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Chapter 5

Societal Burden of the Headache

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Headache is almost a universal experience in that it affects most people at some stage in their lives. Nevertheless, the impact of a headache attack or the headache disorder on the individual and society vary significantly from one person to the next. The individual burden of headache is measured by the degree of pain and suffering, and by the health consequences of the disorder. On the other hand, the burden of headache on society is assessed through cost-of-illness studies, which quantify resources and costs resulting from a disease, which can be complemented by cost-effectiveness evaluations that assess the economic impact of different treatment strategies. Understanding the economic costs of headache to society facilitates informed resource allocation in the overall research and management of the condition. Furthermore, cost-effectiveness analyses allow decision making on the differential, and potentially preferential, funding of specific therapies.

This chapter focuses on the economic costs of headache to society, including medical resource use, lost productivity, and other direct and indirect costs of illness. To date, most published cost-of-illness studies have focused solely on migraine as the prototype primary headache, although tension-type headache is almost five times more prevalent (10). Therefore, the cost estimates presented in this chapter apply mostly to migraine, but we also describe the limited information that is available on resource use and productivity impact of other headaches.

DEFINITION AND METHODS

The costs of an illness are generally defined as follows:

- Direct costs relate to the management and treatment of the disease and cover costs incurred to the healthcare system, social services, patients, or their families.
- Indirect costs are those resulting from the loss of productivity caused by the disease. These can be a consequence of lost working days (absenteeism), reduced productivity while at work (presenteeism), unemployment because of the disease, early retirement, or premature death. Indirect costs may also include social drift; however, to our knowledge, no such data exist for headache.
- Intangible costs relate to patients' suffering and reduced quality of life from the disease.

To assess the burden of migraine to society, cost-of-illness studies using a societal perspective should be used. In terms of specific costs, direct medical costs and indirect costs due to absenteeism and presenteeism are most relevant for this condition. Impaired quality of life from headache is covered in detail elsewhere in this book.

There are several different methodologic approaches to cost-of-illness studies. Concerning the patient population, a study can be prevalence- or incidence-based. In the prevalence-based approach, all costs for patients with the condition incurred during a given time period, generally 1 year, are included. In the incidence-based approach, in contrast, the lifetime costs for patients first diagnosed in a given year are calculated. The first type of studies are useful for budget and planning decisions, and the latter are more suited for estimating the effect of treatment on future costs. Because of the recurrent nature of most headaches, prevalence-based studies are more relevant for this condition.

Depending on the data sources used, a cost-of-illness study can be described as top-down or bottom-up. *Top-down studies* draw on statistical databases and registries, and *bottom-up studies* collect costs directly from a sample of the patient population. The latter approach can be applied either prospectively by following the sample for a given time period or retrospectively by gathering information about resource use through patient charts and questionnaires.

For this overview, published journal articles covering costs of headache and migraine, using the International Headache Society (IHS) criteria, as well as productivity and employment aspects were reviewed. Although a fair number of studies has been conducted regarding the resource use relating to and the general impact of migraine

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and other headaches, only a limited number of studies have reported direct and indirect costs for migraine. As far as possible, studies with a societal perspective and based on the IHS criteria were used. One of the cost studies listed in Table 2, however, does not entirely fulfill these criteria. The direct costs in the study by Hu et al. (8) were based on medical claims data from an insurance database of over 40 employers, which may not be representative of the whole migraine population in the U.S. Although the U.S. study by Osterhaus et al. (18) is often quoted in cost-of-illness reviews, the patient population was drawn from a clinical trial, which is likely to lead to an overrepresentation of moderate and severe patients. Indeed, the estimated costs per patient in this study are very high and lie well above the range of other estimates available for the United States and other countries. Therefore, for the United States, only the costs derived by Hu et al. are used in this overview.

