SEEKING A BALANCE: Weighing the Clinical and Economic Factors of Depression and Anxiety Management in Patient Outcomes
Proceedings of the Economic Working Group Advisory Board, March 2003

HIGHLIGHTS

• Health Care Benefits in the 21st Century: What Employers Are Facing; How They Are Responding

• Mental Health Support Needs: The Employer Perspective In Optimizing Clinical and Economic Outcomes

• MindSET: Tools to Implement A Behavioral Health Initiative In the Workplace

• PANEL DISCUSSION: Does HEDIS Affect Compliance, Length of Therapy, or Outcomes?

• An Economic Analysis of SSRI Length of Therapy

• Improved SSRI Tolerability and Increased Length of Therapy
INTRODUCTION

MARK ZITTER, MBA
CEO, The Zitter Group

Depression is a common, costly, and chronic problem for affected individuals as well as for employers, the health care profession, insurers, and other major stakeholders. Depression—and its frequent concomitant disorder, anxiety—is an inherently complex issue made all the more difficult by nonparity of mental health benefits, social stigma, underdiagnosis, undertreatment, poor patient compliance with medication regimens, and significant associated morbidity and mortality.

To discuss and debate ways in which unnecessary suffering can be reduced and avoidable morbidity and mortality decreased, members of the Economic Working Group attended the second national advisory board meeting last March, in Scottsdale, Ariz. The group includes advisers from every major discipline in managed markets: employers, managed care behavioral health specialists, primary care physicians, quality assurance professionals, psychiatrists, pharmacy directors, researchers, and insurers. Advisers with this breadth of professional diversity and expertise contributed generously to discussions on which this proceedings publication is based. The unique perspectives of these advisers are captured in display quotes throughout this publication.

From the employer viewpoint, we heard presentations by Annette Boyer, RPh, principal for Mercer Human Resource Consulting, and Wayne Lednar, MD, PhD, vice president and director for Corporate Medical, Eastman Kodak Co. These presentations provided insight into employers’ difficulties in sustaining profitability amid an increasingly challenging business environment.

Bob Binder from the GlaxoSmithKline Employer Group Segment presented a portfolio of tools developed by GSK to address employer concerns and issues surrounding depression in the workplace.

A panel discussion provided a forum for three distinct voices: Benjamin Druss, MD, a quality-assurance professional; Larry Pesko, MS, ScD, RPh, a managed care pharmacy director; and David V. Sheehan, MD, MBA, a practicing psychiatrist. Each presented a unique perspective regarding optimal treatment of patients with depression.

An economic analysis of patterns of antidepressant use and related costs was presented by Tim Regan, RPh, CPh, and Thomas Bramley, RPh, PhD, from Applied Health Outcomes. Compelling evidence regarding the excess cost associated with an antidepressant therapeutic regimen of fewer than 90 days, or an augment/switch scenario, was documented with findings from a national database of 57 managed care plans covering 33 million lives.

Sheehan concluded the weekend’s presentations with a review of data on controlled- versus immediate-release selective serotonin reuptake inhibitors, their differing effects on adverse events and tolerability, and how they influence length of therapy and patient outcomes.
Seeking a Balance: Weighing the Clinical and Economic Factors of Depression and Anxiety Management in Patient Outcomes


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The objective of this supplement is to explore the perspectives of a host of professionals concerned with treatment outcomes for patients with depression. To meet this objective, a diverse group of advisers was assembled to present, debate, and exchange viewpoints on the clinical and economic consequences of depression. This group of professionals, with expertise in psychiatry, managed behavioral health, HEDIS, research, pharmacy, the employer segment, and primary care, discussed the inherent conflicts among various market segments — health plans, employers, practitioners, and the quality management arena.

Advisers explored how depression and anxiety are managed in the United States. When asked, “What is the one most pressing problem in managing depression and anxiety” in their organizations, one third of advisers identified the primary care physicians’ suboptimal management of the disease; one third expressed concern over employers’ willingness to pay for quality outcomes in the treatment of patients with depression; and the last third were split evenly on lack of patient compliance and total cost of treatment.

Advisers challenged each other on what constitutes appropriate length of therapy and reviewed national data on health plan performance on the HEDIS antidepressant medication management measures. Economic analyses repeatedly supported the overall cost effectiveness of a longer course of therapy. Because funding comes from two major sources — the government and private employers — cost of care and the role that cost should play in making formulary decisions were examined from several key positions.

Advisers debated the importance of patient compliance and discussed strategies to optimize the pharmaceutical regimen. Participants admitted that although it is easy to talk about what should be happening in the treatment of patients with depression, the realities of the situation in health care today merit an informed multidisciplinary discussion. This was the intent of the Economic Working Group Advisory Board meeting that was facilitated by The Zitter Group. Because the focus was on the treatment of depression and anxiety from a pharmaceutical and medical perspective, other important treatment modalities, such as psychotherapy, were not discussed in depth. The articles in this supplement are not intended to serve as a blueprint for the full range of treatment options available to clinicians.

**PRIMARY FACULTY**

**Annette Boyer, RPh**
Principal
Mercer Human Resource Consulting

**Thomas Bramley, RPh, PhD**
Consultant/Health Economist
Applied Health Outcomes

**Benjamin Druss, MD**
Rosalynn Carter Chair in Mental Health
Associate Professor of Public Health and Psychiatry
Rollins School of Public Health, Emory University

**Wayne M. Lednar, MD, PhD**
Vice President and Director, Corporate Medical
Eastman Kodak Company

**Larry Pesko, MS, ScD, RPh**
Vice President, Pharmacy
Lovelace Health Systems

**Tim Regan, RPh, CPh**
Senior Manager
Applied Health Outcomes

**David V. Sheehan, MD, MBA**
Professor of Psychiatry
University of South Florida College of Medicine

**Mark Zitter, MBA**
CEO
The Zitter Group

**SUPPORTING FACULTY**

**Bob Binder**
Executive Account Manager, Employer Team
GlaxoSmithKline

**DISCLOSURE OF SIGNIFICANT RELATIONSHIPS**

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Stacey Brennan, MD, acknowledges an advisory and speakers bureau relationship with GlaxoSmithKline.

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The content of this supplement was prepared from the transcripts of the Economic Working Group Advisory Board by Susan Keller, Senior Associate, The Zitter Group.
A slowing economy and a demand for increased workforce performance in the presence of reduced staffing levels have resulted in significant challenges for business today. High medical inflation adds to those challenges, making profitability for some employers a daunting goal. Steeply rising medical costs result from a number of factors, not the least of which are an entitlement mentality and consumer demand for life-enhancing services, new technologies, and emerging drug therapies. Another factor contributing to medical inflation is the rising average age of the labor force with its concomitant increase in rates of health risks, such as stress, obesity, high blood pressure, and even poor self-care. Aging baby boomers have had a measurable effect on the cost of health care. For instance, the average per-member, per-month (PMPM) cost of prescription drugs for employees in their 20s is just over $100; in contrast, PMPM pharmacy costs are $442 for employees in their 40s and $992 for employees in their 60s (AdvancePCS Benefits Barometer 2002). Consequently, employers are focusing closely on the cost ramifications of an aging workforce and the increasing use of pharmaceutical products. Employer data indicate that pharmaceutical use and cost increases are frequently associated with gastric disorders, depression, and cardiovascular disease, conditions that are fairly common in the baby boomer age group.

Because HMOs, with controls and access limitations in place, have not consistently saved employers’ health care dollars, as was initially hoped, there has been a large migration to non-gatekeeper PPO products in the past few years. Significant industry consolidation has resulted in less bargaining power for employers. Rising medical costs — from 14 to 20 percent — have caused cost-shifting, whereby employees and unions have less negotiating power than they had previously to mitigate such trends. Pharmacy continues to be viewed by employers as a cost-cutting target and is blamed for spikes in health care expenditures. Among employers, there is a heightened scrutiny relative to drug utilization, particularly with regard to specialty or new drugs — including new generic drugs — and of the movement from use of prescription drugs to utilization of over-the-counter formulations.

Quantifying the rising cost trend

Mercer Human Resource Consulting conducts one of the largest comprehensive annual health-benefit surveys in the United States. The Mercer National Survey of Employer-Sponsored Health Plans examines cost trends and cost-management initiatives regarding pharmacy and medical benefits among employers with 500 or more workers. As illustrated in Figure 1, pharmacy benefit cost increases have been in the double digits for the past several years, naturally a big concern for employers. This is a manifestation of many complex and intertwined factors, including increased product costs and, especially, higher utilization. In 2001 and 2002, the pharmacy benefit trend decreased slightly; that, however, was mainly because of cost shifting, the addition of three-tier copayments, and the adoption of aggressive pharmacy-management strategies.

