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Increasing Use Of New Prescription Drugs: A Case Study

Recent experience with new antidepressants suggests that without more efforts to identify and promote effective use, biomedical innovation may fall short of its promise.

by Sandra M. Foote and Lynn Etheredge

Surging demand for prescription drugs is adding to health care costs and to pressure for Medicare outpatient prescription drug benefits. Demand is fueled by new drugs and other new biomedical technologies. A prime example is growth in sales of antidepressants from $2 billion in 1993 to more than $7 billion in 1998. In this paper we examine factors contributing to this growth as a case study of issues that biomedical innovation poses for health care financing and delivery. To curtail rising plan expenditures, some insurers are beginning to raise patients’ cost-sharing levels. This strategy tempers demand but fails to promote clinically appropriate drug uses. Our large national investment in developing biomedical technology needs to be complemented by more public- and private-sector investment to ensure that available technologies are used in a cost-effective manner.

Advances in biomedical technology (including new drugs, tests, devices, and procedures) are the dominant force driving long-term increases in spending and many other changes in the health care system.1 Over the next few decades breakthroughs in areas such as genetic analysis and drug development may yield radically different therapies, preventive interventions, and cures that are customized to patients’ genetic coding. If so, the twenty-first-century health system could be focused mostly on outpatient diagnosis and prescription drugs, with a precipitous drop in inpatient hospital use. Research funding increases by the pharmaceutical industry and the federal government may accelerate these trends. The number of prescriptions in the United States has already increased from 2.0 billion in 1994 to 2.5 billion in 1998 and is projected to reach 2.9 billion in 2000. Of the $100 billion spent on prescription drugs in 1998, more than 35 percent was for new drugs introduced since 1991.2

Antidepressants provide an interesting case study. The prevalence of mood disorders is high nationally, and antidepressants are the most costly and fastest growing of the top four therapeutic categories of drugs.3 To the extent that experience with antidepressants is relevant to other new drugs and technologies, the case study also raises broader system issues.

Incremental Improvements In Technology

The recent $5 billion increase in annual sales of antidepressants was driven by incremental improvements in existing technology. The older tricyclic antidepressants (TCAs) work
for some patients, but their use is complicated by slow onset of relief, need to adjust doses, unpleasant side effects, and safety concerns (overdoses can be lethal). Newer antidepressants such as Prozac, Zoloft, Paxil, and Celexa are safer and simpler to prescribe and have more tolerable side effects for some patients.

Neither the TCAs nor the newer classes of drugs—known as selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs)—have the characteristics ultimately desirable in an antidepressant. The recent federal report, Mental Health: A Report of the Surgeon General, summarizes the state of the art. Notably, 50–70 percent of patients respond to the first antidepressant they take, whether it is a TCA, SSRI, or SNRI. There are no reliable predictors of which drug will work best for a patient. Fewer than half of the nonresponding patients will respond to a second antidepressant when a switch is made. Placebo response rates vary by the severity of the mood disorder. Among patients with major depression, the placebo response rate is 32 percent of patients; the total response rate with newer antidepressants is 50 percent. As with most medications, it is not known which patients are likely to respond to a placebo, or why they do.

Duration of treatment is also problematic. Many patients stop taking their antidepressant within a month, and nearly 60 percent of patients do not continue for at least six months as recommended to achieve long-term effectiveness. Among reasons for nonadherence are unpleasant side effects and the four-to-six-week interval that often occurs between when patients start taking antidepressants and when they feel better.

In short, there is much room for progress in developing antidepressants that help more patients, give faster relief, and have fewer side effects. The federal government is investing heavily in brain research. Pharmaceutical companies are competing aggressively in drug development, using sophisticated drug discovery and testing techniques. The Food and Drug Administration (FDA) is expediting product approvals. Demand is strong. Therefore, as current brand-name antidepressants come off patent, they are likely to be replaced by successively better antidepressants that will also command price premiums and raise utilization levels.

Expanding Use Of Antidepressants

Currently, if a new drug is introduced that many patients desire and that primary care physicians are comfortable prescribing, the ramp-up in utilization is likely to be dramatic. Prescriptions for antidepressants, for example, have grown from forty million in 1988, when the first SSRI, Prozac, was introduced, to more than 120 million in 1998. The factors that induced rising utilization are powerful and complementary. They include high prevalence of medical problems conducive to treatment with antidepressants, extensive product promotion, willingness of nonspecialists to prescribe, affordability of drugs for insured patients, and public support for patient access.