HEALTHCARE RESOURCE UTILIZATION CAUSED BY MIGRAINE AND OTHER HEADACHES (DIRECT COSTS)

The direct costs of an illness are those incurred in diagnosing and treating the condition (Table 5-1). Migraine has a significant impact on direct costs, which is illustrated by the fact that migraineurs are more likely to consult general practitioners than nonmigraine age- and gender-matched controls. Based on an analysis of U.S. medical claims data from 1989 and 1990, migraineurs had 1.7 times the number of medical claims compared to controls, 4 times the number of emergency department (ED) visits, and nearly 2.5 times as many pharmacy claims (4). A recent hospital survey in the United States indicates that 2.4 million of 90 million ED visits are headache related, representing 2.6% of total ED visits (National Hospital Ambulatory Medical Care Survey 1999; available at: www.cdc.gov/nchs). In other words, headache is the fourth most common cause of ED visits in the United States.

Estimates of the direct cost of headache vary widely, and tend to be based on migraine data (Table 5-2). In population-based European studies, the 2003 scaled direct annual cost of migraine per patient ranged from $33 in Germany (17) to $243 in Spain (2). In the United States, the comprehensive analysis of a large medical claims database yielded an annual cost of $59 per patient, with women contributing over 80% of the total direct costs (8). By comparison, studies that have evaluated the direct cost of migraine in clinical trial participants result in significantly higher figures (e.g., $817 per patient per year [18]). There are several reasons that account for the reported discrepancies in the estimated direct costs of migraine, including the following:

- *Patient population.* Some studies have estimated the direct cost based on data obtained from participants in clinical trials, clearly leading to an overestimate of costs, because these patients are likely to represent the more severe migraine segment.
- *Cost ascertainment.* For example, the estimate from The Netherlands (28) based the number of outpatient visits on a pilot study where hospital representatives and neurologists were interviewed, which might introduce an element of recall bias. Furthermore, most direct cost estimates are based on top-down calculations, which in turn may lead to underestimation. The only exception to this approach is the French bottom-up study by Michel et al. (14).
- *Time period of study.* Estimates of direct yearly cost of migraine are not constant over time. For example, IMS Health data suggest that U.S. migraine medication sales were almost 10 times higher in 1996 and 1997 ($700 million) than in 1993 ($86 million).
- *Definition of direct cost of illness.* For example, Hu et al. (8) included acute migraine medications, in- and outpatient visits, and diagnostic testing for migraine in their calculation of direct costs. Over-the-counter medication use, alternative treatments such as physical therapy or acupuncture, and preventative medications were not taken into account. On the other hand, Michel et al. (14) and van Roijen et al. (28) included the cost of complementary/alternative therapies in their estimates of the total direct cost of migraine.
- *Confounding costs.* For example, Clouse and Osterhaus (4) did not differentiate migraine from nonmigraine medical costs. Because comorbidity is significant in migraineurs, the high direct cost of migraine that Clouse and Osterhaus reported may be an overestimation.
- *Geo-cultural differences.* The use of healthcare resources may vary among countries. For example, complementary therapies may be more commonly used in Europe than in the United States.

TABLE 5-1 Contributing Factors to the Direct Cost of Headaches

Outpatient visits
Inpatient visits and hospitalizations
ED visits
Prescription and nonprescription medications
Diagnostic testing (e.g., CT scan, MRI, LP)
Complementary and alternative treatments (e.g., herbal therapy, physical therapy, biofeedback)

Abbreviations: CT, computed tomography; ED, emergency department; LP, lumbar puncture; MRI, magnetic resonance imaging.

The effectiveness of headache management strategies with respect to the medical cost of migraine has been the focus of several recent publications (e.g., Silberstein et al. [23], Adelman et al. [1], Williams [30], and Goldfarb

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TABLE 5-2 Total Direct Medical Costs of Migraine per Patient and Year[a]

Country	*Total Direct Medical Costs*	*Hospitalization*	*Drugs*	*Outpatient Care*	*Medical Procedures and Devices*	*Reference*
France	76	21	15	24	16	Michel et al. (14)
Germany	33	5	15	13	n/a	Neubauer and Ujlaky (17)
The Netherlands	78	2	7	67	1	Van Roijen et al. (28)
Spain[b]	243	50	28	165	n/a	Badia et al. (2)
U.S.[b]	59	8	17	33	n/a	Hu et al. (8)

