Introduction

Pharmacoeconomics is the application of conventional methods of economic evaluation to the use of medicines. The most basic application of economic assessment in health care is the cost of illness study (COI). The aim of cost of illness analysis is to evaluate the impact of a specific illness on a single patient or on society as a whole in monetary terms, by means of defining the problems involved in medical management of the illness and the consumption of collective resources. In this manner, it is possible to estimate the cost per patient per unit of time (generally one year) so that the total cost of the illness to society can be calculated with reference to epidemiological data. Depending on whether the data used regard the prevalence or incidence of the disease, this estimate can be static or dynamic in nature. The costs of the illness can be classified into direct, indirect and intangible costs. Direct costs comprise the expenditure incurred by the health care system in managing the disease; they measure, in monetary terms, the resources used during the phases of prevention, diagnosis, treatment and rehabilitation of the patient. Indirect costs are the production losses that arise through absence from work because of ill-health. Indirect costs are the costs related to the disease which do not incur direct expenditure and are defined as the variation of economic productivity; they comprise the costs related to loss of working days and reduced working proficiency caused by the illness in question. Intangible costs consist of the mental and physical consequences that the individual may suffer as a result of the illness; the former are related to pain, anxiety and the emotional impact of the illness on the
patient and his family. They are difficult to translate into monetary terms and rarely feature as financial values in cost of illness studies.

The definition of cost of illness has many advantages. In fact, it represents a useful aspect when deciding how to distribute available health resources and makes it possible to evaluate the relationship between the costs sustained and the benefits obtained in providing a specific service, as well as forming a basis for more sophisticated analyses of health expenditure/economical policy.

Migraine is an issue which still does not receive proper consideration and treatment. In fact, the economic impact of migraine on society is enormous, exceeding that related to asthma and comparable to diabetes. Migraine is a chronic disturbance characterized by attacks which may vary greatly from one patient to another in terms of both frequency and duration and may affect the patient during different periods of his life. Epidemiological data show that migraine affects subjects during the most productive period of their life; this is economically significant if one considers the consequent loss of productivity and remuneration. Furthermore, migraine has a high comorbidity rate. Especially if the attacks are frequent, migraine can have serious repercussions on the patient’s work and social life and can thus be considered an illness with high social costs, both in economic terms and in terms of quality of life.

The impact of migraine on society can be studied by means of cost of illness analysis, while the negative effects on the individual, such as impairment of social life and leisure activities, can be measured by evaluating the quality of life (QOL).

This paper only addresses the socio-economic aspects of migraine, not its impact on the quality of life of the patient, his family and friends.

**Direct costs**

Patients in primary care with headache cost at least 87% more to care for than their similar-age and same-gender counterparts without headache [1]. Patients with migraine exactly as much as 1.6-fold higher overall costs in comparison to patients without migraine [2].

Since education, screening and rehabilitation are not relevant issues, the costs of illness related to migraine principally regard diagnosis and treatment. The diagnostic aspect includes medical consultations, with both general physicians and specialists, utilisation of emergency room facilities, hospitalisation and treatment (medication and non-pharmacological treatment). For each diagnostic procedure, from the simplest to the most complex, associated with management of the disease, the working resources absorbed in terms of quantity and time (number of people employed and number of working hours or days consumed) are quantified and awarded a corresspective monetary value. Evaluation of direct costs is generally straightforward, since there is a market price for each activity involved in professional services or procedures. However, as things stand, it is still not possible to precisely quantify the direct costs of migraine because there is general agreement that a high percentage of migraineurs never consult a physician for their illness (between 19% and 44% in the various studies) and that only a small percentage (from 16% to 36%) regularly consult their physician [3–5]. Moreover, the majority of studies point out that results are difficult to compare because the utilisation of health care resources related to migraine is evaluated according to different methods in different countries. The greatest obstacle derives from the organisational differences that exist among national health care systems. However, international literature indicates that direct costs represent only a small percentage of the overall economical impact. In the U.S.A., expenditure amounts to 1 billion dollars per year and accounts for 8% of the total costs related to migraine [6]. It is interesting to note that the direct costs of migraine represent an almost negligible portion of overall health expenditure; in the U.K. they amounted to less than 0.1% of total National Health Service expenditure at the beginning of the 1990s, in the Netherlands 0.3% and in the U.S.A 1.3%. Several studies have shown that in North America, the percentage of migraineurs who have utilised emergency room facilities at least once (estimated between 14% and 18%) is higher, on average, than in European countries [7]. However, in the U.S.A. the costs related to this emergency room treatment were irrelevant, amounting to 0.13–0.34 dollars per year for each migraineur diagnosed [6]. An interesting observation is that the majority of migraineurs who sought emergency room treatment did so on a regular basis: a study based on a 5-month observation period showed that 36% of migraineurs were habitual visitors (mean, 4.2) [8]. In an urban teaching hospital in the U.S.A., 11% of 185 migraineurs accounted for 42.5% of visits [9]. Hospitalisation costs universally represent only a very small portion of total migraine management costs: the rate of hospitalisation is less than 10% and varies from 2% in Denmark to 7% in the U.S.A. [6]. In all the countries analysed, the costs of medical consultation accounted for the predominant part of direct costs of migraine. The majority of consultations were performed by general physicians while between 20% and 40% of migraineurs consulted a specialist: the specialist was a neurologist in 10% of cases. In France and the Netherlands, the specialists most frequently consulted were ophthalmologists and homeopaths [9, 10].