High prevalence of treated conditions. Antidepressants are used primarily in treating mood disorders such as major depression and chronic unremitting depression (dysthymia). These conditions are widespread and often severely disabling. They are the types of conditions for which the research investment rationale is strong—economically, socially, and ethically. Nearly 7 percent of the U.S. population (nearly nineteen million persons) suffer from serious mood disorders each year. About eighteen million of these suffer from major depressive episodes (including unipolar depression and the depressive phase of bipolar disorder). Anyone who experiences such an episode is likely to have at least one recurrence and frequently more if the condition is not effectively treated. Major depression is the second most disabling disease in the world.

Although most patients who take antidepressants have no diagnosis of a mood disorder in their medical records, physicians report in confidential surveys that such disorders are involved in more than 85 percent of cases. The true diagnosis is often masked to
protect patients from stigma or to avoid lower levels of plan benefits associated with treatment of mental illness. Antidepressants also are being used to treat patients whose symptoms are less severe. Some studies suggest that antidepressants are only modestly effective in treating “minor depression.” Yet many physicians prescribe antidepressants for patients with minor depression instead of running the risk that the patients will suffer deepening depression, become disabled, or possibly attempt suicide.

- **New applications of drugs.** Antidepressants also are being used for a growing array of purposes, including treatment of anxiety, obsessive-compulsive disorder, bulimia, panic disorders, posttraumatic stress disorder, and premenstrual syndrome; weight loss; and smoking cessation. In some cases, the conditions treated are “off-label” uses (that is, uses not evaluated by the FDA in approving sale of the product). The FDA restricts pharmaceutical companies from promoting off-label product uses but does not restrict physicians from prescribing medications for new uses before their efficacy and safety are proven. The FDA has recently begun allowing pharmaceutical companies to give physicians findings from clinical trials of off-label product uses. Therefore, such uses are likely to increase.

- **Product promotion.** Manufacturers also have broadened and intensified product promotion. They market to managed care organizations and pharmacy benefit management (PBM) companies, offering price discounts and rebates to gain preferred drug status in plan formularies. Drug representatives promote products directly to physicians. In 1997 the FDA issued draft guidelines that paved the way for direct-to-consumer (DTC) advertising on television. In response, drug manufacturers increased DTC advertising expenditures to $1.3 billion in 1998, an increase of more than 40 percent over 1997. For example, Eli Lilly spent $41 million on consumer-directed advertising of Prozac, a 98 percent increase over 1997 spending, and continued to spend more than $50 million promoting Prozac to physicians. Prozac is the most highly advertised and widely prescribed antidepressant nationally. With sales surpassing $2.2 billion in 1999, Prozac ranked second nationally among all prescribed pharmaceuticals. Some evidence suggests that DTC drug advertising is very effective in motivating patients to visit physicians to request widely advertised drugs. Survey data suggest that nearly 75 percent of consumers who make such requests receive the desired prescriptions.

- **Treatment by primary care physicians.** Improved safety and ease of dosing also have been key to the rapid diffusion of antidepressants. These attributes allow nonpsychiatrists to prescribe antidepressants with confidence. Nonpsychiatrists have driven increasing antidepressant use; their antidepressant prescriptions increased from thirty-two million in 1988 to nearly ninety million in 1998, with virtually all of the increase attributable to SSRIs and SNRIs (Exhibit 1). Nonpsychiatrists now write about two-thirds of antidepressant prescriptions in the United States. Whenever a patient can obtain a prescription from a primary care physician rather than from a specialist, drug utilization is likely to be higher because patients’ access is greater. There are many more primary care physicians than psychiatrists, and they each typically see many more patients than psychiatrists do.

Whether the result is better care for depressed patients or not has been a matter of some concern. Nonpsychiatrists are a large and diverse group of providers and manage many different types of problems. It has proved challenging to gain their adherence to depression treatment protocols. Studies suggest that primary care physicians, particularly obstetrician-gynecologists, tend to be less confident and effective than psychiatrists in diagnosing and treating depression. A greater percentage of patients treated by psychiatrists experience adequate antidepressant doses and duration of treatment. Despite these drawbacks, many experts concur that having nonpsychiatrists provide antidepressants is advantageous because many patients
who need treatment will not seek help from a psychiatrist.

- **Third-party financing.** Demand for new drugs also depends on affordability. The share of prescription drug costs borne by third-party payers has increased steadily, from about 50 percent in 1980 to about 75 percent of current costs. The increase is attributable to flat-dollar copayments under many plans and to many payers’ reluctance to raise copayments in line with rising drug prices. For example, the average price for a thirty-day supply of SSRIs is about $60, compared with about $6 for TCAs. Typically, patient copayments are about $11 for brand-name drugs and about $5 for generics. Even though some payers have instituted multi-tier benefit structures with higher copayments for nonpreferred brand-name drugs, these plans still usually include at least one product from each therapeutic class in the preferred tier.

