Chapter 1
Public Health

Introduction

The assertion that primary headaches are a social disease is now out of the question, being established both by a high prevalence rate and by the impact they produce on the person and society. The negative loop of these premises is overturned on the vertical economic damage they cause, another solid evidence in the scientific literature. This expansion from personal to social damage, in terms of current expenditure of the national health systems, requires as a natural consequence a more efficient organization of the health services dedicated to control, education, rehabilitation, to achieve social care equity. Migraine represents the perfect paradigm of this path.

Machine-Generated Summaries

1. Public Health
   Machine generated keywords: child, tth, cost, migraine patient, adolescent, headache service, gbd, score, brain, mmd, child adolescent, erenumab, costeffectiveness, preventive, udh.

1.1 Epidemiology

Machine generated keywords: tth, risk, china, child, brain, risk factor, cohort, pakistan, prevalence headache, sex, role, city, adolescent, udh, pmoh.

P. Martelletti (ed.), *Migraine in Medicine*,
https://doi.org/10.1007/978-3-030-97359-9_1

Prevalence, burden, and clinical management of migraine in China, Japan, and South Korea: a comprehensive review of the literature

DOI: https://doi.org/10.1186/s10194-019-1062-4

Abstract-Summary

The objective of this review was to determine the unmet needs for migraine in East Asian adults and children.

Studies reporting the prevalence, humanistic and economic burden, and clinical management of migraine in China (including Hong Kong and Taiwan), Japan, and South Korea were included.

The 1-year prevalence of migraine (IHS criteria) among adults ranged from 6.0% to 14.3%.

For children, prevalence of migraine increased with age.

Information on the economic burden and clinical management of migraine was limited, particularly for children.

When reported, migraine was significantly associated with high levels of disability and negative effects on quality of life.

Of individuals with migraine from China, 52.9% to 68.6% had consulted a physician previously, 37.2% to 52.7% diagnosed with headache had not been diagnosed with migraine previously, and 13.5% to 18% had been diagnosed with migraine previously.

Of individuals with migraine from Japan, 59.4–71.8% had never consulted a physician previously, 1.3–7.3% regularly consulted physicians for their headache, and only 11.6% of individuals with migraine were aware that they had migraine.

This review suggests that there are unmet needs for migraine in terms of sufficient and appropriate diagnosis, and better management and therapies for treatment of migraine in East Asia.

More recent, population-based studies assessing disease burden and clinical management of migraine are needed to confirm unmet needs for migraine across East Asia.

Extended: The objective of this comprehensive literature review of the evidence related to the prevalence, burden, and clinical management of migraine in East Asia (China, Japan, and South Korea) was to determine the unmet needs for migraine in both adults and children.

Because of the wide variation in study types, populations, and analysis methods, it was not possible to compare findings between countries.

Introduction

These reviews were focused on the prevalence of chronic migraine and chronic daily headache, and on headache disorders across multiple countries, with little information on migraine-related burden.

The objective of this comprehensive literature review of the evidence related to the prevalence, burden, and clinical management of migraine in East Asia (China, Japan, and South Korea) was to determine the unmet needs for migraine in both adults and children.

The key outcomes were prevalence, disease burden (humanistic or economic), and clinical management of migraine, including health care utilization and clinical practice patterns.

Materials and methods

All studies were to include at least one of the following outcomes of migraine: prevalence, humanistic burden (all reported measures of health-related quality of life [HRQoL], migraine-related disability, and measures of the impact of migraine on aspects of daily living and social activities), economic burden (work-related productivity, direct and indirect medical costs), and clinical management (health care utilization, clinical practice patterns).

Inclusion of each potential publication was then confirmed after a review of the full text to identify publications reporting one or more of the following eligible outcomes: prevalence of migraine, humanistic burden, economic burden, and clinical management as described above.

The data extracted included study characteristics, population characteristics, criteria for migraine diagnosis, prevalence of migraine, outcomes measuring or describing migraine burden (humanistic, work-related productivity, indirect and direct medical costs), health care utilization, and clinical practice patterns.

Results

Mean MIDAS scores from studies conducted in China and Japan [1–3] indicated severe levels of disability among many patients attending headache clinics for migraine.

Of the six studies retrieved, three provided an estimate of the direct or indirect medical costs of migraine or of costs associated with migraine work-related disability [4–6], with all suggesting that the economic impact of migraine was substantial at the time the studies were conducted.