The issue of greatest concern here to employers is that of rising pharmacy and medical expenditures. To further confound the issue, the two cost centers are still in silos, or separated, within many organizations; overall, therefore, it can be difficult for providers or insurers to demonstrate medical savings with increased pharmaceutical expenditure. Yet it also must be remembered that pharmaceutical products represent approximately 15 to 25 percent of the entire health care expenditure; direct medical expenses, about 75 to 85 percent. Therefore, the same percentage increase in the medical benefit is actually 3 to more than 5 times greater than the same increase in the pharmacy benefit.
What influences employers’ decisions?

In the presence of escalating costs, employers must act. A number of factors influence their responses, including:

• Attitudes and beliefs
• Data and evidence
• Internal and external influencers

Many employers believe that pharmacy benefit costs are driven by price increases from pharmaceutical manufacturers and the increased use of new drugs as a result of pharmaceutical marketing. They believe that new drugs are overpriced and overutilized and that benefits derived from drugs are often exaggerated. In reality, the data show that about half of the rise in the drug trend is a direct result of simple increased utilization of pharmaceutical products, which is, in part, a reflection of pharmaceutical agents used as first-line therapy and the use of more drugs due to the increased age of the workforce. Unfortunately, much of the available data are summarized by price and clinical-use markers and are not expressed in business terms that employers can readily understand. To confound the problem, there is a dearth of good studies on pharmaceutical use and its effect on workforce health.

Influencers in employer decision making are both internal and external to the organization. Internally, in most organizations, human resources benefit managers are the primary points of contact. However, in large corporations with multiple work sites, a medical director working with a human resources group is also a prominent model. Unions have some influence, as do employees. In general, chief financial officers and chief executive officers are less involved with employee health benefit decisions, but, depending on the size of the employer, different mixed models exist.

Benefit consultants play a key role, educating employers about trends and helping them to develop strategy. Another growth area includes business leaders, groups, and coalitions. For example, there is an emerging trend for midsized employers to purchase pharmacy benefit services as a collective. Last year, three such collectives were developed solely to examine pharmacy purchasing. The question is: As these collectives get larger and more numerous, how much influence will they have over formulary and health management decisions?

Employer actions to manage the pharmacy benefit

Employers are acting on several fronts to control the pharmacy benefit cost. These initiatives include member cost sharing, enhanced clinical management, and controlling pharmaceutical access; member cost sharing has been the number one area that employers have focused on over the past few years. Copayments are the most common form of cost sharing; the majority of growth has been in the three-tier copayment plan design (Table 1). As opposed to the copayment design, in which the employee pays a fixed-dollar amount for a prescription, the new dialogue is focused on coinsurance, where the employee pays a percentage (generally around 20 percent) of the actual cost of the prescription. Employers that want employees to have more at stake financially are...
slowly changing copayment plans into coinsurance designs.

Employers have yet to look closely at the relationship between copayments and compliance with therapy; presently, they are focused on the percentage of the pharmacy benefit that they support. Currently, an 80/20 split is still the most common. With some of the movement to the three-tier plan designs, however, and with new restrictions on formularies, a minority of employees are sharing up to 50 percent of the pharmacy cost. Intuitively, this is a concern because of the potential effect on compliance; nevertheless, there are no credible studies available to quantify the relationship.

**Carve out or carve in?**

Nearly 70 percent of large employers carve out behavioral health benefits. The issue is one of integration, particularly when the pharmacy benefit is also carved out, which is true for about one third of all large employers. An emerging and promising trend among a handful of large organizations is that when they are selecting a pharmacy benefit manager, a minimum requirement is that the PBM provide data back to a data integrator. Even with data integration, there is virtually no study to show that carving out these benefits actually saves money for the employer. The carve-out trend is a reflection of the cyclical nature of employer purchasing habits. There are 3- to 4-year periods during which self-insured employers question how the health plan is managing the benefit, so they carve out the benefit. Then they become dissatisfied with how the PBM is managing, and they go back to a carved-in model with the health plan. The trend is now toward consideration of carve-ins.

The slight reduction in increases in the pharmacy benefit from a high of 18.3 percent in 2000 to 16.9 percent in 2002 was caused partially by employers’ adoption of more aggressive clinical management programs, such

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**TABLE 1  Employer actions to manage the prescription drug benefit**

<table>
<thead>
<tr>
<th>Member cost share</th>
<th>Most prevalent plan designs</th>
<th>Average copayments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Card plans</td>
<td>Mail order plans</td>
</tr>
<tr>
<td>No cost share</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>Coinsurance</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Copayment</td>
<td>90%</td>
<td>93%</td>
</tr>
<tr>
<td>Single copayment</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td>Two-tier copayment</td>
<td>31%</td>
<td>31%</td>
</tr>
<tr>
<td>Three-tier copayment</td>
<td>51%</td>
<td>51%</td>
</tr>
</tbody>
</table>

**FIGURE 2  Employer actions to manage the prescription drug benefit**

**Enhanced clinical management**

![Figure 2](source: lilly takeda benefit survey)
as managed drug limits, step therapy, and dosage optimization. Figure 2 illustrates various employer actions to manage the pharmacy benefit clinically and the relative prevalence of these initiatives.

Control of pharmaceutical access is yet another strategy utilized by employers to manage the pharmacy benefit. There are several major ways in which this happens:

- Exclusions of predefined discretionary drugs or drug classes
- Approval of drugs for only certain indications
- High copayments, delayed coverage, and/or therapeutic class management

Utilization of any of these strategies does not mean that employers are making formulary decisions, but there are a number that make policy decisions. Particularly within the three-tier benefit, large organizations are starting to ask questions such as, “Does a drug or therapeutic class fit into the second tier or the third tier, and what effect might that placement have on my workforce?” These are the types of questions on which clinical benefit consultants advise and assist benefit managers in thinking through the issues from a workplace perspective. This type of interaction is new and emergent and is being reinforced particularly as new pharmaceutical products are being launched.

### Cost of workplace depression

Affecting 10 percent of the workforce in any given year, depression is one issue that is brought to employers’ attention through briefing papers from consulting firms. In the United States, the annual cost associated with depression is $44 billion, much of which results from lost productivity. Expressed differently, that is 175 million lost workdays and a high rate of short disability. When employers see statistics such as these, their interest is piqued, and they may begin to pay attention to opportunities for managing depression better within their work forces.

Direct and indirect costs also can be expressed on an average per-capita basis; the percentage of employees who miss workdays because of a variety of common conditions is well established in the literature. Statistics such as those in Table 2 can be used as benchmarks to help employers understand how their organization compares nationally.

Productivity, although more difficult to measure, is also of interest to employers. Models developed by Mercer and others suggest that it can be in the economic interest of the employer to allow a higher priced pharmaceutical product on formulary to avert possible side effects associated with less costly drugs or over-the-counter products. Side effects, such as drowsiness or lack of concentration, although difficult to measure, are inherently associated with a negative effect on productivity.

“Health plans realize that the majority of their depressed members are being treating in primary care, in which the plan is bearing the cost. Nonetheless, they’ve carved out behavioral health care, and are questioning the incremental value of providing additional disease management specific to depression. Frankly, they ask us why the carved-out behavioral health companies aren’t providing more disease management to primary care physicians.”

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### Table 2 The national economic burden of five chronic conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Average per-capita health cost</th>
<th>Workers with condition missing work days</th>
<th>Estimated work loss costs (in billions)</th>
<th>Total costs for persons with condition (in billions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mood disorders</td>
<td>$4,328</td>
<td>18%</td>
<td>$11.5</td>
<td>$66.4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>$5,646</td>
<td>10%</td>
<td>$3.5</td>
<td>$57.6</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>$10,823</td>
<td>37%</td>
<td>$3.8</td>
<td>$42.4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>$4,073</td>
<td>8%</td>
<td>$11.5</td>
<td>$121.8</td>
</tr>
<tr>
<td>Asthma</td>
<td>$2,779</td>
<td>20%</td>
<td>$3.4</td>
<td>$31.2</td>
</tr>
</tbody>
</table>

SOURCE: DRUSS 2001

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Employers yet to adopt DM

Most employers with fewer than 20,000 employees still do not offer disease management programs for arthritis, back pain, cancer, hypertension, depression, or other common conditions. About 25 percent of them might offer disease management through their health plans, but very few are offered through an independent vendor. This lack of disease management is a concern because effective programs provide patient management opportunities, education, follow-up, and integrated information that all can be acted upon to improve both...
clinical and economic outcomes. Yet, what employers have been focused on during the last couple of years are benefit design, vendor selection, and vendor consolidation, all higher-level concerns that demonstrate a more rapid payback, in comparison with the specifics of disease management.

