The major aim of the paper is to give an epidemiologist’s viewpoint on several points related to the evaluation of the costs of migraine and to answer some questions that are important if one wishes to decrease the burden of this disease in the general population.

Migraine is a frequent and clear clinical entity with operational criteria, the International Headache Society criteria [1], accepted by the international scientific community, with (probably) a specific, even multifactorial, pathophysiology with (probably) a specific natural history and with (probably) a specific and effective treatment. Thus migraine is a good disease for neurologists, epidemiologists, economists, drug companies and health authorities.

In spite of these favourable criteria for the management of migraine, and for epidemiologic and economic studies, the relationship between migraine and cost is not so easy to study. The main reason is that this relation is not completely determinist, which is a condition for the validity of cost-of-illness studies.

Cost-of-illness studies consist of three components: direct costs, incurred mainly by the healthcare system in diagnosing and treating the disease; indirect costs, in terms of lost production owing to lost working days, diminished productivity resulting from illness or disability, or losses incidental to premature death; and intangible costs, such as pain, suffering, or reduction in quality of life. Many studies have been conducted with this approach. For instance, Hu et al. [2] calculated the annual direct cost of migraine to be US $1 billion in the United States, the annual lost paid workdays cost to be US $8 billion and the estimated reduced productivity cost an additional US $5 billion.

However, many factors interfere with the relationship between migraine and cost, even for direct costs which appear to be the most objective and easy to collect (Fig. 1).
patients with multiple co-morbidities, it is difficult to attrib-
ute these conditions to justify resorting to health care. Thus, in 
reported in migraineurs than in matched controls, and all 
cological and pneumological disorders are far more self-
anxiety, abdominal pain, constipation, diarrhoea, and gynae-
care settings. In fact, Packard [7] showed 22 years ago 
that nothing can be done against migraine [4] and 52% 
believe that orthodox medicine is not effective [5]. The atti-
side the cost. After 
a first consultation, many patients do not return to their 
physician or neurologist. Edmeads [6] analysed in Canada 
the reason: 55% of patients were satisfied with the treatment 
and did not need consultation again; 17% did not return 
because of problems with the medication; and 38% were 
turned-off by their doctors and considered that they were not 
taken seriously. In fact, Packard [7] showed 22 years ago 
that the major aim of a consultation of a migraineur is for 
this patient to obtain explanation and reassurance whereas 
the major aim of the doctor was to obtain pain relief.

Co-morbidity, which refers to the coexistence of two 
medical conditions with a frequency greater than chance, 
also interferes with cost. Psychiatric disorders, epilepsy and stroke are the well known co-morbidities of migraine [8]. But in fact many conditions are more frequent in migraineurs. In the MIGACCESS study [4] conducted with a face-to-face interview in a French representative national sample, we have shown that backache, fatigue, depression, anxiety, abdominal pain, constipation, diarrhoea, and gynaecological and pneumological disorders are far more self-reported in migraineurs than in matched controls, and all these conditions justify resorting to health care. Thus, in patients with multiple co-morbidities, it is difficult to attribu-
te a consultation with a general practitioner (GP) or a hospi-
talization to a single motive. In our opinion, these findings 
justify, in addition to cost-of-illness studies, a comparative 
approach between migraineurs and non-headache subjects to better appreciate the incremental cost related to migraine.

This comparative approach give some surprising results. In the MIGACCESS study, the comparison of use of health-
care services during a six-month period showed that in spite 
of multiple co-morbidities, migraine sufferers used only 
more GP consultations and complementary exams, but not 
the other healthcare services. After adjustment for comor-
biddies and social insurance, the differences between 
migraineurs and controls disappeared. By the same way, in 
the Gazel cohort, which is a French nationwide cohort of 
volunteers from EDF-GDF, the French power company that 
produces and supplies electricity and gas, we found no dif-
fences in absenteeism during four years of follow-up 
between migraineurs and controls after adjustment for age, 
gender and number of health impairments [9]. On the con-
trary, self-assessed performances at work were strongly 
impaired in migraineurs versus controls. The discrepancy 
between objective and subjective burdens implies that the 
public health impact of migraine is lower than that on the 
individual person. Migraineurs may “suffer silently” and 
work during migraine attacks. Another nonexclusive expla-
nation is that migraineurs may adopt a compensory coping 
strategy for health impairments other than migraine: since 
they miss work for their headaches, they may minimise their 
absences for other health impairments.