Findings from a population-based study conducted in Taiwan in 1997–1998 estimated that migraine was responsible for an annual cost of NTD 4873 (USD 149) per person and a total annual cost of NTD 4.6 billion (USD 140 million) per year due to lost work days.

Findings from one population-based study showed that only 24.4% of individuals with migraine had consulted a physician for headache, 64.3% were taking medication for their headache and, of these, most (92.8%) were using OTC medication [7].

Discussion

Findings from the population-based studies retrieved in our literature review showed that migraine prevalence among adults in East Asia ranged from 6.0% to 14.3% in non-elderly adults, which is consistent with worldwide estimates of migraine prevalence [8] and a previous study conducted among Asia-Pacific countries up until 2013 [9].

Consistent with worldwide studies on migraine disability [8], the peak prevalence of migraine in East Asia was among adult women aged 30 to 49 years.

Findings from the International Burden of Migraine Study [10], which surveyed 8726 individuals from predominantly Caucasian populations with chronic or episodic migraine, showed that approximately 50% reported moderate or significant levels of disability (MIDAS grade III or IV) and significantly negative effects on HRQoL for those with chronic migraine.

Consistent with studies in predominantly Caucasian populations [10, 11], the humanistic burden of migraine in East Asia from the available studies has suggested that there are unmet needs for improvements in diagnosis, management, and therapies for treatment of migraine across East Asia.

Conclusion
Combined with the high prevalence of migraine across all countries included in this review, the significant levels of humanistic burden among the available studies suggest that there are substantial unmet needs for migraine with regard to appropriate diagnosis, and better management of and therapies for treatment of migraine across East Asia.

Acknowledgement
A machine generated summary based on the work of Takeshima, Takao; Wan, Qi; Zhang, Yanlei; Komori, Mika; Stretton, Serina; Rajan, Narayan; Treuer, Tamas; Ueda, Kaname. 2019 in The Journal of Headache and Pain.

Incidence, prevalence and disability associated with neurological disorders in Italy between 1990 and 2019: an analysis based on the Global Burden of Disease Study 2019

DOI: https://doi.org/10.1007/s00415-021-10774-5

Abstract-Summary
Neurological conditions are highly prevalent and disabling, in particular in the elderly.

The Italian population has witnessed sharp ageing and we can thus expect a rising trend in the incidence, prevalence and disability of these conditions.

We relied on the Global Burden of Disease 2019 study to extract Italian data on incidence, prevalence and years lived with a disability (YLDs) referred to a broad set of neurological disorders including, brain and nervous system cancers, stroke, encephalitis, meningitis, tetanus, traumatic brain injury, and spinal cord injury.

The most prevalent conditions were tension-type headache, migraine, and dementias, whereas the most disabling were migraine, dementias and traumatic brain injury.

YLDs associated with neurological conditions increased by 22.5%, but decreased by 2.3% in age-standardized rates.

The increase in YLDs associated with neurological conditions is mostly due to population ageing and growth: nevertheless, lived disability and, as a consequence, impact on health systems has increased.

Extended: The Italian population comprised 60.6 million in 2019, with a life expectancy at birth of 83.1 years (ranking third at European level) and 71.0 years of healthy life expectancy years (ranking sixth at European level) [12].

The most prevalent conditions in 2019 were migraine and TTH, with 12.5 and 23.2 million prevalent cases (28.5 million cases when combined), and an increase of 8.2% and 12.8% compared to 1990.

Introduction

The authors of this manuscript evidenced a consistently increasing trend for number of prevalent cases and disability, in addition to burden, for the selected neurological diseases, and hypothesized that the same indices are reasonably expected to further on increase in reason of population ageing and growth: however, no direct information was referred to YLDs associated with neurological disease by country.

The aims of this article are, therefore, the following: to describe the incidence, prevalence and YLDs associated with a broad group of neurological disorders in Italy, and their variation between 1990 and 2019; to address the trends for those NCDs with typical onset in young to adult age (e.g. headache disorders) and for those with typical onset in old age (e.g. Alzheimer's disease and other dementias), as well as for neurological injuries and for communicable neurological diseases; to compare estimates referred to Italy to those of other Western Europe countries.

Methods

This broad group of neurological conditions included both level 3 and level 4 conditions as presented in the GBD, specifically as follows: (a) A set of level 3 NCDs, namely Alzheimer's disease and other dementias, brain and nervous system cancers, epilepsy, MND, MS, PD and stroke, as well as two level-4 ones, namely migraine and TTH.