Although employers understand that depression is an important area of focus for both clinical and economic reasons, there are disconnections from and barriers to appropriate treatment. These include the following:

- Only one-third of individuals with a behavioral health problem seek care.
- Because of the stigma of mental illness, employees do not want their employers to know that they are depressed.
- There is a lack of care coordination for patients with depression.
- Restrictive formularies can reduce access to, and availability of, antidepressants.
- Education for employers, employees, and even health care providers is lacking.

Nevertheless, credible solutions are available. New drug therapies have proven treatment-success rates, and more than 80 percent of them result in fewer side effects than older medications. In addition, behavioral health vendors have been able to demonstrate a solid return on investment when innovative integrated programs are implemented. With measurable results such as these, a discussion of best practices becomes imperative.

From an employer perspective, consideration is now being given to an in-network benefit with liberal or no-visit/no-day limits on behavioral health benefits. In a perfect world, physical health benefits on copayments and deductibles would be in parity with behavioral health benefits. Streamlined administration and performance-based contracting between employers and MCOs would further ensure quality of care. From a health-management perspective, health promotion, member outreach, early detection and intervention, as well as primary care physician guidelines and care coordination are goals to integrate into current treatment programs. Unfortunately, a number of employers are not yet thinking in these terms.

“...a structured, ongoing dialogue between the people who gather the data and the purchasers, the people who are the end-users of those data. Perhaps what’s needed is a fair broker, a consultant, who would use an employer’s own data, which they would trust, to communicate the benefits of varying modes of treatment.”

— BENJAMIN DRUSS, MD

Results of early identification and intervention

When forward-thinking employers did implement a depression management initiative, they saw a decrease in short-term disability and an increase in productivity, and this was important to them. The depression initiative also resulted in a 17 percent drop in office visits. In addition, for each $1 spent on depression treatment, there was a $3.50 savings on medical treatment. This type of health information — expressed in business terms — really means something to the employer. Measurable results help employers see the benefit of early intervention, adequate identification and treatment, and the link with improved economic outcomes. The continuing challenge is to make this clinical/business link to large and small employers alike.

Reference


From an employer’s perspective, how does a business get better at managing disease—both clinically and economically—other than by focusing solely on cost, with a goal of reduced spending? Depression and anxiety are extremely relevant issues for employers. Yet, companies such as Kodak are in the business of capturing and using images; health care is not a core competency. Increasingly, many businesses are realizing that they need the help of all their partners to improve management of disease, enhance employees’ quality of life, reduce—or at least manage—costs, and sustain productivity at high levels.

Why anxiety and depression are important issues for business

Many businesses, even smaller ones, are becoming increasingly global. They are no longer “mom-and-pop” operations in single communities. Frequently, people who work together serve on global virtual teams and have never met. Focused on a business need or product development, they are in different countries around the world and bring to the project diverse cultural issues, backgrounds, and languages that might clash, especially when pressures build and/or pace accelerates.

Work systems are changing. Companies are trying to make systems more efficient with fewer resources and less staffing. With fewer people, everyone has to perform multiple tasks simultaneously and accomplish more. Most businesspersons carry a pager or cell phone, which is rarely turned off, keeping them still “at work” even if they are not at their desks. Working in an office building for a company is becoming a thing of the past. With their laptops, people are working in airport lounges and out of the front seats of their cars. Employees are working faster and longer, in spite of the fact that the workforce is older. The average age of the Kodak workforce is now 46. In other industries, the average age can be years older. A kind of relentless demand is being seen in the 21st century that is becoming characteristic of many businesses, and in combination with family responsibilities, it produces a significant psychological burden on employees as well as increasing rates of anxiety and depression.

Profitability is a key issue for companies today, because for every employee, a company must generate enough cash to pay its costs and then have remaining capital to return to shareholders. In addition, for every employee, there must be enough profitability to cover the health insurance costs of that employee, his or her family members, and the retirees for whom businesses carry financial responsibilities. For Kodak, that is five people for every single employee. Kodak has two retirees for every active employee; General Motors has three, and in some cases, pays first-dollar coverage based on union-negotiated agreements. Thus, employers have a significant challenge, not only to reduce costs but to improve the quality of care that employees and their families receive.

Managers and executives constitute a special group, because if they do not perform well or if they make poor or delayed business decisions, the consequences are enormous and unforgiving. Regardless of a sagging global economy, managers are still expected to have high-performance business outcomes. In addition, these workers typically are hypercompetitive, are driven to succeed, and perceive that they must be invincible, even though they are hurting inside. They frequently feel an imbalance between their work and other aspects of their lives, with work always taking precedence and representing a continual source of demand and stress.

At Kodak, the worldwide goal is to have healthy employees who are safe and productive, working where they do not get hurt and where they can use their skills and talents in an effective and sustainable way. This has be-
come a central statement that helps Kodak leaders judge what they should do to make certain that they create this kind of environment, whether the workforce is age 50, age 20 and mostly female, or decentralized.

“With good care, patients live longer and mitigate the impact of comorbid conditions longer. One might make a compelling argument that high-quality care actually results in reduced overall costs.” — Jeff Weilburg, MD

Major drivers of absenteeism

Table 1 lists a prioritization of reasons for absenteeism that is derived from Kodak’s data, rather than the published literature. These are physician-diagnosed absences of a calendar week or more, not 1- or 2-day absences from colds or flu. The population comprises all U.S. Kodak employees. The real usefulness of this list of causes for employee health-related absenteeism is that it puts psychiatric issues on the map for business management.

For several years, mental health-related absences have escalated in terms of prioritization and with respect to absolute number of workdays lost. For example, in 1996, mental health-related absences were ranked seventh, with more than 5,000 workdays lost. In 2001, these absences were ranked second in frequency, with more than 13,000 workdays lost. To underscore this trend, these data do not capture the contribution of depression or anxiety as an associated comorbid condition; these are only workdays missed because of a primary diagnosis of anxiety, depression, and so forth. In addition, the population in 1996 consisted of an employee base of about 50,000, in comparison with 28,000 in 2001. Thus, the denominator, representing the population, is decreasing, whereas the numerator, or the number of lost workdays, is increasing. Clearly, the current business environment is contributing to a portion of the burden of morbidity that is reflected in this trend.

<table>
<thead>
<tr>
<th>TABLE 1 Causes of health-related absenteeism (≥7 or days in duration), 2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Musculoskeletal disorders</td>
</tr>
<tr>
<td>2. Injury</td>
</tr>
<tr>
<td>3. Psychiatric disorders (including alcohol and substance abuse)</td>
</tr>
<tr>
<td>4. Circulatory disorders</td>
</tr>
<tr>
<td>5. Neoplasms</td>
</tr>
<tr>
<td>6. Digestive disorders</td>
</tr>
<tr>
<td>7. Maternity leave</td>
</tr>
<tr>
<td>8. Respiratory disorders</td>
</tr>
<tr>
<td>SOURCE: KODAK 2002</td>
</tr>
</tbody>
</table>

Costs: direct and more direct

Although direct costs typically are defined as expenditures for medical treatment, employers view indirect costs — overtime, the need for contract labor, missed product launches, defects, waste, lost sales, etc. — as very direct.

“I believe employers are looking for data that support the concept that if you spend more and treat the right patients with the right medications, they get better and go back to work. In other words, optimal timely treatment has an overall positive impact on cost structure.” — John Williams, MD

Table 2 summarizes 2002 expense ratios for total medical and pharmacy claims in the United States for Kodak employees who are younger than 65, the employees’ family members, retirees who have not yet reached the age for Medicare eligibility, and their family members. The simple message is that people spend more on medical treatment than on pharmaceutical products.

For example, for neoplasms, spending on medical care is nearly 5 times that for prescription drugs. Conversely, in behavioral health, there is a greater commonality in dollars. Therefore, prioritizing spending in the absence of prescription drug information would not result in significant attention to psychiatric issues. Yet, the need is high. Looked at differently, a low expense ratio could be construed as an advantage, which illustrates that medical costs are reduced when patients with psychiatric disorders are adequately treated with medication.

