Economic Considerations in the Management of Arthritis

New medications for arthritis that provide the benefits associated with traditional nonsteroidal antiinflammatory drugs—without the accompanying side effects—can reduce health care utilization and related costs.

Arthritis is the most common chronic disease in the United States—a fact that gives its economic impact significant societal relevance. According to the Centers for Disease Control and Prevention (CDC), osteoarthritis (OA) is the most common form of this disease, affecting an estimated 20.7 million Americans or 12.1% of the population of the United States. Rheumatoid arthritis (RA) affects an estimated 2.1 million Americans, or about 1% of the U.S. population. The Arthritis Foundation has estimated that the costs of musculoskeletal diseases amount to approximately 1% of our nation’s gross domestic product, an economic effect in 1992 of $65 billion attributable to health care costs and lost wages. As baby boomers age and the elderly population correspondingly increases, the prevalence and economic burden of arthritis undoubtedly will grow.

Individuals with OA and RA incur higher charges for medical care than their nonarthritic peers from the same community (age- and gender-adjusted). In a study of the population of Olmsted County, Minnesota, Gabriel and colleagues found that individuals with arthritis incurred additional charges not only for the care of their arthritis but also for the care of numerous other comorbid medical conditions. This suggests that these individuals might have a higher prevalence of other chronic conditions than their peers without arthritis.

In addition to the direct costs of treating arthritis, the cost of treating iatrogenic disease in patients with arthritis is substantial. In a population of Medicaid recipients, 25% of patients taking nonsteroidal antiinflammatory drugs (NSAIDs) experienced side effects that required further medical care. The costs of treating these side effects were accounted for primarily by drugs (42%) and physician visits (20%). However, hospitalization for complications, such as gastrointestinal (GI) bleeding, perforation, or obstruction, although uncommon, accounted for 38% of iatrogenic costs.

Because a drug’s tolerability profile can affect its effectiveness, an analysis of health care claims, such as that conducted for the Medicaid population noted previously, will undoubtedly understate the direct costs of NSAID side effects. Benson and colleagues have noted that “upper GI intolerance limits the use of NSAIDs, ultimately compromising their therapeutic potential. In addition to the adverse events themselves, the perceived threat of side effects may limit the efficacy of NSAIDs as physicians react to this fear by prescribing lower dosages of NSAIDs and recommending that patients limit their usage to periods of arthritis flares. As a result, many patients are unable to receive the full antiinflammatory and pain-relieving benefits of NSAIDs.”

An arthritis medication that is both tolerable and efficacious should allow patients to take their medication and control their arthritis symptoms. The economic effect of such a medication would be to offset the iatrogenic costs of traditional NSAIDs.
ECONOMIC BURDEN

Direct Costs

Direct health care costs are those incurred in the care of a patient's condition or disease. Fishman et al. compared the prevalence and direct costs of 18 chronic conditions within a single health plan, Group Health Cooperative (GHC) of Puget Sound.6 More than a third of adult members had one or more chronic conditions in 1992, accounting for approximately 71% of total medical costs. The combined total of patients with arthritis and chronic back/neck pain was by far the most prevalent chronic condition at GHC. Caring for a member diagnosed with arthritis was estimated to cost 150% more than providing care for patients without such a diagnosis after adjusting for age, sex, and other chronic conditions; GI disease increased costs by approximately 111%.

Fishman et al. provided no information regarding the distribution of costs among various conditions. However, a study conducted at Fallon Community Health Plan provided a breakdown of costs attributable to arthritis from July 1, 1993, to June 30, 1994 (see Figure 1). The average annual cost of arthritis-related care for RA was $2,162 per patient. Prescription medications accounted for the majority of costs (63%), followed by ambulatory care (21%) and hospitalizations (16%). Disease-modifying arthritis drugs (DMARDs) such as methotrexate accounted for a large percentage of medication costs (48%), followed by NSAIDs (32%) and antiulcer medications (16%). RA patients averaged 7.7 physician visits per patient per year, including 3.4 visits per patient per year to a rheumatologist.7

Average costs attributable to OA were $543 per patient per year. Hospital care accounted for 45% of the total; medications, 33%; and ambulatory care, 22%. Hospital care for OA was largely attributable to hip and knee replacements and accounted for nearly half of the total cost of care, despite the fact that only 5% of OA patients were hospitalized. Arthritis-related prescription drug costs were estimated to be $173 per person per year. Approximately 46% of prescription medication costs were attributable to antiulcer drug use, or 15% of total OA costs. Approximately 3.3 office visits per year were attributable to OA.7

RA and OA present interesting contrasts. The individual cost of RA is high, but the cost to the health care system is relatively small due to the low prevalence of RA. In contrast, OA may be characterized by infrequent resource use and lower per-patient costs; however, because of the high prevalence of OA, costs to the health care system are higher for OA than RA—seven times higher in the Fallon Clinic study. Antiulcer medications, used to manage NSAID-induced GI side effects, account for a significant portion of costs for OA (15%) and RA (10%).