- **Public resistance to restrictions on coverage.** Finally, demand for new technology is supported by intense political, legal, and social pressures on insurers to provide coverage for new drugs and treatments. The anti–managed care backlash reflects these pressures and public distrust that patients’ interests are adequately protected in insurance authorization processes. Consequently, health plan costs are rising and shifting toward new drugs and other new technologies.

**Implications For Policy And Research**

The rapid diffusion of new antidepressants illustrates how highly Americans value and trust pharmaceutical interventions, even those that involve alterations to brain functioning. As a society we view biomedical technology development as a vital pathway to improving the quality of our lives. New technologies (and vigorous promotion of new products) are changing our perceptions about what constitutes disease and raising our expectations...
about what conditions require treatment. In 1997 David Mechanic wrote, “We are clearly entering a new era in which it is more difficult to balance the possibilities of medicine and public expectations against the willingness to finance them.”

Arguably, the most powerful cost containment tool available to self-insured employers and insurers is benefit design. Raising patient cost sharing reduces plan risks, increases patients’ cost-consciousness, and is a contract matter, not subject to tort law and possible damages. However, this strategy dilutes insurance protection. As patient cost sharing increases, access to new drugs becomes more dependent on the patient’s ability and willingness to pay. An ideal alternative would be to concentrate insurance protection on drugs that are clinically appropriate and cost-effective, thereby aligning the incentives to beneficiaries and physicians in support of obtaining high clinical value for insurance dollars spent. However, as this case study of antidepressants illustrates, this concept is difficult to implement in practice. The clinical issues can be complex, the evidence about cost-effectiveness inadequate, the value judgments controversial, and social resistance powerful. Private-sector insurers are developing various benefit-design strategies to address these issues in their plan contexts.

Federal policymakers confront similar challenges in designing Medicare outpatient prescription drug benefits. Regardless of how the program is structured, it will be important to ensure that patient cost sharing cannot be cancelled out by supplemental insurance and can be refined as more is learned about how to encourage clinically appropriate and cost-effective drug use.

Another means of addressing cost pressures from new drugs is to improve how well the health care system targets their uses to best clinical practices. The management tools, incentives, and knowledge base that would be helpful in promoting this objective are not yet well developed. With few exceptions, individual purchasers, insurers, and providers lack the resources, incentives, and leverage to propel major systemwide improvements in treatment patterns, especially when price competition is intense and provider networks are large and overlapping. Collaborative efforts by the public and private sectors are needed both to promote best clinical practices and to learn more about which practices are best. Opportunities for federal leadership are apparent, particularly in Medicare and in health services research.

Medicare. In modernizing Medicare, policymakers should provide for a robust system of planning for new drugs and biomedical technologies, evaluating clinical practice patterns, and promoting best practices. This will require strong management capabilities, administrative flexibility, and accountability. Given the market share of Medicare beneficiaries, collaborative efforts by fee-for-service Medicare and Medicare+Choice plans could be highly influential in stimulating system improvements.

Health services research. As investment in biomedical research increases, there is a corollary need for more cost-effectiveness research. Manufacturers of pharmaceuticals, medical devices, and diagnostics have no legal obligation and few incentives to generate many of the studies that would be highly desirable, such as those involving the elderly and other major subpopulations, comorbid conditions, and multiple drug needs. While pharmaceutical research and manufacturing companies have more than doubled their research budgets since 1990 to $24 billion a year, less than 6 percent of these funds flow to research on drugs after FDA approval. Similarly, the federal government has doubled the budget of the National Institutes for Health (NIH) since
1990 to more than $15 billion in 1999. This funding supports mainly biomedical research. By contrast, funding for the Agency for Healthcare Research and Quality ($171 million in fiscal year 1999) and for four Centers for Education and Research on Therapeutics ($7.7 million collectively over three years beginning in 1999) are strikingly small investments.20

The United States is a world leader in biomedical research, technology development, and diffusion; a major challenge ahead is to build our capabilities to evaluate new biomedical technologies and use them more effectively.

This paper draws on insights and data provided by an interdisciplinary group of experts convened by the Health Insurance Reform Project and Health Affairs in Washington, D.C., 2 November 1999. Participants included Harry Cain, Thomas Croghan, John Docherty, Howard Goldman, Richard Hegner, Sandra Hittman, John Iguchi, James Ishister, Rosario Lopez, Carol McCall, Robin Strongin, Victor Villagra, James Verdier, Jane Hibbert-White, and Alan Wright. These persons contributed greatly through data, discussions, and comments on drafts. The Robert Wood Johnson Foundation funded the meeting and work on the paper. The authors are solely responsible for the views presented here.

NOTES
5. Important patents for Prozac expire in 2001 and 2003. Generic equivalents may then drive down prices on all antidepressants until improved brand-name antidepressants are introduced.
13. See Note 6.
17. Teitelbaum et al., 1998 Express Scripts Drug Trend Report, 33, 35.