This latter explanation was rejected by the follow-up of the MIGACCESS cohort in which we could separate absen-
teeism due to headache and absenteeism due to other condi-
tions [10]. In this sample, the incremental absenteeism, 
defined as the mean annual absenteeism in the migraine 
sample minus that in the control group, was the same for 
migraine attacks than for other medical reasons. In fact, the 
results from the Gazel cohort could be related to the condi-
tions of work and of absenteeism in EDF-GDF, which is 
actually in France a public firm.

The comparative approach for the evaluation of the cost-
ing of migraine was recently applied in a context other than 
the French healthcare system by Edmeads and Mackell [11]. 
Using population-based survey data from the United States, 
they selected individuals with migraine and a migraine-free 
control group matched for age, sex, employment status and 
number of comorbidities. As in the MIGACCESS study, 
they assessed the prior six months’ direct medical care in 
terms of self-reported hospital days and emergency depart-
ment and physician visits. The results were a little bit differ-
ent from the French study since the differences between 
migraineurs and non-migraineurs were more pronounced 
for physician and emergency department visits and remained 
significant after matching for comorbidities. The same
trends were observed for the loss of productivity. The discrepancies between studies can be explained by different methodological approaches, in particular for the diagnostic criteria of migraine, but the differences between the French and the American healthcare systems and the belief of the efficacy of this system by the patients are certainly the more relevant explanations.

Another type of comparison may be useful to study the consequences of the progress in management of migraine on the burden of this disease. During the past ten years, many new treatments for migraine have become available, and the awareness of migraine has improved. In a disease with recurrent attacks, the efficacy of better treatment strategies can be associated with a decrease in prevalence of migraine due to a decrease in the duration of the disease. In fact, some studies suggested that the prevalence of migraine may be increasing [12], but the authors admitted that this increase could be related to better diagnostic management in primary care. Two recent prevalence studies, in the United States [13] and in France [14], conducted on national representative samples by telephone or by face-to-face interviews did not confirm this increase and showed exactly the same rates at 10-year intervals: 12.1% in 1989 and 12.6% in 1999 in US for migraine classified with the IHS criteria 1.1, 1.2 and 1.7 [1]; and 8.1% in 1990 and 7.9% in 2000 in France for migraine classified with the IHS criteria 1.1 and 1.2. In the French prevalence study, two characteristics of headache were compared at a 10-year interval (Table 1) according to the type of headache.

Interestingly, the intensity of pain decreased significantly in migraine, while it remained unchanged or even increased in other types of headache. On the contrary, the frequency of attacks remained unchanged whatever the type of headache. Taken together, these findings were in favour of a better management of attacks in migraine while the natural history of the disease remained unchanged. In the same study, we introduced the MIDAS score as a measure of indirect costs of headache [15]. In 2000, the proportion of migraineurs with MIDAS grades III and IV was 12.4%, which gives a prevalence of migraine requiring medical attention of 1.6%. Migrainous disorders have the same magnitude of consequences in terms of days lost due to headache (11.5% of grades III and IV), while other types of headache have far less consequences on this indicator (only 2.1% of grades III and IV). Thus in spite of some progress in the management of headaches, migraine remains in 2001 a disease with a major economic burden.

In the future, it will be crucial to take into account all factors interfering with the economic burden of headache (Fig. 1), if we wish to really decrease this burden. In our opinion, a good way is found in works such as the trial published by Lipton et al. [16] comparing stratified care versus step-care strategies for migraine, which controlled several of these factors.

### Table 1 Characteristics of headache in 1990 and 2000 in France, according to type of headache. GRIM I and II studies. Values are percentages of headache subjects

| Headache characteristic | Migraine 1990 | Migraine 2000 | Migrainous disorders 1990 | Migrainous disorders 2000 | Non-migraine headache 1990 | Non-migraine headache 2000 |
|-------------------------|--------------|--------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Intensity of pain       |              |              |                          |                          |                          |                          |
| Mild or moderate        | 23.0         | 37.5         | 44.3                     | 38.5                     | 69.0                     | 63.9                     |
| Severe                  | 57.0         | 39.8         | 43.8                     | 39.6                     | 26.0                     | 28.6                     |
| Very severe             | 20.0         | 7.5          | 10.9                     | 21.9                     | 3.0                      | 7.5                      |
| Frequency of attacks    |              |              |                          |                          |                          |                          |
| <1 per month            | 18           | 16           | 20                       | 21                       | 32                       | 35                       |
| 1 per month             | 31           | 36           | 28                       | 24                       | 23                       | 28                       |
| >1 per month            | 50           | 52           | 52                       | 55                       | 35                       | 27                       |

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