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Impact of Appropriate Pharmaceutical Therapy for Chronic Conditions on Direct Medical Costs and Workplace Productivity: A Review of the Literature

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ABSTRACT

This paper presents the findings of a literature review investigating the economic impact of appropriate pharmaceutical therapy in treating four prevalent chronic conditions—asthma, diabetes, heart failure, and migraine. The goal of the review was to identify high-quality studies examining the extent to which appropriate pharmaceutical therapy impacts overall medical expenditure (direct costs) and workplace productivity (indirect costs). The working hypothesis in conducting the review was that the costs of pharmaceuticals for the selected chronic conditions are offset by savings in direct and indirect costs in other areas. The literature provides evidence that appropriate drug therapy improves the health status and quality of life of individuals with chronic illnesses while reducing costs associated with utilization of emergency room, inpatient, and other medical services. A growing body of evidence also suggests that workers whose chronic conditions are effectively controlled with medications are more productive. For employers, the evidence translates into potential direct and indirect cost savings. The findings also confirm the importance of pharmaceutical management as a cornerstone of disease management. (*Disease Management* 2004;7:61–75)

INTRODUCTION

ESCALATING HEALTH CARE COSTS are a significant concern for policy makers and for employers, who, in the United States, bear a significant share of the total spending burden.¹ In response to this trend, employers have sought ways to limit their health expenditure risks, such as defined contribution plans, benefit reductions, increased out-of-pocket payments (deductibles and co-payments), reduced choices among plans and providers, and tiered benefit plans. The pharmacy budget has been espe-

cially susceptible to these strategies. The potential impact of having a “silo mentality,” in which pharmacy benefit management decisions are made without reference to the total spending picture, has not been well studied.

Chronic conditions represent a public health issue of magnitude. While some conditions affect individuals of all ages, the prevalence for many increases with age. With the average age in the United States climbing, the prevalence of chronic conditions is expected to increase rapidly over the coming decade.

Evidence-based treatment guidelines and

disease management programs for many chronic conditions emphasize appropriate pharmacotherapy as the cornerstone to improving health outcomes and controlling costs. Numerous studies have shown that appropriate medications for chronic conditions reduce symptoms and prevent or delay the onset of complications, resulting in improved health-related quality of life and workplace productivity.² This paper reports on a review of the literature examining cost impact of appropriate pharmaceutical care for selected chronic conditions.

OBJECTIVE

The working hypothesis of this review was that the cost of providing health insurance coverage that includes pharmaceutical treatment for chronic conditions potentially could be offset by the cost savings associated with decreased medical costs and work loss. We conducted a review of the literature describing the impact of appropriate medication use on costs of care, from an employer perspective. Two main categories of costs—direct medical costs associated with health care service utilization, and indirect costs associated with losses to workplace productivity—were examined. While other costs may be associated to different degrees with the studied conditions, this review was limited to the two categories of cost of greatest interest to employers. Workplace productivity was defined to include both absenteeism—missed days from work due to illness—and presenteeism—reduced output or performance for employees who present for work despite illness.

METHODS

Four chronic conditions—asthma, migraine, diabetes, and heart failure—were selected for review, based on their prevalence, costs, and relevance to employers, as well as the use of appropriate pharmacotherapy as a cornerstone of the management of each disease. A literature search, using the MEDLINE database, covering the time period between 1993 and 2003, was conducted to identify published studies in the

peer-reviewed literature examining the impact of appropriate pharmaceutical agents on health care utilization and workplace productivity. Each identified manuscript was reviewed and evaluated on the basis of the following: (1) study design and methods, (2) study population, (3) class and name of drug(s) studied, (4) type(s) of health care use studied, (5) types of workplace productivity studied, (6) impact of therapy on health care use and costs, and (7) impact of therapy on workplace productivity. Reference lists of key publications were reviewed to identify other relevant articles, which, in turn, were obtained and reviewed.

RESULTS

The results of the literature review for each of the four chronic conditions examined are presented, including overviews of the epidemiology of the conditions and associated costs and summaries of the evidence of the impact of pharmaceuticals on direct and indirect costs.