<table>
<thead>
<tr>
<th>TABLE 2 Ratio of medical-treatment claims costs (inpatient and outpatient) to drug-treatment costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disorder type</td>
</tr>
<tr>
<td>Circulatory disorders</td>
</tr>
<tr>
<td>Digestive tract disorders</td>
</tr>
<tr>
<td>Musculoskeletal disorders</td>
</tr>
<tr>
<td>Neoplasms</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
</tr>
<tr>
<td>Respiratory tract disorders</td>
</tr>
<tr>
<td>Endocrine, metabolic disorders</td>
</tr>
<tr>
<td>SOURCE: KODAK 2002</td>
</tr>
</tbody>
</table>

Employers’ needs in behavioral health disease management

Employers offer health benefits to secure high-quality, cost-effective care for their employees. In return, they anticipate increased profitability from having healthier em-
ployees. Therefore, to the extent that treatment goals are expressed only in medical terms, the employer’s needs are not being fully met. Employers need to have the end result of any initiative expressed in business terms that they can both understand and evaluate. Some of these terms are: the return to work, for active employees; the return to school, for children; the return to independent living, for retirees; and functional outcomes. Disease management goals, when expressed in these terms, are enforceable and understandable to employers.

"Within controlled population studies, we have begun to see that if you treat people correctly immediately upon diagnosis, it may cost a great deal of money the first year. After the initial spike, however, cost for treatment — regardless of diagnosis — falls and remains fairly constant. So, I believe that good care does save money, and the data to support that assertion are credible and growing."

— LARRY PESKO, MS, ScD, RPH

In addition to treatment goals that lack functional relevance, there are several other practices in behavioral health that are of concern to employers. These include the following:

• Most decisions are made by primary care physicians, who spend an average of 7 minutes of “face” time with each patient per visit.
• In a system in which specialization is highly endorsed, the patient’s benefits are frequently “carved up,” and pharmacy benefit managers are not communicating with behavioral health specialists, who are not communicating with disease management vendors, who are not communicating back to the health plan or the employer.
• Delayed interventions lead to unnecessary adverse clinical outcomes.
• There is inadequate use of evidence-based guidelines.
• Reliance on medical claims data alone does not provide adequate information for informed decision making.
• Prescriptions are being written with little evidence that counseling is occurring. Because the U.S. health care system is an acute-presentation, complaint-oriented system, the structure to support repeated patient counseling is not evident.
• Faced with an immediate pressure to reduce cost, employers have still not accepted that high-quality care is more cost effective. With credible data to demonstrate this, it is likely that employers will be responsive to this fact. In business, good data drive good decision making.

Early treatment: imperative

First and foremost, treatment of depression and anxiety needs to improve for the patient. In the absence of an accurate diagnosis and good therapy, prolonged morbidity and disability will be the result. There will be unnecessary employer expense, absenteeism, and reduced productivity. Exhaustion of the sick benefit can result in loss of employment. Improperly treated depression and anxiety can cause escalating social margination at home as well as at work.

Early detection and intervention are appropriate roles for the employer and the work group. Supervisors generally know their team members well and can be trained to recognize signs of distress and constructively respond to them with help for the employee. Employers must endorse a workplace in which people care about each other and are prepared to offer support when needed.

“It seems there are models, such as EAPs [Employee Assistance Programs], that would improve the treatment of depression; increase awareness in the workplace; and get people appropriately screened, assessed, and referred into treatment. In treating substance abuse, the EAP industry is ahead of the rest of health care.”

— JONATHON BOOK, MD

To be accountable and active partners in decision making, patients need information on cost as well as on expected clinical outcomes. They must be made aware of the downside of noncompliance and that they, too, are responsible for the success of their therapy. Employers, as well as patients, need to be very involved, in a way they never have been before.

Reference

At GlaxoSmithKline (GSK), the Employer Group Segment works with national and major regional employers, unions, coalitions, and trust funds with 50,000 employees or more. Unions alone represent 16 million people. Eight account managers are dedicated to building relationships and bringing awareness of mental health issues to this significant business segment. The needs of smaller employers also are taken into account. To effectively reach them, GSK has three additional account managers that work solely with business coalitions that represent 11,000 various employers and 33 million employees within the United States.

By strengthening employer relationships across a spectrum of work sites, the Employer Group Segment strives:

• To understand employer issues and concerns
• To assist in measuring disease costs and drivers
• To establish demonstration programs for optimum health outcomes
• To justify a balanced approach to employee health care purchasing and management

A number of tools have been developed to accomplish these tasks. For example, the MindSET program collection is specific to mental health, particularly depression and related anxiety disorders. The GSK Web site contains MindSET materials that employers can download and customize. Additional National Committee for Quality Assurance certified disease management programs are also available through GSK’s Web site as part of this employer initiative. With groups such as Tower Perrin, the GSK Employer Group Segment has created and refined actuarial tools that can be utilized within employer segments to understand the impact of depression and anxiety on a particular business. Demonstration projects are in place to test many of these tools.

The goal of MindSET is to measure costs associated with illness; for example, the program shows how absenteeism affects a particular marketplace and demonstrates the areas in which those costs might be reduced. MindSET can also be used to plan and implement behavioral health interventions in the workplace. Utilization of MindSET increases awareness of behavioral health issues, assists in Health Insurance Portability and Accountability Act–compliant screening to identify behavioral health disorders, and promotes the use of behavioral health benefits. MindSET consists of two fundamental components: a Workplace Kit and an Economic Burden of Depression in the Workplace Actuarial Model.

**MindSET in the workplace**

The MindSET kit contains step-by-step implementation instructions on how to assess organizational needs, communicate with health plans, and arrange and implement a behavioral health initiative. Among other aids, the kit contains a PowerPoint presentation for a “Lunch and Learn” program and a variety of promotional materials and tips to assist a local health coordinator to set up a health fair within the work site. Fact sheets and brochures educate employers and employees about behavioral health disorders and where to go for help.

**Economic burden of depression in the workplace actuarial model**

This actuarial model — developed in conjunction with Towers Perrin — evaluates an employer’s data to produce a detailed, economic picture of the impact of depression in a particular workplace. It allows managed care organizations and employers to estimate the direct medical costs, as well as lost productivity costs, of depression and related comorbid conditions, and then to assess the economic impact of treatment. The figure on the following page represents data from an actual employer with nearly 22,000 employees.

Demographically, the female-to-male ratio is extremely close. In our sample, 1,360 employees have received diagnoses of depression and have been treated accordingly. In this output of the model, differential costs for the employees with depression versus those without are broken down by category: lost productivity, prescription costs, and direct medical costs. The difference is nearly $1,000 per employee. In the aggregate,
In addition, GSK has the ability to perform outreach and to provide education for community physicians, within the network, to meet specific employer needs.

Conclusion

Most employers are not sophisticated when it comes to health care issues: General Motors spends its time concentrating on cars; McDonald’s, mostly on hamburgers. Corporations that are savvy about health care are the exception, not the rule.

First, it can be difficult to impress on employers that doing “the right thing,” in terms of depression disease management, not only is good for their employees but also is prudent from their own economic standpoint.

Second, there are some inherent conflicts between employers and managed care, specifically in terms of how the two entities view costs. Indirect costs that affect the employer, such as absenteeism or presenteeism (when an employee is in attendance but is either offering little or no value or, in fact, is having a negative effect on quality or on the performance of others because of some impairment, such as illness, medication side effect, lack of sleep, or substance abuse) are not normally considered by the provider or health plan. That inherent conflict is something to resolve, and the employer must be aware of this conflict with any of the plans and programs just described.

Finally, some employers have expressed concern that if they implement these projects, they will identify additional people with untreated depression. Although they believe an accurate diagnosis is appropriate, they are concerned that the added treatment burden will further escalate costs. What the Towers Perrin model demonstrates, however, is that if patients with depression are treated adequately, they become a more economically attractive group, from a productivity and absenteeism perspective, than those not treated at all.