In monetary terms, the cost of medical consultation in the U.S.A. is 59 dollars and 54 dollars, respectively, for each migraineur diagnosed. Quite a substantial number of
patients seek help from non-pharmacological therapy; expenditure for this type of treatment was 106 million florins in the Netherlands, about 10-fold higher than the amount spent on medications. The amount spent on specialist visits was estimated to be 1.5 million florins [10].

The direct costs of treatment of a migraine attack include: eventual emergency room visit, cost of anti-migraine medication, cost of any “rescue” remedies (if the first drug proves ineffectual 2 hours after administration) and the cost of any medication required to treat side effects.

A very high percentage of patients with migraine only take non-prescription medication. In a recent Canadian study conducted on the general population, only 12% of migraine sufferers used medicines that required a prescription. In France, 15% of migraineurs used drugs given by family or friends. In this population-based study, only 17% of the migraineurs knew the name of at least one drug from a list of all migraine medications, and only 10% had actually tried one of them [9]. In the U.S.A., the annual cost of prescription medicines is estimated to be about 300 million dollars [6].

In Italy, little information is available regarding the direct costs of migraine. The largest recent study was M.E.T.E.O.R. (Migraine Epidemiology – Therapy and Economics: an Outcome Research Study) whose scope was to evaluate the quality of life in migraineurs and the economic impact of migraine on the consumption of resources, as well as the prevalence of migraine in the population as a whole. The study was carried out in 1998 by means of questionnaires issued to patients visiting general physicians throughout the country. Out of a total of 71,588 patients assessed, 8,293 complained of migraine. The direct cost factors considered were: out-patient visits, hospital admissions, diagnostic procedures and medications [11].

The number of visits performed in the sample examined was 2,115 amounting to a total cost of 68,795,000 million lire. Of these visits, 55% were out-patient in a general medical division, 8.6% home visits, 8% emergency room and 27.8% specialist. The average annual cost per patient was 96. There were 61 in-patients in the sample examined, amounting to a total cost of 216,408,000 million lire and an average annual cost per patient of 304,050 lire. However, the costs of hospitalisation account for 26% of the total, due to the high cost of admissions. As far as diagnostic investigations are concerned, 1,046 tests were performed for a total cost of 87,395,400 million lire: 54.1% of these were blood tests, 20.1% electroencephalograms, 17.3% plain X-rays of the head, 5.1% computed tomography (CT) or magnetic resonance imaging (MRI) of the brain and 1.5% plain X-rays of the cervical spine. The average cost per patient was 122,790 lire. The cost of anti-migraine medication was estimated as 57,708,086 million lire, of which only 0.8% was spent on anti-depressants, tranquillisers and preventive medication. The average annual cost per patient was 83,900 lire, of which only 720 lire for anti-depressants, tranquillisers and preventive medicines. These findings indicate that the great majority of medications are taken to treat the symptoms of a migraine attack and are similar to those described in a Canadian prevalence study which reported that between 6% and 12% of migraineurs have received prophylactic treatment [3].

By examining the overall data related to the direct costs of migraine management, the following considerations are possible: too many migraineurs do not seek medical advice, often preferring to cure themselves or not trusting the treatment advised by doctors; and there is a high tendency to drop out of follow-up after first consultations and to utilise emergency room facilities. On the other hand, it is clear that such patients find the response of medical staff, both general physicians and specialists, too often unsatisfactory. In Canada, Edmeads [12] studied the reasons why 65% of patients did not return to their primary care physician or neurologist: 55% were satisfied with the treatment and did not require further consultation, 38% were not satisfied with the consultation, because it was too hurried and because “they did not feel as if they were being taken seriously” and only 17% did not return because they experienced side-effects of the medication.