Asthma

Asthma is one of the most prominent public health issues in children and adults.^{3,4} In the United States, asthma affects approximately 15 million individuals³ and is the most common illness in children and adolescents.⁵ On an annual basis, 5,000 deaths, 500,000 hospitalizations, and 2 million emergency department (ED) visits are attributed to asthma.⁶⁻⁸ Furthermore, asthma has been estimated to cause 14 million school absence days and 14.5 million work absence days annually.⁶ Accordingly, health care costs are substantial and were estimated to be \$12.7 billion in 1998.^{7,9} The average annual cost per patient has been estimated at \$1,238.¹⁰

The majority of asthma-related costs (58%) are related to direct medical care expenditures, of which 45% are associated with hospitalizations, outpatient hospital visits, and ED visits and 43% with prescription medications.⁹ However, indirect costs—which include non-medical economic losses such as days missed from work and school, caregivers' costs, premature

retirement, and death—represent 42% of the total health care expenses for the disease.⁹

Pharmacological therapy, along with patient education, control of asthma triggers, and the monitoring of asthma severity with objective measures of lung function, plays a central role in the National Heart, Blood, and Lung Institute's (NHBLI's) asthma treatment guidelines.³ Despite these guidelines, the current use of controller medications is seriously suboptimal.^{11–13} Long-term-control medications, used to prevent and control disease symptoms while simultaneously reducing the frequency and severity of asthma,³ include inhaled and systemic corticosteroids, cromolyn sodium and nedocromil, long-acting beta2-agonists, methylxanthines, and leukotriene modifiers. Although inhaled corticosteroids are universally considered the most effective controllers and recommended as first-line therapy,^{3,4} recent evidence from clinical trials indicates that the synergic association of beta2-agonists and corticosteroids might be beneficial for more effective long-term treatment, leading to improvements in lung function and symptoms, as well as a decreased need for rapid relief, short-acting medications.^{3,4,14} As a result, the 2002 updated NHBLI asthma guidelines recommend that the preferred treatment for patients with moderate to severe asthma be the addition of long-acting inhaled beta2-agonists to low-to-medium doses of corticosteroids.¹⁵

Impact of asthma drug therapy on health care utilization and direct costs. Several studies have documented an association between the increased use of inhaled corticosteroids among patients with asthma and a decrease in utilization of costly health care resources, namely, hospitalizations^{16–19} and ED visits.²⁰ One large population-based study²¹ showed that the use of inhaled steroids was associated with a 50% decrease in risk of hospitalization. A recent review¹⁶ suggested that regular use of inhaled corticosteroids can decrease asthma hospitalizations by up to 80%. A large retrospective study of acute hospitalization among 6 million people in Sweden between 1978 and 1991¹⁸ showed that increased sales of inhaled corticosteroids were significantly related to a downward trend in the total number of bed-days related to asthma.

Studies investigating the relative risk of return visits to the ED among users and nonusers of inhaled corticosteroids indicate that patients who use inhaled corticosteroids following discharge from the ED have a significantly lower risk of subsequent ED visits²² and that inhaled corticosteroid therapy can reduce the risk of rehospitalization among elderly asthmatics.²³ Perhaps most important is the finding that the regular use of inhaled corticosteroids is associated with a decrease in asthma mortality rates.^{24,25}

Studies consistently show that proper adherence to national asthma guidelines is associated with better clinical outcomes, lower health care utilization,¹¹ and lower total health care costs,²⁶ while poor adherence to therapeutic regimens is associated with excess health care utilization and costs.^{27,28} A study of adults with persistent asthma in France²⁹ found that poorly controlled asthma was associated with a 2.5-fold increase in utilization costs, compared with well-controlled asthma. Another study³⁰ showed that the mean medication cost of patients whose medication use was at variance with treatment guidelines was double that of other asthma patients (\$89 vs. \$42), and the mean total health care cost of the non-guideline-compliant patients was almost three times that of other asthma patients (\$496 vs. \$182). A study in the Medicaid population²⁶ found that patients being treated with corticosteroids had lower total health care costs (by 24%) than patients without. These results are consistent with asthma cost-effectiveness models, which suggest that the use of inhaled corticosteroids in adults with mild to moderate asthma can decrease costs and improve quality of life.³¹

The impact of asthma on workplace productivity. A number of studies document the deleterious effects of asthma on quality of life and work productivity.^{32–38} Recent results from the 2000 Behavioral Risk Factor Surveillance System (using data from 163,773 respondents) indicate that adult asthmatics have significantly more physically unhealthy days, mentally unhealthy days, and days with activity limitation compared with adults without asthma.³⁹

The impact of asthma on work-related im-

pairment could be substantial. One population-based study³⁸ found that nearly a quarter of working asthmatics changed their job or duties because of their condition, another quarter reported missing at least one partial or complete work day in the last four weeks because of their asthma, and almost one-fifth rated their effectiveness on the job as less than or equal to 90% in the last four weeks. Similar findings were reported by Ungar and Coyte,³² who noted that most productivity loss among asthmatic patients results from restricted days rather than complete absenteeism. In light of the high rates of absenteeism to begin with, this additional cost to work productivity should be of special concern to employers.