What employers can do

Employers are encouraged to implement a comprehensive depression management program. This entails:

- Initiation of stress management and depression education programs to increase disease awareness among employees
- Education of supervisors to recognize the signs and symptoms of depression
- Encouragement of employees to contact trained employee assistance program personnel for referrals for diagnosis and treatment
- Ensuring that depression identification and education are integral parts of every health care initiative

Example: an average employer

Effect of depression on lost productivity, prescription costs, and direct medical costs:

<table>
<thead>
<tr>
<th>Employees with depression</th>
<th>Employees without depression</th>
<th>$941 difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost productivity</td>
<td>Prescription costs</td>
<td>Direct medical costs</td>
</tr>
<tr>
<td>$608</td>
<td>$320</td>
<td>$772</td>
</tr>
<tr>
<td>$320</td>
<td>$294</td>
<td>$785</td>
</tr>
<tr>
<td>$785</td>
<td>$163</td>
<td>$316</td>
</tr>
</tbody>
</table>

Demographics:
- 10,000 employees
- 11,800 dependents
- 21,800 covered lives total
- 52:48 female-to-male ratio
- Average employee age: 39
- Average salary: $37,489
- 1,360 employees with depression
- Copayments represent typical cost-sharing provisions

SOURCE: GLAXOSMITHKLINE

Reference

Depression increases morbidity, mortality

Depression complicates the prognosis for individuals who suffer from comorbid conditions, such as coronary artery disease, diabetes mellitus, stroke, and cancer (Takeshita 2002). Depression also creates an increased risk for development of those diseases among otherwise healthy individuals.

In a study to examine the effect of depression on development of coronary heart disease (CHD) and its sequelae, researchers found that men and women with prior depression had an increased risk of developing CHD: Adjusted odds ratios for CHD were 1.73 for depressed women and 1.71 for depressed men. Depression also increased the risk of mortality from CHD in men (Ferketich 2000).

Penninx (2001) found that the risk for cardiac mortality among persons with and without cardiac disease was significantly elevated among individuals with major and even minor depression: Adjusted odds ratios for cardiac mortality (95 percent confidence interval) were
3.0 for patients who suffer from major depression and 1.6 for those with minor depression.

**Depression and suicide**

In another study, Isacsson (1996) used a large data set from the Swedish National Data Center and examined suicide rates in depressed individuals who were either treated with antidepressants or not treated. The treated population numbered approximately 40,000, and the untreated population numbered 85,000. The calculated risk for suicide in treated patients with depression was 141 per 100,000 person years; in the untreated population, the risk was 259 per 100,000 person years, or 1.8 times higher. The authors concluded that antidepressants could effectively reduce the risk of suicide among depressed patients. Yet, at that time, only 1 in 5 persons with major depression was treated with an antidepressant. Increasing the use of these medications has had a reductive effect on suicide rates in Sweden.

**Depression and resource utilization for chronic medical conditions**

As illustrated in Figure 1, the presence of depression significantly increases expenditures among patients with common chronic medical conditions such as back pain, diabetes, headache/migraine, and heart failure. These data are from the OCI1 database and include almost 250,000 people (OCI 2001).

Katon (1990) administered the National Institute of Mental Health Diagnostic Interview Survey, Version 3A, to 119 patients who used health care resources extensively (so-called high utilizers of health care). Their findings include the following: 70 percent had a lifetime history of major depression; 23 percent, panic disorder; more than 40 percent, generalized anxiety disorder; 24 percent, somatization disorder; and 25 percent, alcohol abuse and dependence. Katon concluded that high utilizers with a psychiatric diagnosis represented a major cost driver — not of psychiatric overutilization but of general medical overutilization (Figure 2).

**High cost of suboptimal treatment**

In a study published in 1996, Thompson evaluated patterns of antidepressant use and their relationship to cost of care. Cumulative charges included costs for drugs, physician visits, hospital outpatient care, and hospital inpatient care. Patterns of antidepressant use were defined as early discontinuation (fewer than 60 days); switching/augmentation, or partial compliance (60 to 90 days); and more than 90 days of use. The early discontinuation group, which included patients who received 60 days or fewer of treatment with an antidepressant over a 12-month interval, incurred total overall costs of $5,610. In contrast, those who were treated for more than 90 days, who were considered compliant and received at least 90 days of therapy with their initial selective serotonin reuptake inhibitor (no switching/augmentation), had the lowest overall mean cost, $3,393, over the 12-month follow-up period (Thompson 1996).

This study confirms the counterintuitive notion that there are higher overall health care costs for those taking medications for a shorter time. The expectation might be that there are higher costs among patients consuming more medication, yet the inverse is true. The longer a patient is taking medication, the lower the aggregate costs become.

**Economic trend**

Applied Health Outcomes (AHO) corroborated Thompson’s results using the TennCare Data Set. These data cover 1.4 million lives and approximately 22,000 patients taking antidepressants. AHO looked at the total amount billed by month in a 12-month period, beginning with the initiation of an antidepressant course of therapy (Figure 3). This data set illustrates stabilization of charges after 6

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1 OCI is an application service provider that owns the largest private collection of integrated health benefits and risk-management data.
months. Comparing the sixth month with the first, we can calculate a reduction of 15.9 percent in costs. At 6 months, however, a physician might get a letter from the managed care company reiterating that Agency for Healthcare Research and Quality (AHRQ) guidelines recommend that patients with depression be treated for 6 months. The implication of the letter is clear: A patient who has been treated for 6 months should discontinue the medication. So what does the physician do? He or she might discontinue the patient’s therapy due to concern that his or her prescribing patterns are being scrutinized, with possible personal financial repercussions. If discontinuation occurs, what are the likely scenarios? To determine the outcome of discontinuation versus continuation of treatment, Geddes (2003) researched relapse prevention and explored optimal length of therapy for antidepressants.

**The Geddes study**

To determine long-term antidepressant treatment outcomes, data were collected from 31 randomized trials involving 4,410 subjects. The patients, who had responded to acute treatment, were treated largely in 8-week trials and then were assigned to a continuation treatment phase, intended to prevent relapse. At discontinuation, whether it was at 6 months, 1 year, or 2 years, patients were monitored for at least 1 additional month. In view of the brevity of the follow-up period, this is a best-case outcome scenario. Had follow-up been longer, extrapolated to 2, 3, 4, 5, or 12 months, the outcomes might have been worse, because they would include the people who suffered relapse during the more-extended time frame.

Geddes (2003) found, however, that continuing treatment with antidepressant medication reduced the odds of relapse by 70 percent, in comparison with patients who discontinued therapy or who were given placebo. On average, across all the data, 41 percent of patients taking placebo suffered relapse, in comparison with 18 percent taking antidepressants. In other words, the absolute risk of relapse is high when antidepressants are discontinued.

In reference to the stabilization of costs graph, this can mean that after 6 months, if a patient discontinues medications, there may be relapse within 1 or 2 months and, from an economic perspective, the patient is going to start back at week 1 with exaggerated costs. If physicians just stay the course a bit longer and stabilize the patient, the frequency of visits to the psychiatrist or the primary care physician actually decreases.

Geddes categorized patients into two primary groups and two subsets of those groups. The primary group...
differentiation was based on either 1 or 2 years of treatment after randomization. Within these two groups, they further distinguished patients on the basis of whether they had received 1 to 2 months or 4 to 6 months of treatment before the study. Geddes found that among patients who had been treated for 2 years or more, those who had undergone 1 to 2 months prior antidepressant treatment had a 33-percent rate of relapse during the trial, whereas those with 4 to 6 months of prior antidepressant treatment had a 24-percent rate of relapse during the trial. Rates of relapse for controls were 65 and 62 percent, respectively. Rates of relapse for patients with 1 year of follow-up were lower, as might be expected with a shorter period of observation.

The salient point here is the 9-percent difference (33 versus 24 percent) in the rate of relapse between the two groups treated for 2 years or more. This indicates that even a small difference in prior treatment has a positive effect on outcome. The overall message is that the longer patients continue receiving treatment after an acute episode of depression, the less likely they are to suffer relapse than if they receive no appropriate treatment at all or if they discontinue their medication therapy after 12 months.

Getting patients into remission

The goal of treatment of depression and anxiety disorders is always remission, which is defined as 70 percent or more improvement according to a standardized instrument. The definition of response is less precise. In some of the published literature, response is defined as 34 percent or greater improvement; in other studies, it is 50 percent improvement. Nevertheless, that is not good enough and is the reason placebo “response rates” appear robust. If the expectation for the outcome of active treatment is so poor, it is easy for a placebo to achieve what appears to be a reasonable response. Yet, when standards for remission are set at 70 percent or more improvement, there is a significant difference between placebo and active treatment response rates. This concept is clearly illustrated in Figure 4, which shows placebo versus active treatment with paroxetine during a 32-week course of study among patients diagnosed with general anxiety disorder.

