Development and validation of tools for the assessment of the burden and disease-management of headache disorders in Europe

Inauguraldissertation

zur
Erlangung der Würde eines Doktors der Philosophie
vorgelegt der
Philosophisch-Naturwissenschaftlichen Fakultät
der Universität Basel

von

Colette Marie ANDREE
aus Differdingen, Luxemburg

Basel, 2009

Genehmigt von der Philosophisch-Naturwissenschaftlichen Fakultät auf Antrag von:

Prof. Dr. Stephan Krähenbühl

PD. Dr. Peter Sandor

PD. Dr. Kurt Hersberger

Basel den 23. Juni 2009

Prof. Dr. Eberhard Parlow

Dekan

TABLE OF CONTENTS

1 Summary

Headache, including migraine, is a common and disabling neurobiological disorder which is under-recognized, under-treated, commonly mismanaged and it imposes a substantial health burden.

The principle aim of my dissertation was to review the existing data about these findings in order to develop and validate scientific instruments to improve the methodology and the scientific value of future headache impact studies on which headache disease-management recommendations at EU level will be based upon.

My dissertation's working objectives were:

- To review the literature published between 1988 and 2007 for studies reporting the prevalence and impact of headache disorders and new relevant review papers at European level from 2005-2007
- To develop and validate a first scientific instrument in a questionnaire format for gathering headache impact information from a representative multi-cultural population sample of migraine sufferers in Luxembourg
- To develop and validate a second instrument in a questionnaire format for gathering headache prevalence and impact information in a standardized way from headache sufferers in Europe.

In my first study I made a literature survey in order to summarize what is known on the subject, as a support for my future studies to assess the prevalence and impact of primary headache disorders in Europe with similar methodology and the same research instrument. The analysis revealed that according to a recent health economic survey in Europe migraine is the most costly among the neurological disorders. Several studies suggest that migraine and other disorders lead to widespread suffering, reduction of quality of life, and marked impairment of participation, both in work and social activities. Most studies have yielded

relatively reliable data only for migraine, whereas the impact of tension-type headache is virtually unknown or only very incompletely known for most dimensions of headache impact. Some data do suggest, however, that this headache may be as important from a health economic and a public health perspective as migraine.

These findings allowed me to analyze the gaps and to the collection of population-based data from various countries relevant for estimation of indirect (mostly absenteeism from work and reduced working efficiency when having headache) and direct costs (related to medication, consultations, investigations and hospitalisations). The impact on ability to get education and participate in the workforce should be taken into consideration as well as the impact on love life and family planning. To get a complete picture, one should also ask about the effect on the life of partners and children, and on the possible impact even when headache free (e.g. fear of the next attack). The quality of life of headache patients should be measured by validated instruments.

In my second study we developed and validated a 77-item-self reporting questionnaire to run a pilot study to assess the burden of migraine (BURMIG), including headache characteristics, migraine associated disability, comorbidities, management, and the consequences on the patients lives. We translated BURMIG into 4 languages (French, Portuguese, German and English) and tested it in 130 headache patients (20 from pain clinics, 17 from primary care doctors and 93 from the general public) in Luxembourg. We performed a linguistic and a face-content validation and tested the questionnaire for its comprehensiveness, internal consistency and for its test-retest-reliability at an interval of one month (completion rates were 79.6%, and 76,4%, for test and retest, respectively). Retest-reliability for the different parts of the questionnaire varied between 0.6 to 1.0 (Kappa coefficient), with an intracorrelation coefficient of 0.7–1.0. The internal consistency was between 0.74 to 0.91 (Cronbach's alpha).

These findings allowed me to propose the BURMIG questionnaire to evaluate the burden of migraine in the multicultural population of Luxemburg in four languages English, German, French and Portuguese.

Based on the results of my pilot study in Luxemburg with BURMIG questionnaire, we developed in my third study a 103-item-self reporting questionnaire (EUROLIGHT) to assess the burden of primary headache disorders on those affected by them including headache characteristics, associated disability, comorbidities, disease-management and quality of life. We validated the questionnaire in 5 languages with 426 headache patients (131 in UK, 60 in Italy, 107 in Spain, 83 in Germany/Austria, and 45 in France). After a linguistic and a face-content validation we tested the questionnaire for comprehensibility, internal consistency and test-retest reliability at an interval of one month. In the different countries, response rates were between 73% and 100%. Completion rates over 90% were 69% and 82%. Test-retest reliability varied between -0.27 to 1.0 depending of the nature of the expected agreement. The internal consistency was between 0.69 and 0.91.

These findings allowed me to propose the EUROLIGHT questionnaire to evaluate the burden of primary headache disorders at European level. It can be used in English, German, French, Italian and Spanish. Further language validations have already been done for Portuguese, Dutch and Lithuanian.

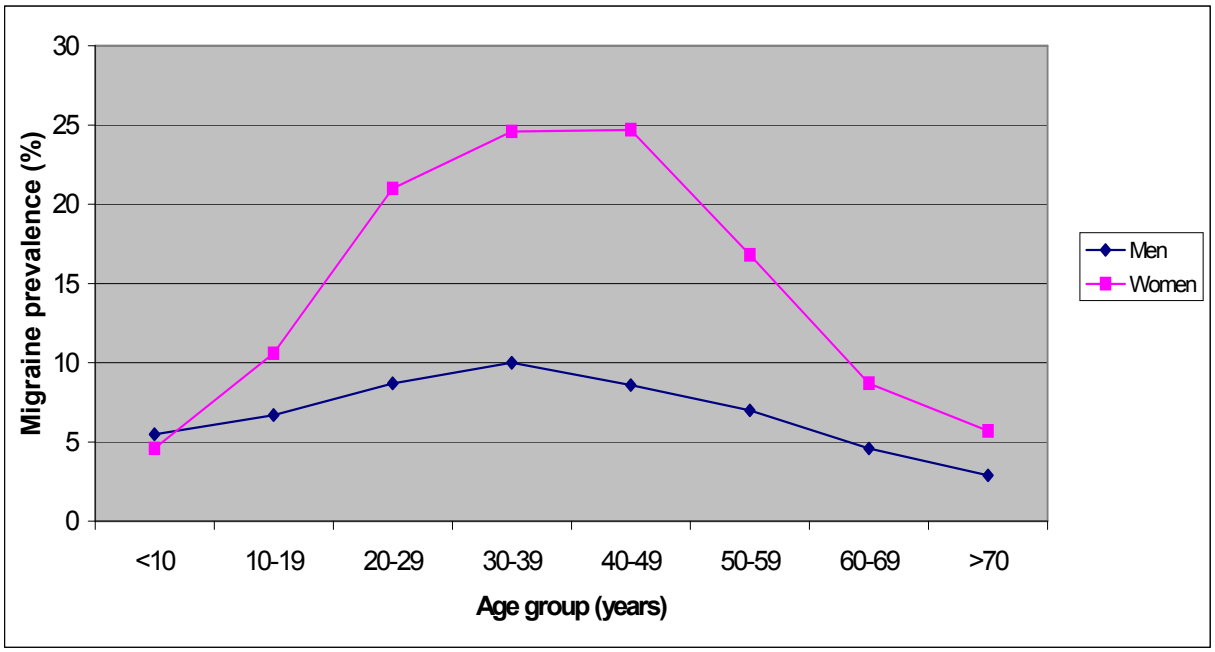
The studies show that primary headache disorders are disabling neurobiological disorders but under-recognized, under-treated and commonly mismanaged. With the support of major stakeholders we developed a first and then a second scientific instrument in a questionnaire format and we validated both instruments to gather qualitative as well as quantitative data that describe the clinical, economic and humanistic dimensions of primary headache disorders to produce systematic data to complement epidemiological evidence of the burden and disease management of primary headache disorders in Europe.

2 Introduction

2.1 Headache Disorders and Public Health

Headache is a symptom of a range of neurobiological disorders, including some of the most common and ubiquitous. Adults aged 20-50 years are the most likely sufferers [(1)] but children and adolescents are affected to [(2)]. The term headache disorder encompasses a number of conditions which vary in severity, incidence and duration. As a consequence establishing their overall prevalence has been difficult. Migraine is the more thoroughly investigated, and better understood, Onset of migraine is from childhood onwards but most commonly in the 20s and 30s [(3)] (Figure 1) and relatively infrequently after the age of 40 years; therefore, prevalence increases from the first to fourth decades and thereafter declines [(4)] . Migraine may nevertheless be a significant health issue among children [(5)].

Figure 1 Migraine prevalence related to age in men and women, average of 10 studies



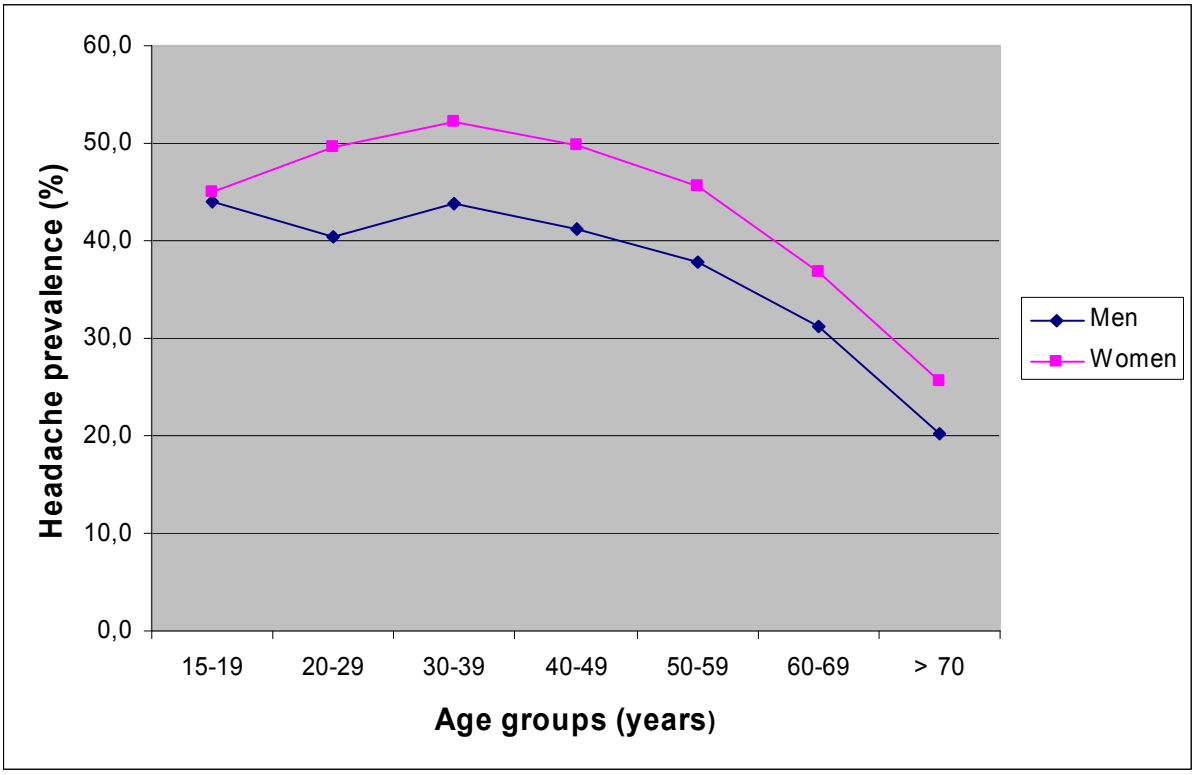
(Reproduced from Stovner et al [(5)] with permission from European Journal of Neurology)

Overall, migraine has a variable prevalence worldwide. Over 12% of the general population have regular migraine attacks. The frequency of migraine attacks is highly variable, from 1/year in some to more than 1/week in as many as 25% of sufferers [6]. The average may be as high as 21 episodes per sufferer per year [7]. Extrapolation of migraine attack prevalence and attack incidence suggest that 3000 migraine attacks occur every day for each million. Probably everywhere, significantly more women are affected than men, in a ratio of 2-3:1. [8].

Other forms of nearly every day headaches, estimated as high as 1 in 25 of adults, are associated with long-term morbidity.

Tension-type headache is the most widespread of headache disorders [9] .Onset is often in the teenage years and prevalence peaks in the fourth decade and then declines [10] (Figure 2)

Figure 2 Headache prevalence related to age in men and women, average of 3 studies



(*Reproduced from Stovner et al [5] with permission from European Journal of Neurology)*

Overall, one-year prevalence may exceed 60% although it is apparently lower in some countries. A large part of the population have mild and infrequent tension-type headache (once monthly or less), with 20-30% experiencing headache episodes more often. Tension-type headache is also more common in women, in a ratio of 1.5 :1 [8].

What is undisputed is that migraine and tension-type headache are the most prevalent headache disorders and, both with disabling potential, they have the greatest impact on public health. Nearly all migraine sufferers and 60% of those with tension-type headache experience reductions in social activities and work capacity **[11-14].**

The World Health Organization (WHO) places migraine among the world's top 20 leading causes of disability [15], with an impact that extends far past the suffering individual, to the family and community. The WHO report defines the "burden" of migraine to include the economic and emotional difficulties that a family experiences as a result of migraine, as well as the lost opportunities - the adjustments and compromises that prevent other family members from achieving their full potential in work, social relationships and leisure. These human aspects of migraine are more difficult to assess and quantify, the report says, but are nevertheless vital to fully understanding the implications of the disorder.

Migraine is estimated to account for 2.0% years of life lost due to a disability in women of all ages. In both sexes of all ages, migraine is responsible for 1.4% of total years of life lost due to a disability (Table 1). Years of life lost to a disability is defined as years of "healthy" life lost in states of less than full health.

Table 1 Leading causes of years of life lost due to a disability:

	Females All Ages	**% Total**
1	Unipolar depressive disorders	14
2	Iron-deficiency anemia	4.9
3	Hearing loss, adult onset	4.2
4	Osteoarthritis	3.5
5	Chronic obstructive pulmonary disease	2.9
6	Schizophrenia	2.7
7	Bipolar affective disorder	2.4
8	Falls	2.3
9	Alzheimer's and other dementias	2.2
10	Obstructed labour	2.1
11	Cataracts	2.0
12	**Migraine**	**2.0**
13	Congenital abnormalities	1.9
14	Asthma	1.8
15	Perinatal conditions	1.8
16	Chlamydia	1.8
17	Cerebrovascular disease	1.8
18	Protein-energy malnutrition	1.6
19	Abortion	1.6
20	Panic disorder	1.6

The World Health Organization (WHO) recognition of migraine as a major global disorder, therefore, is a major step toward relieving the burden of headache around the world. People with migraine score highly on scales of general physical and mental-ill health. According to the WHO disability assessment, the disability of a day with severe migraine is in the highest disability category, the same disability category than quadriplegia. Despite this, both the public and the majority of healthcare professionals tend to perceive headache as a minor or trivial complaint. As a result, the physical, emotional, social and economic burdens of headache are poorly acknowledged in comparison with those of other, less prevalent, neurological disorders [16].

In a health economic report on the [17]) by the European Brain Council (EBC), migraine came out as the most costly of the purely neurological disorders. Data were available only for migraine, but there were indications that other headaches could result in as high costs as migraine.

There is a lack of worldwide studies on the different headache sub-types. Those carried out have employed different methodologies although headache definitions were standardized by the International Headache Society in 1988 [18]. What is undisputed is that migraine and tension-type headache are the most prevalent headache disorders and, both with disabling potential, they have the greatest impact on public health.

Information is needed to achieve greater recognition and transparency. Headache, particularly chronic and recurrent headaches are a major liability in the quality of life in Europe. Migraine cost alone are estimated in EU-25, Norway, Iceland and Switzerland at 27 billion Euros.

2.2 Studies performed

After my active participating in the Headache Disorders and Public Health Meeting, called by the Department of Mental Health and Substance Dependence, Non-communicable Diseases and Mental Health Cluster of the World Health Organization, held at WHO headquarters, Geneva, 13-14 March 2000, I decided to initiate a project to allow measuring the impact of headache disorders in Europe in a reliable way.

I collected the official support from all major stakeholders: public bodies, clinicians, headache experts, representatives of patients' organization and representatives of scientific organizations (European Headache Federation, International Headache Society) and the World Health Organization to support my idea which can be followed up in the trilogy of studies of my dissertation.

In my first study I gathered information for action to know the scale and scope of the problem: I did a comprehensive Medline search for population-based studies of headache and migraine used the search terms *headache epidemiology* or *migraine epidemiology* or *headache prevalence* or *migraine prevalence* or *headache impact* or *migraine impact* or *migraine burden* or *headache burden t*o put together all the existing worldwide evidence of the burden attributable to headache.

References listed in relevant publications were also examined. All identified articles were screened for various aspects of methodology and design, and type of content, in order to select methodologically adequate studies for collecting prevalence and impact studies in the future.

I my first study I could show that there were important methodological differences and unbridgeable various formulae to calculate the burden of headache. This study allowed me to detect the gaps and to define the needs for content and for methodology to collect the different socio-economic and humanistic areas of headache disorders in a reliable way.

As I wanted to know the impact attributed to headache disorders, I initiated in my second study a national pilot project in Luxembourg, to define and to validate the content for a scientific instrument allowing to collect reliable migraine impact data and to validate this instrument in a multicultural environment.

I persuaded the Ministry of Research in Luxembourg to support this project with a national research grant allowing my second study to be independent of pharmaceutical company financial support.With the support of major stakeholders I put together a questionnaire containing primary measures of headache, secondary measures of disability and disease management.

The data were organized into eight major themes: Epidemiology, diagnosis and assessment, issues of care of people with headache disorders (use of system, disease

management, treatment outcome/ patient satisfaction), impact on lifestyle, impact on society, impact on quality of life and comorbidity. To my knowledge such a tool had so far not been developed. After approval by the national data protection and the national ethics committees, I undertook a validated translation of the content into German, French, English and Portuguese and complete validations tests (face content, language validity, test-retest reliability, internal consistency, construct validity, comprehensiveness, completion rate and response rate).
As a result I could proof that this scientific tool in a questionnaire format, called BURMIG, was a valid scientific instrument to collect reliable migraine impact data in the multicultural environment of the Luxembourgish population.

In my third study I initiated the first European project to define the content for a scientific instrument allowing collecting reliable headache impact data and to validate and to implement this instrument in 10 European countries.

After expert exchange at national and EU level, involvement of the stakeholders including health authority structures, practitioners and patients organisations, we adapted the BURMIG questionnaire taking into account the raised adaptation issues from the consortium. The resulting questionnaire comprised general epidemiology information (age, gender, working situation, language) headache criteria, medical consultation habits and given diagnosis; socio-economic information and global burden of migraine (work loss, socio-economic functioning, WHOQoL, a WHO quality of life assessment questionnaire for comparing quality of life of different health conditions, the hospital anxiety and depression scale HADS, a validated scales for the evaluation of depression and anxiety as co-morbidities of headache, questions about disease management, their outcome, satisfaction and needs of treatment and finally questions about the implication of headache on the social environment and the social acceptance of the headache disorder.

Once approved by the data protection and ethical committees in each of the 7 validation countries (France, Italy, Germany, Austria, UK, Luxembourg, Spain), the questionnaires were translated according to an approved language validation procedure in the national languages A new informatics tool was developed for the data input of the questionnaires at country level and then the questionnaires were validated for face content, language validity, test-retest reliability, internal consistency, construct validity, comprehension/completion rate and response rates in the 7 different countries.

The content of the questionnaire was adapted according to the results of the statistical analysis. We then translated the resulting questionnaire, named EUROLIGHT, according to an approved language validation procedure in the 8 European languages (English, French, German, Italian, Dutch, Lithuanian, Spanish and Portuguese) and it is actually used as the new scientific instrument for collecting impact data on headache disorders in 10 different countries representative of the different regions of Europe. The detailed report on the development and validation of the Eurolight questionnaire is shown in my study 3.

2.3 References

1 Pryse-Phillips W., Findlay H., Tugwell P., Edmeads J., Murray T.J.,Nelson R.F. A Canadian population survey on the clinical, epidemiologic and societal impact of migraine and tension-type headache. Can J Neurol Sci 1992; 19: 333-339.

2 Linet M.S., Stewart W.F., Celentano D.D., Ziegler D., Sprecher M. An epidemiologic study of headache among adolescents and young adults; JAMA 1989; 261: 2211-2216.

3 Rasmussen B.K. Epidemiology of headache in Europe. In: Olesen J., ed. Headache Classification and Epidemiology. New York: Raven Press, 1994; 231-237.

4 WHO: Headache disorder and public health neurological diseases & neuroscience wh/msd/mbd/00.9.

5 Stovner LJ, Zwart JA, Hagen K, Terwindt G, Pascual J. Epidemiology of headache in Europe. Eur. J Neurol. 2006;13:33-45.

6 Stewart W.F., Lipton R.B. Migraine epidemiology in the United States.in: Olesen J, ed. Headache Classification and Epidemiology. New York:Raven Press, 1994; 239-246.

7 Edmeads J., Findlay H., Tugwell P., Pryse-Phillips W., Nelson R.F.,Murray T.J. Impact of migraine and tension-type headache on life-style, consulting behaviour and medication use: a Canadian population survey. Can J Neurol Sci 1993; 20: 131-137.