Individuals with arthritis incur additional charges not only for the treatment of arthritis per se but also for the care of numerous other comorbid medical conditions.8 Similar findings recently have been reported by Lee et al. from their analysis of members enrolled in United HealthCare. These investigators found

Figure 1. Breakdown of the Direct Costs of Arthritis

Cost Breakdown of Rheumatoid Arthritis

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<thead>
<tr>
<th>Cost Category</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Analgesics and Steroids</td>
<td>3%</td>
</tr>
<tr>
<td>Antiulcer Medications</td>
<td>10%</td>
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<tr>
<td>DMARDs</td>
<td>30%</td>
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<tr>
<td>Hospital</td>
<td>16%</td>
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<tr>
<td>NSAIDs</td>
<td>20%</td>
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<tr>
<td>Ambulatory Care</td>
<td>21%</td>
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Cost Breakdown of Osteoarthritis

<table>
<thead>
<tr>
<th>Cost Category</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Analgesics and Steroids</td>
<td>3%</td>
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<tr>
<td>Antiulcer Medications</td>
<td>15%</td>
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<tr>
<td>NSAIDs</td>
<td>15%</td>
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<tr>
<td>Hospital</td>
<td>45%</td>
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<tr>
<td>Ambulatory Care</td>
<td>22%</td>
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*Antiulcer medications represent 46% of total medication costs
that the incremental cost of caring for a member who had been diagnosed with OA was nearly twice that of caring for a member of the same age and gender without OA: $145 per member per month (PMPM) versus $74 PMPM. The same analysis showed that the cost of caring for members with RA was 155% higher than the cost of caring for members without RA: $158 PMPM versus $62 PMPM.

Other than NSAID-related diseases of the digestive system, the most common comorbid condition that these investigators found was “mental disorders.” In this United HealthCare study, mental disorders were found to be 79% more common in OA patients than in nonarthritis patients who were matched by age and gender. Other investigators also have found that depression is common among arthritis patients. Approximately 27% of arthritis patients in Oxford Health Plan reported symptoms of depression, compared with 16% of controls. Investigators found that the prevalence of patient-reported symptoms of depression increased from 15.8% in patients with mild arthritis to 30.4% in patients with moderate arthritis to 49.8% in patients with severe arthritis.

**Indirect Costs**

The indirect costs of a disease include the costs of lost wages, lost productivity, and lost days from work. Indirect costs of arthritis have been estimated to be four times greater than the per capita direct costs of arthritis. Indeed, the biggest economic impact of RA in patients 18-65 years of age is a one- to two-thirds reduction in their workload capacity. In addition:

- Meenan et al. found that patients with RA incur a 50%-63% reduction in their expected income.
- Fex et al. found that 78% of RA patients had to adjust their work conditions to remain employed, including transferring to a different job, changing work tasks, modifying the workplace, and reducing work hours.
- Martinez et al. reported that 66% of female RA patients received Social Security disability payments.

Because OA develops primarily in the elderly, it is difficult to assess indirect costs due to lost wages. However, according to the CDC, OA is second only to chronic heart disease as the most common primary diagnosis leading to the receipt of Social Security disability payments. Given the higher prevalence of OA compared with RA, and the increasing age of the U.S. population, the economic implications of the indirect costs of OA can be expected to become even more substantial in the next 20 years.

**COST OF USING NSAIDS**

NSAIDs are among the most widely used therapeutic categories of medication. A Roper-Starch survey of NSAID risk estimated that 16.8% of Americans use NSAIDs regularly to relieve symptoms such as pain and inflammation of arthritis. The antiinflammatory and analgesic effects of NSAIDs reduce an arthritis patient’s pain and swelling, which in turn results in improvements in functional status and quality of life. The costs of NSAIDs, however, need to be weighed against the side effects, and an evaluation of NSAID costs should include not only prescription costs but also the costs of NSAID-induced adverse events. Such an approach provides a more complete understanding of the costs of NSAID usage.

**NSAID-related Gastropathy**

Symptomatic ulcers and potentially life-threatening ulcer complications such as upper gastrointestinal bleeding, perforation, and gastric outlet obstruction are reported in 2% to 4% of patients who take NSAIDs for a year. Singh has estimated that 16,500 persons die each year of ulcer complications associated with NSAID therapy. For persons hospitalized with GI bleeding or perforated ulcers, the average payment in 1994 was estimated to be $13,150.