[a]US$, scaled to 2003 Prices.
[b]Not including OTC drug costs; ED visits included under hospitalization costs.

et al. [6]). Silberstein et al. (23) retrospectively reviewed information stored in a U.S. health use database. A period prior to the use of preventive drugs was compared to a period when patients were prescribed a prophylactic therapy. In addition, patients were eligible only if they were using sumatriptan for acute treatment. The authors' results suggested that the cost of acute medications and total healthcare costs are reduced when preventative therapies are used. These data, when recalculated to account for the cost of preventative therapy, indicate that cost reduction on prophylactic agents is highest with generic treatments such as amitriptyline and propranolol (1). Cost improvement with valproate is observed beyond 6 months of treatment in high-end sumatriptan users. Williams et al. (30) used data from a clinical trial to project the differential effect of stepped versus stratified care on total direct migraine cost in the United Kingdom. Stratified care was estimated to reduce the medical cost of migraine by approximately £5 per patient per year, which is a substantial number given the high prevalence of the condition. Last, Goldfarb et al. (6) reviewed medical claims in a health maintenance organization in the United States and found that limiting the monthly use of sumatriptan reduced the total prescription drug cost, but did not have any significant influence on the monthly total direct cost of migraine.

PRODUCTION LOSS CAUSED BY MIGRAINE AND OTHER HEADACHES (INDIRECT COSTS)

Considerations for Measurement and Valuation of Indirect Costs

Two key measures relevant for the assessment of the indirect costs of migraine and other headaches are absenteeism and reduced productivity when working with headache symptoms (presenteeism). Although absenteeism is a relatively common concept in cost-of-illness studies, reduced productivity can be less apparent and more difficult to quantify. For migraine and other headache patients, however, costs resulting from reduced productivity often constitute the major indirect cost, with more lost work days resulting from this than from work absence. There are two major methodologic challenges inherent to the assessment of workplace productivity: choosing an appropriate measurement and a valuation method. The chosen approach can have a significant impact on the resulting cost estimates, which, for example, was illustrated by a comparison of different methods in the study by van Roijen et al. (28).

Measurement of affected work days can either be performed retrospectively or prospectively. A retrospective design may introduce recall bias into patients' estimates, and results are often sensitive to the length of the recall period. This problem can be avoided by choosing a prospective design, where patients record work performance on a daily basis. To achieve as objective estimates as possible, however, such an approach would need to be complemented by independent assessments, for example, by supervisors, or by using defined output parameters to generate a comprehensive assessment of headache impact on work performance. In addition to the issues of recall bias and objectivity, the calculation method for the number of work days lost because of reduced productivity can have a considerable impact on results. The following variations illustrate the major approaches that have been used:

- The estimated days at work with migraine/headache symptoms are multiplied by patients' self-assessed level of performance. This approach has been used in a large number of studies and is sometimes also referred to as using lost work day equivalents.
- The estimated number of hours worked with migraine/headache symptoms are multiplied by the number of attacks per month and patients' self-assessed level of performance. This was used, for example, by Osterhaus et al. (18), who suggested that the method is likely to have underestimated the impact on work productivity in their study because the lower estimate of time lost per week was scaled up to 1 month. On the other hand, as van Roijen et al. (28) pointed out, this method can also imply that all attacks occur during working hours, which in turn leads to an overestimation of indirect costs.