8 Rasmussen B.K. Epidemiology and socio-economic impact of headache. Cephalagia 1999; 19 Suppl 25: 20-23.

9 Steiner T.J. Disadvantage and discrimination: components of the F$rden of headache. Evidence presented to the meeting.WHO March 2000, Headach Disorders and Public Health.

10 Rasmussen B.K. Epidemiology of headache in Europe. In: Olesen J.,ed. Headache Classification and Epidemiology. New York: Raven Press, 1994; 231-237.

11 Osterhaus J.T., Gutterman D.L., Plachetka J.R. Healthcare resource and lost labour costs of migraine headache in the US.PharmacoEconomics 1992; 2: 67-76.

12 Kryst S., Scherl E. A population based survey of the social and personal impact of headache. Headache1994;.**34**:344-350.

13 Stewart W.F., Lipton R.B., Simon D. Work-related disability: results from the American migraine study. Cephalalgia 1996; **16**: 231-238.

14 Schwartz B.S., Stewart W.F., Lipton R.B. Lost workdays and decreased work effectiveness associated with headache in the workplace. J Occupat Environm Med 1997; 39: 320-327.

.

15 The world health report 2001: mental health, New Understanding, New Hope. Geneva: WHO, 2002.

16 American Association for the Study of Headache, International Headache Society. Consensus statement on improving migraine management. Headache 1998; 38:736.

17 Andlin-Sobocki P, Jönsson B, Wittchen HU, Olesen J (2005) Cost of disorders of the brain in Europe. Eur J Neurol 12:1-27.

18 Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Headache Classification Committee of the International Headache Society. Cephalalgia. 1988;8 Suppl 7:1-96.

3 Impact of headache in Europe: A review for the Eurolight project

Lars Jacob Stovner[1,3], Colette Andree[2,3]

[1]Norwegian National Headache Centre
Department of Neuroscience, Norwegian University of Science and Technology
and St. Olavs Hospital, Trondheim, Norway
[2]CRP Santé, Luxembourg
[3]On behalf of the Eurolight Steering Committee

3.1 Abstract

A recent health economic survey in Europe has suggested that migraine is the most costly among the neurological disorders, and several studies also suggest that migraine and other disorders lead to widespread suffering, reduction of quality of life, and marked impairment of participation, both in work and social activities. The present literature survey was made in order to summarize what is known on the subject, as a preparation for an EU-supported study to assess the impact in several EU countries with similar methodology and the same research instrument.

Previous studies have yielded relatively reliable data only for migraine, whereas the impact of tension-type headache is virtually unknown or only very incompletely known for most dimensions of headache impact. Some data do suggest, however, that this headache may be as important from a health economic and a public health perspective as migraine. In future studies it is important to get population-based data from various countries relevant for estimation of indirect (mostly absenteeism from work and reduced working efficiency when having headache) and direct costs (related to medication, consultations, investigations and hospitalisations). Also, the impact on ability to get education and participate in the workforce is very relevant, as is the impact on love life and family planning. The quality of life of headache patients should be measured by validated instruments. To get a complete picture, one should also ask about the effect on the life of partners and children, and on the possible impact even when headache free (e.g. fear of the next attack).

3.2 Introduction

For a just and rational distribution of means to health-care services and health related research, reliable data on the individual and societal impact of different disorders are crucial. In recent years several initiatives have been launched to raise the awareness that headache is not only a nuisance for some individuals, but that it entails widespread suffering and loss of opportunities for patients and their families, and large cost for the society. The recently published report on the prevalence and burden of headache [(1)] is a premise for the campaign "Lifting the burden: The Global Campaign to reduce the burden of headache" [(2)]. In Europe, much data on both the economic costs of migraine have been collected and presented in connection with the "Cost of Brain Disorders in Europe" project [(3)], in which migraine is treated along with many of the other (neurological and psychiatric) "brain disorders". The Eurolight project (www.eurolight-online.eu) is an initiative supported by the EU aiming to fill in the main holes in our knowledge by performing studies on headache prevalence and impact in selected European countries (Austria, France, Germany, Italy, Lithuania, the Netherlands, Spain, UK). A pilot study is first performed in Luxembourg. The present review of the existing literature on both economic and non-economic impact was performed as a preparation for the Eurolight study, partly to assess the current state of knowledge, and partly to be able to create a questionnaire to measure all the most relevant aspects of headache impact. The present study presents the results of this review and a proposition of the main dimensions that ought to be covered in the headache impact instrument to be used in the Eurolight study.

3.3 Economic impact of headache

Headache may have considerable economic consequences, both for the patient and for the society as a whole. There are more studies about the societal costs than about the individual economic losses of the patients.

3.3.1 Relation to socioeconomic status, education and employment

In a large Norwegian study (the HUNT study), both migraine and headache in general was associated with low socioeconomic status [4] which has also been found in North America [5, 6] but not in some smaller European studies [7-11]. The question whether this is a consequence or a cause of headache is not satisfactorily answered, but in one Swedish study, half of the patients reported a negative influence of migraine on their ability to pursue studies and one third a negative influence on their finances [9]. In a US study it was found that headache patients have somewhat reduced labour force participation [12], but employment status has not been found to be related to headache in some European studies [7-13].

3.3.2 Absenteeism from work

In two relatively old studies, one from Finland in 1979 [14] and one from San Marino in 1986 [15], 7% of working individuals had been absent from work in the previous year due headache. In a Danish study from 1992 [16], 43 % of migraineurs (5% of the population) and 12% of TTH patients (9 % of the population) had been absent from work during the last year due to headache, i.e. a total of 14 % of the population. In a Swedish study from 2004 [9] 65 % of migraineurs reported some degree of absence from either school or work during the last year. These data are, however, of relatively limited interest from an economical viewpoint as they do not indicate how many days the headache sufferers are away from work.

The number of days with work absence due to headache is relatively consistent across studies from different countries. In some previous studies it has varied between 2 and 6 days per year among headache patients in general [17], and between 1.5 and 4.2 days per year in migraineurs [9]. A study among migraineurs in Sweden revealed that 35 % were never absent from work due to migraine, and 54 % were absent 1-2 days per year [9]. Compared to headache free individuals, migraine patients in the HUNT study from Norway lost on average 4.4 workdays per year and persons with non-migrainous headache lost 2.5 workdays per year [18]. In the Danish study from Copenhagen [16], the TTH patients who had been absent seem to have been as much or more absent from work than the migraine patients, and the number of workdays lost due to migraine was 270 and to TTH 820 per 1000 persons per year, i.e. a total of 1090 days. In a study from England in 2003 [13], 15% had been absent from work or had reduced ability to work due to headaches in the last three months. Per year, headache accounted for 1327 missed and 5213 reduced ability days per 1000 workers per year, representing 0.5% and 2.0 % of all working days in the adult population, irrespective of headache status. This study did not relate absenteeism to different headache diagnoses. In an English study from 2003, an estimated 5.7 workdays per year was missed by migraineurs working or attending to school [8]. This seems to be higher than in France where a diary-based registration of absenteeism published in 1999 showed that migraineurs were away from work 2.18 days per year due to headache [19].

3.3.3 Effectiveness when working with headache

Working with migraine results in a 35% productivity loss on average according to some European studies [20]. This figure is, however, largely based on migraineurs' self-report, which may give a too high estimate according to a recent US study from a workplace [21]. In this study, it was found that the working ability assessed by self-report was much lower than the

objectively measured working efficiency (20 vs 8%). The relatively small decline in working ability led the authors to conclude that workers with even relatively severe headache find creative ways to cope with the pain and maintain standards.

3.3.4 Health economic studies

For the headache part of the "Cost of Brain Disorders in Europe" project, a literature search for studies containing cost data for migraine and other headaches identified 8 European studies evaluating the direct or indirect costs of migraine from a societal perspective [20], from France [22-23], Germany [24], The Netherlands [25], Spain [20] (26), Sweden [27] and the UK [28-29]. No studies analysing the cost of TTH or other non-migraineous headaches were found. There were large variations in costs across the six European countries where data were available, ranging from around €100 per patient per year in Sweden to nearly €900 in Germany. These variations are probably mostly due to different methodologies and differences in the year when the studies were conducted. An important finding was that the vast majority of total costs, between 72% and 98%, were indirect costs, due to lost productivity, either in the form of work absence or reduced efficiency levels when working with migraine. Women tended to lose more work days than men, but indirect costs were similar due to lower salaries and labour force participation amongst women. The direct costs, related to consultation, diagnostic investigations, treatments, and hospital admissions accounted for less than 30% of total costs in most studies.

The cost estimate for migraine in the European report was based on an average of the most representative cost estimates, from the UK, Germany and France. An average annual cost of €585 per migraine patient was estimated for these Western European countries. The 1-year prevalence of migraine was 14% among adults in Europe according to the review of epidemiological studies [1], i.e. 41 million adult Europeans with active migraine. Per patient

migraine was the least costly disorder among the brain disorders. However, due to the high prevalence, the total cost of migraine was estimated to be €27 billion for whole Europe in 2004, which was the highest cost among the purely neurological disorders. Many of the psychiatric afflictions were even more costly according to this review. It is, however, likely that the available cost data in Europe would tend to underestimate the actual costs of headache, mainly because no cost data existed on the most common headache type (TTH), but also because children and adolescents were not considered, and because cost connected with more expensive medication (triptans) were not included, since most cost studies were performed before this class of drugs were introduced.

In a separate paper summarizing the prevalence and cost data for headache in Europe [30] a more speculative estimate for the cost of headache, rather than migraine alone, was derived by using the results of the Danish [31] and British [32] population-based studies which demonstrated that around 1100 to 1300 days per 1000 workers were missed due to headache each year. The British study also suggested that the number of days with reduced efficacy was around four times higher than the number of days missed. Assuming a reduced efficiency of 35% when working with headache, and that the direct costs of headache constitute the same proportion of the total costs as for migraine, the average total cost per headache patient was estimated to be roughly €420 per year (of which €390 would be due to indirect costs and €30 due to direct medical costs). Since headache in general was found to affect nearly 50 % of Europeans, this estimate, if true, would make headache a much more costly disorder than migraine alone.

It is of interest to compare the European cost study [3] with more recent cost studies in some individual European countries. In one study from Spain [33] the annual costs of migraine was only about 50% of the sum given in the European Cost study for the same country. The difference may partly be explained by somewhat lower prevalence figures (12 versus 14 %)

for migraine used in the Spanish study, but the main difference may be that this study did not employ a bottom-up design, but used published statistics and data to estimate resource use and productivity losses, which may have led to an underestimation of some costs. A recent study from France [34], restricted to the direct costs in 1999, found that these costs were at least twice as high (€ 128) as in the European migraine cost study (<€60). This study included both "strict" migraine (IHS 1.1 and 1.2) and "migraineous disorder" (IHS 1.7, corresponding to 1.6 in ICHD-2), which together affected 17% of the population. For the whole country the direct costs amounted to more than 1 billion €, which was 0.068% of the gross national product. Non-migraineous episodic headache, affecting 9.2% of the population, entailed a considerably lower cost of €28.

It may also be of interest to compare the European studies with one US study using a quite different methodology to assess direct costs. In this study, all types of medical care costs (not only those related to headache) were derived from the claims records of a large health plan, whereas diagnostic status (migraine or not) and comorbid and demographic status was ascertained using a telephone interview among members of the health plan [35]. Migraineurs incurred on average $700 more per year in total medical care costs than the controls. Interestingly, this statistically significant difference disappeared when psychiatric comorbidity variables (anxiety and depression) were entered into the model. The much higher costs per patient in this than in the French study [34] and Spanish study [33] may therefore at least partly be due to the differences in cost assessment methodology, indicating that the direct costs specifically related to migraine and not to comorbid disorders are most reliably assessed by a direct method, questioning patients about use of health-care resources.

Medication for headache constitutes an important part of the direct costs. In France in year 2000, the most frequently used acute medications for migraine were paracetamol, salicylates and NSAIDs. Triptans were used by 8 % of migraineurs, and prophylactic

treatment was used by 6% (36). In Denmark 26% of migraineurs had used triptans in 2001, but less than 5% of those with pure migraine had used prophylactic medication [37].

3.4 Non-economic impact

From a purely humanitarian perspective, but also from a public health perspective, the pain, suffering and disability caused by headaches are as important as the economic consequences. In a study performed in young women in 9 Western European countries, 86 % of migraineurs stated that their life would have been better if they did not suffer form migraine [38]. A German study showed that, on average, patients with migraine or TTH had around one month every year affected by headaches [10]. The main burden of headache is carried by a minority of sufferers, and a Swedish study has shown that 27% of migraine patients had 68% of all attacks [9]. Three to four % of the European population have headache half of the days or more per month [1].

3.5 Disability

It has been calculated that in the US, 300 000 persons stay in bed each day (24 hours) due to headaches [39]. A Swedish study has shown that the disability is not only related to the attacks since many migraine patients report impairment also between attacks [40]. Nine % of patients report that they have some residual disability since they do not recover completely between attacks, and in addition, many patients live in a constant worry about the next attack [9-38].

In some studies the level of disability due to migraine has been evaluated with the Migraine Disability Assessment Scale (MIDAS). With this instrument, days with work absence (job or household chores), days with ≥50% reduction in productivity, and days with inability to participate in social activities is counted during a 3 month's period. In France,

among those with active migraine 22% (1.5% of the whole population) had grades III or IV (moderate or severe disability, indicating 11 days or more during the last 3 months' period when headache affected work/household chores 50% or more, or leisure activities) [36]. MIDAS III or IV were about twice as common among migraineurs in one US study (54%) [41], as it was in the multinational Latin American study (50 %) [42]. Among patients with headache in general (both migraine and non-migraineous headache, comprising 70% of the study population), 10.3% (7.2% of the population) had MIDAS grade III or IV [13]. Comparing the percentage of the general population with MIDAS disability grade III-IV due to migraine in France (1.5%) [36] with the percentage with same disability due to headache in general in England (7.2 %) [13], it seems that non-migraineous headache cause more disability on a population basis than migraine. The HALT (Headache-Attributed Lost Time) index is a close derivative of MIDAS (http://www.liftingtheburden.org/ → Resources → Burden measure) to be used for headache burden studies which will be conducted by the by the Lifting The Burden Campaign [43].

In the World Health Organisation (WHO), the preferred measure of disease burden is "Disability Adjusted Life Years" (DALYs), which is a sum of the years of life lost (YLL) and the years lived with disability (YLDs). The YLDs are determined by the incidence and duration of the disorder, and by a disability weight ranging between 0 and 1 [44]. Although migraine entails no increased mortality (i.e. YLL =0), migraine was number 19 of the leading causes of DALYs among women aged 15-44, and with regard to YLDs, it was number 19 for both sexes, and number 12 for women, irrespective of age. Using the WHO data for a calculation of the burden of "brain disorders" (i.e. the psychiatric and neurological disorders) in Europe, the weight of migraine was lower than that of the major psychiatric disorders, dementias, stroke and injuries, but higher than that of epilepsy, multiple sclerosis and Parkinson's disease [45].

In a recent report on the global prevalence and burden of headache disorders, the burden of migraine and TTH were measured in a similar way as the DALYs by combining data on prevalence, mean number and duration of headache attacks, and headache intensity, from studies containing such information. For the world as a whole, it was demonstrated that TTH resulted in a higher population burden (approximately 55 % of total burden) than migraine (45 %). The data for Europe indicated an even higher burden due to TTH compared to migraine [(1)]. If one uses the European data from this study it can be calculated that the hours with migraine headache would add up to between 34 and 100 hours per year, if distributed on each adult individual in the population. The data on TTH are too scarce to use for similar calculations.

3.6 Studies using validated QoL-instruments

The SF-36 is a validated instrument to measure quality of life (QoL), containing 8 dimensions. One US study [(46)], recruiting migraine patients from a medication trial, demonstrated that migraineurs had lower QoL than the general US population, most marked for bodily pain, physical role limitations and social functioning.

A Dutch population-based study found that migraine had a negative influence on all a dimensions compared to controls. The negative influence on QoL was larger than that of e.g. asthma, and it increased with increasing headache frequency [(47)]. Two population-based studies from Spain among chronic daily headache sufferers showed a marked negative influence, most marked for those with medication overuse, but similar for those with a headache of a migraine or a tension type [(48)]. One of these showed that the headache frequency may have a greater impact than headache intensity on QoL [(48)], and the other that chronic headache with medication overuse was associated with a decrease in all QoL aspects studied with SF-36, most marked for role physical and bodily pain [(49)]. A study from UK

showed that migraineurs with high or moderate disability had a marked reduction on all dimensions on the SF-36 [50]. One Swedish study compared SF-36 results in the two sexes and in participants with different pain conditions. There was a gender difference for headache, which in men influenced physical function, physical role and bodily pain most, and in women vitality, social functioning, emotional functioning and mental health [51]. In a French study, migraineurs had significantly lower scores than headache free controls on all SF-36 dimensions, and lower scores on the pain dimension than those with other headaches or with TTH [52].

One study comparing migraineurs in the US and the UK used a shorter QoL instrument, the SF-12, which contains a physical and a mental component [53]. In both countries, migraineurs had lower scores than controls on both components also after adjusting for socioeconomic status and for depression. However, in those with both migraine and depression, the QoL was significantly reduced in comparison to those who were not depressed.

In another French study, using a disease-specific QoL instrument called QVM, the QoL was found to be lowest among those with chronic headache, intermediate among migraineurs and highest among subjects with other forms of episodic headache [54].

The total burden of headache patients may not only be related to the headache per se, but also to comorbid conditions. European population-based studies have demonstrated that depression and/or anxiety occur 2-3 times more often among migraineurs than in the general population [55-56]. Depression adds to the reduction in QoL in migraine [53]. This comorbidity may be as important for non-migrainous headache [57], but it is not known how this comorbidity influences the QoL in other headaches. In addition, it has been found that headache is also comorbid with other bodily pain, both in Finnish children [58] and Norwegian adults [59].

3.7 Family impact of migraine

Migraine also affects the patients' spouses and children. In a population-based Swedish study [9], the % of migraine sufferers who reported a negative impact of migraine was 76% for attendance to work, 67% for family situation, 59% for leisure time, 48% for pursuing studies, 46% for sexual life, 37 % for their social position, 31% for love, 30% for their financial situation, 27% for making a career, and 11% for making friends.

One study has measured the impact on the family in two population samples of similar size in US and UK [60]. The impact was very similar in both countries. More than 60 % of patients reported a marked impact on the ability to do household chores because of their migraine during the past 3 months, and it was markedly reduced also in 20 % of the patients' partners. Almost 46 % of patients, and 24 % of partners had missed days of family or social activities due to the proband's migraine, and 16% of patients and 12 % of partners had avoided making plans for family or social activities due to the proband's migraine. As to the impact on the children of patients, more than 60 % stated that it had a moderate to marked influence on the relation with their children, 40% stated that they would have been a better guardian or parent without migraine, more than 10% stated that their children had missed school, and 10 % that their children had been late to school because of their headache. Fourty six % stated that they would have been a better partner without headaches, and 5% stated that they had had fewer children because of headache, 0.4% that they had avoided having children, and 15% that they had avoided oral contraception. Compared with a control group, the partners of migraine patients were significantly more dissatisfied with the demands, responsibility and duties placed upon them, and with their ability to perform.

3.8 Conclusions

Health economic studies have documented that the costs of headache disorders are huge, the costs only for migraine amounting to €27 billion in the EU countries, and the cost for other headaches are probably as large. However, better population-based cost studies, are needed to assess the cost involved with TTH. Headache sufferers tend to have lower income and education, and more of them may be unemployed, but it is still uncertain whether this is true for most European countries, and also whether it may be a cause of or an effect of headache. It is also amply documented that migraine confers a high degree of disability with more forced absence from work and leisure activities, and migraineurs also has a measurably reduced quality of life. In addition, there is a marked impact on family life, and headaches also put considerable strains on partners and children. A minority of headache sufferers chose to have fewer children than they would have had if they had not had headaches.

Based on the present review we have identified some main domains, summarized in the Table 1, which should be covered in order to capture as much as possible of the headache burden. The investigations should be performed in population-based samples, and to assess the whole burden, it is particularly important that also TTH and not only migraine is included. The fact that results on most aspects of headache vary considerably between different European countries highlights the need to study several countries with the same methodology and instrument. All these methodological aspects will be taken care of in the studies of the Eurolight project which are now ongoing. We believe that the results from these studies will provide the evidence needed to let headache disorders get the resources for treatment and research that they deserve according to the burden that it places on people in Europe.

Table 1 The main domains that should be covered in headache burden studies

Economic burden	
Direct cost	Medication, consultation, investigations, hospitalisations
Indirect costs	Workdays lost,
	Decreased effectiveness when working with headache
	Lost career and education opportunities
Non-economic burden	
Disability	MIDAS or HALT
	Time with disability:
	Headache frequency x duration x intensity/disability
Impact outside attacks	Residual disability and fear of next attack
Quality of Life	SF 36, SF 12, WHOQual etc
Family impact	Impact on the life of partner and/or children
	Impact on marriage and love life
	Impact on family planning and/or contraception
Psychiatric complaints	Various scales to measure anxiety and/or depression as consequent or comorbid disorders

3.9 References

1. Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A, Steiner T, Zwart JA (2007) The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia 27:193-210.

