but little advantage in pain relief or functional recovery and a higher rate of complications — creating a dilemma that deserves further scrutiny.[4] Another unresolved question concerns the use of spinal fusion or disk replacement for patients with only back pain and degenerated disks.[4] European trials have reached conflicting conclusions, though the discrepancies may be explained by differences in nonsurgical treatments; structured rehabilitation incorporating cognitive–behavioral therapy seems to be nearly equivalent to surgery for such patients.

So who needs back surgery? The consensus seems to be that patients who were excluded from these trials because of major motor deficits need surgery, as do some with major spine trauma. For these patients, surgery may preserve life or function. Absent major neurologic deficits, patients with herniated disks, degenerative

spondylolisthesis, or spinal stenosis do not need surgery, but the appropriate surgical procedures may provide valuable pain relief. In such situations, decisions should be made jointly by well-informed patients and their physicians.[5]

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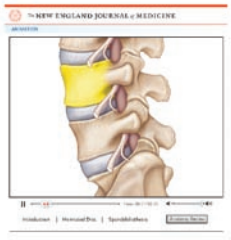

An animated illustration showing spinal diskectomy and fusion (produced with assistance from James N. Weinstein, D.O., Dartmouth Medical School) can be viewed at www.nejm.org.