Approximately 30% to 40% of long-term NSAID users experience symptoms of dyspepsia. Although dyspepsia may not appear to be as serious as other NSAID-induced GI toxicities, its high prevalence and significant cost can place a financial burden on the payors of health care. A recent study estimated the economic implications of dyspepsia in arthritis patients by comparing resource use and costs between arthritis patients with and without dyspepsia. Arthritis patients with dyspepsia had higher costs for both inpatient ($4,430 vs. $2,967) and outpatient ($3,042 vs. $1,919) services than nondyspeptic arthritis patients. The magnitude of cost differences between patients with and without dyspepsia highlights the economic implications of dyspepsia in arthritis patients.

**NSAID-induced Anemia**

Estimates of the prevalence of anemia among arthritis patients range from 39% to 53%. Of all reported cases of anemia, 77% are “anemia of chronic disease” (i.e., due to the rheumatic disorder itself), while the remaining 23% of reported cases are due to iron deficiency caused by blood loss. NSAIDs also can cause anemia, presumably due to clinically and subclinically apparent blood loss caused by the chronic erosive effects of NSAIDs in the GI tract.

**NSAID-induced Platelet Dysfunction**

NSAIDs have the reversible effect of inhibiting platelet aggregation and as a result increase a patient’s bleed time. NSAID-induced platelet dysfunction is a contributing mechanism to the chronic GI blood loss that leads to anemia. NSAID-induced platelet dysfunction also can complicate elective and nonelective surgery for both the patient and provider. In cases of emergent/elective surgery, patients who are anticoagulated with an NSAID will bleed more during a procedure and may incur higher health care costs. In cases of elective surgery (e.g., hip or knee replacement), patients are required to discontinue the use of their NSAIDs for at least three days prior to a procedure. Often this three-day window

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The authors suggested that problems with lack of efficacy or with tolerability of NSAIDs were possible reasons for the low duration of use.

**IMPROVING GI SAFETY AND TOLERABILITY**

When NSAID toxicity occurs, a patient's health-related quality of life is diminished, and a significant financial burden is placed on the payor (see Figure 2). GI intolerance alone leads to significant healthcare resource use. The diagnostic work-up of dyspeptic symptoms often requires the use of costly procedures such as GI endoscopy, which is used in an estimated 25% of diagnosed cases of dyspepsia. Antibacterial medications are prescribed for nearly half of the patients who present with NSAID-induced GI distress. A recent analysis of a managed care claims database revealed that the rate of coprescribing antibacterial medications (i.e., proton pump inhibitors, H2 receptor antagonists, and misoprostol) was 57% higher among arthritis patients who used NSAIDs than in those who did not use NSAIDs. In fact, the incidence of antibacterial medication use was higher than that of the coprescribed NSAID.

The availability of an agent that would provide the antiinflammatory effects of an NSAID without the accompanying side effects should improve the quality of patient care and curb the costs of NSAID-related toxicities. In 1999, a new class of medications, the specific cyclooxygenase-2 (COX-2) inhibitors, has become available for the management of pain associated with arthritis. These agents have the potential to help people manage their arthritis. However, the indiscriminate use (e.g., use for the short-term management of acute pain) of these agents can unnecessarily affect a health plan's pharmacy budget. For the purposes of this discussion, the specific COX-2 inhibitor, celecoxib, will be used as the basis for modeling the economic implications of an agent that provides the antiinflammatory effect of NSAIDs without their accompanying side effects.

Burke et al. previously demonstrated that the cumulative incidence of moderate-to-severe GI tolerability of celecoxib is similar to that of placebo and that the rate associated with traditional NSAIDs is significantly higher (p < .01). From their results, the excess rates of NSAID-induced GI adverse events can be determined. For the purposes of this discussion, the annual excess rate of GI adverse events associated with NSAIDs is the difference between the annual rate projected with NSAIDs and that projected with celecoxib or a placebo. The annual excess rates of the most significant NSAID-induced GI adverse events (i.e., hospitalized events, symptomatic ulcers, GI distress and anemia) are displayed in Table 1.

Using the excess event rates listed in Table 1, the number of events that could be avoided through the effective use of a more tolerable agent can be estimated in a given population. For example, a representative health plan that covers one million lives would be expected to have approximately 50,000 arthritis NSAID-users (prevalence of
arthritis NSAID-users in a group-model HMO population has been estimated to be 5%.

If each of these 50,000 arthritis NSAID-users was given a more tolerable agent instead of an NSAID to manage their pain, the health care plan would prevent an estimated 5,900 cases of GI distress per year, as well as 3,200 cases of ulcers, 420 hospitalizations, and 1,350 cases of anemia. Table 1 lists the estimated number of avoidable events in a population of one million covered adult lives.