Missed work and restricted days affect employees with asthma, as well as employees who have children with asthma. One study documented that among full-time working parents of children with asthma, 39% of parents whose children awakened one to three times, and 69% of parents whose children awakened four to seven times within a month's period, missed at least one day of work in that month.³⁵ In an effort to estimate the patient-level costs of asthma care to children, Ungar and Coyte³⁷ found that the indirect costs associated with parent productivity loss were 12% of the total health care costs, and almost half of the cost of medication, which accounted for 31% of the total. Given these facts, it is not surprising that, in one of the first studies to estimate the expense of asthma for a major U.S. employer,³³ asthma wage-replacement costs due to absenteeism and disability (40%) accounted for almost as much as those due to direct medical care (43%).

Undertreatment of asthma can lead to higher direct medical costs as well as substantial indirect costs to employers, through absenteeism, impaired productivity and the ramifications of decreased quality of life among employees.⁴⁰ Conversely, asthma patients with better asthma control have been shown to have lower health care costs, less work impairment, and a better quality of life.⁴¹ An increasing number of studies demonstrate that appropriate pharmacotherapy within the context of comprehensive asthma disease management programs can improve clinical outcomes, cost outcomes, and work productivity.^{42,43} Knoell et al⁴⁴ demonstrated that

patient adherence to medication guidelines led to improved work productivity. Similarly, outcomes of a population-based asthma management program showed an increase in quality of life, as well as a decrease in absenteeism for those who attended the program.⁴⁵

The estimated cost savings to managed care organizations or employers who participate in asthma disease management programs can be substantial. For example, results from the Asthma Self-Management Program (ASMP) demonstrated that the estimated cost savings due to a reduction in the utilization of health care services were \$175,317. Since the cost of participating in the program was \$49,500, participating organizations yielded a net savings of \$125,817, or a return on investment of 254%.⁴⁶ One asthma intervention program, which trained providers to follow national asthma guidelines, estimated that the annual resource savings after the intervention amounted to \$4,845 per patient.⁴⁷

Diabetes

In 2001, approximately 16.7 million adults in the United States were thought to have diabetes, and 7.9% of adults were diagnosed with the disease.⁴⁸ The number of individuals with diabetes is expected to continue to increase, rising to almost 22 million by 2025.⁴⁹ These individuals are at greater risk for neurological, peripheral vascular, cardiovascular, renal, and ophthalmic diseases than the non-diabetic population.⁵⁰⁻⁵³ In 2002 the total direct and indirect costs attributable to diabetes were estimated to be \$132 billion, averaging approximately \$10,900 per diabetic.⁵⁰ This review focuses primarily on type 2 diabetes, which accounts for 90% or more of all cases of diabetes.^{54,55} Although type 2 diabetes is often asymptomatic in its early stages, as it progresses, it frequently results in serious long-term complications⁵⁶⁻⁵⁸ and lower quality of life.⁵⁹⁻⁶¹

The American Diabetes Association (ADA) treatment guidelines for type 2 diabetes focus on maintenance of glycemic control and screening for and attempting to prevent the onset or progression of complications.⁵⁷ Other treatment approaches can include collaboration between health practitioners and patients,^{62,63} and disease management, which has been as-

sociated with significant reductions in health care cost and use.^{64,65} While recommended treatment strategies for type 2 diabetes vary by individual case, at initial diagnosis they frequently include some combination of diet and exercise.⁵⁷ As the disease progresses, for the majority of patients non-pharmacological interventions alone become insufficient to keep blood glucose levels within target ranges, often leading to the introduction of oral medications—alone, in combination, or together with insulin.⁶⁶ However, patient compliance with treatment guidelines and preventive care standards has been shown to be less than optimal, especially in cases with more complicated treatment regimens.^{67–70} According to longitudinal study data, the number of patients who are able to maintain glycemic control using only one medication also decreases over time, and 50% in three years and 75% in nine years need multiple therapies to remain within acceptable levels.⁶⁶ Medications to address complications are also frequently an important part of the treatment regimen.⁵⁷