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TABLE 5-3 Impact of Migraine and Other Headaches on Work Absence and Productivity[a]

Country	Work Absence (Days/Year)	Lost Time Due to Reduced Efficiency (Days/Year)	Efficiency Level During Migraine (%)	Reference
France	2.2	N/A	N/A	Michel et al. (16)
The Netherlands	3.2	2.7	72	Van Roijen et al. (28)
U.K.				Cull et al. (5)
Men	1.5	4.1	58	
Women	2.1	4.6	56	
U.S.				Stewart et al. (27)
Men	3.8	N/A	42	
Women	8.3	N/A	34	
U.S.				Schwartz et al. (21)
Migraine headache	3.2	4.9	N/A	
Tension-type headache	0.3	1.2	N/A	
Other headaches	1.6	4.9	N/A	
U.S.				Von Korff et al. (29)
Migraine headache (IHS 1.1, 1.2)	2.8	3.0	41	
Migraineous headache (IHS 1.7)	1.0	1.9	28	
Other headaches	0.5	2.9	24	
Average	2.5	3.4	44	

[a]Unless otherwise indicated, figures refer to migraine only.

- Patients' estimates of the additional hours they should have worked during the past 2 weeks to make up for productivity losses; working with a headache were used by van Roijen et al. (28). This approach yielded considerably lower results than the two described previously, but was deemed by the authors to be the most direct and thus reliable estimate.

Another issue that applies to all cost-of-illness studies is the valuation of lost work days and productivity. There are two possible approaches to this, the human capital and the friction cost method. The human capital method, which is most commonly used, values lost productivity using gross earnings. This approach does not capture lost opportunity costs or income related to career advancement. The friction cost method, on the other hand, uses the time it takes a company to adapt to the productivity loss caused by a sick employee as a valuation basis. This often results in lower cost estimates than the human capital approach, is related to some estimation difficulties, and introduces the potential for additional bias. In the case of migraine and other headaches, the two methods should not yield significantly different results, because work absence generally is quite short.

Different Components of Indirect Cost Caused by Migraine and Other Headaches

As mentioned, the two major indirect cost components for migraine and other headaches are from absenteeism and reduced productivity. An additional important aspect is the impact of headache on patients' labor force participation and social status. However, very few studies have dealt with this issue, probably because of the difficulty of valuing lost productivity arising from unemployment or missed employment opportunities.

Table 5-3 summarizes the impact of migraine and other headaches on work absence and productivity in terms of the number of days lost per year and the efficiency level when working during a migraine attack. On average, 2.5 days are lost per year because of absenteeism, and an average productivity level of 44% when working with migraine leads to the loss of an additional 3.4 days per year. The estimates vary across countries, which to a large extent depends on different methodologies. For example, the estimates by Michel et al. (15) for France and von Korff et al. (29) for the United States are based on prospective diary studies; the conservative estimates presented for The Netherlands and the United Kingdom are based on 2-week and 12-month recall periods, respectively. The costs by gender derived by Stewart et al. (27) are comparatively high because the study focused on the most severe headache attacks. In nearly all studies, reduced work productivity results in more work days lost per year than absenteeism, which is also reflected in the indirect cost estimates presented in Table 5-4. Depending on the study, reduced work productivity accounts for 40 to 90% of indirect costs, with a tendency to dominate costs resulting from work absence. Although not covered in existing studies, absenteeism of the spouse because of their partner's headache is a potential further

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TABLE 5-4 Total Indirect Costs of Migraine per Patient and Year[a]

Country	*Total Indirect Costs*	*Short-Term Absence From Work*	*Reduced Productivity at Work*	*Reference*
France	N/A	389	N/A	Michel et al. (16)
Germany[b]	973	564	409	Neubauer and Ujlaky (17)
The Netherlands	314	153	161	Van Roijen et al. (28)
Spain[b]	555	66	489	Badia et al. (2)
U.K.	595	175	419	Cull et al. (5)
U.S.[b]	702	416	286	Hu et al. (8)

[a]US$, scaled to 2003 prices.
[b]Based on productivity metrics from secondary sources.

indirect cost, which should be investigated further in the future.