Remission rates continue to increase throughout the entire length of the study, whereas rates among patients taking placebo decline. At the end of 8 months of treatment, 70 percent of the patients experience 70 percent or better improvement, the previous definition of remission. However, it takes an extended period of time to get them to this level of improvement, and, of importance, remission can occur at any time (GlaxoSmithKline 2001). Therefore, patients must be maintained on treatment for a long period of time. The longer the treatment, the higher is the likelihood of remission.

Rates of remission for patients with depression follow a very similar pattern. For example, Thase found that incomplete remission is predictive of complete relapse. He classified patients into responders and “remitters” and demonstrated that among remitters, the probability of remaining symptom free was much higher. Patients who were treated until they achieved remission had better outcomes at all time points than did those who were not treated until they received remission; in addition, remitters were less likely to suffer relapse (Thase 1992).

Recovery from major depression: 10-year follow-up

The longest study done by the federal government on the question of recovery from major depression is the National Collaborative Depression Study, which includes a nationwide cohort of people who received diagnoses approximately 20 years ago with an index episode of major depression. The researchers assessed the cumulative probability of recovering from an index episode of major depression. When researchers examined probability of recovery from a second, third,
fourth, or even fifth episode, the proportion of patients who recovered at any one point in time was similar to the others. In addition, duration of recurrent major depressive episodes was relatively uniform, averaging approximately 20 weeks (Solomon 1997).

Recently, Keller (2002) assessed the cumulative probability of recurrence after recovery from an episode of depression. He found that once a patient has experienced three episodes of depression, the probability that he or she will suffer from another is 95 percent within 2 years. Because depression is a chronic illness, nearly everybody who suffers an episode of major depression will eventually experience another.

Therefore, the question is this: Why would any pharmacy benefits manager or any health plan assume that patients can discontinue antidepressant therapy and live happily ever after, regardless of the HEDIS measures? Arbitrary discontinuation of medication is indefensible. There is no chronic disease in which a physician can treat the condition, then stop the medication, and expect the patient to live happily ever after. The data supporting this conclusion are overwhelming.

**VIEW OF A MANAGED CARE PHARMACY DIRECTOR**

*Larry Pesko, MS, ScD, RPh*

Many of the studies in the literature are conducted through the use of formal methods in sterile environments that are removed from real-world practice. These studies and clinical evaluations do not reflect the experience or perspective of an integrated health system pharmacy director, a practicing clinician, or an average patient.

Bench research is well controlled, and investigators know exactly what outcomes they are attempting to formalize, but those outcomes frequently have little or no application to what goes on in the field. Field research, of course, is representative of what takes place in real life; however, in this type of research, it is very difficult to control the variables. The following presentation is based on the interface between some well-documented published literature and how the results of those studies play out, or are interpreted, in a real-world scenario.

According to AHRQ statistics, the prevalence of major depressive disorder ranges from 4.8 to 8.6 percent of the population at any given time. These statistics, applied to a managed care plan that covers 250,000 lives, imply that between 12,000 and 21,500 members will probably experience some sort of major depressive disorder that necessitates treatment, including treatment with antidepressant medications. To treat these health plan members with major depressive disorder adequately, the AHRQ guideline on depression in primary care recommends that the acute treatment phase be of a sufficient length to achieve remission of depressive symptoms, followed by 4 to 9 months of chronic, or continuation, therapy to prevent recurrence.

The literature, however, supports the findings that only 40 to 70 percent of patients adhere to their antidepressant drug regimen during the acute phase of therapy (Simon 1993) and that only 15 to 50 percent of patients adhere to their antidepressant drug regimen during the continuation phase (Melfi 1998).

**Economics of depression therapy**

To put prevalence and adherence into economic terms, the average cost to a health plan — after discounts — for 1 year’s supply of antidepressant medication for one patient is approximately $720. This amount is not an average wholesale price or a fictitious number; it is based on real-world data. When extrapolated to a health plan with 250,000 members, the per-patient cost of antidepressant therapy becomes an aggregate of about $6.7 million annually. These are real costs, fully discounted, for medications only. Divided among all members of the health plan, whether they have depression or not, this $6.7 million costs each member $26.80 annually.

These amounts are based on actual usage and are reflected in the studies referenced previously. However, if a health plan were to meet the current national guidelines for therapy, meaning that all patients with a diagnosis of depression would be given antidepressant medications and continue taking them for the acute and continuation phases of therapy, annual costs would rise to $53.60 for each health plan member, double the current expense.

However focused a pharmacy director may be on costs, he or she will maintain that the most expensive drugs are those that do not work or those that are not taken. Health plans spend a great deal of money in treating depressed patients, and yet outcomes remain inadequate. In many cases, less-than-optimal outcomes are a result of patient noncompliance, defined as less than 75 percent of the course of therapy utilized within the period of time under consideration. If patients were compliant with evidence-based national recommendations on the optimal course of therapy, health plans would be far more successful in lowering their overall medical costs, benefiting not only employers but also insurance companies in terms of reduced medical expenses.

**VIEW OF A QA EXPERT**

*Benjamin Druss, MD*

Making decisions about health care costs and quality relies on the use of data to the fullest extent possible and simultaneously on the realization that all data have limitations. However imperfect, data form the basis of the four current guidelines on optimal length of antidepressant therapy and were used in the development of all HEDIS measures (Table 1 on page 18).
Despite having been developed almost a decade apart, all of these guidelines are actually quite similar. The guideline that the National Committee for Quality Assurance, the authors of HEDIS, relied on most significantly — and the one most widely known — is that of the U.S. Agency for Health Care Policy and Research (AHCPR, now AHRQ) Depression Guideline in Primary Care. The AHCPR guideline recommends treatment throughout the acute phase, which is essentially the time until remission of depressive symptoms. It further recommends treatment during the continuation phase, which it defines as a second period lasting 4 to 9 months. Interestingly, all of these guidelines suggest discontinuing antidepressant therapy after the continuation period and then observing patients for recurrence of depressive symptoms. Maintenance therapy beyond the continuation period is recommended only for individuals at high risk, who are typically defined as patients who have experienced recurrent depressions.

Recent literature

One relevant and compelling look at the data can be found in the article by Geddes (2003), referred to earlier by Sheehan.

Although Geddes addressed the benefits of antidepressants in reducing the risk of relapse for at least 12 months, the article does not make a strong recommendation to continue antidepressants after that period. Rather, it encourages clinicians to use their judgment in identifying patients who seem to be at high risk, focus on this subpopulation, and look into the issue of potentially lowering the threshold for longer-term maintenance treatment below that currently outlined in the four main guidelines.

HEDIS antidepressant measures

There are three evidence-based HEDIS antidepressant measures. The first measure concerns the optimal number of contacts that a depressed patient should have with a practitioner; the focus of this measure is the effective management of medications (see box, “Three HEDIS Antidepressant Measures”). The second measure addresses the pattern of medication usage during the acute stage, or the first 3 months. With regard to this measure, there is broad consensus among practitioners. According to the final measure, all adult members in whom a new episode of depression is diagnosed should continue antidepressant therapy for a period of at least 6 months. This differs slightly from the AHCPR guideline that recommends discontinuation of medication after 4 to 9 months of continuation treatment: that is, treatment after remission of symptoms.

Health plan performance on HEDIS measures

Regardless of consensus on or clarity of the measures, performance by participating HMOs is lackluster. Table 2 summarizes 2002 performance data on the HEDIS continuation phase measure. The HMOs that report HEDIS data cover approximately 90 percent of the people in managed care plans in the United States; thus, results can be considered representative of patterns of care nationwide among patients enrolled in commercial managed care plans.

Among plans that report performance on this measure, less than 40 percent of people, on average, take an antidepressant throughout the 6-month continuation period. This is significant, because the guidelines recommend that treatment continue throughout this phase. The debate arises with regard to the need for treatment after 6 months. Even in the highest-scoring plans — the 75th percentile — less than 50 percent of patients who began taking a new antidepressant received the full 6 months of treatment.

Another interesting fact about the HEDIS depression metrics is that their values are considerably lower than overall plan performance on the majority of other HEDIS measures. For example, overall plan compliance with other general health metrics is approximately 60 percent, whereas depression compliance tends to be approximately 40 to 50 percent.