2. Steiner TJ (2004) Lifting the burden: The global campaign against headache. Lancet neurology 3:204-205.

3. Andlin-Sobocki P, Jönsson B, Wittchen HU, Olesen J (2005) Cost of disorders of the brain in Europe. Eur J Neurol 12:1-27.

4. Hagen K, Vatten L, Stovner LJ, Zwart JA, Krokstad S, Bovim G (2002) Low socio-economic status is associated with increased risk of frequent headache: a prospective study of 22718 adults in Norway. Cephalalgia 22:672-679

5. Stewart WF, Lipton RB, Celentano DD, Reed ML (1992) Prevalence of migraine headache in the United States. Relation to age, income, race, and other sociodemographic factors. JAMA 267:64-69.

6. Breslau N, Davis GC, Andreski P (1991) Migraine, psychiatric disorders, and suicide attempts: an epidemiologic study of young adults. Psychiatry research 37:11-23.

7. Rasmussen BK (1992) Migraine and tension-type headache in a general population: psychosocial factors. Int J Epidemiol 12:1138-1143.

8. Steiner TJ, Scher AI, Stewart WF, Kolodner K, Liberman J, Lipton RB (2003) The prevalence and disability burden of adult migraine in England and their relationships to age, gender and ethnicity. Cephalalgia 23:519-527.

9. Linde M, Dahlöf C (2004) Attitudes and burden of disease among self-considered migraineurs--a nation-wide population-based survey in Sweden. Cephalalgia 24:455-465.

10. Gobel H, Petersen-Braun M, Soyka D (1994) The epidemiology of headache in Germany: a nationwide survey of a representative sample on the basis of the headache classification of the International Headache Society. Cephalalgia 14:97-106.

11. Launer LJ, Terwindt GM, Ferrari MD (1999) The prevalence and characteristics of migraine in a population-based cohort: the GEM study. Neurology 53:537-542.

12. Stang P, Von Korff M, Galer BS (1998) Reduced labor force participation among primary care patients with headache. J Gen Intern Med 13:296-302.

13. Boardman HF, Thomas E, Croft PR, Millson DS (2003) Epidemiology of headache in an English district. Cephalalgia 23:129-137.

14. Nikiforow R, Hokkanen E (1979) Effects of headache on working ability: a survey of an urban and a rural population in Northern Finland. Headache 19:214-218.

15. Benassi G, D'Alessandro R, Lenzi PL, Manzaroli D, Baldrati A, Lugaresi E (1986) The economic burden of headache: an epidemiological study in the Republic of San Marino. Headache 26:457-459.

16. Rasmussen BK, Jensen R, Olesen J (1992) Impact of headache on sickness absence and utilisation of medical services: a Danish population study. J Epidemiol Community Health 42:443-446.

17. Stovner LJ, Zwart JA, Hagen K, Terwindt G, Pascual J (2006) Epidemiology of headache in Europe. Eur J Neurol 13:333-345.

18. Fiane I, Haugland M, Stovner L, Zwart JA, Bovim G, Hagen K (2006) Sick leave is related to frequencies of migraine and non-migrainous headache-The HUNT Study. Cephalalgia 26:960-967.

19. Michel P, Dartigues JF, Duru G, Moreau J, Salamon R, Henry P (1999) Incremental absenteeism due to headaches in migraine: results from the Mig-Access French national cohort. Cephalalgia 19:503-510.

20. Berg J (2004) Economic evidence in migraine and other headaches: a review. Eur J Health Econom 5:S43-S54.

21. Pransky GS, Berndt E, Finkelstein SN, Verma S, Agrawal A (2005) Performance decrements resulting from illness in the workplace: the effect of headaches. J Occup Environ Med 47:34-40.

22. Michel P, Auray J, Chicoye A, Dartigues J, Lamure D, Duru G, Henry P, Salamon R (1993) Prise en charge des migraineux en France: Coût et recours aux soins. J Econ Med 11:71-80.

23. Auray JP (2006) Impact socio-economique de la migraine et des cephalees en France. CNS Drugs 20 Spec no.1:37-46.

24. Neubauer G, Uljaky R (2002) Migraine-a disease and its costs. Pharm Unserer Zeit 31:494-497.

25. van Roijen L, Essink-Bot ML, Koopmanschap MA, Michel BC, Rutten FF (1995) Societal perspective on the burden of migraine in The Netherlands. Pharmacoeconomics 7:170-179.

26. Lainez MJA, Monzon MJ: The socioeconomic impact of migraine in Spain. In Reducing the burden of headache. Oxford: Oxford University Press; 2003:255-259.

27. Björk S, Roos P: Economic aspects of migraine in Sweden. In Working paper no8 Institute for Health Economics, Lund. 1991:5-24.

28. Blau N, Drummond M: Migraine. London: Office of Health Economics; 1991:26-30.

29. Cull R, Wells N (1992) The economic cost of migraine. Br J Med Econ 2:103-115.

30. Berg J, Stovner LJ (2005) Cost of migraine and other headaches in Europe. Eur J Neurol 12 Suppl 1:59-62.

31. Rasmussen BK, Jensen R, Olesen J (1992) Impact of headache on sickness absence and utilisation of medical services: a Danish population study. J Epidemiol Community Health 46:443-446.

32. Boardman HF, Thomas E, Croft PR, Millson DS (2003) Epidemiology of headache in an English district. Cephalalgia 23:129-137.

33. Badia X, Magaz S, Gutierrez L, Galvan J (2004) The burden of migraine in Spain: beyond direct costs. Pharmacoeconomics 22:591-603.

34. Pradalier A, Auray JP, El Hasnaoui A, Alzahouri K, Dartigues JF, Duru G, Henry P, Lanteri-Minet M, Lucas C, Chazot G *et al* (2004) Economic impact of migraine and

other episodic headaches in France: data from the GRIM2000 study. Pharmacoeconomics 22:985-999.

35. Elston Lafata J, Moon C, Leotta C, Kolodner K, Poisson L, Lipton RB (2004) The medical care utilization and costs associated with migraine headache. J Gen Intern Med 19:1005-1012.

36. Lucas C, Chaffaut C, Artaz MA, Lantéri-Minet M (2005) FRAMIG 2000: medical and therapeutic management of migraine in France. Cephalalgia 25:267-279.

37. Lyngberg AC, Rasmussen BK, Jørgensen T, Jensen R (2005) Secular Changes in Health Care Utilization and Work Absence for Migraine and Tension-type Headache: A Population Based Study. Eur J Epidemiol 20:1007-1014.

38. Dueland AN, Leira R, Burke TA, Hillyer EV, Bolge S (2004) The impact of migraine on work, family, and leisure among young women -- a multinational study. Curr Med Res Opin 20:1595-1604.

39. Hu XH, Markson LE, Lipton RB, Stewart WF, Berger ML (1999) Burden of migraine in the United States: disability and economic costs. Arch Intern Med 159:813-818.

40. Dahlöf CG, Dimenäs E (1995) Migraine patients experience poorer subjective well-being/quality of life even between attacks. Cephalalgia 15:31-36.

41. Hamelsky SW, Lipton RB, Stewart WF (2005) An assessment of the burden of migraine using the willingness to pay model. Cephalalgia 25:87-100.

42. Morillo LE, Alarcon F, Aranaga N, Aulet S, Chapman E, Conterno L, Estevez E, Garcia-Pedroza F, Garrido J, Macias-Islas M *et al* (2005) Prevalence of migraine in Latin America. Headache 45:106-117.

43. Steiner TJ (2005) Lifting the burden: the global campaign to reduce the burden of headache worldwide. J Headache Pain 6:373-377.

44. Leonardi M, Steiner TJ, Scher AT, Lipton RB (2005) The global burden of migraine: measuring disability in headache disorders with WHO's Classification of Functioning, Disability and Health (ICF). J Headache Pain 6:429-440.

45. Olesen J, Leonardi M (2003) The burden of brain diseases in Europe. Eur J Neurol 10:471-477.

46. Osterhaus JT, Townsend RJ, Gandek B, Ware JE (1994) Measuring the functional status and well-being of patients with migraine headache. Headache 34:337-343.

47. Terwindt GM, Ferrari MD, Tijhuis M, Groenen SM, Picavet HS, Launer LJ (2000) The impact of migraine on quality of life in the general population: the GEM study. Neurology 55:624-629.

48. Guitera V, Muñoz P, Castillo J, Pascual J (2002) Quality of life in chronic daily headache: a study in a general population. Neurology 58:1062-1065.

49. Colás R, Muñoz P, Temprano R, Gómez C, Pascual J (2004) Chronic daily headache with analgesic overuse: epidemiology and impact on quality of life. Neurology 62:1338-1342.

50. Lipton RB, Liberman JN, Kolodner KB, Bigal ME, Dowson A, Stewart WF (2003) Migraine headache disability and health-related quality-of-life: a population-based case-control study from England. Cephalalgia 23:441-450.

51. Bingefors K, Isacson D (2004) Epidemiology, co-morbidity, and impact on health-related quality of life of self-reported headache and musculoskeletal pain--a gender perspective. Eur J Pain 8:435-450.

52. Michel P, Dartigues JF, Lindoulsi A, Henry P (1997) Loss of productivity and quality of life in migraine sufferers among French workers: results from the GAZEL cohort. Headache 37:71-78.

53. Lipton RB, Hamelsky SW, Kolodner KB, Steiner TJ, Stewart WF (2000) Migraine, quality of life, and depression: a population-based case-control study. Neurology 55:629-635.

54. Duru G, Auray JP, Gaudin AF, Dartigues JF, Henry P, Lantéri-Minet M, Lucas C, Pradalier A, Chazot G, Hasnaoui AE (2004) Impact of headache on quality of life in a general population survey in France (GRIM2000 Study). Headache 44:571-580.

55. Lipton RB, Hamelsky SW, Kolodner KB, Steiner TJ, Stewart WF (2000) Migraine, quality of life, and depression: a population-based case-control study. Neurology 55:629-635.

56. Kececi H, Dener S, Analan E (2003) Co-morbidity of migraine and major depression in the Turkish population. Cephalalgia 23:271-275

57. Zwart JA, Dyb G, Hagen K, Odegard KJ, Dahl AA, Bovim G, Stovner LJ (2003) Depression and anxiety disorders associated with headache frequency. The Nord-Trondelag Health Study. Eur J Neurol 20:147-152.

58. Anttila P, Metsahonkala L, Mikkelsson M, Helenius H, Sillanpaa M (2001) Comorbidity of other pains in schoolchildren with migraine or nonmigrainous headache. J Pediatr 138:176-180.

59. Hagen K, Einarsen C, Zwart JA, Svebak S, Bovim G (2002) The co-occurrence of headache and musculoskeletal symptoms amongst 51 050 adults in Norway. Eur J Neurol 9:527-533.

60. Lipton RB, Bigal ME, Kolodner K, Stewart WF, Liberman JN, Steiner TJ (2003) The family impact of migraine: population-based studies in the USA and UK. Cephalalgia 23:429-440.

4 Development of a self-reporting questionnaire, BURMIG, to evaluate the burden of migraine

Colette Andrée [1,2*], Michel Vaillant [1*], Christelle Rott [1], Zaza Katsarava [3], Peter S. Sándor [4]

[1] Centre d'Etudes en Santé, Centre de Recherche Public – Santé, Luxembourg, Luxembourg

[2] Department of Pharmaceutical Sciences, University of Basle, Switzerland

[3] Department of Neurology, University of Essen Germany

[4] Department of Neurology, University Hospital, Zurich, Switzerland

* These authors contributed equally to the work.

4.1 Abstract

We developed a 77-item-self reporting questionnaire to assess the burden of migraine (BURMIG), including headache characteristics, migraine associated disability, comorbidities, management, and the consequences on the patients' lives. We translated BURMIG into 4 languages (French, Portuguese, German and English) and tested it in 130 headache patients (20 pain clinic, 17 primary care and 93 general public) in Luxembourg. We performed a linguistic and a face-content validation and tested the questionnaire for its comprehensiveness, internal consistency and for its retest-reliability at an interval of one month (completion rates were 79.6%, and 76,4%, for test and retest, respectively). Retest-reliability for the different parts of the questionnaire varied between 0.6 to 1.0 (Kappa coefficient), with an intracorrelation coefficient of 0.7–1.0. The internal consistency was between 0.74 to 0.91 (Cronbach's alpha).

The questionnaire BURMIG is suitable to evaluate the burden of migraine and can be used in English, German, French and Portuguese. .

4.2 Background

Migraine is a common and disabling neurobiological disorder [(1)] which is under-recognized and under-treated [(2, 3)]. It imposes a substantial health burden, with nearly all migraine sufferers experiencing impairment of social activities and of work capacity [(4, 5)]. The World Health Report 2002 [(3)] ranks migraine as number 12 in women and number 19 in both genders amongst all causes of disability in the world. In spite of this, it is estimated that only about 50% of migraine patients are diagnosed and therefore treated adequately [(6-10)]. There are a few validated questionnaires such as the ID migraine to diagnose migraine, and the migraine

disability assessment score (MIDAS) to assess disability in the last three months, but there is no comprehensive questionnaire to assess migraine associated burden.

The physical and emotional impact of migraine on individual sufferers, their care-takers, family and colleagues is poorly acknowledged and this is true as well for the social and economic burden of migraine on society in comparison with those of other, less prevalent, neurological disorders [9, 11-13].

We aimed to develop and validate a questionnaire to assess the burden of migraine after having translated it into the main languages in order to use it in subsequent studies in different linguistic populations.

4.3 Methods

4.3.1 Questionnaire

We designed a questionnaire combining elements from established questionnaires and added further questions concerned with disease management and social consequences of headache. Priority areas for the questionnaire were defined with joint support from NGO'S (Swiss Migraine Trust Foundation, Migraine Action Association UK, Switzerland and Luxembourg), several international headache experts (see acknowledgements) and the Luxembourg Ministry of Health. Ethics committee approval for the study was obtained from the National Ethic and Research Board of Luxembourg.

The resulting questionnaire contains 77 items, 17% of them are open questions. In the first part, the respondents are asked for biographical details such as age, gender, their most spoken language and their employment status. For the purpose of migraine diagnosis, the questions from "ID migraine" [14] are included. Specific information on headache, such as age of onset, the average number of headache days per month during the last 3 months and

symptoms before and after the headaches are gathered as well as information on general health, and previous and current disorders using items from the World Health Organization Disability Assessment Schedule II (WHODAS II) [15], the Migraine Disability Assessment Scale (MIDAS) [16] and the Patient Health Questionnaire-9 (PHQ-9) [17]. Participants are asked about the influence of headaches on their job and family life as well as whether they had ever consulted medical doctors, about the diagnosis that was made and about the medication that had been prescribed. Psychosocial circumstances having worsened the headaches, limitations in social activities, conceptions of headache and the need of support from health professionals to improve the headaches are also assessed.

4.4 Evaluation of the questionnaire

The testing of the questionnaire included face, content and language validity; the stability of the questionnaire over one month, a period of time during which little or no change is expected (Test-retest reliability); the extent to which the questionnaire is able to discriminate between respondents with more or less severe disease status (construct validity), and the extent to which individual items in a questionnaire correlate with other items relating to the particular area of investigation (internal consistency). The respective methodology is detailed below.

4.4.1 Study population

Patients with headache were recruited from primary care centres, pain clinics and lay organisations. The idea behind this recruitment was to test the questionnaire in different settings. Selection for the primary care setting was done by doctors in general practice from the personal acquaintance of the project team. For the pain clinic setting the patients were selected from the pain clinic of the Centre Hospitalier de Luxembourg (Central Hospital in

Luxembourg). When consulting because of headaches, both of these patient groups were asked by their physician to complete the questionnaire. For a third group of headache patients, headache sufferers with different employment settings were consecutively recruited by the national occupational health service and by a patient organization.

The samples size needed to investigate internal consistency, construct validity and for test-retest reliability was estimated by using the kappa formula (see below). Assuming an absolute precision of 0.18 (given the validated parts of the questionnaire), we estimated that 73 responses to the main questions in the second test would enable a Kappa value of ≥ 0.5 to be detected with a power of 0.95 (two-tailed $\alpha = 0.05$). Thus allowing for a 60% response rate, 135 subjects were considered necessary.

4.4.2 Face, content and language validity

Initial content validity was explored through systematic review by experts, and face validity was tested by pre-piloting with 23 volunteers. All questions which had not been used before in the respective language in validated questionnaires were translated using a forward-backward method with 2 different native translators. Comprehensiveness was piloted with native speaker volunteers.

4.4.3 Test-retest reliability

Questions were categorized by the amount of change expected, as described previously for the development of a comparable questionnaire [18], primarily based on the time frame of the question and blinded to the results as follows: ‘no change expected’; ‘change unlikely’; ‘1 unit change expected’; ‘3 unit change expected’; ‘change likely’.

The data from the two periods of answering the questionnaire were compared to assess test-retest reliability. For categorical data, this was estimated by using agreement measures as

percentage agreement, Kappa values, Mac Nemar's S test and Bowker's S test. Percentage agreement gives an estimate of within-patient agreement. The Kappa coefficient indicates when the observed agreement exceeds chance-agreement; a value above 0.6 is generally considered as acceptable. The Mac Nemar's S provide a measure of agreement when used between two measures of the same questionnaire in the same patient. The null hypothesis of the Bowker's S test is that the probabilities of cells in the square table satisfy symmetry. It was used for r x c tables where r>2 or c>2. For the questions with discrete integer data; intraclass correlation coefficient (ICC) was calculated using a 2-way random effects model for agreement.

4.4.4 Construct validity

Comparisons between these samples were made for the total scores of the WHODASII, MIDAS and PHQ9. Comparison between categorical scores of the 3 samples was performed by using a chi-square test. Continuous values of the scores were also used for comparison and a one way-ANOVA was used with the score as dependent variable. Normality was assessed with a Kolmogorov-Smirnov test; if significant, data were log-transformed and analysed if normally distributed. Otherwise the Kruskall-Wallis test was used.

4.4.5 Internal consistency/Content:

Where appropriate, cross-tabulations were used to check for internal consistency. Blocks of questions corresponding to ID, WHODASII, MIDAS and PH9 were compared in terms of correlations. This was done in order to verify if they measure the same construct in a multilingual context and in the newly designed questionnaire. The Cronbach's alpha coefficient was used to explore the overall consistency of the ID, WHODAS II, MIDAS and PHQ-9 questionnaires. The larger the overall alpha coefficient, the more likely that items

contribute to a reliable scale. A value of 0.70 suggests an acceptable reliability coefficient; smaller reliability coefficients are seen as inadequate. A coefficient alpha after deleting each variable independently from the scale was calculated to determine how each item reflects the reliability of the scale. When the coefficient increases after an item is deleted from the scale, one can assume that the item is not correlated highly with other items in the scale. Conversely, if the coefficient decreases, it can be assumed that the item is highly correlated with other items in the scale.

4.5 Results

4.5.1 Population and frequency of headache in the samples

130 questionnaires were completed leading to a response rate of 65% (Fig 1).
Out of this sample, 15.4% (n=20) were from the Pain clinic, 13.1% (n=17) from the primary care centre and 71.5% (n=93) from the lay organisation (Table 1). Fifty-two persons (40%) responded in German, 1 (0.8%) in English, 72 (55.4%) in French and 5 (3.8%) in Portuguese. Eighty-four percent were women, mean age was 41.9 ± 11.5, the gender distribution was significantly different (p=0.03) between centres. There was no statistically significant difference in age, age at onset of headaches, work status and diagnosis of migraine between the 3 groups. Headache frequencies were unequal between centres (p=0.02) with higher headache frequencies in subjects at the pain clinic. In the primary care setting, most individuals were in the 4-9 days/month category. In the pain clinic, most of the patients had headache on ≥15 days/month. The general public population had a similar profile as the primary care setting.

Out of 130 subjects of the whole population, 28 did not answer all the MIDAS questions leading to the unfeasibility to calculation of the total score. Thus 102 subjects only had the

total score. When re-running the comparison without the unhealthy subjects, only 10 subjects out of the 28 had no total scores. 49 subjects had the total score.

Figure 1 Tests and samples used in the different steps of the BURMIG questionnaire validation.