The American Migraine Study II (11), a nationwide population-based survey from 1999, covered a range of migraine-related issues, including healthcare use and the impact of migraine on work, school, and household activities. According to this study, 31% of all migraine patients missed at least 1 day of work or school during the previous 3 months because of their headache. Moreover, the majority of migraineurs (76%) did not carry out any household work during a migraine attack. Fifty-one percent of respondents thought their productivity at work or school was reduced by at least 50% during a migraine attack, compared to 67% reporting similarly reduced productivity for household activities. In general, little research has been conducted on the impact of headache on unpaid labor. Van Roijen et al. (28) included time spent on household work in their analysis, but did not find any significant differences in time spent compared to controls. This result was probably a result of the retrospective measurement method, which was not sufficiently refined to quantify small differences between groups.

To assess the impact on work performance attributable specifically to headache rather than other causes, the concept of incremental absenteeism has been addressed in a population-based French study (15; for incremental resource use see Michel et al. [16]). Comparing work absence among migraineurs with a control group, the lost work days from causes other than migraine were assumed to be the same for both groups, with the remaining days being attributed to migraine. Overall, migraineurs were absent 2.2 days per year because of headaches, compared to 0.5 days in the control group. In addition, migraineurs were absent 9.0 days because of other medical reasons, compared to 7.3 days for controls. This study found that migraineurs have higher absenteeism rates than "average" workers, not because of their headache but because of other medical reasons, because they avoid taking sick leave during days with headache. To assess the incremental indirect cost of migraine without any comorbidities, such as depression or anxiety, a further control group would have been required.

Although most research on lost productivity has focused on migraine, some studies have also covered tension-type headache and other headaches (e.g., Schwartz et al. [21] and Von Korff et al. [29]). These studies suggest that migraine leads to a higher number of total work days lost per patient than other headaches, with the largest difference seen in the number of days absent from work (Table 5-3). However, when taking the prevalence rates into account, absence caused by tension-type headache is likely to have a larger societal impact. This is suggested by the results of a Danish population-based study (19), where the absence rate in the total population due to migraine was 5% during 1 year, compared to 9% for tension-type headache. In this study, tension-type headache led to three times as many lost work days as migraine: per 1000 persons, 820 work days were lost because of tension-type headache during 1 year, compared to 270 work days for migraine. Further research is required in this area to gain a more in-depth understanding of the impact of nonmigraine headaches on productivity. Overall, the existing evidence suggests that the burden of primary headaches is considerably larger than for migraine alone.

In general, indirect costs relating to lost productivity are based on patients who are employed. Few studies have examined the impact of headache on labor force participation. The existing evidence suggests that increasing severity is related to significantly reduced employment rates. Moreover, several U.S. studies have shown a higher prevalence of migraine in lower income than higher income groups, where income or education were used as measures of socioeconomic status (e.g., Stang and Osterhaus [24] and Stewart et al. [26]). However, this relationship has not been confirmed in studies from other countries (11).

Von Korff et al. (29) showed that patients with more frequent headaches worked significantly fewer days per week than those with less frequent headaches. For example, patients with up to 12 headaches over 3 months worked for an average of 3.8 days per week, compared to 2.9 days for those with more than 24 headaches per 3 months. This suggests that people with frequent headaches may not only

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lose more work days, but also have reduced labor force participation. Moreover, the 40% most severely affected migraineurs accounted for all lost work days owing to absence and around 75% of lost work days owing to reduced productivity. A similar correlation between pain intensity and lost work days has also been shown by Schwartz et al. (21).

A 2-year cohort study in the United States compared the employment status of 662 primary care patients suffering from headache with that of 1024 patients with back pain (25). Pain severity was grouped into five levels, which served to classify patients into good, mixed/fair and poor outcomes. Twelve percent of headache patients were unemployed at one or more of the three study interviews. Unemployment was highest at 25% among headache patients with poor outcome, compared to 7% for those with good outcome. The significant impact of outcomes on work-related disability is also illustrated by the proportion of patients unable to obtain or keep full-time employment at one or more of the study interviews owing to their headache: only 4% of those with good outcomes were negatively affected in their employment status, compared to 36% of those with poor outcomes. From a sociodemographic viewpoint, age, gender, and education were related to increased difficulty for headache patients in finding or maintaining full-time employment. Women, younger patients (18 to 24 years old), and those with lower education levels were more likely to have reduced labor force participation. Additional negative influencing factors included depressive symptoms and migraine headaches. Overall, the unemployment rates for headache were somewhat lower than for back pain, which tends to be of a more chronic nature and of longer term duration than headache. The results illustrate the considerable impact of headache especially on severe patients' employment status and opportunities, highlighting the need for development of targeted management strategies in this patient population.