Impact of diabetes drug therapy on health care utilization and direct costs. Diabetes and its complications have substantial impacts on health care utilization.^{50,71–79} According to 2002 data from the ADA, the estimated ratio of annual per capita medical expenditures for individuals with and without diabetes was approximately 5:1 (\$13,243 vs. \$2,560, respectively).⁵⁰ Previous studies support the findings that patients with type 2 diabetes have noticeably higher medical costs than similar patients without diabetes.^{73,77}

Brown et al⁷⁴ assessed medical costs attributable to the progression of cardiovascular and renal disease in patients with type 2 diabetes and found that an individual's medical costs increased from baseline by 50%–360% for cardiovascular disease and by 65%–771% for renal disease, both depending on the stage of the disease. The authors emphasized the role of aggressive therapeutic treatments in lowering costs through a reduction in microvascular and macrovascular complications. Caro et al⁷⁵ estimated the average direct costs of diabetes-related complications would amount to more than \$47,000 per person over 30 years of

age. In their model, the major contributors to these costs included macrovascular diseases (52% of total), nephropathy (21%), neuropathy (17%), and retinopathy (10%).⁷⁵ However, they noted that the ability to translate a reduction in the risk of complications into cost savings depends on the cost of the treatment involved.

The direct medical costs of diabetes are often determined by examining a variety of health care expenditures, including but not limited to hospitalization, medication, nursing home, and physician costs.^{71,79–83} Estimates of the direct medical costs of diabetes have increased rapidly over the past few years.^{50,71} Among the factors contributing to the direct costs of diabetes overall, inpatient health care utilization consumes the largest portion (greater than 60%) of total health care expenditures.^{71,79} In 1997, the direct medical costs for diabetes were estimated at \$44.1 billion.⁷¹ A 2002 study more than doubles this figure, estimating direct costs at \$91.8 billion.⁵⁰

Medication costs have been found to contribute less than 10% of total health care expenditures related to diabetes,⁷⁹ though costs may increase significantly over time, with the onset of major complications.⁷³ However, limited research exists on the specific impact of medications on direct costs associated with the disease. In a treatment simulation model, patients who used oral medications and achieved glycemic control, as defined in the model, were found to have average annual costs \$422 lower than those patients who did not achieve control.⁸⁴ An economic analysis as part of a randomized controlled clinical trial showed that intensive glycemic control was a cost-effective means of delaying the onset of complications, with a cost reduction of \$1,862 associated with each year spent free of complications.⁸⁵ The average total cost per patient of standard medical practice has been estimated to decrease by approximately \$438 with use of an oral medication (metformin), compared with conventional treatment (primarily diet).⁸⁶ And a study that investigated the impact of various treatment methods on total direct costs found that treatment with a class of oral medications—sulfonylureas—lowered the annual costs over no treatment by \$213.⁸⁷

The impact of diabetes on workplace productivity. Significantly fewer studies have been conducted to investigate the indirect costs of diabetes and type 2 diabetes in particular.^{50,71,82,88} Although not specific to type 2 diabetes, a number of studies have assessed the economic implications of work disability and productivity losses for individuals with all types of diabetes.^{71,89–93} In particular, work disability, whether measured in days or in quarters, has been shown to be substantially impacted by diabetes.^{50,90,92,93} In 2002, indirect costs attributable to diabetes in general, as measured by restricted or lost work, premature mortality, and permanent disability, were quantified as \$10,759, \$21,558, and \$7,494 billion, respectively—amounting to \$39,810 billion in total indirect costs.⁵⁰

Relatively recent results from an evaluation of the health economic benefit of improvement in glycemic control in patients with type 2 diabetes point to significantly favorable health economic outcomes in the form of higher retained employment, greater productive capacity, decreased absenteeism, fewer bed-days, and fewer restricted-activity days.⁸⁸ The savings realized in the study were \$304 per 1,000 person days for bed-days and \$1,615 per 1,000 person days for restricted activity days. It has also been shown that diabetes medication in general contributes to large savings in terms of work days for employees with the disease, with an average of 16 days saved because of treatment, taking compliance rates into account.⁹¹ This translates into a net savings to employers of \$1,475, in 1996 dollars. Additionally, individuals on blood glucose-lowering agents who are able to achieve better glycemic control have been demonstrated to have fewer physical symptoms and enhanced well-being,⁹⁴ as well as having a significantly reduced risk of having cardiovascular and microvascular complications,^{95,96} although the risks of hypoglycemia must be balanced against the benefits of tight control.⁵⁷