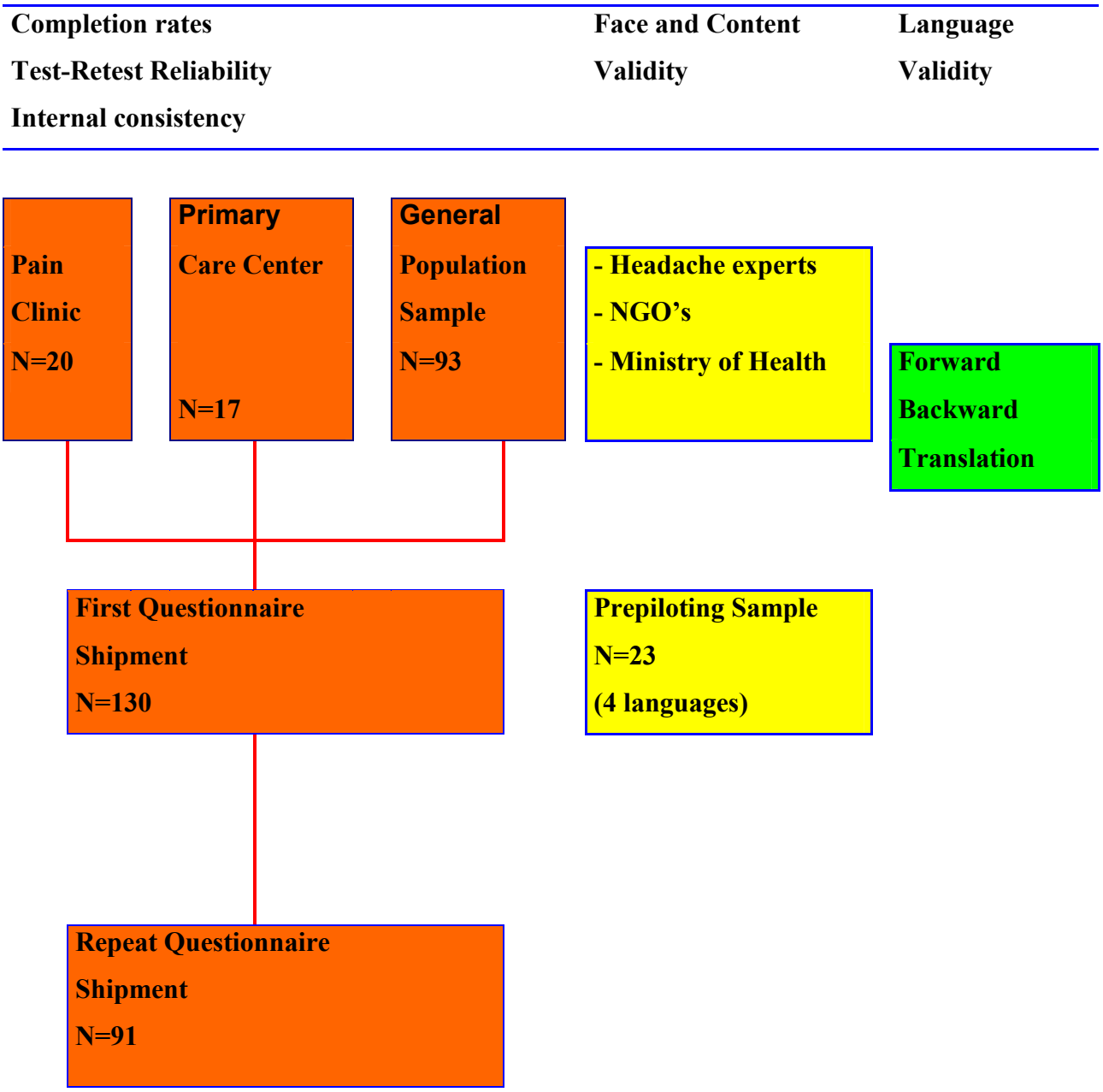


Table 1 Socio-demographic and headache characteristics of the validation sample

		Primary care	**Pain clinic**	**General public**	**All**	**p-value**
Age	Year (mean ± sd)	38 ± 13	39 ± 10	43 ± 11	41 ± 11	0.14
Gender	M/F (%)	0/100	30/70	16/84	16/84	0.03
Work Status	Economic workers (%)	70	75	73	73	0.95
Diagnosis	Migraine	88	70	76	77	0.45
	days/month (%)					
	< 1 (%)	0	0	2	2	
Headache	1 to 3 (%)	29	30	21	24	
frequency	4 to 9 (%)	35	10	45	38	
	10 to 14 (%)	18	15	19	18	
	>15(%)	18	45	12	18	0.02
Age of onset	Year (mean ± sd)	24 ± 10	20 ± 11	20 ± 10	20 ± 10	0.36

4.5.2 Completion rates

Completion rates for the items of the questionnaire varied between 5.83% and 100%. As the questionnaire included some questions with more than one possible choice or sub-questions, only the principal item was kept to evaluate questions with good completion rates. Thus, 63 % questions were found to have completions rates of 90% or more. Questions where there were several choices tended to have completion rates around 10%. There was no difference for completion rates between genders or language groups. Completion rates of the second questionnaire varied from 5.41% to 100% and were very similar to the first questionnaire (63% of questions with completion ≥ 90%).

4.5.3 Test-retest reliability

Out of the 130 subjects recruited for the validation process, 91 subjects replied a second time to the questionnaire sent one month later. Seventy nine single items (incl. sub-questions) were used to assess reliability, excluding open questions; 67.1% of the items (n=53) were over an 80% agreement whereas 13.9% (n=11) ranged between 60% and 80% and 19% (n=15) were below a 60% agreement.

The Kappa coefficient ranged from 0.23 to 0.99. Questions categorized as 'no change expected' (0.86 to 0.99) and 'change unlikely' (0.68 to 0.99) showed a good agreement (Table 2). From the items categorized as '1 unit change expected' or '3 unit change expected' the kappa showed values ranging from 0.45 to 0.92, indicating a poor agreement for some questions; unsurprisingly, from the items categorized as 'change likely' the kappa value showed lower values ranging from 0.23 to 0.77. Questions which showed the smallest agreement were the items from the WHODAS II, PHQ9 and questions 5 and 6 from the MIDAS.

Table 2 Test –Retest reliability with percentage agreement and Kappa values

	% Agreement	Kappa	p-value for Kappa
No change expected	79.12 – 98.90	0.86 – 0.99	<0.0001
Change unlikely	79.12 – 98.90	0.68 – 0.99	<0.0001
± 1 unit change expected	90.11 – 96.70	0.45 – 0.92	<0.0001
± 3 unit change expected	72.53 – 84.62	0.45	<0.0001
Change likely	54.95 – 89.01	0.23- 0.77	<0.0001

Mac Nemar's S test showed no significant differences. Only one item was significant (p=0.03) with the Bowker's S test: No agreement was observed for 'Feeling tired or having little energy' from the question 25 (PHQ9) between the two measures. The intra-class

correlation coefficient for quantitative answers is detailed in Table 2. Values were significant for questions 15 (from WHODAS II) and 18 (from MIDAS) (Table 3).

Table 3 Test –Retest reliability with McNemar's coefficient for 2x2 tables, Bowker's coefficient for more than 2 classes variables and Intraclass correlation for continuous variables.

	Statistic	**p-value**
McNemar's coefficient	0.11 – 3.57	0.74 - 0.06
Bowker's coefficient	0 – 10.07	0.03 - 1.00
Intra-class correlation	0.79 – 0.99	0.04 – 0.92

4.5.4 Construct validity

The mean frequency of headache days was significantly different between the 3 samples (Table 5). While few subjects had high headache frequency in the primary care and general population samples, a large proportion (45% of subjects) in the pain clinic sample had ≥15 headache days per month. However, there was no difference between the 3 samples in terms of average disability attributed to headaches (MIDAS total score) or of depression (as measured by PHQ9). The mean scores of WHODASII, MIDAS and PHQ9 were not different between the 3 samples (Table 6) except for a significant pair-wise difference between the pain clinic and the general population sample with the MIDAS total score ($p<0.05$) (Table 4).

Table 4 Internal consistency

	Raw	**Standardized**
ID Migraine Screener ™	0.26	0.26
WHODAS II Questionnaire	0.80	0.91
MIDAS Questionnaire	0.68	0.74
PHQ-9 Questionnaire	0.85	0.84

A subanalysis was carried-out after omitting patients (n=71) with headache from the general population sample in order to better discriminate WHODASII, MIDAS and PHQ9 values between levels of headaches. The remaining general population sample (n=22) was assumed completely healthy while the pain clinic sample was supposed to be the most affected group. Results showed a clear trend (p=0.06) for the mean number of days with headaches and the presence of depressive disorder (p=0.09). A highly significant difference was observed between the general population sample, the pain clinic and the primary care sample for MIDAS scores (p-value=0.0005) but not for the PHQ9 depressive disorder estimate (Table 5).

The mean WHODASII score did not show any significant difference in this subanalysis while for MIDAS and PHQ9, total scores were significantly different (Table 6).

When further analysing pair-wise relationships between the 3 samples, differences ($p<0.05$) were observed between the MIDAS score of the pain clinic sample and the general population sample when including all subjects, and also between the PHQ9 scores of the primary care and the general population sample (Table 6) when excluding incompletely healthy subjects from the general population sample.

Table 5 Construct validity for Frequency of headaches, MIDAS, and PH9 categorical scores

	Whole population sample					**Healthy subjects**		
	Primary care	Pain clinic	General population sample	ALL	Chi Square	General population sample	ALL	Chi Square
N (mean days per month of headaches)								
Less than 1 day	0 (0%)	(0%)	2 (2.15%)	2		1 (4.55%)	1	
1 to 3 days	5 (29.41%)	6 (30%)	20 (21.51%)	31		7 (31.82%)	18	
4 to 9 days	6 (35.29%)	2(10%)	42(45.16%)	50		9(40.91%)	17	
10 to 14 days	3 (17.65%)	3 (15%)	18 (19.35%)	24		4 (18.18%)	10	
>15 days	3 (17.65%)	9 (45%)	11 (11.83%)	23		1 (4.55%)	13	
Total	17 (13.08%)	20 (15.38%)	93 (71.54%)	130	0.0238	22 (37.29%)	59	0.0629
MIDAS score								
Minimal or infrequent disability	3 (23.08%)	4 (23.53%)	14 (19.44%)	21		9 (47.37%)	16	
Mild or infrequent disability	0 (0%)	0 (0%)	10 (13.89%)	10		5 (26.32%)	5	
Moderate disability	6 (46.15%)	2 (11.76%)	18 (25%)	26		4 (21.05%)	12	
Severe disability	4 (30.77%)	11 (64.71%)	30 (41.67%)	45		1 (5.26%)	16	
Total	13 (12.75%)	17 (16.67%)	72 (70.59%)	102	0.159	19 (38.78%)	49	0.0005
Depressive disorder								
No	14 (82.35%)	17 (85%)	86 (92.47%)	117		22 (100%)	53	
Yes	3 (17.65%)	3 (15%)	7 (7.53%)	13		0 (0%)	6	
Total	17 (13.08%)	20 (15.38%)	93 (71.54%)	130	0.3179	22 (37.29%)	59	0.0977

Headache days, the MIDAS score as a measure of disability and the presence of depression are detailed for the different samples of participants according to their origin. On the right hand side of the table, the subset of healthy participants (without headache) in the generation population sample is detailed.

Table 6 Pairwise differences of WHODASII, MIDAS and PH9 scores between groups

	General population sample				Without unhealthy subjects			
	N	Mean	SD	p-value	N	Mean	SD	p-value
WHODAS-II score12								
Primary care	13	25.85	15.15	0.5752	13	25.85	15.2	0.3015
Pain clinic	15	21.3	18.42		15	21.3	18.4	
General population sample	84	24.14	15.09		21	17.59	12.8	
MIDAS score								
Primary care	13	22.92	22.73	0.2588*	13	22.92	22.7	0.0039*
Pain clinic	17	38.47	33.87		17	38.47	33.9	
General population sample	72	22.71	20.84		19	7.37	7.11	
Score PHQ-9								
Primary care	17	9.24	4.51	0.219	17	9.24	4.51	0.0049**
Pain clinic	20	8.1	5.62		20	8.1	5.62	
General population sample	93	7.53	4.59		22	4.95	2.57	

* Significant pairwise difference between pain clinic and general pop at the 5% level (Tukey post-hoc ANOVA tests)

** Significant pairwise difference between primary care and general pop at the 5% level (Tukey post-hoc ANOVA tests)

4.5.5 Internal consistency/Content:

The standardized values of the Cronbach's alpha to test the consistency of (ID, WHODASII, MIDAS and PH9 tested in the new questionnaire were 0.26, 0.91, 0.74 and 0.84, respectively. Questions categorized by the amount of change expected and compared between the test and the retest time to assess the internal consistency showed a 80% to 100% agreement except for open questions where more than 70% change was observed.

4.6 Discussion

We described the development and methodological testing of a self-reporting questionnaire to evaluate the burden of migraine in the general population.

Completion rates for each question were generally good with the vast majority between 60% and 90%. A small number of questions showed low completion rates which can be explained by the fact that they were part of multiple choice questions. Some other questions did not have to be answered in all participants since they applied only to subgroups. Questions from WHODAS II and PHQ9 showed both, good completion rates, and good reliability. For methodological purposes, we had defined the amount of change expected for each question before administering the questionnaire. Questions where a change had been expected actually showed higher amounts of change and lower reliability. This means, that these items were used in an appropriate way and that they can be used as part of a questionnaire on the impact and burden of migraine and headaches. The question “Feeling tired or having little energy” from PHQ9 was found to have little re-test reliability at one month interval which can be explained by the transient character of this item.

Internal consistency was evaluated independently for each scale tested within in the questionnaire. It was found to be excellent for the MIDAS and somewhat smaller for questions from WHODASII and PHQ9.

Construct validity was found to be acceptable when samples were adequately chosen to discriminate between levels of headache. However, questions from WHODAS showed a poor discrimination between headache patients and the general population. This can be explained by the fact that this tool is not specifically designed for headache sufferers. The headache specific MIDAS, as expected, showed good discriminative power.

4.6.1 Disease Management

Regarding questions on disease management, agreement ranged from 77% to 98% (except for multiple choice questions). Kappa coefficient ranged from 0.68 (0.62 with multiple choice questions) to 1.00 which indicates good agreement between the 2 steps.

The majority of the questions about private and social influence were of the multiple choice type and scored poorly in terms of percentage agreement (10-30%), but had a good retest reliability (kappa coefficients ranging from 0.52 to 0.97). These questions were therefore stable with time and could be used in a large study with a period of recruitment lasting a few months.

4.6.2 Changes brought to the final questionnaire

In the disease management part, two questions on medical doctor consultations were merged into one question allowing a better completion.

In one question on the temporal relation between headache and other problems, in addition to “before”, and “after” a third item “during” was added.

4.7 Conclusions

A new questionnaire, BURMIG, was developed with the aim to estimate the burden of migraine. It uses established and previously validated items for diagnosis and measurement of disability and depression. Questions related to disease management and the influence on daily living were added. The resulting questionnaire was tested in a sample in the Grand Duchy of Luxembourg. Reliability and consistency of BURMIG were found to be comparable to previously published questionnaires. Therefore, this tool is suitable to study larger populations of headache patients.

4.8 Acknowledgements:

The authors are indebted to all physicians, psychologist, pharmacists and patient organizations for their contributions to this study and are especially grateful for the help offered by T. Steiner, Ch. Pull, S. Chatterjis, R.Lipton, J. Schoenen, and A. Mc Gregor. We also thank particularly the 'comité de pilotage': Dr Alexandre Bisdorff, Hôpital Emil Mayrisch, Service Neurologie, Dr Catherine Boisanté, Centre Hospitalier, Centre De Traitement de la Douleur, Dr Robert Goerens, Direction de La Sante, Mme Marie-Anne Kaiffer, Patientevertriedung, Mme Marie-Lise Lair, Crp-Santé CES, Dr Nicole Majery, Service de Sante au Travail Multisectoriel, Mme Joséane Martens-Paulus, Syndicat des Pharmaciens, Dr René Metz, Centre Hospitalier, Service Neurologie, Prof Charles Pull, Centre Hospitalier, Service Psychiatrie Ambulatoire et de Liaison, Mme Véronique Schambourg, Syndicat des Pharmaciens, Dr Yolande Wagener, Direction de la Santé.

4.9 Funding

The study was funded by the Luxembourg Ministry of Research and the Swiss Migraine Trust Foundation.

4.10 References

1 Goadsby, PJ, Lipton R, Ferrari MD. Migraine--current understanding and treatment. N Engl J Med. 346(4): 257-70, 2002.

2 Headache disorders and Public Health. Education and Management, Implications. Geneva: WHO World Health Organization, Department of Mental Health and Substance Dependence WHO/MSD/MBD/00.9. Report No.:WHO/MSD/MBD/00.9.

3 WHO. The world health report 2001: Mental health, New Understanding, New Hope. Geneva: WHO, 2002.

4 Mounstephen AH, Harrison RK. A study of migraine and its effects in a working population. Occup Med (Lond) 1995;45:311-317.

5 van Roijen L, Essink-Bot ML, Koopmanschap MA, Michel BC, Rutten FF. Societal perspective on the burden of migraine in The Netherlands. Pharmacoeconomics 1995;7:170-179.

6 Lipton RB, Amatniek JC, Ferrari MD, Gross M. Migraine. Identifying and removing barriers to care. Neurology 1994;44:S63-68.

7 Lipton RB, Diamond S, Reed M, Diamond ML, Stewart WF. Migraine diagnosis and treatment: results from the American Migraine Study II. Headache 2001;41:638-645.

8 Osterhaus JT, Gutterman DL, Plachetka JR. Healthcare resource and lost labour costs of migraine headache in the US. Pharmacoeconomics 1992;2:67-76.

9 Rasmussen BK. Epidemiology and socio-economic impact of headache. Cephalalgia 1999;19 Suppl 25:20-23.

10 Stang PE, Osterhaus JT. Impact of migraine in the United States: data from the National Health Interview Survey. Headache 1993;33:29-35.

11 Edmeads J, Findlay H, Tugwell P, Pryse-Phillips W, Nelson RF, Murray TJ. Impact of migraine and tension-type headache on life-style, consulting behaviour, and medication use: a Canadian population survey. Can J Neurol Sci 1993;20:131-137.

12 Kryst S, Scherl E. A population-based survey of the social and personal impact of headache. Headache 1994;34:344-350.

13 Lipton RB, Bigal ME, Kolodner K, Stewart WF, Liberman JN, Steiner TJ. The family impact of migraine: population-based studies in the USA and UK. Cephalalgia 2003;23:429-440.

14 Lipton RB, Dodick D, Sadovsky R, et al. A self-administered screener for migraine in primary care: The ID Migraine validation study. Neurology 2003;61:375-382.

15 WHODAS-II, Disability Assessment Schedule [online]. Available at: http://www.who.int/icidh/whodas.

16 Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. Neurology 2001;56:S20-28.

17 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16:606-613.

18 Boardman HF, Thomas E, Millson DS, MacGregor EA, Laughey WF, Croft PR. North Staffordshire Headache Survey: development, reliability and validity of a questionnaire for use in a general population survey. Cephalalgia 2003;23:325- 331.

4.11 Appendix BURMIG questionnaire

Evaluation of the Influence and Management of Headache and Migraine in Luxembourg

Please answer the survey questions honestly regarding your own current health. If you are a primary caregiver for someone else, such as a parent, you may also participate on their behalf. For this questionnaire, it is important that you give an answer to all questions. If you need assistance you can call 45.32.13-54 Monday-Thursday 9h00-17h00.

GENERAL INFORMATION (please tick the correspondent cases)

Question 1: **What is your age: _____(years)**

Question 2: **Gender:** ❑ male ❑ female

Question 3: **What language do you speak at home? (please tick the one you speak mostly at home):**

❑ Luxembourgish ❑ French ❑ German ❑ Portuguese
❑ English ❑ Other :

Question 4: **What is your actual working situation? (Please tick all applicable)**

❑ Full time employed ❑ Self-employed ❑ Retired ❑ Other

❑ Part-time employed ❑ Student/school ❑ Housekeeping/Child care

ABOUT HEADACHE

Question 5: **At what age did you start getting headaches?**

_____ (years)

Question 6: **What is the average number of <u>days per month</u> on which you suffered from headaches <u>during the last 3 months:</u>**

❑ less than 1 day/month ❑ 1-3 days/month ❑ 4-9 days/month
❑ 10-14 days/month ❑ 15 or more days/month

Question 7**:** **Think about (the last 3 months):**

- Are you nauseated or sick to your stomach when you have a headache?

❑ Yes ❑ No

- Does light bother you when you have a headache?

❑ Yes ❑ No

- Has a headache limited your activities for a day or more?

❑ Yes ❑ No

Question 8: **Do you experience problems <u>before, during</u> or <u>after</u> your headache:**

❑ Yes, **before** my headache**:** duration: _____hours (e.g. 2 days = 48 hours)

❑ Yes, **during** my headache**:** duration: _____hours

❑ Yes, **after** my headache**:** duration: _____hours

❑ No

If yes please tick which ones:	**before**	**during**	**after my headache**
❑ Feeling tired	❑	❑	❑
❑ Feeling dizzy	❑	❑	❑
❑ Speech difficulty	❑	❑	❑
❑ Unusual hunger	❑	❑	❑
❑ Visual disturbances (Blurred or altered vision)	❑	❑	❑
❑ Mood changes	❑	❑	❑
❑ Swollen limbs	❑	❑	❑
❑ Other(s):_____	❑	❑	❑

HEALTH AND LIFE (World Health Organization Disability Assessment Schedule II)

Question 9: **How do you rate your overall health in the past 30 days ?**

❑ Very good ❑ Good ❑ Moderate ❑ Bad ❑ Very Bad

The questions in this section ask about difficulties due to health conditions. Health conditions include diseases or illnesses, other health problems that may be short or long lasting, injuries, mental or emotional problems, and problems with alcohol or drugs.
Think back over the last 30 days and answer these questions thinking about how much difficulty you had because of your headache doing the following activities you usually do them. For each question, please tick only one response.