The total indirect costs of migraine per patient are summarized in Table 5-4. Estimates range from $314 per patient per year in The Netherlands to $973 in Germany. These variations are to a large extent caused by differences in methodology. For example, in The Netherlands, the most conservative estimate for lost productivity was used, whereas the German estimate is based on gross domestic income for the economically active population rather than average income levels. If an average daily wage were used instead, the indirect costs for Germany would be approximately 50% lower. Available gender-specific data indicate that although women on average tend to lose more days of work because of migraine, the resulting indirect costs for women are similar to or even lower than those for men because of lower salary levels and proportionally reduced labor force participation among women.

IMPACT OF TREATMENT ON THE BURDEN OF HEADACHE

In the context of the societal burden of headache, it is of particular interest for decision makers to understand the impact that different treatment strategies have on the disease and its costs. The relevant methodology for this type of assessment is cost-effectiveness analysis, where two treatment alternatives are compared in terms of costs and outcomes. This is often done as part of clinical trials, where new therapies are evaluated in relation to standard care. In the area of migraine, cost effectiveness has become particularly relevant with the introduction of the triptans during the 1990s, which are more effective but also more expensive than older treatments. Most economic evaluations have been conducted for sumatriptan, and indicate that treatment with this product class is cost saving from a societal perspective, at least in more severely affected patients (3). In moderately and severely affected patients, the higher medical costs related to triptan use are offset by savings in terms of improved work productivity. In addition, selected studies have assessed the value of different management strategies for migraine.

In a prospective, observational outcomes study in the United States, both the cost effectiveness and the cost benefit of sumatriptan was analyzed from a societal perspective (12). Resource use and disability time at work and social activities for migraine patients enrolled in a managed care organization were collected during 6 months following the initiation of therapy with sumatriptan. Initiation of sumatriptan resulted in a decrease of disability owing to migraine from 28 days to 17 days per patient during the study period. Total medical costs were higher with sumatriptan therapy, because drug costs increased by $296 per patient compared to nontriptan therapy. This was offset by savings of $1516 per patient in terms of disability time and slightly reduced fees for physician and ER visits. Overall, the net cost saving to society was $1249 per patient following initiation of sumatriptan, corresponding to annual savings of $2498 per patient.

An international clinical trial compared the effectiveness of two treatment strategies for migraine in terms of headache response and disability time (22). The baseline strategy consisted of stepped care, where all patients initially received analgesics, and only moved on to migraine-specific therapy if they did not respond to first-line treatment. The second treatment strategy involved stratified care, where initial medication was based on an assessment of each patient's needs, meaning that those patients most severely affected during attacks generally received migraine-specific therapy. The clinical trial showed that stratified care, with zolmitriptan as the migraine-specific drug, was more effective than stepped care. Based on these study results, a cost-effectiveness analysis was performed for the United Kingdom, using prospective data from a