Non-fatal outcomes for the individual disorders included in this residual category need to be approximated by assuming the same YLDs/YLLs ratios estimated for the main fatal neurological disorders, which can be a precise approach for those conditions associated to relevant mortality (e.g. Huntington's disease), but not for those associated to little or no mortality (e.g. myasthenia gravis).

Changes over the period were also analysed at the group level, i.e. young to adult-age onset NCDs, older age onset NCDs, neurological injuries, and communicable neurological diseases.

Results

With regard to incidence, a consistent decrease both for counts and age-standardized rates was observed for stroke, meningitis, tetanus and TBI, whereas a consistent increase both for counts and age-standardized rates was observed for TTH, MS, dementias and MND.

As for prevalence, a consistent decrease both for counts and age-standardized rates was observed for meningitis and tetanus, whereas a consistent increase both

for counts and age-standardized rates was observed for migraine, TTH, MS and MND.

For PD, stroke, TBI and SCI the trend was increasing when counts were taken into account, and decreasing in age-standardized rates; for migraine, TTH and dementias and brain and nervous system cancers the trend was increasing when counts were taken into account, and stable in age-standardized rates; finally, for encephalitis, the trend was decreasing in age-standardized rates, and stable in counts.

Discussion

There has been a dramatic increase in the counts and age-standardized rates of incidence and prevalence of some conditions with typical onset in old age, in particular for Alzheimer disease and other dementias, brain and nervous system cancers and MND.

The increase in YLDs was due to a clear epidemiological change mostly for young to adult-onset conditions, for which age-standardized YLD rates increased by 5.0%, whereas for old-age onset disease the variation herein observed was mostly an effect of population ageing and growth as age-standardized YLDs rates decreased by 13.7%.

Incidence, prevalence and YLDs associated with Alzheimer's disease and other dementias have more than doubled in Italy over the 1990–2019 period, but not in terms of age-standardized rates, where only for incidence a minor increase was found, suggesting that such an increase is a consequence of population ageing.

Conclusions

We reported information on incidence, prevalence and disability associated with neurological disorders in Italy relying on the GBD 2019 estimates.

Our results show that headache disorders are still the most prevalent and disabling conditions, and that epidemiological patterns have changed between 1990 and 2019.

Our work pinpoints a worrisome rise in incidence and prevalence for conditions with typical onset in older ages, particularly dementias and PD as an effect of population ageing; for MND, on the contrary, estimates suggest a consistent increase which cannot be explained by population ageing only, but also as an effect of prolonged survival.

The increase is mostly due to population ageing and growth, with the only exceptions of MND and MS (for which classification changes and the inclusion of less severe varieties can be also implicated), and points out the increased survival for many of these conditions.

Acknowledgement

A machine generated summary based on the work of Raggi, Alberto; Monasta, Lorenzo; Beghi, Ettore; Caso, Valeria; Castelpietra, Giulio; Mondello, Stefania; Giussani, Giorgia; Logroscino, Giancarlo; Magnani, Francesca Giulia; Piccininni, Marco; Pupillo, Elisabetta; Ricci, Stefano; Ronfani, Luca; Santalucia, Paola; Sattin, Davide; Schiavolin, Silvia; Toppo, Claudia; Traini, Eugenio; Steinmetz, Jaimie; Nichols, Emma; Ma, Rui; Vos, Theo; Feigin, Valery; Leonardi, Matilde. 2021 in Journal of Neurology.

Epidemiology, work and economic impact of migraine in a large hospital cohort: time to raise awareness and promote sustainability

DOI: https://doi.org/10.1007/s00415-021-10715-2

Abstract-Summary
Migraine is not routinely assessed at work, making impossible to realize its impact and the potential benefit of migraine-related health strategies.

We aimed to assess epidemiology, work and economic impact of migraine in a workplace cohort of a tertiary hospital.

Through a web questionnaire, we screened participants for migraine, collecting demographic data, work characteristics, work impairment due to headache (WPAI), treatments and healthcare resource utilization.

Migraine caused an overall economic loss for the hospital of 439,848.90 €/month, as a result of utilization of healthcare resources at the workplace (136,028.0 €/month) and indirect costs (absenteeism + presenteeism: 303,820.90 €/month).

Only 110 participants (HFEM + CM) were responsible for half of indirect costs (165,017.2€/month).

Although healthcare professionals have greater knowledge on health issues, migraine is underdiagnosed and undertreated, leading to a significant economic loss for the hospital.