Question 10: **In the last 30 days, how much difficulty did you have in:**

	None	Mild	Moderate	Severe	Extreme/ cannot do
Standing for long periods such as 30 minutes ?					
Taking care of your household responsibilities?					
Learning a new task, for example, learning how to get to a new place?					
How much of a problem did you have joining in community activities (for example, festivities, religious or other) in the same way as anyone else can?					
How much have you been emotionally affected by your health problems?					
Concentrating on doing something for ten minutes?					
Walking a long distance such as a kilometre [or equivalent]?					
Washing your whole body?					
Getting dressed?					
Dealing with people you do not know?					
Maintaining a friendship?					
Your day to day work?					
Overall, how much did these difficulties interfere with your life?					

Question 11: **Overall, in the past 30 days, how many days were these difficulties present?**

Record number of days: _____

Question 12: **In the past 30 days, for how many days were you totally unable to carry out your usual activities or work because of any health condition?**

Record number of days: _____

Question 13: **In the past 30 days, not counting the days that you were totally unable, for how many days did you cut back or reduce your usual activities or work because of any health condition?**

Record number of days: _____

Please answer the questions 14-19 about ALL the headaches you have had over the last three months. Write the answer on the line next to each question.
Write zero if you did not do the activity in the last 3 months.

Question 14: **On how many days in the last 3 months did you miss work or school (because of your headaches)?**

Record number of days: _____

Question 15: **How many days in the last 3 months was your productivity at work or school reduced by half or more (because of your headaches)? (Do not include days you counted in question 14 where you missed work or school)**

Record number of days: _____

Question 16: **On how many days in the last 3 months did you not do household work (because of your headaches)?**

Record number of days: _____

Question 17: **How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches? (Do not include days you counted in question 16 where you did not do household work)**

Record number of days: _____

Question 18: **On how many days in the last three months did you miss family, social or leisure activities (because of your headaches)?**

Record number of days: _____

Question 19: **On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 day, count each day)**

Record number of days: _____

Question 20: **Over the last 2 weeks, how often have you been bothered by any of the following problems?**

Please answer Question 20 not only in relation to your headache but how you felt in general

	Not at all	Several days	More than half the day	Nearly every day	
Little interest or pleasure in doing things					
Feeling down, depressed, or without hope					
Trouble falling/staying asleep, sleeping too much					
Feeling tired or having little energy					
Poor appetite or overeating					
Feeling bad about yourself – or that you are a failure or have let yourself or your family down					
Trouble concentrating on things, such as reading the newspaper or watching television					
Moving or speaking so slowly that other people could have noticed or the opposite – being so fidgety or restless that you have been moving around a lot more than usual					
Thoughts that you would be better off dead or of hurting yourself in some way					

DISEASE MANAGEMENT

Question 21: **Have you consulted a medical doctor for one of the following reasons <u>since your headaches started:</u>**

Please tick all that are applicable:

❑ Head trauma ❑ Hypertension ❑ Sleeping problems

❑ Depression ❑ Anxiety or Panic disorder ❑ Allergies

❑ Eating problems ❑ Asthma ❑ Other : _____

❑ No other reason

Question 22: H**ow many doctors have you already consulted because of your headaches?**

❑ 0 ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ more

Question 23: **If you have already consulted a doctor because of your headaches, did the doctor tell you what kind of headache you suffer from?**

❑ Yes ❑ No

If yes, what kind:

❑ Migraine ❑ Tension headache ❑ Cluster ❑ Stress

❑ Neck problems ❑ Other ❑ I do not remember

Question 24: **How many doctors have you consulted because of your headaches during the last 12 months?**

❑ 0 ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ more

If you have not consulted a doctor because of your headaches during the last 12 months, why not?

❑ my headache improved

❑ my headache did not get better despite the medical consultation more than 12 months ago

❑ other reasons:_____

Question 25: **Have you <u>ever</u> been given any tests to investigate your headaches ?**

❑ Yes ❑ No

If Yes, which one(s):

How many? (number) year(if possible)

❑ MRI of my head …….…… ……

❑ EEG ……

❑ CT scan of my head ……

❑ In depth interview about my headache ……

❑ Other:…… ……..……

Question 26: **Do you currently take any drugs to relieve your headache once it has started?**

❑ Yes ❑ No

If yes, please indicate what drug(s) you are currently taking to relieve your headache: (Please tick all that are applicable, more than one tick possible)

❑ Aspirine, Aspro, Aspégic ❑ Naramig ❑ Family recipe

❑ Dafalgan ❑ Panadol ❑ I do not remember

❑ Ibuprofen, Brufen, Nurofen ❑ Panadol + Codéine

❑ Imitrex ❑ Primpéran ❑ Motilium

❑ Maxalt ❑ Relert ❑ Zomig

❑ Other(s) ……

Question 27: **Looking back <u>at the last three months</u>, on how many days each month did you take medication to relieve your headaches?**

❑ less than 1 day/month ❑ 1-3 days/month ❑ 4-9 days/month

❑ 10-14 days/month ❑ 15 days days/month

Question 28: **How many different drugs have you ever tried to relieve your headaches?**

❑ None ❑ one ❑ 2-4 ❑ 5-7 ❑ more

Question 29: **If there was a drug which would relieve your headaches, how much do you think it would change your quality of life?**

❑ no change at all ❑ slight change ❑ complete new life

Question 30: **Do you currently use a treatment (medication on a daily base or alternative/complementary therapies) to prevent your headache?**

❑ Yes ❑ No

If Yes, which one(s): ……

Question 31: **How many different treatments (medication on a daily base or alternative/complementary therapies) have you ever tried to prevent you from getting a headache:**

❑ none ❑ one ❑ 2-4 ❑ 5-7 ❑ more

If applicable, how successful do rate these treatments to prevent you from getting a headache

Treatment:

…….. ❑ not at all ❑ a little ❑ fair ❑ very

…….. ❑ not at all ❑ a little ❑ fair ❑ very

…….. ❑ not at all ❑ a little ❑ fair ❑ very

…….. ❑ not at all ❑ a little ❑ fair ❑ very

Question 32: **Have you ever controlled or do you currently control your headaches using one of the following self-management techniques?**

❑ Diet/healthy life style ❑ Sports ❑ Food supplements

❑ Meditation/relaxation ❑ Other method(s) of self-management_____

❑ None of the above

If applicable, how successful do rate the methods?

Method:

…….. ❑ not at all ❑ a little ❑ fair ❑ very

…….. ❑ not at all ❑ a little ❑ fair ❑ very

…….. ❑ not at all ❑ a little ❑ fair ❑ very

…….. ❑ not at all ❑ a little ❑ fair ❑ very

Question 33: **Taking into account everything you do to treat your headache, how well do you think you control your headache?**

❑ not at all ❑ a little bit ❑ quite well ❑ completely under control

Question 34: **Please tick of the following services those which you would appreciate to be present to improve your headache:**

Education for the patient ❑

Consultation with a health professional with specialist knowledge of headache ❑

Individualized care ❑

Telephone Helpline ❑

Written information, brochures ❑

Self management courses ❑

Help with medication 'withdrawel' and rehabilitation support ❑

Internet website ❑

Self-help group meetings ❑

Public forum ❑

Information in the press media ❑

Books ❑

Research studies ❑

Other suggestions: …...……

PRIVATE AND SOCIAL IMPACT

Question 35: **Have headaches ever influenced your job situation/career, school choice, job choice?**

❑ Yes ❑ No

If yes, tick all that are applicable:

❑ Less chance /missed promotion

❑ Restricted my job's choice

❑ Afraid of losing my job

❑ Lost my job

❑ Could not pass my exams

❑ Had to change my workplace

❑ Less opportunity to get a job

❑ Had to change school

❑ Bullying

❑ Reduce my working time

❑ Other: _____

Question 36: **At your working place do you encounter situations which worsen your headache, like: (Skip this question if not applicable)**

❑ Light

❑ Air conditioning

❑ Computer screen

❑ Noise

❑ Working positions (e.g. uncomfortable or badly positioned chairs, standing too long etc.)

❑ No relaxation facilities or opportunities

❑ Other: ……

Question 37: **When you talk about your headache do you feel that others understand?**

Your family	❑ No	❑ to some extent	❑ Yes
Your friends	❑ No	❑ to some extent	❑ Yes
Your work colleagues	❑ No	❑ to some extent	❑ Yes
Your employer	❑ No	❑ to some extent	❑ Yes

Most people know about my headache:

❑ Yes ❑ No

Question 38: **Have headaches ever influenced your family situation/partnership?**

❑ Yes ❑ No

If yes, tick all that are applicable:

❑ Arguing ❑ Feeling guilty

❑ Isolation ❑ Divorce

❑ Frustration ❑ Breaking up

❑ Other: _____

Question 39: **Are there any hobbies/social activities which you enjoy doing/participating in, but which you had to limit or which you had to give up/could not participate in because of headache?**

❑ Yes ❑ No

If yes, which ones: ……

……

Question 40: **Do you feel that your social life is constrained because of headache?**

❑ not at all constrained ❑ to some extent ❑ completely

Question 41**: Please tick any popular myths or misconception about headache you are confronted with:**

None ❑

Headache just hurts; you should be able to cope with it easily ❑

Headache only affects weak people ❑

Headache affects people who can't cope with stress ❑

Headache is just putting it up, is just all in the mind ❑

Headache is just an excuse ❑

Only women get headaches ❑

Other: ……

Thank you for taking the time to fill in this question, we value your views!

6 Development and validation of the EUROLIGHT questionnaire to evaluate the burden of primary headache disorders in Europe

Colette Andrée[1,2], Michel Vaillant[1], Jessica Barre[1], Zaza Katsarava[3], Jose Miguel Lainez[4], Marie-Lise Lair[1] , Michel Lanteri-Minet[5], Christian Lampl[6] , Timothy J Steiner[7], Lars Jacob Stovner[8], Cristina Tassorelli[9], Peter S Sándor[10]

[1] Centre d'Etudes en Santé, Centre de Recherche Public – Santé, Luxembourg, Luxembourg

[2] Department of Pharmaceutical Sciences, University of Basle, Switzerland

[3] Department of Neurology, University of Essen, Germany

[4] Department of Neurology, Hospital Clínico Universitario. University of Valencia, Spain

[5] Centre Hospitalo-Universitaire de Nice, France

[6] Department of Neurology and Pain Medicine, Konventhospital Barmherzige Brüder, Linz, Austria

[7] Division of Neuroscience and Mental Health, Imperial College London, London,UK

[8] Norwegian national Headache Centre, St. Olavs University Hospital and Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway

[9] IRCCS Neurological Institute C. Mondino Foundation, Italia

[10] Department of Neurology, University Hospital, Zurich, Switzerland

5.1 Abstract

We developed a 103-item-self reporting questionnaire to assess the burden of primary headache disorders on those affected by them, including headache characteristics, associated disability, comorbidities, disease-management and quality of life. We validated the questionnaire in 5 languages with 426 participants (131 in UK, 60 in Italy, 107 in Spain, 83 in Germany/Austria, and 45 in France).

After a linguistic and a face-content validation we tested the questionnaire for comprehensibility, internal consistency and test-retest reliability at an interval of one month. In the different countries, response rates were between 73% and 100%. Test-retest reliability varied between -0.27 to 1.0 depending of the nature of the expected agreement. The internal consistency was between 0.69 and 0.91.

The EUROLIGHT questionnaire is suitable to evaluate the burden of primary headache disorders, and can be used in English, German, French, Italian and Spanish.

5.2 Background

Headache disorders, including migraine, are common and disabling [1] but under-recognized and under-treated [2, 3]. Consequently, they impose a substantial population burden of ill-health. It is well documented that migraine impairs work and social activities [4, 5]. The *World Health Report 2001* [3] ranks migraine 12th in women and 19th overall amongst all causes of disability in the world. Less is known about other primary headache disorders, but tension-type headache (TTH), being more prevalent, may impose an even higher population disability burden than migraine [6]. Yet this is poorly acknowledged, along with the physical and emotional impact of headache on those directly affected, their carers, family and colleagues, and the social economic burden of headache. For example, fewer than half of people with

migraine are correctly diagnosed, a prerequisite for receiving adequate treatment [7-11]. In comparison with other, less prevalent neurological disorders, headache attracts little attention and is generally accorded low priority [10, 12-14].

The EUROLIGHT project (www.eurolight-online.eu) is an initiative supported by the EC Public Health Excecutive Agency and a partnership activity within *Lifting The Burden*: the Global Campaign to Reduce the Burden of Headache Worldwide (www.l-t-b.org). One of its main objectives is to gather up-to-date and reliable knowledge of the prevalence and impact of migraine, TTH and chronic daily headache across Europe. There is no validated instrument for collecting the data that will achieve this. Therefore, the EUROLIGHT steering committee has developed the EUROLIGHT questionnaire.

This instrument is based largely on the BURMIG questionnaire, and has additions from instruments developed by *Lifting The Burden* [15] .The BURMIG questionnaire was developed in 2004 for a population-based survey of the burden of migraine in the Grand Duchy of Luxembourg. It incorporated previously validated tools for diagnosis, disability assessment and recognition of depression, and added questions on disease management and impact on quality of life[16]. It proved to be consistent and reliable for the Luxembourg population. In order to develop the EUROLIGHT questionnaire for use in different European countries, and also to encompass other headache disorders, the BURMIG questionnaire was revised. We integrated sections to assess disability burden, measure general and disease-specific quality of life (QoL), detect anxiety and depression, and enquire into disease management.

The aim of the present study was to assess the test-retest reliability and validity of the EUROLIGHT questionnaire for use throughout Europe. A pilot validation study in the UK was followed by a multi-country study in France, Luxembourg, Germany, Austria, Italy and Spain.

5.3 Materials and Methods

5. 3.1 Questionnaire development

The content of the BURMIG questionnaire was reviewed and thoroughly revised by the steering committee of the EUROLIGHT project. Priority areas for revision had been defined in a pilot study [16] with support from several patient organisations (Migraine Action Association UK, Switzerland and Luxembourg), international headache experts (see acknowledgements) and the Luxembourg Ministry of Health. The additional or amended items were incorporated into the EUROLIGHT questionnaire after a full literature review of studies on headache burden [17].

The final EUROLIGHT questionnaire (see appendix) contains 103 items, 7% of which are open questions, 15% numeric questions (*ie*, requesting a number for answer) and 78% categorical (requesting the respondent to place a tick in a box). The first section is biographical (age, gender, language and employment). Next are screening questions for headache (life-time and 1-year prevalence), followed by a section on chronic daily headache. The following questions diagnose the headache that the patient considers to be the most bothersome (if more than one headache type is identified). This approach recognised the virtual impossibility of accurately diagnosing, by self-administered questionnaire, more than one headache type in the same individual. The diagnostic questions, for migraine and TTH, were based on the criteria of the International Classification of Headache Disorders, 2nd edition (ICHD-II) [18]. Further questions relate to age at onset and frequency of headache during the previous 3 months. This section is followed by questions about headache yesterday (point prevalence), and then by sections on the use of health-care resources (medicines, investigations, consultations, *etc*) and the impact of headache on work, family life and social activities (including the Headache-Attributed Lost Time (HALT) Index [19]), both for those

with headache and for their household partners. A set of questions determined body mass index (BMI), a risk factor, if high, for frequent headache. Finally, there were questions on general health derived from the World Health Organization Quality of Life bref (WHOQOL - Bref) [20] and the Hospital Anxiety and Depression Scale (HADS) [21].

5.4 Evaluation of the questionnaire

The EUROLIGHT questionnaire was assessed for face, content and language validity; for test-retest reliability over one month, a period of time during which little or no change in the respondent's headache is expected; for the extent to which it could discriminate between respondents with more or less severe disease (construct validity); and for the extent to which individual items correlated with other items relating to the particular area of enquiry (internal consistency). The respective methods are detailed below.

All parts of the study conformed to the ethical standards described in the Declaration of Helsinki. Ethics committee approval was obtained from the National Ethics and Research Board of Luxembourg.

5.4.1 Study population

People with headache were recruited by different means in five countries. In England, they were recruited from the members of Migraine Action UK. In France, consecutive patients were recruited in the Department of Evaluation and Treatment of Pain within the Neurosciences Clinic, University Hospital, Nice. In Luxembourg, people with headache were recruited from the French-speaking employees of CRP-Santé by email. The subjects from Luxembourg and France participated in the evaluation of construct validity. The sample from Germany was derived from an existing data bank of the German Headache Consortium, University Hospital of Essen, a population-based cohort including people with and without

headache. In Austria, consecutive patients were recruited in the Department of Neurology and Pain Medicine, Konventhospital Barmherzige Brüder, Linz; healthy subjects were enrolled from the personnel working at the hospital and their families. In Italy, 50% of subjects with headache came from the waiting list of the Applied Neurological Research Centre of the C Mondino Foundation and 50% were members of the headache patient organization, AI.Ce. Healthy subjects were enrolled from the staff of the research centre. In Spain, respondents with or without headache were recruited from people attending general practitioners for other reasons than headache.

5.4.2 Face, content and language validity

Initial content validity was explored through systematic review by experts, and face validity was tested by pre-piloting with 23 volunteers. All questions not used previously in validated questionnaires in a particular language were forward-and-back translated by two native translators, with reconciliation by a bilingual headache expert. Comprehensibility was tested by native language-speaking volunteers.

5.4.3 Test-retest reliability

Questions were categorized by the amount of change expected within the relevant time frame, as described previously for the development of a comparable questionnaire [(22)], as follows: “no change expected”; “change unlikely”; “up to 1 unit change expected”; “up to 2 units change expected”; “up to 3 units change expected”.. Respondents in this study completed the questionnaire twice, the second time after an interval of one month. At retest they were blinded (beyond what they might have recalled) to their responses on the first occasion.

To assess test-retest reliability, the two sets of answers were compared. For categorical data, agreement measures were the percentage agreement rate, Kappa values, McNemar’s S

test and Bowker's S test. Percentage agreement measures absolute within-patient agreement. The Kappa coefficient indicates whether this agreement exceeds what might be expected by chance: a value >0.6 is generally considered acceptable. For the questions with discrete integer data, the intraclass correlation coefficient (ICC) was calculated using a 2-way random effects model for agreement.

5.4.4 Construct validity and internal consistency

Construct validity was intended to be assessed partly by comparing headache-free participants with headache sufferers and partly by measuring the internal consistency of answers to related questions. In the course of this part of the study, it transpired that some participants recruited as "healthy" were in fact reporting occasional headaches. Construct validity assessment was therefore based on headache frequency rather than presence or absence (low frequency = 0-3 and high frequency >3 headache-days/month). Comparisons between low-frequency and high-frequency headache sufferers were made for the total scores of the WHOQoL, HALT index and HADS. Comparisons between categorical scores of those diagnosed with migraine, other episodic headache and chronic daily headache were performed by chi-squared test. Continuous scores were compared by one way-ANOVA, with the score as dependent variable. Normality was assessed by Kolmogorov-Smirnov test; if this was significant, data were log-transformed and re-analysed if normally distributed; otherwise the Kruskall-Wallis test was used.

Where appropriate, cross-tabulations were used to check for internal consistency. Blocks of questions corresponding to the ICHD-II criteria, WHOQoL, HALT index and HADS were explored for consistency using Cronbach's alpha coefficient: the larger this coefficient, the more likely it was that items contributed consistently to a scale, with a value of >0.70 suggesting acceptable consistency. Recalculating the alpha coefficient after deleting each

question within a set determined how each contributed to the reliability of the scale: when the coefficient increased after a question was deleted, its responses were not highly correlated with those to other questions in the set; conversely, if the coefficient decreased, they were highly correlated.

5.4.5 Sample size calculation

To our knowledge there is no method to calculate the sample size needed to assess face content, language validity, construct validity and internal consistency in a questionnaire validation study. Therefore the sample size calculation was based on the test-retest reliability. Assuming an absolute Kappa precision of 0.18 (based on parts of the BURMIG questionnaire that had been validated previously), we estimated that 73 responses to the main questions in the second test would enable a Kappa value of ≥0.5 to be detected with a power of 0.95 (two-tailed $\alpha = 0.05$). Thus allowing for a 60% response rate, 135 subjects were considered necessary.

5.5 Results

5.5.1 UK Pilot study

Before translations, the English version of the questionnaire was tested in a pilot study of 200 members of Migraine Action UK; 136 questionnaires were returned of which five were deleted from the database because they were duplicated or incomplete. Thus the response rate was 65 %. Of the 131 included respondents, 83 answered a second questionnaire one month later, but 10 of these were excluded because incomplete identification the link impossible to the previously completed questionnaire. Therefore the response rate for retest was 63% (Table 1).