Evidence points to the value of early intervention and tight glycemic control in helping to delay or reduce the long-term consequences of diabetes, and significant research has been aimed at describing and identifying interventions that

could accomplish these goals.^{81,84,89,97,98} Because the cost of complications may greatly increase the costs of health care utilization for individuals with diabetes,⁷³ one focus of interventions is on the prevention and management of such complications. Research has suggested that interventions aimed at preventing one individual's complications related to renal disease would result in total economic savings of \$60,000 over three years.⁸¹ In the management of type 2 diabetes and in the avoidance of complications leading to both direct and indirect costs, oral medications play an integral part.^{97,98}

Heart failure

The lifetime risk of developing heart failure for both men and women has been estimated at 20% (1 in 5).⁹⁹ While heart failure is most prevalent in people over the age of 65 years, prevalence in the 55–64 year age range is 3% for women and 5% for men.¹⁰⁰ Risk factors associated with early onset of heart failure (such as obesity, high blood cholesterol, and hypertension) are on the rise in working adults (35–64 years old), raising concerns of increased incidence of heart failure in younger people.

The total direct costs of heart failure are predicted to exceed \$22.1 billion in 2003.¹⁰¹ While total costs include the costs of hospitalizations, physicians' office visits, nursing home stays, home health care, and pharmacotherapy,¹⁰¹ the main cost drivers are frequent hospitalizations and readmissions.¹⁰² Readmission costs account for almost 30% of total inpatient care costs.¹⁰³

In his discourse on the economic burden of heart failure, O'Connell¹⁰⁴ estimates that “. . . if pharmacologic and behavioral approaches were combined (in the management of the condition), the five-year mortality rate could be reduced by as much as 50 percent.” There is no cure for heart failure. The goals of treatment are to relieve symptoms, enhance functional capacity, and improve survival, while reducing costs related to hospitalizations.¹⁰⁵

Impact of heart failure drug therapy on health care utilization and direct costs. Reducing the rate of hospitalization and readmission is recog-

nized as the key to decreasing the cost of care for heart failure.¹⁰⁶⁻¹⁰⁹ Multiple clinical trials suggest that use of appropriate drug therapies may be the most effective way to reduce the cost of care while reducing morbidity and mortality: Drug therapies can reduce hospitalization from 12% to 35%, depending on the agent.¹¹⁰⁻¹¹² Drugs like angiotensin converting enzyme (ACE) inhibitors and beta blockers have proved not only to slow the pathophysiological processes involved in heart failure, relieve symptoms, and improve survival, but also to reduce hospital days and readmissions in all stages of heart failure.¹¹³⁻¹²⁵ In fact, ACE inhibitors, beta blockers, diuretics, and digoxin have recently been recommended as first-line pharmacotherapy for heart failure by the American College of Cardiology and the American Heart Association.¹¹⁵

ACE inhibitors have demonstrated a potential net savings of \$36 million due to reduction in hospitalization.^{113,126} For instance, the ACE inhibitor ramipril has been shown to decrease heart failure hospitalizations by 12%.¹¹¹ The SOLVD trial demonstrated that the enalapril group had a 26% reduction in the risk of death or hospitalization for worsening heart failure compared with the placebo group.¹²⁷ One cost consequence analysis, based on clinical trial results,¹²⁸ has shown that use of the ACE inhibitor fosinopril achieved an overall cost savings of \$1.6 million per 1,000 patients.^{129,130} Another study, a cost-effectiveness analysis of the ACE inhibitor captopril for heart failure patients, using SAVE data, found that use of captopril therapy resulted in a cost per life year saved of \$1,460.¹³¹

The literature also contains a number of compelling studies describing the impact of beta-blocker therapy on utilization, overall medical costs, and survival of patients with heart failure. Clinical trials have demonstrated that carvedilol therapy reduced mortality by 65% and hospital admissions by 22%, and reduced overall costs of care by approximately \$14,530.¹³²⁻¹³⁴ A study using data from the US Carvedilol Heart Failure Trials Program has also shown that carvedilol reduced the risk of hospitalization for any reason by 29%, the risk of cardiovascular hospitalization by 28%, the risk of heart failure hospitalization by 38%,

and the mean number of hospitalizations for heart failure by 53%.¹³⁵ These studies have also documented that the cost per life-year saved for carvedilol was \$29,477 under limited benefits assumptions and \$12,799 under extended benefits assumptions.¹³⁶ A number of other studies have similarly demonstrated the effectiveness of beta-blockers carvedilol and bisoprolol in reducing the rate of hospitalization and the cost of care.^{120,133,137-139}