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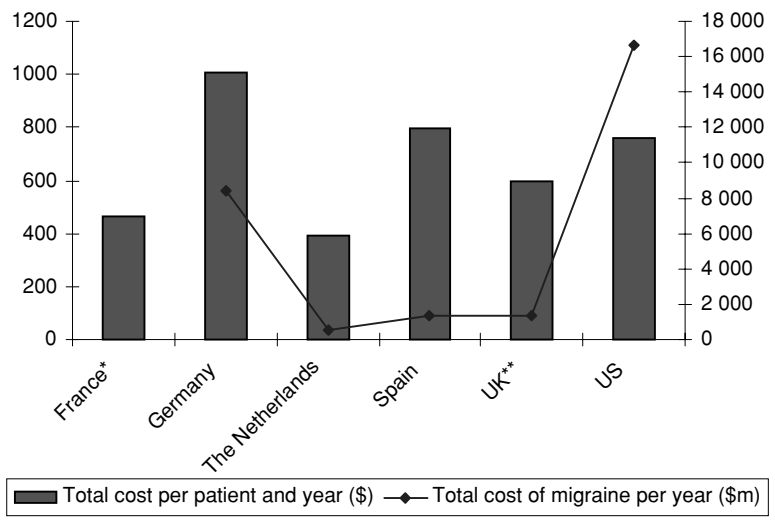

FIGURE 5-1. Total annual cost of migraine per patient and country, scaled to 2003 prices ($). *Not including the costs of reduced productivity. **Indirect costs only.

societal perspective. Although average healthcare costs were higher for stratified care, the average productivity costs were considerably lower, resulting in lower costs overall. Although these results were not statistically significant, stratified care had the highest probability of being cost effective.

CONCLUSION

Based on selected available estimates, the annual cost of migraine alone ranges from $400 to about $800 per patient (Fig. 5-1). Taking prevalence rates into account, this leads to estimated annual societal costs of $1.4 billion in the United Kingdom and $16.6 billion in the United States. The difficulty of comparing results across studies illustrates the need for a more standardized methodology for cost-of-illness analyses in this field. Ideally, such studies should capture every relevant cost item through population-based samples for all primary headaches.

The fact that indirect costs constitute the vast majority of societal costs of migraine and other headaches indicates that there is substantial room for improvements in the diagnosis and management of the condition. This also ties in with the findings of the 1999 American Migraine Study II (9), which showed that although the diagnosis of migraine has increased since 1989, about 50% of all migraineurs in the United States remain undiagnosed. Thus, the increase in consultation and diagnosis does not seem to have gone hand in hand with an increased use of prescription medication to treat migraine. This highlights the importance of increasing awareness of the issues surrounding migraine and other headaches both among patients and physicians, to enable more patients to receive and maintain optimal treatment. Smaller studies of headache programs in selected workplace settings suggest that active patient education and management can have a positive impact on resource use, work absence, and patient quality of life (e.g., Harpole et al. [7], Mannix et al. [13], and Schneider et al. [20]). Therefore, in the future, larger scale evaluations of the effectiveness of different management strategies need to be placed into the context of the overall costs of headache to society. The lessons that can be drawn from such findings can in turn facilitate a reduction of the burden of headache both on patients and on society.

REFERENCES

1. Adelman JU, Adelman LC, Von Seggern RL, et al. Does migraine preventive medication actually reduce resource utilization? *Headache*. 2003;43:1116–1118.
2. Badia X, Magaz S, Gutierrez L, et al. The burden of migraine in Spain: beyond direct costs. *Pharmacoeconomics*. 2004;22:591–603.
3. Caro JJ, Getsios D. Pharmacoeconomic evidence and considerations for triptan treatment of migraine. *Expert Opin Pharmacother.* 2002;3:237–248.
4. Clouse JC, Osterhaus JT. Healthcare resource use and costs associated with migraine in a managed healthcare setting. *Ann Pharmacother.* 1994;28:659–664.
5. Cull RE, Wells NE, Miocevich ML. The economic cost of migraine. *Br J Med Econ.* 1992;2:103–115.
6. Goldfarb SD, Duncan BS, Dans PE, et al. HMO direct costs and health care resources use after implementation of a monthly limit on sumatriptan. *Am J Health Syst Pharm*. 1999;56:2206–2210.
7. Harpole LH, Samsa GP, Jurgelski AE, et al. Headache management program improves outcome for chronic headache. *Headache*. 2003;43:715–724.
8. Hu XH, Markson LE, Lipton RB, et al. Burden of migraine in the United States: disability and economic costs. *Arch Intern Med*. 1999;159:813–818.
9. Lipton RB, Diamond S, Reed M, et al. Migraine diagnosis and treatment: results from the American Migraine Study II. *Headache*. 2001;41:638–645.
10. Lipton RB, Scher AI, Stewart WF. Overview of headache prevalence, burden, and management. In: Olesen J, Steiner TJ, Lipton RB, eds. *Reducing the burden of headache*. Oxford: University Press; 2003: 3–14.
11. Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*. 2001;41:646–657.