Table 1. Socio-demographic and headache variables for the validation samples in different countries

		UK		Italy		Spain		Germany-Austria		France	
		Test	**Re-test**	**Test**	**Re-test**	**Test**	**Re-test**	**Test**	**Re-test**	**Test**	**Re-test**
Age	Year (mean ± sd)	49.9 ± 11.5	51.3 ± 11.3	38.18 ± 11.67	38.18 ± 11.67	40.44 ± 11.11	40.71 ± 11.01	41.10 ± 11.08	39.43 ± 11.69	50.14 ± 11.75	50.98 ± 11.08
N		131	83	60	60	107	107	83	61	45	43
Gender[1]	M/F (n)	21/110	17/65	17/42	18/42	28/79	28/76	29/53	19/41	9/35	8/35
Work status(%)	full-time earning	45.9	40.0	68.33	68.33	79.44	78.85	56.25	53.33	68.89	65.12
	part-time earning	28.7	25.0	5.00	5.00	8.41	8.65	22.50	23.33	6.67	4.65
	full-time student	2.3	-	16.67	16.67	7.48	8.65	10.00	13..33	4.44	2.33
	unemployed but seeking employment	1.5	3.7	5.00	6.67	0.93	.	2.50	1.67	6.67	11.63
	unemployed and not seeking employment	7.0	3.7	5.00	3.33	3.74	3.85	6.25	8.33	13.33	16.28
	retired	18.6	27.5					2.50	.		
				21.55 ± 4.86	21.47 ± 4.78	20.60 ± 3.84	20.65 ± 3.86			19.65 ± 3.51	19.78 ± 3.37
Age of finishing education	Year (mean ± sd)	19.8 ± 5.5	20.5 ± 7.0					16.00 ± 1.97	15.98 ± 2.28		
Income	GBP/year (mean ± sd)	40524 ± 78018	37379 ± 24609	11.86	13.56	8.05	10.23	28324 ± 27338	29617 ± 26201	21.21	20.59
				42.37	38.98	33.33	31.82			24.24	23.53
Partner	(%)	81.5	85.4	33.90	37.29	28.74	23.86	62.65	65.57	18.18	26.47
				6.78	5.08	11.49	15.91			36.36	29.41
Headache frequency	days/month (%)			5.09	5.08	18.39	18.18				
	< 1	1.5%	3.7%					15.38	10.42	70.45	70.73
	1 to 3	12.2%	17.1%	86.67	86.67	66.36	68.57	50.77	50.00		
	4 to 9	34.3%	33.9%					16.92	27.08		
	10 to 14	25.9%	23.2%					7.69	6.25	2.27	2.56
	>15	25.9%	23.2%	8.89	9.09	11.90	10.00	9.23	6.25	15.91	12.82

[1]Not all subjects answered the question about gender

Completion rates were ≥90% for 86% of single questions at both test and retest. Questions with <90% completion rate were those related to income, questions from the HALT Index and those related to impact on children. One question about the "level of control" over headaches seemed especially difficult to answer, with completion rates of 49% and 55% at test and retest. A question on preventative medications had three response fields (name of medication and how long it had been taken in weeks or months); the first field had completion rates of 45% and 40% for test and retest while the two other fields fell below 10%. Questions on investigations such as MRI and CT also showed completion rates below 10%.

Of the 188 questions and sub-questions of the questionnaire, 79 were analyzed by Kappa coefficient, 55 by ICC, 20 by McNemar test and 59 by Bowker S test to evaluate the reliability (**Error! Reference source not found.**). Because of the nature of responses to them, and the high likelihood of change between test and retest, the reliability of the open-text-field questions could not be quantified.

Among the questions categorized as "no change expected", two of those analyzed by Kappa coefficient were responsible for lowering the rate of agreement (<30%) while all others analyzed in this way showed test-retest agreements of 40-100% (**Error! Reference source not found.**). The Kappa coefficient varied from 0.26 to 1, with questions from the HADS contributing most (from 0.36 to 0.55) to a low value. For questions with quantitative responses, analyzed by ICC, the rate of agreement varied from 1% to 74%, with the extreme low value due to a diagnostic question asking the number of days with headache (Appendix, question 18). Most of these questions were in the range 20% to 25%. The ICC was good for these questions.

For the questions categorized as "up to 1 unit change expected", only a third had agreement rates of <60%. Age had the highest value (98%). These questions were also associated with low Kappa coefficients: only one quarter of them had coefficients >0.5.

Only two questions were categorized “up to 2 units change expected”; these had 12% and 100% agreement rates with Kappa coefficients of 0.16 and 0.66. Six questions were categorized “up to 3 units change expected”: one had an agreement rate of 36%, with a Kappa coefficient of 0.21, which is not a good result, and 5 HALT Index questions showed agreement rates of 25-52 %, with an ICC varying from 0.83 to 0.92, which is a good result.

For questions with two response options, McNemar’s S test showed a significant difference for one question, which asked whether the respondent had a headache yesterday (Appendix, question 32). A change of response to all questions about headache yesterday is expected between test and retest. Only three items were significant ($p<0.05$) on Bowker’s S test: no agreement was observed for questions attempting to measure lost work due to headache (Appendix, question 36 and 37) and the question about how headache was accepted at work (Appendix, question 53).

Internal consistency was evaluated independently for the blocks of questions derived from WHOQoL, the HALT index and HADS. The standardized values of Cronbach’s alpha were, respectively, 0.93, 0.88 and 0.90.

Following this pilot study, the phrasing and the response options of some questions were modified. In general, however, the pilot study showed that the questionnaire was well understood and yielded satisfactory completion rates; therefore, no questions were deleted or added.

5.5.2 Validation study in other countries

The slightly amended questionnaire was translated for validation in the other countries.

5.5.2.1 Populations

The numbers of subjects participating in each country is given in Table 1. There was a female preponderance in all countries. Most respondents were full- or part-time employed or self-employed, while students, unemployed and retired people accounted for 10 to 20%. Average age was 40 years except in France where it was 50 years.

5.5.2.2 Response Rates

Numbers of responders in each country are given in Table 1, varying between 66% and 100%. In Spain, one questionnaire was deleted from the database as it was incomplete.

5.5.2.3 Completion rates

Completion rates for each question were adjusted according to expectation. A rate >100% meant that the participant was not expected to answer a particular question but nevertheless did: for example, some respondents answered that they had not had headache yesterday, but still had taken medicines to relieve headaches on that day. Per country, the percentages of respondents with completion rates over 90% were: Germany-Austria: 69%; Spain 75% ; Italy 65%; France: 82%.

Certain questions had low completion rates. For the question on duration of use of preventative drugs (Appendix, question 45), the rate was <30% in Italy and <10% in the other countries. The questions concerning MRI and CT scans had completion rates <10% in Italy, <30% in Spain and <20% in Germany-Austria. The HALT-Index questions had low completion rates in France, ranging from 52% to 61%.

5.5.2.4 Test-retest reliability

In Italy, 141 questions (including some sub-questions) were used to assess reliability (open questions were excluded, as they could not be quantified). Of these, 42% (n=59) showed >80% agreement, 10% (n=14) ranged from 40% to 80% and 48 % (n=66) had <40% agreement (**Error! Reference source not found.**). In Spain, 149 questions were used (again including sub-questions and excluding the open questions). Of these, 46% (n=69) had >80% agreement, 16 % (n=23) ranged between 40% and 80% and 38 % (n=57) had <40% agreement. In Germany-Austria and in France, 116 questions were used (including sub-questions and excluding open questions), of which 36% (n=42) showed >80% agreement, 21% (n=24) ranged between 40% and 80% and 43% (n=50) had <40% agreement.

Two "no change expected" questions were identified as largely responsible for lowering the rate of agreement below 40%. The first (Appendix, question 15) asked for the medication usually taken to treat chronic daily headache; some participants may not have understood well enough the accompanying text to the question. The second (Appendix, question 56) question asked how well subjects were able to control their headache. In this category, two other questions had low reliability scores. The first asked for the number of days with headache (Appendix, question 18), giving respondents the reply options of "every day" or stating the number of "days/month" or "days/year". The second asked the duration of headache in minutes, hours or days (Appendix, question 20).

Of "up to 1 unit change expected" questions, 26 out of 48 in Italy had agreement rates of <60% (only 11 having Kappa coefficients of >0.5). Corresponding numbers were 29 of 48 in Spain, 24 of 46 in Germany-Austria and 22 of 48 in France; in all countries these questions accounted for the low Kappa coefficients. The question about investigations e.g MRI and CT . (Appendix, question 48) unsurprisingly also had low agreement rates. Questions on the effects of headache on education, career and family planning (Appendix, question 50-76), with 4-6

Table 2. Test –Retest reliability of questionnaire (percent agreement; Kappa values and IntraClass Correlation Coefficient values for variables of 2 modalities; McNemar's coefficient for 2x2 tables and Bowker's coefficient for variables with more than two response options.

	UK			Italy			Spain			Germany-Austria			France-Luxembourg		
	% Agreement	Kappa	p-value	% Agreement	Kappa	p-value	% Agreement	Kappa	p-value	% Agreement	Kappa	p-value	% Agreement	Kappa	p-value
No Change Expected	2.-99	0.26 – 1	<0.0001 – 0.0004	2. - 100	0.65-1.00	<.0001	1. – 98	-0.01 – 1.00	<.0001 – 0091	2.-97	-0.07 – 1.00	<0.0001 – 0.0087	2.-98	-0.06 – 1.00	<.0001 – 0.71
± 1 unit change expected	1. – 100	-0.03 – 0.95	<0.0001 – 7894	2. - 100	-1.04	<.0001-0.74	1. – 100	-0.19 – 1.00	<.0001 – 0.90	2-100	-0.27 – 1.00	<0.0001 – 0.87	2.-100.00	-0.14 – 1.00	<.0001 – 0.80
± 2 unit change expected	12. - 100	0.16 – 0.66	<0.0001 – 0.0115	13	.	.	13	0.35	<.0001	10	0.47	<0.0001	33	0.27	0.0096
± 3 unit change expected	36	0.21	0.0002	13	0.46	<.0001	12	0.28	<.0001	10	-	-	30	0.17	0.0807
	% Agreement	ICC	p-value	% Agreement	ICC	p-value	% Agreement	ICC	p-value	% Agreement	ICC	p-value	% Agreement	ICC	p-value
No Change Expected	1.-73	0.76 - 0.097	0.05-0.80	3. - 95	0.16-0.99	0.02-0.72	7. – 86	-0.06 – 0.99	0.06 – 0.56	2.-85	0.13-0.99	0.14-1.00	2.-93	0.72 – 0.99	0.0781 – 0.8118
± 1 unit change expected	98	0.99	<0.0001	100	1	.	97	0.99	0.1	97	0.89	0.95	100	0.99	0.0272
± 2 unit change expected	-	-	-	58 - 65	0.60-0.97	0.03-0.69	55 – 60	0.89 – 0.95	0.05 – 0.85	28-38	0.55-0.94	0.14-0.96	23-33	0.58 – 0.94	0.0409 – 0.4332
± 3 unit change expected	25-52	0.83-0.99	<0.0001-0.66	Dez 65	0.83-0.93	0.10-0.01	8 – 69	0.80 – 0.83	0.12 – 0.28	8.-64	0.89-0.99	0.15-0.21	16-65	0.80 – 0.86	0.0348 – 0.4198
Change likely	1.-31	0.55-0.99	0.32-0.93	2. - 100	-3.55	0.01-1.00	1. – 100	-27.15 – 0.99	0.06 – 1.00	2.-100	-3.24	0.13-0.87	2.-100.00	-6.64 – 0.99	0.0004 – 0.8790
	Not significant		Significant		Not significant		Significant		Not significant		Significant		Not significant		Significant	
	Statistic	p-value	Statistic	p-value	Statistic	p-value	Statistic	p-value	Statistic	p-value	Statistic	p-value	Statistic	p-value	Statistic	p-value
McNemar's coefficient	-	-	-	-	0-3	1-0.1025	4-14	0.0455-0.0002	0-4	1-0.0588	-	-	0-3	1-0.083	-	-	0-2	1-0.1573	4-6	0.0455-0.0143
Bowker's coefficient	-	-	-	-	0-6	1-0.81	8	0.046	0-9	1-0.5	54.8-64.8	<0.0001	0.3-10	0.95-0.12	31.36-35	<0.0001	0-9	1-0.17	22	0.0012
Intra-class correlation	0.6-1	0.32-0.63	0.89-0.99	0.048-<0.0001	-3-1	0.42-0.90	0.93-0.97	0.013-0.034	-27-1	0.061-0.18	0.88	0.046	-2-1	0.87-1	-	-	-7-1	0.52-0.74	0.84-0.99	0.0004-0.041

possible response options, had agreement rates of <10% in Italy. As multiple responses could be chosen, completion rate was calculated for each possibility. As a consequence, percentage changes were very low for all responses other than "no". Three questions of the WHOQOL and one from the HADS showed significant Bowker S tests in Germany-Austria, Spain and France, meaning that there was lack of reliability over time.

There was one question with "up to 2 units change expected", and this had very low agreement rates: Italy 13%, Germany-Austria 10% with Kappa=0.47, France 33% with Kappa=0.27, Spain PA=13% with Kappa = 0.35.

Of questions in the category "up to 3 units change expected", only one had low agreement rates: in Italy (3%, Kappa=0.46), Spain (12%, Kappa =0.28) and France (30%, Kappa=0.17). However, the poorest agreement was for the HALT index, the reliability of which was measured by the ICC associated with the percentage agreement rate: in Italy, 58-65% with ICC = 0.60 to 0.97; in Spain 90-100 % with ICC = 0.88 to 0.95; in Germany-Austria 28-38% with ICC = 0.55 to 0.94 and in France 23-36% with ICC = 0.58 to 0.94.

5.5.2.5 Construct validity and internal consistency

The four populations were relatively similar overall with respect to age, gender and employment status. However, there were significant differences in each country between headache sufferers and participants without headache (Table 3). Age was higher in the French speaking sample with high headache frequency. Males were more frequent amongst the "headache-free" participants, except in Italy. There were more employed persons amongst people with headache in Italy and Germany-Austria compared with Spain and France-Luxembourg (significantly for France-Luxembourg).

Table 3. Internal consistency of question blocks (WHOQoL, HALT, HADS) (standardized values of Cronbach's alpha)

	UK	Italy	Spain	Germany-Austria	France-Luxembourg
WHOQoL	0.93	0.86	0.86	0.9	0.82
HALT index	0.88	0.81	0.86	0.91	0.69
HADS	0.9	0.88	0.89	0.91	0.78

Internal consistency was evaluated independently for each block of questions derived from WHOQoL, HALT index and HADS. The standardized values of Cronbach's alpha were high in all cases, indicating excellent consistency.

It is indicative of good construct validity that the mean scores for WHOQoL, HADS overall, HADS anxiety (HADS A) and HADS depression (HADS D) were significantly different between those with and those without headache in each country. In addition, the HALT index, used to compare groups with low and high headache frequencies in France-Luxembourg, showed significantly higher scores in the latter.

We further investigated construct validity by comparing those with different types of headaches (migraine, other episodic headache or chronic daily headache) (Table 5). The mean scores of WHOQoL were significantly different between these in each country. The mean HADS, HADS-A and HADS D scores were significantly different between these in each country except Spain. The mean scores of the HALT index were significantly different in each country except France-Luxembourg.

Table 4. Construct validity for WHOQoL, HADS and HALT index in relation to headache status.
* one subject was excluded due to a high score of 261

			Country	Headache	No headache	ALL	p-value
Age	Year	(mean ± sd)	Italy	38.5 ± 10.9	37.4 ± 13.4	38.2 ± 11.7	0.4692
			Spain	39.4 ± 10.9	42.9 ± 11.4	40.4 ± 11.1	0.119
			Germany and Austria	42.9 ± 9.9	37.8 ± 12.5	41.1 ± 11.1	0.0597
			France and Luxembourg	47.8 ± 13.1	37.1 ± 11.8	41.8 ± 13.4	<.0001
Gender	M	(%)	Italy	25	36.8	28.8	0.34
			Spain	16.2	48.5	26.2	0.0005
			Germany and Austria	26.4	51.7	35.4	0.0219
			France and Luxembourg	17.1	37.2	28.3	0.0326
Work Status	Economic workers	(%)	Italy	73.2	57.9	68.3	0.24
			Spain	75.7	87.9	79.4	0.1492
			Germany and Austria	82.7	71.4	78.8	0.2401
			France and Luxembourg	68.3	86.6	78.5	0.0335
WHOQoL		(mean ± sd)	Italy	27.5 ± 4.6	32.6 ± 3.2	29.1 ± 4.9	<.0001
			Spain	28.1 ± 5.2	30.2 ± 4.7	28.8 ± 5.1	0.0382
			Germany and Austria	30.3 ± 5.9	34.0 ± 4.6	31.5 ± 5.8	0.012
			France and Luxembourg	27.7 ± 5.2	32.2 ± 3.7	30.3 ± 4.9	<.0001
HADS		(mean ± sd)	Italy	13.3 ± 6.3	4.3 ± 3.7	10.4 ± 7.0	<.0001
			Spain	12.5 ± 6.9	8.5 ± 7.0	11.2 ± 7.2	0.0047
			Germany and Austria	12.4 ± 7.8	6.1 ± 6.3	10.3 ± 7.9	0.0003
			France and Luxembourg	17.4 ± 6.5	11.6 ± 6.5	14.2 ± 7.1	<.0001
HADS Anxiety		(mean ± sd)	Italy	6.9 ± 3.7	2.4 ± 2.4	5.5 ± 3.9	<.0001
			Spain	6.7 ± 4.0	4.1 ± 4.0	5.9 ± 4.2	0.0005
			Germany and Austria	7.3 ±4.0	3.4 ± 3.4	5.9 ± 4.2	<.0001
			France and Luxembourg	9.9 ± 3.6	7.1 ± 3.7	8.3 ± 3.9	0.0003
HADS Depression		(mean ± sd)	Italy	6.2 ± 3.6	1.9 ± 1.8	4.8 ± 3.8	<.0001
			Spain	5.7 ± 3.8	4.4 ± 3.5	5.3 ± 3.7	0.095
			Germany and Austria	5.1 ± 4.6	2.6 ± 3.2	4.3 ± 4.3	0.0091
			France and Luxembourg	7.5 ± 3.6	4.7 ± 3.8	5.9 ± 3.9	0.0005
HALT Index		(mean ± sd)	Italy				
			Spain				
			Germany and Austria				
			France and Luxembourg	28.7 ± 65.7	1.9 ± 3.5	9.5 ± 36.3	<.0001
HALT Index*		(mean ± sd)	Italy				
			Spain				
			Germany and Austria				
			France and Luxembourg	12.1 ± 14.2	1.9 ± 3.5	4.7 ± 9.0	<.0001

Table 5. Construct validity for WHOQoL, HADS and HALT in relation to headache diagnoses

		Italy				Spain				Germany-Austria				France			
Variable		**N**	**Mean**	**SD**	**p**	**N**	**Mean**	**SD**	**p**	**N**	**Mean**	**SD**	**p**	**N**	**Mean**	**SD**	**p**
WHOQOL	others headaches	20	30	3,9	0,0031	47	30	4,7	0,0182	41	32	3,7	0,0041	12	25	5,4	0,0285
	migraine	12	30	5,1		25	27	5,3		9	24	7,8		16	30	4,8	
	chronic daily headaches	15	25	3,7		9	25	3,7		6	28	8,1		11	27	3,4	
HADS	others headaches	19	9	6,1	0,0118	47	11	6,7	0,5368	44	10	6,7	0,0169	12	23	4,8	0,0038
	migraine	12	12	7,7		24	12	6,8		10	18	6,7		15	16	6,3	
	chronic daily headaches	16	16	4,7		8	15	8,6		6	16	11,0		12	18	4,9	
HADS_A	others headaches	20	5	3,7	0,0293	47	6	4,3	0,3914	45	6	3,8	0,0738	12	12	3,1	0,0372
	migraine	12	7	4,6		25	6	3,6		10	9	3,3		16	9	3,4	
	chronic daily headaches	16	8	2,7		8	8	3,8		6	8	5,5		12	10	3,3	
HADS_D	others headaches	19	4	2,8	0,0122	47	5	3,4	0,6366	44	4	3,4	0,013	13	10	2,4	0,0047
	migraine	12	6	4,2		24	6	3,6		10	8	4,3		16	6	3,3	
	chronic daily headaches	16	8	3,2		9	7	5,2		6	8	7,4		13	8	2,8	
HALT	others headaches	17	16	34,2	0,0004	35	8	13,7	<0.0001	24	2	3,2	0,0003	4	27	18,7	0,121
	migraine	12	19	11,3		23	16	16,9		7	35	54,8		6	8	5,4	
	chronic daily headaches	16	67	61,6		9	50	34,3		2	72	53,7		4	68	128,9	

HADS: Hospital Anxiety and Depression scale

HADS_A: HADS-Anxiety, HADS_D: HADS-Depression

5.6 Discussion

This paper describes the development and testing of the EUROLIGHT questionnaire to evaluate the burden of headache disorders in different European populations. The questionnaire originated in the BURMIG questionnaire, and was revised after a systematic literature review and discussions among headache experts and lay persons in the EUROLIGHT steering committee. The English version was tested in a UK pilot study, and after some minor amendments the resulting questionnaire was translated and tested in a German version in Austria and Germany, a French version in France and Luxembourg, a Spanish version in Spain and an Italian version in Italy.

