Justice Department’s request for a rehearing. As of mid-September, it was not known whether Ashcroft will appeal to the Supreme Court. In 1997, before the second Oregon vote, the Court upheld laws in New York and Washington that prohibited physician-assisted suicide and unanimously ruled that there is no constitutional right to assisted suicide. The Court, however, left the states free to legalize the practice.

Although the specific issues are different, the assisted-suicide and medical marijuana cases raise the question of whether the Justice Department is defending the Controlled Substances Act or using the act to advance a political agenda. Even people who personally oppose physician-assisted suicide have objected to the repeated federal efforts to interfere with Oregon’s law. As has been discussed for years, the federal government could defuse the controversy over the medical use of marijuana by reclassifying it to schedule II or a lower classification. As a schedule II substance, marijuana would be tightly regulated but accessible for medical purposes.

5. Oregon v. Ashcroft, 368 F.3d 1118 (9th cir. 2004).

When the British National Health Service (NHS) was established in 1947, its clinical standards were aligned with those of individual clinicians and their professional organizations. If the emerging NHS had tried to challenge the traditional freedom of clinicians, the medical profession would have walked away from it.

Almost 60 years later, however, attitudes have changed. Medical practice based on evidence, rather than on anecdote and opinion, has gained credence. Yet studies during the 1990s showed that the results of clinical research were poorly incorporated into routine care and that inappropriate variations in the standards of clinical practice abounded, in the United Kingdom as well as in the United States. There was also gross geographic variation in access to medicines by NHS patients. So-called postcode prescribing (differential treatment according to one’s area of residence) had become a national scandal. Neither the public nor the medical profession could understand why, in a health care system funded by general taxation, such differential access was allowed to occur. Something had to be done.

The “something” was the establishment, in 1999, of the National Institute for Clinical Excellence (NICE), a new part of the NHS, tasked with advising health care professionals on how to provide patients with clinical care of the highest attainable standard. NICE carries out its mission in three ways. The appraisals program assesses the clinical effectiveness and cost-effectiveness of drugs, devices, and diagnostic tools and provides advice on whether and how they should be used in the NHS. It has, to date, produced reports involving nearly 250 individual products. The guidelines program develops advice, based on assessments of clinical effectiveness and cost-effectiveness, about the management of individual medical conditions. And with its interventional procedures program, NICE plays the role of a regulatory authority (like the Food and Drug Administration [FDA] in the United States), assessing the safety and efficacy of drugs and devices. Like the FDA, the institute does not consider cost-effectiveness in these assessments, but an intervention that is classified as safe and effective may subsequently undergo a formal appraisal to establish its cost-effectiveness.

All the appraisals and guidelines provided by NICE are grounded in a systematic review of the available evidence, including, when appropriate, data from observational studies as well as from randomized, controlled trials — a combination that the
Clinical Effectiveness

Cost-Effectiveness

Conclusion

<table>
<thead>
<tr>
<th>Population</th>
<th>Clinical Effectiveness</th>
<th>Cost-Effectiveness</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>Children with growth hormone deficiency or growth failure (Turner’s syndrome or Prader–Willi syndrome)</td>
<td>According to randomized, controlled trials and uncontrolled studies, height gain of 8.7–10.7 cm in boys and 7.7–9.5 cm in girls</td>
<td>Incremental cost-effectiveness of £25,000–£124,950 ($39,000–$194,922) per quality-adjusted life-year</td>
<td>Increase in height worthwhile and cost-effective, given lifelong value and psychological importance to child</td>
</tr>
<tr>
<td>Adults with growth hormone deficiency</td>
<td>Effects on cardiovascular risk factors and bone mineral density uncertain; according to observational studies and small randomized, controlled trials (which did not replicate current United Kingdom endocrinologic practice), some improvement in health-related quality of life</td>
<td>Use only in patients who have a severe deficiency, as indicated on insulin-tolerance test; have significantly impaired health-related quality of life; receive treatment for other pituitary hormone deficiencies; and have predefined improvement in health-related quality of life after 9 months of therapy</td>
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* Information is from the National Institute for Clinical Excellence.3,4

The institute believes provides the best estimate of the size of a given effect, which is an essential component of a rigorous estimate of cost-effectiveness. Cost-effectiveness is usually modeled on the basis of the available data and, if possible, expressed in terms of the incremental (i.e., additional) cost per quality-adjusted life-year gained. Judgments about whether interventions are cost-effective, in the context of the NHS, are made on a case-by-case basis and represent an attempt to resolve the tensions among efficiency, equity, and opportunity costs.2