A common problem in the care for patients with heart failure is the underprescription and underuse of appropriate drugs such as ACE inhibitors and beta blockers.¹⁴⁰⁻¹⁴⁴ For instance, only slightly more than 50% of heart failure patients receive ACE inhibitor therapy, while patients at all levels of severity should be receiving it.¹⁴⁴ Therefore, an objective of cardiovascular quality improvement and disease management programs should be to increase the use of such life-saving and cost-effective treatment regimens.

The impact of heart failure on workplace productivity. The published literature on the impact of heart failure on workplace productivity is limited. This may be attributable in part to the relatively new science of productivity measurement, and to the significantly higher prevalence of diagnosed heart failure in the older, non-working population. In a 2001 report¹⁴⁵ the National Committee for Quality Assurance (NCQA) applied its economic model to estimate the number of working people with heart disease who are enrolled in health plans that provide Health Plan Employer Data and Information Set (HEDIS[®]) data (also see <http://www.ncqa.org>). The NCQA compared the indirect costs associated with heart failure for its accredited health plans (that is, health plans that meet minimum treatment standards for heart disease) and non-accredited health plans. They reported that, for a population of 1,248,304 workers with heart disease (based on prevalence data), a total of 2,917,000 missed or unproductive workdays were avoided and \$501,000,000 in sick-day wages was saved by the accredited health plans that provided the appropriate outpatient treatments for patients diagnosed with heart disease.¹⁴⁵

Migraine

Migraine headache is a highly prevalent¹⁴⁶ chronic condition, which manifests as acute episodes. Migraine is frequently misdiagnosed¹⁴⁷ and undertreated.¹⁴⁸ The prevalence of migraine headache is three times as high for women as it is for men (18% vs. 6%).¹⁴⁹ The highest prevalence of migraine occurs between ages 25 and 44 years, a time when many women are highly productive in their professional career, family responsibilities, and social life.¹⁴⁹

The direct and indirect costs of migraine headache in the United States are significant. In 1994, the associated health care costs for migraine headache were approximately \$1 billion.¹⁵⁰ Estimates range from \$17 billion in 1986 to \$13 billion in 1994 for annual losses associated with lost workplace productivity secondary to migraine headache.^{150,151} A 1998 survey comparing patients with and without migraine found that over a 6-month period, patients with migraine had higher direct medical costs (by \$107), due largely to greater frequency of physician and ED visits, and greater lost productivity, for a total incremental 6-month cost of migraine of \$313.¹⁵² Another study estimated the annual employer cost of migraine associated with lost productivity at \$3,309 per migraine.¹⁵³

Fortunately, significant advances have been made in migraine pharmacotherapy, with the availability of the triptans, a class of drugs introduced in the 1990s. A large number of studies have demonstrated improvement in patients' health-related quality of life¹⁵⁴⁻¹⁶¹ and reductions in patients' lost workplace productivity associated with initiation of triptan therapy.^{155-157,162-164} These improvements are clearly of importance to the individual with migraine headaches. However, employers and health care purchasers would be interested in knowing whether the benefit(s) of a migraine-specific medication (ie, decreased medical costs, decreased lost workplace productivity) are greater than its associated costs, thus potentially offsetting the cost of migraine therapy and producing a net benefit from the employer's economic perspective.

Impact of migraine drug therapy on health care utilization and direct costs. A recent literature re-

view by Caro and Getsios¹⁶⁵ demonstrates that a large number of investigations have examined the impact of triptan therapy on health care use and the associated direct costs of individuals with migraine headache. Most of these studies specifically evaluated sumatriptan, the first commercially available triptan, and a widely used migraine pharmacotherapy, although several other triptans have since become available. The majority of investigations have demonstrated that sumatriptan therapy is associated with reductions in health care use. For example, a prospective, observational study examining the change in health care use of 178 patients with migraine in a managed care organization found significant decreases in the mean number of physician office visits, ED visits, and medical procedures in the six months after sumatriptan therapy was initiated.¹⁶⁶ Because the triptans are more expensive than traditional non-triptan therapies, some studies have indicated that net direct medical costs may increase following initiation of triptan therapy. However, these studies generally have not considered the non-medical and indirect cost savings associated with improvement in appropriate management, and reduction in medical utilization.