As a wise man once said, “It’s better to light a candle than to curse the darkness.” This aphorism can serve as a metaphor for the HEDIS measures. Before these measures were developed in the late 1980s, health care practitioners were indeed “fumbling around in the dark” as far as measuring quality was concerned. Although HEDIS is still a work in progress, it also can be viewed as a very viable attempt to balance data from research with measures that can and will be used in medical practice in the real world. Recently, a few major articles critiquing HEDIS have been published. The authors of these articles have examined who actu-

### Table 1: Guidelines for duration of medication use

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Published</th>
<th>Recommended continuation period*</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.K. Defeat Depression Consensus</td>
<td>1992</td>
<td>4–6 months</td>
</tr>
<tr>
<td>U.S. AHCPR Depression in Primary Care</td>
<td>1993</td>
<td>4–9 months</td>
</tr>
<tr>
<td>American Psychiatric Association</td>
<td>2000</td>
<td>4–5 months</td>
</tr>
<tr>
<td>British Association for Psychopharmacology</td>
<td>2000</td>
<td>6 months</td>
</tr>
</tbody>
</table>

*All recommend maintenance therapy beyond this period only for individuals with recurrent depression.
ally is complying with the measures and whether clients are just demanding the HEDIS data with little or no action being taken as a result. Some of those criticisms are justified, but HEDIS is certainly the best set of guidelines currently available, and it is far better than no attempt to measure quality at all. If there is no means of measuring the quality of health care, all that can be determined is cost.

In summary, there seems to be a clear consensus among practitioners, as well as reports in the literature such as Geddes’s study, that treatment should be maintained through the acute phase (which is measured from remission of symptoms) and then continue for some time (typically at least 6 months). There are questions regarding the wisdom of keeping patients on antidepressant therapy after this continuation phase is complete. Geddes advocated that more work be done in this area to evaluate the potential benefits of continuing therapy after that time. Finally, regardless of whether patients need to continue therapy after 6 months, health care providers certainly have to work hard just to achieve compliance in the acute and continuation phases.

References

Three HEDIS antidepressant measures

**Optimal practitioner contacts for medication management.** This issue concerns the percentage of members age 18 and older as of the 120th day of the measurement year in whom a new episode of depression was diagnosed, who were treated with antidepressant medication, and who had at least three follow-up contacts with a primary care practitioner or mental health practitioner during the 12-week acute phase. At least one of the three follow-up contacts must be with a prescribing practitioner (e.g., a licensed physician, a physician assistant, or another practitioner with prescribing privileges).

**Effective acute-phase treatment.** This issue concerns the percentage of members age 18 and older as of the 120th day of the measurement year in whom a new episode of depression was diagnosed, who were treated with antidepressant medication, and who continued taking an antidepressant drug during the entire 84-day (12-week) acute phase.

**Effective continuation-phase treatment.** This issue concerns the percentage of members age 18 and older as of the 120th day of the measurement year in whom a new episode of depression was diagnosed, who were treated with antidepressant medication, and who continued taking an antidepressant for at least 180 days (6 months).

**TABLE 2 Continuation measure: 2002 values for HMOs**

<table>
<thead>
<tr>
<th>Health plan rank</th>
<th>% of members with a new episode of depression with at least 6 months of treatment with antidepressant medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>25th percentile</td>
<td>33.7</td>
</tr>
<tr>
<td>Median</td>
<td>39.6</td>
</tr>
<tr>
<td>75th percentile</td>
<td>46.0</td>
</tr>
</tbody>
</table>

**SOURCE:** NCQA 2002


NCQA. HEDIS 2003 Antidepressant Medication Measures. Washington: NCQA.


Two studies are presented here: the TennCare Database Study and a discontinuation analysis from the National Managed Care Database, managed by Applied Health Outcomes and possibly the largest managed care database on depression in the country.

The TennCare study was derived from a Tennessee managed Medicaid population of 1.4 million lives. The objectives for the study were to:

- Examine the relationship between length of therapy and total health care costs by using retrospective medical, behavioral health, and pharmacy claims data, and
- Evaluate the economic benefits of longer selective serotonin reuptake inhibitor (SSRI) antidepressant therapy in a managed Medicaid population.

To quantify the economic burden of early discontinuation, researchers in the TennCare Study modeled elements of their methods after a study designed by Thompson (1996).

Thompson found that patients who were fully compliant and continued antidepressant therapy for 90 days or longer had incurred $2,200 less in total annual health care costs than had patients who received therapy for fewer than 60 days. Thompson also found that the most costly cohort comprised patients with evidence of switching or augmenting SSRI therapy ($7,590 annually). The TennCare Study defined patient cohorts more broadly to include compliance with antidepressant therapy for fewer than 90 days, 91 to 179 days, and more than 180 days — and examined the cost ramifications (Figure 1).

SSRI therapy in the TennCare population was discontinued by 24 percent before 3 months and by 45 percent by 6 months. Only 34 percent of patients remained compliant and were still taking antidepressant therapy more than 180 days after the index prescription. Although the >180-day cohort and the augment/switch group had the highest monthly pharmacy charges — approximately $280 and $325, respectively — overall medical charges for hospitalization, professional fees, physician visits, and outpatient care were lowest for the >180-day cohort. Early discontinuation, therefore, is a costly issue from both an economic and a quality perspective, inasmuch as persistency of antidepressant therapy is a HEDIS measure. The TennCare analysis also revealed that although costs do fluctuate during the first 6 months of treatment for compliant patients, they stabilize at 6 to 7 months and remain stable at 12 months. With data such as these, the development of effective intervention strategies can begin to change inadequate patterns of care and improve outcomes and costs in the treatment of depression and anxiety.

Findings from the National Managed Care Database

One of the criticisms of the TennCare analysis was that the study population was not representative of those found in most managed care plans. To address that valid concern, a subsequent study was conducted with data from a much larger managed care population that included more than 33 million lives, 57 health plans, and 750,000 patients receiving therapy with SSRIs (Bramley 2003).

This geographically diverse study population is deemed representative of national age and gender distribution. Longitudinal integrated data, allowing for utilization and tracking of treatment patterns, were compiled for analyses of time to discontinuation of therapy, cost of discontinuation, rates of discontinuation, and rates of switching and augmentation among patients taking an immediate-release SSRI (Figure 2). A follow-up analysis was also conducted on discontinuation rates of a controlled-release SSRI introduced after initial study commencement.

Study inclusion criteria

All subjects:
- Were defined as “new starts,” which meant they had taken no antidepressants for a 6-month period before study enrollment
- Received a diagnosis of depression or anxiety; no other mental health disorders were included
- Were at least 18 years of age
Were continuously eligible for health plan membership for 12 months after the index date.

Among this national managed care population, discontinuation was defined as a medication treatment gap of 15 days or more. The two largest cohorts were the switch/augment group (34 percent) and those who discontinued antidepressant therapy before 60 days (30 percent). Among all the patients, including the switch/augment cohort, 72 percent of patients taking an immediate-release SSRI discontinued therapy before reaching the minimum 180 days of treatment. Obviously, there is a problem with keeping people on therapy, and it seems as though a number of factors might influence that.

Medical cost by cohort

Not surprisingly, total 6-month pharmacy costs for all medications in addition to antidepressants were highest for the >90-day cohort ($690) and lowest for the <60-day cohort ($415). Switching/augmenting was also in the upper range, at approximately $675 for the 6-month follow-up period.

In terms of hospital costs incurred for any reason, a different picture emerges with regard to the >90-day cohort. In this case, their total 6-month hospital costs are the lowest of all, at approximately $850, whereas the switch/augment cohort’s costs were the highest, at $1,200. Therefore, hospital costs decreased with persistency of SSRI therapy beyond 90 days. In measuring total medical 6-month costs, the switch/augment group was again the most costly, at just over $1,700, and the >90-day cohort was the least costly, at less than $1,300.

Treatment patterns analysis

The initial study commenced Jan. 1, 2001, and a treatment patterns analysis began April 1, 2002, coinciding with the availability of the controlled-release SSRI antidepressant paroxetine.1 Two issues were particularly germane to this treatment patterns analysis: the effects of the controlled-release product on length of therapy as well as on switching/augment rates. The following analysis includes patients taking paroxetine (n=1,416) and patients taking immediate-release medications (n=45,128) over the same length of time. The researchers found that throughout the study period, 6 percent of patients taking paroxetine switched or augmented therapy, compared to 11 percent of patients taking an immediate-release product. This demonstrates a compelling 44 percent reduction in patients who switched/augmented their SSRI therapy with paroxetine versus the immediate-release SSRIs.