These results compare favorably to those of other disease states. For example, the West of Scotland Coronary Prevention study (WOSCOP), which has been a basis for using HMG-CoA reductase inhibitors for the primary prevention of coronary artery disease, showed that 46 hospitalizations could be avoided per year if 10,000 persons with hypercholesterolemia were treated with Pravastatin. In comparison, if 10,000 arthritis sufferers were treated with a more tolerable agent, the available evidence indicates that 84 hospitalizations could be avoided per year. In addition, approximately 1,180 cases of GI distress, 640 cases of symptomatic ulcers, and 270 cases of anemia could be prevented.

In order to establish the cost of each of the adverse events included in the current analysis, an analysis of claims was conducted with a large, nationwide managed care organization. The cost per case of each of the adverse events included in the analysis was estimated to be: GI distress, $481/case; ulcer, $983/case; serious GI complications requiring hospitalization, $6,193/case; and comparator NSAID-induced anemia, $669/case. The cost of each event can then be applied to the number of avoidable events to estimate the total annual cost to the health plan of these avoidable events. Table 1 also lists these costs.

Another way to view these results is in terms of annual cost per arthritis patient. Figure 2 represents the direct medical costs that can be attributed to avoidable NSAID-induced GI adverse events. GI distress accounts for 29.9% of excess costs or $56.76 per patient per year (PPPY); ulcers account for 33.2% of excess costs ($62.91 PPPY); serious GI events account for 27.4% of excess costs ($52.02 PPPY); and NSAID-induced anemia accounts for 9.5% of excess costs ($18.06 PPPY).

These analyses indicate that the effective utilization of an agent that provides the antiinflammatory effect of an NSAID without the accompanying side effects could offset acquisition costs of such a drug. Therefore, the use of such an agent in arthritis patients who now use NSAIDs would not only be expected to reduce the number of NSAID-induced GI events but also would be expected to reduce medical costs associated with the treatment of those adverse events.

CONSIDERATIONS FOR MANAGED CARE PHARMACISTS

The availability of the COX-2 inhibitors has raised concerns and questions within managed care organizations. What will the cost of these new agents be? Will the economic benefits of avoiding events offset the cost of treatment? Will these agents be used inappropriately in the short term management of pain or as first line therapy? What will be the impact of direct-to-consumer advertising?

Robert Seidman, Pharm.D., vice president of pharmacy, WellPoint Health Networks, shares these concerns. In Dr. Seidman's view, the objective of providing new pharmaceuticals at an affordable price is becoming increasingly difficult with the pace of new drug approvals by the U.S. Food and Drug Administration. In an effort to manage the pharmacy budget impact of the COX-2 inhibitors, he and his colleagues at WellPoint Health Networks have established prior approval criteria for these agents. Before physicians can prescribe a COX-2 inhibitor, patients must fulfill at least one of the following criteria: active bleeding or bleeding disorder, concomitant anticoagulant use, previous documented history of NSAID-induced gastropathy, or at least two GI complication risk factors documented by the physician.

Joseph Fox, M.D., medical director of The M-Plan, shares many of the same concerns. However, he and his colleagues were "pleasantly surprised by the pricing of the two [COX-2 inhibitors]" and they are "encouraged by the preliminary safety data," Fox says. Consequently, the M-Plan's Pharmacy and Therapeutics committee has decided to place one of the COX-2 inhibitors on the formulary. Dr. Fox also plans to watch the post-release safety data very closely and will continue to review this new class as more information becomes available.

With new and improved drugs such as the COX-2 inhibitors, managed care pharmacists are presented with the challenge of incorporating these new therapies into disease management and pharmaceutical care programs. Just as the introduction of the HMG-CoA reductase inhibitors advanced the treatment of cardiovascular diseases and significantly increased managed care pharmacy budgets, so do the COX-2 inhibitors represent a significant advancement in the management of arthritis and cause similar concerns related to costs. Just as managed care pharmacy not only survived but arguably benefited from the advent of the HMG-CoA reductase inhibitors, it seems likely that managed care pharmacy will manage and find positive impacts resulting from the introduction of the COX-2 inhibitors for the treatment of arthritis.

Arthritis imposes a significant financial burden on society, managed care organizations, and on other payors...
of health care. The side effects associated with NSAIDs contribute significantly to this financial burden. New treatments that provide the antiinflammatory effects of NSAIDs without the accompanying side effects can reduce the consumption of certain health care resources. This reduced health care utilization has the potential to offset the costs of these newer treatments. The challenge facing managed care pharmacy is to continue to improve arthritis-patient care by providing innovative drug therapies to those who would benefit while managing the increased drug spending that is inevitable with these new therapies.

References