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GRBT050-05 Olesen- 2057G GRBT050-Olesen-v6.cls July 8, 2005 1:25

12. Lofland JH, Kim SS, Batenhorst AS, et al. Cost-effectiveness and cost-benefit of sumatriptan in patients with migraine. *Mayo Clin Proc*. 2001;76:1093–1101.
13. Mannix LK, Solomon GD, Kippes CM, et al. Impact of headache education program in the workplace. *Neurology*. 1999;53:868–871.
14. Michel P, Auray J-P, Chicoye A, et al. Prise en charge des migraineux en France: coût et recours aux soins. *Journal d'Economie Médicale*. 1993;11:71–80.
15. Michel P, Dartigues JF, Duru G, et al. Incremental absenteeism due to headaches in migraine: results from the Mig-Access French national cohort. *Cephalalgia*. 1999;19:503–510.
16. Michel P, Pariente P, Duru G, et al. MIG ACCESS: a population-based, nationwide, comparative survey of access to care in migraine in France. *Cephalalgia*. 1996;16:50–55.
17. Neubauer G, Ujlaky R. Migraine—a disease and its costs. *Pharm Unserer Zeit*. 2002;31:494–497.
18. Osterhaus JT, Gutterman DL, Plachetka JR. Healthcare resource and lost labour costs of migraine headache in the US. *Pharmacoeconomics*. 1992;2:67–76.
19. Rasmussen BK, Jensen R, Olesen J. Impact of headache on sickness absence and utilisation of medical services: a Danish population study. *J Epidemiol Community Health*. 1992;46:443–446.
20. Schneider WJ, Furth PA, Blalock TH, et al. A pilot study of a headache program in the workplace: the effect of education. *J Occup Environ Med*. 1999;41:202–209.
21. Schwartz BS, Stewart WF, Lipton RB. Lost workdays and decreased work effectiveness associated with headache in the workplace. *J Occup Environ Med*. 1997;39:320–327.
22. Sculpher M, Millson D, Meddis D, et al. Cost-effectiveness analysis of stratified versus stepped care strategies for acute treatment of migraine: The Disability in Strategies for Care (DISC) Study. *Pharmacoeconomics*. 2002;20:91–100.
23. Silberstein SD, Winner PK, Chmiel JJ. Migraine preventive medication reduces resource utilization. *Headache*. 2002;43:171–178.
24. Stang P, Osterhaus J. Impact of migraine in the United States: data from the National Health Interview Survey. *Headache*. 1993;33:29–35.
25. Stang P, von Korff M, Galer BS. Reduced labour force participation among primary care patients with headache. *J Gen Intern Med*. 1998;13:296–302.
26. Stewart WF, Lipton RB, Celentano DD, et al. Prevalence of migraine in the United States: relation to age, income, race and other sociodemographic factors. *JAMA*. 1992;267:64–69.
27. Stewart WF, Lipton RB, Simon D. Work-related disability: results from the American migraine study. *Cephalalgia*. 1996;16:231–238.
28. Van Roijen L, Essink-Bot ML, Koopmanschap MA, et al. Societal perspective on the burden of migraine in The Netherlands. *Pharmacoeconomics*. 1995;7:170–179.
29. Von Korff M, Stewart WF, Simon D, et al. Migraine and reduced work performance: a population-based diary study. *Neurology*. 1998;50:1741–1745.
30. Williams P, Dowson AJ, Rapoport AM, et al. The cost effectiveness of stratified care in the management of migraine. *Pharmacoeconomics*. 2001;19:819–829.