As to test-retest reliability, good response rates were achieved, and completion rates for each question were generally good with the majority (65% to 80%) above 90%. A small number of questions required modification in the light of likely causes for low completion rates. Sub-questions asking for the total number of days or occasions were deleted as they were not completed by respondents. Questions with text field for respondents to fill in also had to be avoided. Questions from WHOQoL and HADS showed good completion rates, and good reliability. This was not the case for the HALT index, especially in France.

For methodological purposes, we had defined the amount of change expected for each question before administering the questionnaire. Questions where a change had been expected did show higher amounts of change, indicating that these items were understood correctly and therefore can be used as part of the EUROLIGHT questionnaire.

The reliability coefficients also showed convincing results. Kappa and ICC showed values above the defined significance threshold (see Methods). However a small number of questions needed to be modified to increase the reliability of the questionnaire.

Internal consistency was found to be excellent for WHOQoL, HADS, HADS A, HADS D and the HALT index.

Construct validity was found to be acceptable in different countries as the relevant questions were able to discriminate between groups of respondents with different headache frequencies and diagnoses. The tools WHOQoL, HADS and HALT index used within the questionnaire discriminated well between those with and those without headache. In headache sufferers alone, questions from the HADS showed a low discrimination between headache types, which is unsurprising, as comorbidity is known to differ little between headache type but more according to headache frequency [23-25]. The headache-specific tool HALT showed good discriminative power in most counties, although not in France and Luxembourg.

For questions on disease management, test-retest agreements ranged from 77% to 98% (except for questions with multiple response options). Kappa coefficients ranged from 0.68 (0.62 for questions with multiple response options) to 1.00, which indicates good agreement.

The majority of questions about private and social impact were of the type with several response options, and these scored poorly in terms of agreement rate (10-30%) but had a good test-retest reliability (Kappa coefficients ranging from 0.52 to 0.97). As the responses to these questions were stable over time we believe that they truly reflected the headache impact on patients' lives over a certain period and not only how they perceived it on that day.

It is a weakness in the development of the questionnaire that the diagnostic questions have not yet been validated against a gold standard method for diagnosing headaches (interview and examination by a headache expert), which is mandatory when diagnostic accuracy is of paramount importance [26]. Diagnostic validation should be done in the population to be studied and, since the present study was mostly performed among headache patients who had already been diagnosed and treated, this was not done. When the population-based studies with the EUROLIGHT questionnaire are performed, some sort of validation in the different countries is planned in order to assess the diagnostic precision of the questionnaire.

5.7 Conclusion

The EUROLIGHT questionnaire was developed in order to estimate the burden of headache disorders in Europe. Established and recently validated tools for diagnosis, disability and comorbidity were supplemented with more detailed questions on disease management and impact on school, work, family, social life and quality of life. The resulting questionnaire was tested in UK, Italy, Spain, Germany, Austria, France and partly in the Grand Duchy of Luxembourg.

Reliability and consistency were found to be comparable to those of previously published questionnaires [16, 22]. The validation process resulted in relatively minor changes.

We believe the final EUROLIGHT questionnaire, at least in the 5 languages that have been tested, will give a reliable and valid picture of the impact and burden of primary headache disorders in European populations. Since headache is a considerable burden for people everywhere, we hope that the questionnaire can be adapted for use in many other countries and cultures.

5.8 Acknowledgements:

The authors are indebted to patient organizations within the World Headache Alliance for their contributions to this study and are especially grateful for the help offered by S. Chatterji, R. Lipton, J. Schoenen and A. MacGregor.

5.9 Funding

EUROLIGHT is a European initiative supported by a grant of the EC, Executive Agency for Health and Consumers (EAHC) and promoted by the Centre of Public Research, Luxembourg. EUROLIGHT is a partner within *Lifting The Burden*: the Global Campaign to Reduce the Burden of Headache Worldwide.

5.10 References

1 Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Headache Classification Committee of the International Headache Society. Cephalalgia. 1988;8 Suppl 7:1-96.

2 Crisp AH. Delivery of postgraduate medical education--who pays? Br Med J. 1977;1:1397-9.

3 WHO. The world health report 2001 : mental health, New Understanding, New Hope. Geneva: WHO, 2002.

4 Mounstephen AH, Harrison RK. A study of migraine and its effects in a working population. Occup Med (Lond). 1995;45:311-7.

5 van Roijen L, Essink-Bot ML, Koopmanschap MA, Michel BC, Rutten FF. Societal perspective on the burden of migraine in The Netherlands. Pharmacoeconomics. 1995;7:170-9.

6 Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A, et al. The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia. 2007;27:193-210.

7 Lipton RB, Amatniek JC, Ferrari MD, Gross M. Migraine. Identifying and removing barriers to care. Neurology. 1994;44:S63-8.

8 Lipton RB, Diamond S, Reed M, Diamond ML, Stewart WF. Migraine diagnosis and treatment: results from the American Migraine Study II. Headache. 2001;41:638-45.

9 Osterhaus JT, Gutterman DL, Plachetka JR. Healthcare resource and lost labour costs of migraine headache in the US. Pharmacoeconomics. 1992;2:67-76.

10 Rasmussen BK. Epidemiology and socio-economic impact of headache. Cephalalgia. 1999;19 Suppl 25:20-3.

11 Stang PE, Osterhaus JT. Impact of migraine in the United States: data from the National Health Interview Survey. Headache. 1993;33:29-35.

12 Edmeads J, Findlay H, Tugwell P, Pryse-Phillips W, Nelson RF, Murray TJ. Impact of migraine and tension-type headache on life-style, consulting behaviour, and medication use: a Canadian population survey. Can J Neurol Sci. 1993;20:131-7.

13 Kryst S, Scherl E. A population-based survey of the social and personal impact of headache. Headache. 1994;34:344-50.

14 Lipton RB, Bigal ME, Kolodner K, Stewart WF, Liberman JN, Steiner TJ. The family impact of migraine: population-based studies in the USA and UK. Cephalalgia. 2003;23:429-40.

15 Steiner TJ, Martelletti P (eds). Aids for management of common headache disorders in primary care. *J Headache Pain* 2007; 8 (suppl 1): S1-S47

16 Andrée C, Vaillant M, Rott C, Katsarava Z, Sandor PS. Development of a self-reporting questionnaire, BURMIG, to evaluate the burden of migraine. The journal of headache and pain. 2008;9:309-15.

17 Stovner L, Andrée C, On behalf of the Eurolight Steering Committee. Impact of headache in Europe: a review for the Eurolight project. The Journal of Headache and Pain. 2008;9:139-46.

18 The International Classification of Headache Disorders. 2nd Edition. Cephalalgia. 2004;24:1-160.

19 Steiner TJ. The HALT and HART indices. J Headache Pain 2007; 8 suppl 1: S22-S25.

20 The WHOQOL Group, (1998), Development of the World Health Organization WHOQOL-BREF Quality of Life Assessment, Psychological Medicine, vol. 28, p.551-558.

21 Zigmond, A. S. & Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale. Acta Psychiatrica Scandinavia 67;361-370. (Psychological Medicine, 1997, 27; 363-370. Copyright 1997 Cambridge University Press).

22 Boardman HF, Thomas E, Millson DS, MacGregor EA, Laughey WF, Croft PR. North Staffordshire Headache Survey: development, reliability and validity of a questionnaire for use in a general population survey. Cephalalgia. 2003;23:325-31.

23 Zwart JA, Dyb G, Hagen K, Odegard KJ, Dahl AA, Bovim G, Stovner LJ. Depression and anxiety disorders associated with headache frequency. The Nord-Trondelag Health Study. Eur J Neurol. 2003;20:147-52.

24 Aamodt AH, Stovner LJ, Hagen K, Zwart JA. Comorbidity of headache and gastrointestinal complaints. The Head-HUNT Study. Cephalalgia. 2008;28:144-51.

25 Aamodt AH, Stovner LJ, Langhammer A, Hagen K, Zwart JA. Is Headache Related to Asthma, Hay Fever, and Chronic Bronchitis? The Head-HUNT Study. Headache. 2007;47:204-12.

26 Stovner LJ. Headache epidemiology: how and why? J Headache Pain. 2006;7:141-4.

Appendix: EUROLIGHT questionnaire

Lifting The Burden

The Global Campaign to Reduce the Burden of Headache Worldwide

A partnership in action between the World Health Organization, World Headache Alliance, International Headache Society and European Headache Federation

Impact of headache questionnaire - Eurolight

To be answered by headache sufferers
AND
by people who do not suffer from headaches

Eurolight is a partnership activity within Lifting The Burden: WHO's Global Campaign to Reduce the Burden of Headache Worldwide, supported by a grant of the European Union Executive Agency for Health and Consumers and promoted by the Centre of Public Health Research in Luxembourg.

Center identifier	_____
Your date of birth	**Day___ /month____ /year___**

Thank you for answering the following questions. Please begin by entering today's date, and then answer all questions on this day.

1	Please enter today's date	**Day___ /month____ /year___**

2	What is your age? **_____ years**
3	What is your gender? (please tick one box) **male** ☐ **female** ☐
Social situation questions	
4	Which of these is closest to your personal situation? (please tick one box only) **employed or self-employed** ☐ **homemaker or housewife** ☐ **student** ☐ **unemployed** ☐ **retired** ☐
5	Are you now married or living with a household partner? (please tick one box) **no** ☐ **yes** ☐
6	What is your total net household income per year? (please tick one box) **less than 18 000 €** ☐ **between 18 000€ and 29 999 €** ☐ **between 30 000 € and 41 999 €** ☐ **between 42 000 € and 59 999 €** ☐ **more than 59 999 €** ☐
7	How old were you when you left full-time education? **_____years** **still in process** ☐
8	What is your native language (the language you first learned to speak)? **enter name of language: _____**
9	What language do you usually speak in your own home? **enter name of language: _____**
Screen questions	
10	Have you ever had a headache? (please tick one box) **no** ☐ (if no, go directly to question 74) **yes** ☐

11	Have you had a headache during the last year? (please tick one box) **no** ☐ (if no, go directly to question 74) **yes** ☐
12	During the last 30 days, on how many of these days did you have a headache? (please enter number of days between 0 and 30) **_____ days** If you answered 15 or more, please continue with questions 13-16. Otherwise, go directly to question 17.
Daily headache questions You have said that you had headache on 15 or more days in the last month. Please think about these headaches.	
13	How long, during each day, do these headaches usually last? (please enter the number of minutes or hours) **_____ min or _____ hr**
14	Do you usually take any medication to treat these headaches? (please tick one box) (please note that this question is about treatment to relieve the headache, not daily treatment to prevent headache) **no** ☐ (if no, go directly to question 17) **yes** ☐
15	What medications do you use <u>most</u> to treat these headaches? (please note that this question is only about treatment to relieve headache) (if you use no medications at all for these headaches, please tick the box) **none** ☐ **name the most-used medications: _____**
16	Altogether, on how many days in the last 30 days did you take these medications? (please enter number of days between 0 and 30) **_____ days**

"Most bothersome headache" questions

These are questions on the headaches that interfere most with your life. These headaches may be the same as the headaches you have just described, or they may be different headaches if you have more than one type of headache.

17

Please think about your headaches. Do you think they are all of one type, or are they of more than one type? (please tick one box)

one ☐

more than one ☐

If you answered one, the next questions are to diagnose this headache. Please start at question 18.

If you answered more than one, please start also at question 18 but from now on focus only upon the headache type that on the whole bothers you most (*ie*, interferes most with your life).

Diagnostic questions

18

How often do you have this type of headache?
(please tick box or enter the number of days per month or per year)

everyday ☐ **_____days/month** **_____days/year**

19

How long does this type of headache usually last?
(please enter the number of minutes, hours or days)

_____ min **_____hr** **or** **_____ days**

20

Is your last answer (to question 19) with or without having taken medication?
(please tick one box)

with ☐

without ☐ (if you answered "without medication", please go to question 22)

21

How long would it last if you did not take medication?
(please enter the number of minutes, hours or days)

_____ min **_____hr or _____ days**

22

How bad is this headache usually? (please tick one box)

not bad ☐ **bad** ☐ **very bad** ☐

23

There are many ways of describing a headache, but most headaches are either throbbing or pressing.
Thinking still of this type of headache, which best describes the pain? (please tick one box)

throbbing or pulsating
(this means varying in time with the heart beat) ☐

pressing, squeezing or tightening ☐

24	Is the pain of this headache usually on only one side of the head? (please tick one box) **no** ☐ **yes** ☐
25	Does exercise (like walking or climbing stairs) tend to make it worse? (please tick one box) **no** ☐ **yes** ☐
26	Thinking still of this type of headache, how does it affect your ability to do day-to-day activities? (please tick one box) **can do everything as normal** ☐ **cannot do some things** ☐ **can do nothing** ☐
27	With this headache, do you usually feel sick (as though you may throw up)? (please tick one box) **no** ☐ **yes** ☐
28	With this headache, are you usually actually sick (do you throw up)? (please tick one box) **no** ☐ **yes** ☐
29	When you have this type of headache, does daylight or other lighting bother you? In other words, do you prefer to be in the dark? (please tick one box) (this question refers to ordinary levels of light, not bright lighting) **no** ☐ **yes** ☐
30	When you have this type of headache, does noise bother you? In other words, do you prefer to be in the quiet? (please tick one box) (this question refers to ordinary levels of noise, not very loud noise) **no** ☐ **yes** ☐
31	Has a doctor ever given you a diagnosis for this headache? (please tick one box and, if applicable, enter the diagnosis) **no** ☐ **If yes, please write the diagnosis: _____** **yes** ☐

The next series of questions are specifically about any headache you had yesterday (the day before you fill in your answers). This may be the same headache as the one you have just been describing, or it may be a different type of headache if you have more than one type.
It is very important that the answers you give are about yesterday and not any other day.

Questions about yesterday

32	Did you have a headache yesterday? (please tick one box) **no** ☐ (if no, go directly to question 44) **yes** ☐
33	Was this the type of headache you have just been describing? (please tick one box) **no** ☐ **yes** ☐
34	Please now think about the headache you had yesterday. How long did it last? (please tick one box) **less than 1 hour** ☐ **1-4 hours** ☐ **5-12 hours** ☐ **more than 12 hours** ☐
35	How bad was your headache yesterday? (please tick one box) **Not bad** ☐ **Bad** ☐ **Very bad** ☐
36	Please now think about everything you wanted to do yesterday if you had not had a headache. How much of this did you actually do? (please tick one box) **Nothing** ☐ **less than half** ☐ **more than half** ☐ **everything** ☐
37	Was yesterday a workday for you (either at your job or at school)? (please tick one box) **no** ☐ (if no, go directly to question 41) **yes** ☐

38	Because of your headache, were you absent from work or school yesterday? (please tick one box) **No** ☐ **Absent less than half the day** ☐ **Absent more than half the day** ☐ **Absent the whole day** ☐ (if absent the whole day please go to question 40)
39	If you went to work or school with your headache yesterday, how much of your work did you get done? (please tick one box) **Nothing** ☐ **less than half** ☐ **more than half** ☐ **everything** ☐ (if everything, please go to question 41)
40	Will you be able to make up for this today or later? (please tick one box) **no** ☐ **yes** ☐
41	This question is about household work or general chores that you wanted to do yesterday if you had not had headache. How much of this did you actually do? (please tick one box) **Nothing** ☐ **less than half** ☐ **more than half** ☐ **everything** ☐
42	This question is about leisure and social activities that you wanted to do yesterday if you had not had headache. How much of this did you actually do? (please tick one box) **nothing** ☐ **less than half** ☐ **more than half** ☐ **everything** ☐

43

What treatment did you take for the headache you had yesterday?
(please tick the box if you took nothing; otherwise, please list the names and amounts of all medications taken yesterday)
nothing at all ☐

List medications: (please list medications for headache, not for any other illnesses)	**how many times you took each yesterday**
______	_____

Health care questions

The aim of the following questions is to help us know how much health care should be available to meet the needs of people with headache.

44

Many different medications may be used to treat headache. This question is about any of these medications you may have taken for headache in the last 30 days
Please tick the first box if you took nothing at all in the last 30 days. Otherwise, please look at these lists, and think about which of these you have used in the last 30 days.
Please tick one box by each medication.

Nothing at all ☐

	Not used	**Used once**	**Used more than once**
almotriptan (Almigran)	☐	☐	☐
eletriptan (Relert)	☐	☐	☐
naratriptan (Naramig)	☐	☐	☐
rizatriptan (Maxalt)	☐	☐	☐
Sumatriptan, Imitrex, Merck-sumatriptan	☐	☐	☐
zolmitriptan (Zomig)	☐	☐	☐
ergotamine Dihydergot, Dystonal (Cafergot)	☐	☐	☐
domperidone Motilium (Zilium)	☐	☐	☐
Metoclopramide Primperan, (Docmetoclo, Dibertil)	☐	☐	☐
Aspirine Acetylsalicylique acide (Sedergine, Dispril)	☐	☐	☐
Diclofenac Voltaren, Motifene	☐	☐	☐
Ibuprofene Brufen, Nurofen, Spidifen,(Advil-mono)	☐	☐	☐
Naproxene Aleve, Apranax (Naprosyne)	☐	☐	☐
Paracetamol Dafalgan, Panadol, perdolan (dolprone)	☐	☐	☐
Proprietary combination drugs:			
Migpriv (acetylsalicylate lysine, metoclopramide	☐	☐	☐

44 cont

Please list any other medications you have used to treat your headache in the last month?

Name(s) of medication(s): (please list medications for headache, not for any other illnesses)	**Used once**	**Used more than once**
_____	☐	☐
_____	☐	☐
_____	☐	☐
_____	☐	☐

45

Medications to *prevent* headaches are usually taken daily. Are you taking any of these?
Please enter the name(s) and, by each one, for how long in weeks or months you have been taking it.