The impact of migraine on workplace productivity. Many studies have demonstrated that triptan therapy is associated with reductions in time lost from work and non-work activities, and their associated indirect costs.¹⁶⁵ In an investigation examining the differences in time lost from work and non-work activity before and after the initiation of sumatriptan therapy, Lofland et al¹⁶⁶ showed that, on average, the number of workdays missed due to migraine decreased by 0.5 days and 0.7 days in the three and six months, respectively, after starting sumatriptan. In addition, individuals reported working on average four days with migraine symptoms in the three months before starting sumatriptan, but six months after the initiation of sumatriptan this had decreased to two days. A cost-effectiveness and cost-benefit analysis of data from this study¹⁶⁷ showed an overall net cost savings after sumatriptan therapy initiation of \$1,249, and an incremental cost-effectiveness ratio of \$25 for each additional mi-

graine-disability-day avoided. Biddle et al¹⁶⁸ demonstrated through a decision tree analysis an annual incremental net benefit of sumatriptan over usual therapy of \$114–\$540 per patient, with the higher costs of sumatriptan (in comparison with usual therapy) being offset by reductions in health care use and lost productivity. Other researchers, including Caro et al,¹⁶⁹ have demonstrated similar net savings.

DISCUSSION

Four chronic conditions were considered in this literature review, which sought to summarize key published studies on the epidemiology and economic impact of these conditions, with a focus on the economic impact of pharmacotherapy on total direct medical cost and workplace productivity. Care guidelines for asthma, diabetes, heart failure, and migraine all emphasize the critical role of pharmaceuticals in managing these conditions. This review provides support for the role of pharmaceuticals in managing clinical, humanistic, and economic outcomes.

These findings may be helpful to employers who are considering offering a pharmacy benefit or restructuring existing benefits. This review did not investigate the extent to which different levels of benefits (eg, tiered benefits with different levels of co-payments) foster or impede the likelihood that patients will be prescribed appropriate therapy, and will fill prescriptions and adhere to provider recommendations. However, we do demonstrate that the literature suggests a consistent benefit to employers—in regard to both direct medical cost savings and avoided losses to workplace productivity—in making appropriate pharmacotherapy available to employees (at least for these four prevalent and costly chronic conditions).

The findings are limited to published studies. It is possible that “publication bias,” in which only findings in favor of certain medications get published, overestimates the contribution of pharmacotherapy to cost management for the four conditions studied. This review also focused on key studies with measurement of economic outcomes; it is possible that some relevant studies either were not iden-

tified through this review or that economic data in contrast with the findings cited above were not included in the review. However, all relevant identified articles, whether they supported or refuted the hypothesis of the economic benefit of appropriate pharmacotherapy, were reviewed and are cited as appropriate. The focus of this review also was on the *appropriate* use of pharmacotherapy. Real world effectiveness and cost-effectiveness may be mitigated by patient adherence and other factors that may be encountered less frequently in the research environment. The cost savings associated with appropriate pharmaceutical use also are sensitive to changes in drug pricing. Furthermore, few of the studies discussed examined utilization and costs in the long term, beyond one or two years. Despite these concerns, a large majority of published evidence makes a compelling case for the potential economic benefit of appropriate pharmacotherapy in accordance with current care guidelines.

Finally, much research remains to be done to better establish the linkages between pharmacotherapy and workplace productivity. The science of productivity measurement is still developing, and controversy about which approach is most appropriate (eg, human capital, friction cost, or other approaches) continues. Measurement of presenteeism also is a developing field. The early evidence identified in this literature review suggests direct relationships between appropriate drug use and workplace productivity, but additional high-quality studies are needed.

CONCLUSIONS

The findings of this review strengthen the arguments for appropriate pharmacotherapy as a cornerstone for disease management efforts. Employers should be concerned with ensuring that employees have access to needed medications, and are educated and supported so as to be adherent to provider recommendations. Appropriate pharmaceutical agents help to counter the detrimental effects of chronic conditions on patients, thereby improving health status, reducing utilization of higher cost health care resources, and decreasing time lost

from workplace productivity. The evidence suggests that increased costs for disease-specific pharmaceutical therapy, in accordance with current care guidelines, may be offset by savings in a combination of direct and indirect medical costs.

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