NICE has a full-time staff of about 100 people who consolidate evidence, perform economic modeling, and manage the evaluations and reviews commissioned by the institute. But the appraisals and guidelines issued by NICE are developed by independent (and unpaid) members of advisory bodies drawn (through advertising and referral) from the NHS, clinical academia, and associated disciplines (particularly economics and statistics); these bodies also include patients and patient advocates. In drawing its conclusions, the institute actively seeks the views of relevant professional and patient organizations, as well as manufacturers, and encourages them both to submit evidence and to respond to drafts of NICE documents. In the case of technology appraisals, these stakeholders also have the right to appeal to the institute’s board of directors, although they do not necessarily get their way in the end; indeed, all the appraisals and advice issued by NICE have attracted criticism from some quarter. As the examples presented in the Table demonstrate, some conclusions and recommendations are relatively straightforward, whereas other decisions are bedeviled by incomplete evidence.

The products of the institute are formally regarded as advice to the health care professionals in the NHS. Nevertheless, the NHS has a legal obligation to make available, within three months, the financial resources necessary for its members to implement NICE’s advice on the use of health care technologies — resources that, according to the government, are already in the budgets of primary care trusts and hospital trusts. Although the institute does not have the legal power to ban the use of any interventional procedures that it determines to be unsafe or ineffective, it is virtually inconceivable that any health care professional in either the public sector (the NHS) or the private sector would undertake to use such a procedure, given the requisite preparations for implementing a new procedure of any kind.

The implementation of NICE’s clinical guidelines is more complicated. The NHS is expected to adopt these guidelines in full, but all concerned recognize that the implementation of any recommended changes may take time because complex infrastructural changes are often required. Local NHS organizations are therefore expected to develop their own implementation schedules that take into account local circumstances.
account their individual circumstances and the complexity of the tasks at hand.

NICE started life as a highly controversial experiment. It remains controversial, but it is no longer an experiment. And yet much remains to be done. First, the existence of the institute would be pointless if its advice and assessments failed to have real effects. At the time it was founded, implementation was not part of its charter. From now on however, NICE will be taking direct responsibility for ensuring that its advice is adopted into routine clinical care, by developing and disseminating a range of appropriate implementation “tools.”

Second, NICE’s clinical guidelines offer a means of influencing broad areas of clinical practice rapidly. Within five years, the institute could cover virtually all of the commonly seen causes of illness and preventable death. NICE therefore seeks to expand its capacity to develop and issue guidelines, as circumstances allow, with the long-term aim of covering all major causes of illness and death.

Third, the British government has recently announced that as of April 2005, NICE will also address matters of public health, providing advice about measures for improving the health of the population—for example, by reducing levels of smoking, alcohol consumption, and obesity. In this new realm, assessments will again be based on measures of both effectiveness and cost. Many believe that it would make sense, too, for the institute to assume responsibility for issuing advice on screening and immunization.

Perhaps surprisingly, NICE has earned the broad support of health care professionals in the United Kingdom, as well as that of the public and members of Parliament. Although the institute’s authority and relationships are peculiar to the political and cultural conditions in its home country, the methods it uses are easily transferable to the United States and other countries. Indeed, there has been considerable transatlantic interest in the type of guidance NICE provides—interest indicated by the 10,000 daily hits on the institute’s Web site from U.S. visitors. Perhaps George Bernard Shaw was wrong, after all, when he described England and America as two countries divided by a common language.

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Expecting the Unexpected — Drug Safety, Pharmacovigilance, and the Prepared Mind

Anne Trontell, M.D., M.P.H.

When a new drug is first marketed, findings regarding its efficacy and safety are commonly based on the experience of several thousand people who have been treated in controlled clinical trials. Despite extensive testing, rare adverse events (those that occur in less than one patient per thousand) can easily escape detection, and unforeseen interactions with coexisting clinical conditions or other drug therapies may remain unexplored. As a result, the characterization of the full safety profile of a new drug relies heavily on clinicians’ careful observation of its effects in “real world” practice that is far removed from clinical-trial conditions. Discovery in an observational science such as pharmacovigilance depends on the capacity to recognize and investigate unexpected clinical events that are manifest once a new drug is in use. The detection of such unanticipated effects hinges on what Pasteur called “the prepared mind.”

In this issue of the Journal, Bennett and colleagues (pages 1403–1408) demonstrate the power and importance of the detection, analysis, and re-