A time-to-discontinuation analysis — illustrated in Figure 3, page 22 — evaluated the time between the index date of April 1, 2002, and the discontinuation of therapy, as defined by a gap of more than 15 days in therapy.

Beginning at 30 days, the discontinuation rate for patients taking immediate-release SSRIs was 23 percent higher than that for patients taking paroxetine.

One additional difference should be noted in study design. The majority of manufacturers of immediate-release SSRIs participate in what are known as persis-

1 Throughout this article, “paroxetine” refers to Paxil CR.
tency, or refill-reminder, programs with all the major chain pharmacies, such as Eckerd, Rite-Aid, and Walgreens. These programs would not, in all likelihood, affect switch/augment rates, but they do anecdotally have a rather significant effect on length of therapy. These programs are designed so that after 30 days, if patients have not filled their antidepressant prescriptions, they get a phone call from a pharmacist or a nurse. The caller explains the importance of continuing to take the medication and reiterates the reason it was prescribed initially. The caller encourages patients to refill their prescriptions, and, as a result, refill rates are extremely high, sometimes doubling the expected length of therapy. During the study period, however, paroxetine was not part of any such refill-reminder program. In view of this information, the 23 percent lower rate of discontinuing paroxetine not only is statistically significant but also may translate into even greater reductions in the future in comparison with the immediate-release SSRIs.

When people cannot continue on therapy for longer than 90 days, or when they augment or switch, an economic penalty emerges. Conversely, as length of therapy increases, there is evidence of decreased medical utilization. Patients taking paroxetine appear less likely to change therapies and have greater persistency with therapy. This trend of better persistence is a viable proxy for improved economic and clinical outcomes.

References

“In psychiatry, there are case management programs being developed. One that has proved to be extremely useful is called the Assertive Community Treatment for Schizophrenic Patients. Programs such as these should be considered as one of the solutions for antidepressant noncompliance as well.”
— Sabah Chammas, MD

![FIGURE 3 Time-to-discontinuation analysis](source: Bramley 2003)
As anyone with a background in business well knows, it is far more cost effective to retain an existing customer than to secure a new one. The same maxim can be translated into prescribed pharmaceuticals. For example, Lin (1995) studied Medicaid patients who were prescribed antidepressants (selective serotonin reuptake inhibitors [SSRIs], tricyclic antidepressants [TCAs], and others) and determined their dropout rates over a 6-month period. Lin found that approximately 28 percent of patients had stopped taking their medications by week 4, and 43 percent had stopped by week 9. At the end of 6 months, only 21.7 percent of patients were still taking their index medications. These are not isolated findings: Lin’s results (Figure 1) have been replicated by other researchers.

Dropout rates were slightly higher with the tricyclic antidepressants than with the SSRIs, but overall rates were cause for concern, particularly because a great number of these patients should be taking antidepressants over long periods. A practitioner or health care administrator might reasonably ask, “What is the point of investing in depression disease management programs and prescribing medications to patients if the majority will be noncompliant?”

To improve patient outcomes, the dropout rate must be reduced and patient compliance with length of therapy must be increased. Given that patients stop complying largely because of adverse side effects, a key characteristic for a new SSRI formulation became increased tolerability and reduced adverse effects, especially nausea. This led to the application of the Geomatrix technology.

The Geomatrix technology provides a delivery system that controls the amount, timing, and location of drug release; it has been favorably tolerated by patients, and the rate of dropouts due to adverse effects is low in comparison with that of dropout with placebo. The controlled-release (CR) paroxetine tablet has two basic components: the outer enteric film-coated layer of the tablet, which consists of a degradable barrier, and the inner layer, which contains the active drug. The degradable polymeric matrix controls the dissolution rate of paroxetine over a period of approximately 4 to 5 hours. Data suggest that this unique pharmacokinetic profile has demonstrated benefits in terms of patient tolerability and reduced patient dropout rates. Once ingested, the CR paroxetine tablet travels down the digestive tract to the stomach, where the active drug is protected from degradation by the enteric coating, thus al-

**FIGURE 1 Compliance**

*High dropout rates undermine treatment success*

<table>
<thead>
<tr>
<th>Week</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>28% dropout</td>
</tr>
<tr>
<td>8</td>
<td>43% dropout</td>
</tr>
<tr>
<td>12</td>
<td>52% dropout</td>
</tr>
</tbody>
</table>

In a study of Medicaid patients prescribed antidepressants, 21.7% remained on treatment for an adequate term of 6 months.

following absorption of the drug farther down in the small intestine and reducing the nausea.

**Adverse events**

There are a number of pooled analyses with the CR paroxetine: four in depression, three in panic disorder, and one recently in social anxiety disorder. Others are still under investigation. Figure 2 represents a summary of some of those data. In treatment-emergent nausea, there is an initial rise in the percentage of patients experiencing this adverse event and then a gradual decline until week 12, when virtually all cohorts report the same low rate of nausea.

![FIGURE 2 Treatment-emergent nausea](image)

* p < .05 CR vs. Paroxetine.
Source: GlaxoSmithKline

![FIGURE 3 Overall dropouts due to adverse events](image)

* p < .0008 Paroxetine vs. Placebo.
Source: GlaxoSmithKline

“*I would say, ‘Get it right the first time.’ Cost is probably not the number one issue with physicians. So, considering that they are troubled by a large percentage of patients coming back to them because they are having an adverse effect, if the prescription is the right one the first time, that will decrease the physicians’ workloads and make life simpler.*”

— Dennis Glick, MD

Overall rates of dropout due to adverse events in the pooled depression trials are illustrated in Figure 3. For placebo, dropout rate was 5.8 percent; for CR paroxetine, 9.8 percent; and for immediate-release (IR) paroxetine, 16.2 percent. Those differences are statistically significant, with a 40 percent reduction in dropout rate of CR paroxetine in comparison with the IR formulation.

Because depression has a 10 percent prevalence in the population, a reduction in dropouts among this many people translates into a much more favorable profile in terms of compliance and length of therapy.

**Efficacy**

In addition to greater tolerability, CR paroxetine seems to provide efficacy equal to or greater than that of IR paroxetine, as measured by the Hamilton Depression (HAM-D) Rating Scale. A HAM-D score of 7 or less indicates remission, which is approximately equivalent to...
an improvement of 70 percent or more. Figure 4 illustrates statistically significant results among cohorts of patients receiving CR paroxetine, IR paroxetine, or placebo.

“When patients discontinue use of one drug, typically they do not begin the second drug the next day. In fact, there’s an intermediate period of time when they are probably untreated and can go into a clinical deterioration, from which it is harder for them to recover.”
— Wayne Lednar, MD, PhD

The observed (OC) cohort is observed cases: that is, results from patients who actually attended at each visit. A last observation carried forward (LOCF) analysis includes all patients who were randomly assigned to treatment and who returned for at least one on-treatment visit. For any patient who drops out of treatment or misses a visit, his or her last observation is carried forward. In this way, all patients who took the effective treatment, including dropouts, are included in the final analysis. This is the most conservative analysis that can be done in a clinical trial. It represents a worst-case scenario.

“There are good research data available in the past few years that challenge the conventional wisdom of starting with what appears to be an equally efficacious but lower-cost drug as first-line therapy. More and more data are showing clearly that starting with the best therapy first for a particular disease — whether surgery or pharmaceutical therapy — is less costly across all the conditions that the patient has.”
— Bernard Bloom, PhD

Weight gain
Another area of clinical interest in the treatment of depression is weight change. The standard measure of meaningful weight change is an increase or decrease in body weight by greater than 7 percent from baseline, which is, on average, equivalent to about a 10-pound change in weight. With CR paroxetine, slightly more people lost 10 pounds than gained 10 pounds. In contrast, data on the IR formulation indicate that more patients gained than lost weight. This difference was not statistically significant, but the study was not powered to detect weight shift. Some patients may favor CR over IR paroxetine for this reason.

In summary, the importance of patient compliance with therapy cannot be overstated. Any formulation that improves compliance and increases length of antidepressant therapy, resulting in overall lower utilization of health care, should be carefully considered. An improved adverse-event profile that translates into significantly reduced dropout rates has a potentially enormous effect when extrapolated to the millions of sufferers of chronic depression.

References
GlaxoSmithKline, data on file.