Name(s) of medication(s):	**Weeks**	**Months**
_____	_____	_____
_____	_____	_____

46

Botulinum toxin (Botox or Dysport) is used sometimes as a treatment for headaches, although it is not proven to be helpful.
Have you been treated with Botulinum toxin for your headaches in the last year?

no ☐ **yes** ☐

47

Many people with headache treat themselves, but others need professional advice.
Have you had professional advice about your headaches in the last year? Who from, and how many times?
Please tick all boxes that apply and, for each ticked box, enter the number of times in the last year.

no-one ☐

		Number of times
nurse	☐	_____
physical therapist (physiotherapist, osteopath, chiropractor)	☐	_____
primary-care doctor (GP)	☐	_____
headache specialist	☐	_____
hospital emergency room	☐	_____
other (please specify):_____	☐	_____

48	Most people with headache do not require any investigations, but occasionally these tests are done. Because of your headaches, have you had any of these tests in the last year? (please tick <u>all</u> that apply) **MRI brain scan** ☐ **CT brain scan** ☐ **x-rays of the neck** ☐ **eye tests (for glasses)** ☐ **blood tests** ☐ **other (please specify): _____** ☐ **None of the above** ☐
49	Have you, in the last year, been admitted to hospital because of your headaches? (please tick the no or yes box and, if yes, also tick the box to indicate the total number of days you spent in hospital) **No** ☐ **yes** ☐ **If yes, how many days:** **1** ☐ **2** ☐ **3-7** ☐ **More than 7** ☐
Impact questions The next questions are about the effects your headaches have on your own life	
50	Have your headaches interfered with your education? (please tick all boxes that apply <u>because of your headaches</u>) **no** ☐ **yes, I did less well** ☐ **yes, I gave up early** ☐

51	Do you believe your headaches have made you less successful in your career? (please tick all boxes that apply <u>because of your headaches</u>) (if this question is not applicable to you, please tick no and go directly to question 54) **no** ☐ **yes I have done less well** ☐ **Yes I have taken an easier job** ☐ **Yes I have taken long-term sick leave** ☐ **Yes, I have retired early** ☐ **Yes, I am on a disability pension** ☐
52	Have your headaches resulted in reduced earnings? (please tick one box) (if this question is not applicable to you, please tick no and go directly to question 54) **no** ☐ **yes** ☐ **not applicable** ☐
53	Do you feel that your employer and work colleagues understand and accept your headaches? (please tick one box) **no** ☐ **yes** ☐ **not applicable** ☐
54	Do you feel that your family and friends understand and accept your headaches? (please tick one box) **no** ☐ **yes** ☐
55	Do you avoid telling people that you have headaches? (please tick one box) **no** ☐ **yes** ☐
56	Taking into account everything you do to treat your headaches, do you feel you are in control of your headaches? (please tick one box) **always** ☐ **often** ☐ **sometimes** ☐ **rarely** ☐ **never** ☐
The next questions are about lost time because of your headaches.	
57	On how many **days** in **the last 3 months** could you **not go** to work or school because of your headaches? (please enter the number of days missed completely during the last 3 months) _____
58	On how many **days** in **the last 3 months** could you do **<u>less than half</u>** your usual amount in your job or schoolwork because of your headaches? (please enter the number of days; do <u>not</u> include days you counted in question 57 where you missed work or school) _____
59	On how many **days** in the **last 3 months** could you **not do any** household work because of your headaches?(please enter the number of days lost completely during the last 3 months) _____

60	On how many **days** in the **last 3 months** could you do **less than half** your usual amount of household work because of your headaches? (please enter the number of days; do not include days you counted in question 59 where you did not do any household work) _____
61	On how many **days** in the **last 3 months** did you **miss** family, social or leisure activities because of your headaches? (please enter the number of days) _____
The following questions aim to understand how much your headaches affect you even when you do not actually have an attack. Please think carefully about the last day when you did not have a headache.	
62	On that day, were you anxious or worried about your next headache episode? (please tick one box) **no** ☐ **yes** ☐
63	On that day, was there anything you could not do or did not do because you wanted to avoid getting a headache? (please tick one box) **no** ☐ **yes** ☐
64	On that day, did you feel completely free from all headache-related symptoms? (please tick one box) **no** ☐ **yes** ☐
The next three questions are about the effects your headaches have **on your relationships, love life and family planning.** Please answer no to any that do not apply.	
65	Have your headaches affected your family planning? (please tick all boxes that apply because of your headaches) **no** ☐ **Yes, I have had fewer children** ☐ **Yes, I have avoided having children** ☐ ***(the next answer is only for women)*** **Yes, I have avoided oral contraception** ☐
66	During the last 3 months, have your headaches caused difficulties in your love life? (please tick one box) **no** ☐ **yes** ☐
67	Have your headaches caused a relationship to break down? (please tick one box) **no** ☐ **Yes, they have caused separation** ☐ **Yes, they have caused divorce** ☐

68	Do you have children of school age (please tick one box) **no** ☐ If you ticked no, please go directly to question 71 **yes** ☐
69	During the **last 3 months**, have <u>your</u> headaches caused one or more of your children to **miss** school? (please tick one box) **no** ☐ **yes** ☐ if yes, estimate the **total number of missed days:** _____
70	During the **last 3 months**, have **<u>your</u>** headaches **prevented** you from caring for your children? (please tick one box) **no** ☐ **once** ☐ **more than once** ☐
71	Are you currently living with a partner (please tick one box) **no** ☐ **yes** ☐ if you are not now living with a partner, please go directly to question 79
72	During the **last 3 months**, have **<u>your</u>** headaches caused your partner **to lose** time from work? (please tick one box) **no** ☐ **yes** ☐ if yes, enter the **total number of days lost**: _____
73	During the **last 3 months**, have **<u>your</u>** headaches caused your partner **to miss** social activities? (please tick one box) **no** ☐ **yes** ☐ if yes, enter the **total number of occasions missed:** _____
The next five questions are **about your household partner**. Whether you have headaches yourself or not, we would like to know if your partner has headaches and, if so, how they affect <u>your</u> life	
74	Has your partner had a headache in the last year? (please tick one box) **no** ☐ if no, go directly to question 79 **yes** ☐

75	During the last 30 days, on how many days did he/she have a headache? (please enter the number of days between 0 and 30) **_____ days**
76	During the last 3 months, have your partner's headaches caused <u>you</u> to lose time from work? **no ☐ once ☐ more than once ☐**
77	During the last 3 months, have your partner's headaches caused <u>you</u> to miss social activities? (please tick one box) **no ☐ once ☐ more than once ☐**
78	During the last 3 months, have your partner's headaches caused difficulties in your love life? (please tick one box) **no ☐ yes ☐**

The next three series of questions are general, **to be answered by everyone**, with or without headaches.

Body mass index questions
Your answers to these questions will give an indication of your level of fitness.

79	What is your weight? (please enter your weight in kilograms <u>or</u> in stones and pounds) **_____ kg**
80	What is your height? (please enter your height in centimeters <u>or</u> in feet and inches) **_____ cm**
81	What is your waist measurement? (please enter the measurement in centimeters <u>or</u> in inches) Please take a tape measure and put it around your waist or take a string put it around your waist and then measure the length of the string with a ruler **_____ cm**

Quality of life questions (WHOQoL)

This set of eight questions, developed by the World Health Organization, are for everybody, whether they have headaches or not. They will help us compare people with headaches and people without.

The questions ask how you feel about your quality of life, health or other areas of your life. Each question has five response options. **Please choose the answer that appears most appropriate by ticking the box in the appropriate column.** If you are unsure about which response to give to a question, the first response you think of is often the best one.

Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life **in the last 4 weeks.**

		very poor	**poor**	**neither poor nor good**	**good**	**very good**
82	How would you rate your quality of life?	☐	☐	☐	☐	☐
		very dissatisfied	**dissatisfied**	**neither satisfied nor dissatisfied**	**satisfied**	**very satisfied**
83	How satisfied are you with your health?	☐	☐	☐	☐	☐
84	How satisfied are you with your ability to perform your daily living activities?	☐	☐	☐	☐	☐
85	How satisfied are you with yourself?	☐	☐	☐	☐	☐
86	How satisfied are you with your personal relationships?	☐	☐	☐	☐	☐
87	How satisfied are you with the conditions of your living place?	☐	☐	☐	☐	☐
88	Do you have enough energy for everyday life?	☐	☐	☐	☐	☐
89	Have you enough money to meet your needs?	☐	☐	☐	☐	☐

Depression and anxiety questions (HADS)
The final series of questions ask about depression and anxiety, both of which are common in the general population. Please read each item and place a firm tick in the box which comes closest to how you have been feeling **in the past week.** Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought out response.

		Most of the time	**A lot of the time**	**Time to time, occasionally**	**Not at all**
90	I feel tense or "wound up"	3	2	1	0
		Nearly all of the time	**Very often**	**Sometimes**	**Not at all**
91	I feel as if I am slowed down	3	2	1	0
		Definitely as much	**Not quite so much**	**Only a little**	**Not at all**
92	I still enjoy the things I used to enjoy	0	1	2	3
		Not at all	**Occasionally**	**Quite often**	**Very often**
93	I get a sort of frightened feeling like "butterflies in the stomach"	0	1	2	3
		Very definitely and quite badly	**Yes, but not too badly**	**A little, but it doesn't worry me**	**Not at all**
94	I get a sort of frightened feeling like something awful is about to happen	3	2	1	0
		Definitely	**I don't take as much care as I should**	**I may not take quite as much care**	**I take just as much care as ever**
95	I have lost interest in my appearance	3	2	1	0
		As much as I always could	**Not quite so much now**	**Definitely not so much now**	**Not al all**
96	I can laugh and see the funny side of things	0	1	2	3

		Very much indeed	**Quite a lot**	**Not very much**	**Not at all**
97	I feel restless as if I have to be on the move	3	2	1	0
		A great deal of the time	**A lot of the time**	**From time to time but not too often**	**Only occasionally**
98	Worrying thoughts go through my mind	3	2	1	0
		A much as I ever did	**Rather less than I used to**	**Definitely less than I used to**	**Hardly at all**
99	I look forward with enjoyment to things	0	1	2	3
		Not at all	**Not often**	**Sometimes**	**Most of the time**
100	I feel cheerful	3	2	1	0
		Very often indeed	**Quite often**	**Not very often**	**Not at all**
101	I get sudden feelings of panic	3	2	1	0
		Definitely	**Usually**	**Not often**	**Not at all**
102	I can sit at ease and feel relaxed	0	1	2	3
		Often	**Sometimes**	**Not often**	**Very seldom**
103	I can enjoy a good book or radio or TV programme	0	1	2	3

6 Discussion

My dissertation shows that despite the advances in understanding the pathogenesis of migraine and other primary headache disorders, the existence of well-established diagnostic criteria and the availability of effective and safe treatments for headache disease-management, migraineurs and other primary headache sufferers continue to experience significant pain and disability [(1)].

The physical, emotional, social and economic burdens of headache are poorly acknowledged

compared to less prevalent neurological disorders [2].

So far there was no reliable comparable data on the different dimensions of headache burden in Europe. There was also no valid instrument for measuring the different dimensions of headache burden and no definition of indicators to build such an instrument. The impact of migraine for example has been mostly estimated based on pharmaceutical company studies on migraine and the loss of productivity at work, these studies being realized with the main objective to obtain an optimal price for the migraine attack treatment drug of the company [3].

With my studies we could demonstrate for the first time that it was possible to realize pharmaceutical industry independent studies in that area of research. We could also proof that in headache disorder it was possible for different stakeholders (medical professions and patient organisations) to work together in a consortium, to develop together the first instrument (BURMIG) to evaluate the different dimensions of migraine burden in a multicultural environment and to develop together the first instrument (EUROLIGHT) to evaluate the different dimensions of headache burden at European level.

Choosing Luxembourg as the country to do the multicultural test run for the validation of the BURMIG instrument proved to be a good choice. Until then Luxembourg was not known as European scientific point of interest in the neurological field.

I haven chosen Luxembourg not only because it is my home country but with its multicultural aspects and languages, is well suited for a pilot European project. The country offers a clear structure and for this similar reason surveys about headaches have been made and publicized years ago in the republic of San Marino [4].

There was no existing data about prevalence and impact of headache in Luxembourg and based on the BURMIG questionnaire we developed and validated in my second study, we could recently present the first prevalence and impact results for migraine in Luxembourg [5,6].

After the successful validation of the EUROLIGHT instrument we could start in October 2008 to use the EUROLIGHT instrument for collecting the data of the different dimensions of headache burden in 10 European countries (France, Germany, Ireland, Spain, Netherlands, Italy, Austria, UK, Luxembourg and Lithuania) representative of the different regions of Europe, involving in each country a non-headache sufferers group as a control group.

The European scientific research body on headache disorders, the European Headache Federation (EHF), has officially signed an agreement as associative partner for our Eurolight research and has committed themselves to base the next European Headache Treatment Guidelines presented at the European Headache Congress in Nice (France) in September 2010 on the outcome of the data from the EUROLIGHT questionnaire.

Our 3 studies got also accepted by the World Health Organisation as an official activity contribution to the World Health Organisation campaign 'Lifting the burden'

6.1 References

1 WHO: Headache disorder and public health neurological diseases & neuroscience wh/msd/mbd/00.9.

2 Berg J, Stovner LJ. Cost of migraine and other headaches in Europe. Eur J Neurol 2005;12 Suppl 1:59-62.

3 Andlin-Sobocki P, Jönsson B, Wittchen HU, Olesen J (2005) Cost of disorders of the brain in Europe. Eur J Neurol 12:1-27.

4 R D'Alessandro, G Benassi, P L Lenzi, G Gamberini, T Sacquegna, P De Carolis, and E Lugaresi. Epidemiology of headache in the Republic of San Marino. J Neurol Neurosurg Psychiatry. 1988 January; 51(1): 21–27.

5 Andrée C, Vaillant M, Lair ML et al. Report on prevalence of migraine in Luxembourg. (Data on file, National Center of Research Luxembourg).

6 Andrée C, Vaillant M, Lair ML et al. Report on impact of migraine and other primary headache disorders in Luxembourg. (Data on file, National Center of Research Luxembourg).

7 Conclusion

Without knowing the size and dimensions of the burden of a health problem it is difficult to make clear recommendations about disease-management, the content of medical profession education and to raise public awareness. The future will show whether my work of developing the first instruments to measure in a reliable way the different dimensions of headache burden as well as measuring the problems in headache disease-management will, together with the resulting new treatment guidelines, prompt health care providers and decision makers to re-examine clinical and pharmacy practice patterns and lead to better care.

8 Acknowledgements

I would like to thank

The members of my family, my parents Denise and Paul, my partner Stephan, my friends especially Jürg for supporting me during the work and for believing in me that I could finish the work.

PD. Dr. Peter Sándor and PD. Dr. Kurt Hersberger for giving me advice and for reviewing my work.

Prof. Dr. Stephan Krähenbühl for heading my doctor examination.

The team of the National Center of Public Health Research in Luxembourg as well as

Prof. Dr. Timothy Steiner (Imperial College, London) and Prof. Dr. Lars Stovner (St. Olavs Hospital, Trondheim, Norway) for their collaboration and support and the Luxembourg National Research Fund for supporting the printing of this document.

Curriculum vitae

Colette Marie Andrée

Address	Oberwilerstr. 48 CH-4103 Bottmingen
Tel.	+41 61 423 10 80
Mob	+41792112252
Fax	+41 61 423 10 82
E-mail:	migraine_action@vtxmail.ch

Professional Experience

1986 – 1988	Hoffmann-La Roche, Basle, Marketing Trainee - International Medical Advisor Rheumatology.
1988 - 1991	Ciba-Geigy AG, Basle, Product Manager Cardiovasculars.
1991- 1994	Janssen Pharmaceutica AG, Baar, Switzerland, Line Manager for Neurology, Allergology and Cardiovasculars.
1994 - 2007	Swiss Migraine Trust Foundation (NGO). Executive Director.
2001- present	Swiss Migraine Action. Program Director.
2004 - present	University Basle. Dep. Pharmaceutical sciences. Coordinator 'Health Care'.
2004 - 2007	National Center of Public Health Research, Luxembourg, CRP-Santé, Project initiator and project leader, National Research project.
2007- present	CRP-Santé, Project initiator and project leader, European Commission Research project.
2007- present	Health Invest AG, Baar, Switzerland, honorary CEO.

Memberships and organizational experience

- Administrative Secretary Swiss Neurology Society (1992-1994)
- Co-Founder and Director of the 'Swiss Migraine Trust Foundation (1994-2006)
- Foundation Member of the Swiss Headache Society, Therapeutic. Committee (1996)
- Foundation Member of the World Headache Alliance (WHA) (1997), Member of WHA steering committee (1997-2003)
- Member Swiss Industrial Pharmacists (1998-present)
- Advisory Board for Grünenthal, Novartis, Robapharm, Vifor, Bayer (1998-present)
- Educator 'continuous learning' for the Swiss Pharmacists Association (1998-present)
- Co-Founder and Director of the 'Swiss Migraine Action (2000-present)
- Foundation Member of the European Headache Alliance (EHA) (2006)
- Steering committee Member and Secretary EHA (2006-2008)
- Evaluator for the EC for the 7th Framework ICT (Integrated Projects) (2007-present)
- Reviewer for the EC for the FP6 Framework (Streps) (2007-present)
- Member of the Task Force for Chronic Diseases Public Health Executive Committee (EC) (2007-present)
- Member of the Swiss Society for Pharmaceutical Sciences (2008-present)
- Working Partner of the 'Global Burden of Headache' Campaign of the World Health Organization (WHO) (2008-present)

Education

1972 - 79	High School, Sciences (Biology, Chemistry, Physics, Mathematics, Latin), Luxembourg
1979 - 83	Basle University, Chemical Institute, BSc chem
1983 - 86	Basle University, Pharmaceutical Institute, MSc pharm
2006 -.09	PHD dissertation under the direction of Prof. Dr. Stephan Krähenbühl, Department of Pharmaceutical Sciences, University Basle and PD. Dr. Peter Sandor, University Hospital Zurich
Date of Birth:	15.04.60
Nationality:	Luxemburgish
Language spoken:	Fluent in French, German, English; Mother tongue Luxemburgish; some knowledge Dutch, Spanish and Italian
Citizenship:	Holder of a C Permit in Switzerland

Publications

- Headache Disorders and Public Health, WHO/MSD,MBD/00.9 (contribution writing)
- Andrée C, Migräne, Schweizer Apothekerzeitung, 12/2006, 475-478.
- Andrée C, Behandlung der Migräne, med.pharm.drog.hosp 01/06.
- Andrée C, Migräne: Der besten OTC-Empfehlung auf der Spur, med.pharm.drog.hosp 02/06.
- Andrée C, Prophylaxe bei Migräne, pharmaJournal 2006; 22:27-29.
- Andrée C, Vaillant M, Lair ML et al. Report on prevalence of migraine in Luxembourg. (Data on file, National Center of Public Health Research Luxembourg, 2006).
- Bisdorff A, Sobocki P, Cloos JM, Andrée C, Graziano ME. Cost of disorders of the brain in Luxembourg. Bull. Soc. Sci. Méd. p 347-Nº 3/2006.

- Andrée C, Kopfschmerzen und Migräne, Apotheken Handbuch der Schweiz 2007, 329-335.
- Andrée C, Migräne: Anfallbereitschaft vermindern, Psychiatrie & Neurologie 02/07,10-11.
- Andrée C, Gap assessment: identifying areas for future SANCO action (contribution for headache) July 2007.
- Andrée C, Highlighting the Impact of Headache in Europe. Neurologie & Psychiatrie 3/2008, 24-26.
- Andrée C, Vaillant M, Lair ML et al. Report on impact of migraine and other primary headache disorders in Luxembourg. (Data on file, National Center of Public Health Research) Luxembourg 2008.
- Stovner L, Andrée C, On behalf of the Eurolight Steering Committee. Impact of headache in Europe: a review for the Eurolight project. The Journal of Headache and Pain. 2008, 9:139-46.
- Andrée C, Vaillant M, Rott C, Katsarava Z, Sándor P. Development of a self-reporting questionnaire, BURMIG, to evaluate the burden of migraine. August 2008. The Journal of Headache and Pain, 309-315.
- Alexandre Bisdorff, Colette Andrée, Michel Vaillant, Peter S. Sándor. Prevalence and impact of headache-associated dizziness. Submitted May 2009, accepted August 2009, Cephalagia.
- Andrée C, Vaillant M, Barre J, Katsarava Z, Lainez MJ, Lair ML, Lanteri-Minet M, Lampl C, Steiner TJ, Stovner LJ, Tassorelli C, Sándor. Development and validation of the EUROLIGHT questionnaire to evaluate the burden of primary headache disorders in Europe. Submitted June 2009 accepted August 2009, Cephalalgia.

Information and education material for medical professions and for headache sufferers

- Annual magazine ‚Querkopf/Casse-tête' 2001, 2002, 2003, 2004, 2005
- Patient brochure ‚Headache and Migraine'2003, second edition 2007
- DVD and Video 'Free YOUR body free YOUR head' (Video 2003, DVD 2005)
- Adult Headache Calendar (2004, second edition 2007),
- Children Headache Brochure and Headache Diary (2005, second edition 2006)

- Assisted teaching, Headache CD, Swiss pharmacy assistants (2006)
- Educational brochure, Headache in the Pharmacy, (2006, third edition 2008)
- Assisted teaching, Module Migraine, Pharmasquare, (contribution support), University Basle (2008-present)
- National Headache Website www.migraine-action.ch design and content development (2005-2009)
- Project Website www.eurolight-online.eu design and content development (2006-2009)

Scientific Posters

Andrée C, Vaillant M, Rott C, Sándor P. A self-reporting questionnaire on the burden of migraine (BURMIG): development, reliability and validity. International Headache Conference, Kyoto 2005.

Andrée C, Vaillant M, Rott C, Lair M-L, Wagener Y, Schank J.M, Sándor P. Migraine and other headache prevalence in the Grand Duchy of Luxembourg: First results. International Headache Conference, Kyoto 2005.

Andrée C, Vaillant M, Sándor P. Disability due to headache as measured using WHODAS II, the World Health Organization Disability Assessment Scale. European Headache Congress, Valencia 2006.

Andrée C, Vaillant M, Rott C, Sándor P Andrée C, Vaillant M, Sándor P. Factors related to the impact of different headache types. The Luxembourg Burden of Migraine (BURMIG) study European Headache Congress, Valencia 2006.

Andrée C, Dargent G, Lair ML. Eurolight: Knowledge is needed for action in Europe International Headache Conference, Stockholm 2007.

Bisdorff A, Andrée C, Vaillant M, Sándor P. Le vertige, compagnon négligé des maux de tête. Société des Sciences Médicales, Luxembourg 2007.

Colette A, Vaillant M, Sándor P. Depression as comorbidity in different types of headache. What is the effect of headache frequency? International Headache Conference, Stockholm 2007.

Other public documents

More than 100 press articles in lay press about headache and migraine in Switzerland, Luxembourg, Spain, Austria, France, Germany 1996-2009 (Astrea, Beobachter, Gesundheitstipp, Pulstipp, Wir Eltern,..)

Over 50 radio interviews about headache in Switzerland, Luxembourg, Spain, Austria, Germany, France (1995-2009)

TV Headache reports: DOC, Mona Lisa, , RTL Santé, Santé France, RTL Lux (2000-2009). Health TV Programm Gesundheitssprechstunde, Puls (2004-2007)

Invited speaker

World Health Organization (WHO), Neurological disorders and Public Health, Geneva 2000

International Headache Congress (IHC), London 2000

International Children Headache Congress, Vienna 2002

International Headache Congress, Kyoto (IHC) 2005

European Headache Congress in Valencia 2006

European Commission, DG SANCO Task Force on Major and Chronic Diseases Luxembourg,

December 2007

National Headache Congress, Pavia 2004, Padua 2006, Pavia 2008

National Headache Congress, Madrid April 2008

International Headache Congress, Philadelphia (IHC) 2009

Regular invited teacher on headache and on other health subjects

Swiss Drugstore School

CAP

AGFAM

Swiss Pharmacy Association