### Indirect costs

The indirect costs of migraine are determined by the economic evaluation of the loss of productivity. In fact, the symptoms of a migraine attack forced many migraineurs to stay away from work or to work at a reduced level of effectiveness. The number of hours lost as a result of a lower level of effectiveness is calculated by the product of the number of hours of work at reduced level of effectiveness multiplied by the percentage of effectiveness lost. The total number of working days lost is calculated by adding the number of days lost through reduced effectiveness to the number of days lost through absence. The obvious limit of this analysis is that, since the parameter adopted is the amount of working time lost by the migraineur, the economic evaluations may vary considerably according to the remuneration levels of the individuals considered and the type of work performed. For example, it is not easy to evaluate the economic aspect of loss of productivity of a housewife, student or writer. Reduced levels of effectiveness account for 70% of all the work lost: in fact, all the studies agree that the majority of days lost are not due to absence, but to a lower level of effectiveness while continuing to work during a migraine attack. Although evaluation of loss of productivity linked to migraine is extremely subjective, the residual level of effectiveness calculated in the various studies is fairly similar, between 56% and 72% [13].
Recent studies have demonstrated that, in European countries, the working days lost as a result of migraine vary from 1.9 to 3.2 per patient per year. In all the studies, regardless of nationality, women stay away from work more often than men. Stewart and colleagues [14] reported an average 7.4 working days lost (4.38 for men and 8.3 for women). This observation, dissimilar to other reports, probably derives from the fact that the migraine attacks considered were predominantly severe [14].

In the U.S.A. during a 3-month observation period, migraineurs lost an average of 1 working day from migraine, corresponding to 4 days per year, higher than in previous studies [15]. Work loss was not uniformly distributed among migraine sufferers but was directly influenced by the severity of the illness, evaluated in terms of intensity and frequency of the migraine attacks. In fact, 77% of the lost workdays were attributable to just 20% of the most severely affected patients [15].

Therefore, to optimise the cost/benefit ratio of treatment, the most expensive types of treatment should be administered to patients in whom migraine causes the highest grade of disability. It is well-known that migraine has a high comorbidity rate which may play an important role in the assessment of absenteeism in migraineurs [16]. This comorbidity manifests with symptoms related to pain, psychological disturbances or psychosomatic disease; the presenting symptom is often headache so that migraine sufferers are not always able to precisely identify the cause of their illness. Consequently, it is not always possible to distinguish between the number of days absent due to comorbidity and those due to migraine itself. Michel and associates [9], by employing the principle of incremental absenteeism (comparison of the number of days absent in migraineurs to those in a group of non-sufferers), found that the increase of absenteeism from illness in migraineurs, as compared to the control group, is not due to headache but to other health problems. The monetary equivalent of the loss of working productivity related to migraine, including days lost in absences from work and by loss of productivity, has been calculated in various studies performed in different countries. These figures are usually calculated using economic indexes and extrapolated to the total working population with migraine derived from estimates of the prevalence of migraine specific for sex and age. The extent of the range of the difference results depends on the different evaluation methods used, particularly the different remuneration levels and the exchange rates between different currencies.

Ferrari [7] took several estimates performed in different countries in the 1980s and early 1990s, and calculated them in relation to the value of the dollar in 1993. By doing so, he found that migraine was responsible for indirect annual costs of 32 million dollars in Sweden, 22 570 million dollars in Australia, 1.1 billion dollars in Spain and the U.K. and 1.2 billion dollars in the Netherlands [7]. In the U.S.A. the loss of productivity from migraine amounted to the equivalent of more than 12 billion dollars in 1998 [6]. The loss of working productivity obviously depends on the number of attacks, their intensity and duration. Therefore, the correct choice of treatment for each patient is also important in monetary terms. Rapidly effective treatment, without recurrences of migraine symptoms or side effects that require specific treatment or impair normal activities, reduces the costs of illness.

Triptans are highly effective drugs which are far more expensive than ergots and non-steroid anti-inflammatory drugs, but which are responsible for more frequent recurrences in comparison to other anti-migraine drugs. The cost/benefit to employers for the use of sumatriptan (the only triptan available at the time of the study [17]) was assessed: it brought about a reduction in the number of workdays lost from 2.75±3.03 to 0.8±1.64 (-71%) and a reduction in the number of workdays at reduced proficiency from 6.0±7.32 to 4.76±8.40 (-20%). Since the monthly cost of the drug was 43 dollars and the amount of money saved monthly by the employer 435 dollars, the benefit/cost ratio was 10 to 1. In a sample of 178 patients observed over a period of 6 months in the U.S.A., the use of sumatriptan reduced the number of medical consultations by 34% (general physicians) and also decreased (though not significantly) the number of emergency room consultations [17].

Conclusions

There is strong evidence that improvement in the management of migraine patients (early diagnosis and effective treatment) represents a significant intervention option not only for ensuring better quality of life for migraine sufferers but also for reducing the costs of this illness.

The social impact of migraine is mainly sustained by sufferers and their employers, whereas probably not more than 10% is sustained by the employment infrastructures. Undoubtedly, greater involvement of general physicians in management of patients with migraine, combined with more specific training for specialists, would not only increase the number of specialist health services available for the more difficult cases, but would ensure early diagnosis and proper treatment of migraine. Accordingly, early diagnosis and proper treatment would reduce the direct costs: less diagnostic tests and hospitalisation, less frequent migraine attacks as a result of preventive therapy and, therefore, less consumption of symptomatic drugs. On the other hand, it also seems clear that better patient education is necessary for prevention of migraine, encouraging patients to monitor their attacks and to vary the medication used according to the severity of the attack (stratified care).
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