These results urge companies to assess migraine and promote stronger and migraine-specific health strategies at the workplace as a way to improve their own economic sustainability and the burden of migraine in their workforce.

Extended: Future studies should also aim to evaluate different work settings, the cost–benefit effects of health strategies and their translation in terms of employees' wellbeing and companies' sustainability.

Adequate strategies to correctly diagnose, treat and prevent migraine should be promoted in the near future within every hospital or company as a way to improve economic sustainability.

Introduction
Migraine has enormous costs for society.

In the European Union, for example, the total annual cost of migraine was estimated at €111 billion [13].

At a national level, several studies have estimated global migraine costs and savings [14, 15], whereas in companies employers have not been able to promote comprehensive evaluations of migraine economic impact at work, with limited data available at present [16–19].

In hospitals, for example, healthcare resources may be directly used at workplace, adding direct costs to the indirect ones and generating an even higher economic impact.

We decided to describe and quantify epidemiology, working and economic impact of migraine in a workplace cohort of a Spanish tertiary hospital.

Methods

Through a structured questionnaire based on the International Classification of Headache Disorders—3 (ICHD-3) [20] criteria, we screened participants for migraine and tension-type headache (TTH).

We collected data about headache frequency, acute medication intake and preventive treatments currently used.

We also asked participants about all complementary tests performed due to headache in this time frame.

We assessed migraine impact through Headache Impact Test (HIT-6) [21] and specifically working impact through Work Productivity and Activity Impairment Questionnaire (WPAI) [22].

We used the WPAI to estimate work time loss (absenteeism) and work impairment (presenteeism).

Absenteeism cost (€/month): MHW*8 (work hours/day) *5 (work days/week) *percentage of work time loss/week due to headache (time lost/time lost + time worked) *4 (weeks/month).

Presenteeism cost (€/month): MHW* productivity loss in a migraine day while working [(Work time − work time loss)/work time) * Productivity Impairment (from WPAI)] *headache monthly frequency.

We assessed statistical significance between migraine subdiagnoses (LFEM, HFEM and CM) by Pearson's Chi-square when comparing categorical variables.

Results

In participants with migraine, 76.8% (365/475) had low-frequency episodic migraine (LFEM: < 10 headache days/month), 12.6% (60/475) high-frequency episodic migraine (HFEM: 10–14 headache days/month) and 10.5% (50/475) chronic migraine (CM: > 14 days/month).

Work time loss (absenteeism) due to headache in the last seven days was reported by 14.7% (70/475) of participants, resulting in a percentage of work time missed/week of 6.7% [16.6] for LFEM, 8.1% [18.1] for HFEM, 7.9% [65.7] for CM.

Eighty point four percent (382/475) reported impairment at work (presenteeism) due to headache in the last seven days, resulting in a percentage of work productivity loss of 8.8% [11.7] for LFEM, 21.4% [16.0] for HFEM, 34.4% [33.3] for CM.

Discussion

Our study describes the migraine "status quo" in a hospital workplace cohort, observing a monthly economic impact of 439,848.90 €/month (indirect costs + healthcare resource utilization at workplace) for the hospital, translating higher monthly cost per patient than the one estimated by national-based surveys [23].

In terms of direct costs, migraine-specific acute medications, such as triptans, could potentially reduce healthcare resource utilization in those who respond [24], representing a saving strategy for hospitals since healthcare resources are directly used by employees at workplace.

Our focus was to show migraine-related costs and impact in a specific setting, rather than in the general population, providing a model for company leaders to evaluate the work and economic impact of migraine in their workforce, in line with the Plan of Action promoted by the WHO on Workers' Health [25].

Conclusions
Migraine strikingly impacts hospital economy, as a result of employees' global productivity loss (absenteeism + presenteeism).

The direct use of healthcare resources by employees at workplace generates direct costs that weight on as added costs for the hospital.

Acknowledgement
A machine generated summary based on the work of Caronna, Edoardo; Gallardo, Victor José; Alpuente, Alicia; Torres-Ferrus, Marta; Pozo-Rosich, Patricia. 2021 in Journal of Neurology.

Association of migraines with brain tumors: a nationwide population-based study

DOI: https://doi.org/10.1186/s10194-018-0944-1

Abstract-Summary
This study aimed to investigate the risk of migraine occurrence in the preceding years among patients diagnosed with brain tumors and unaffected controls.

Conditional logistic regressions were performed to calculate the odds ratio (OR) and the corresponding 95% confidence interval (CI) to present the association between brain tumors and having previously been diagnosed with migraines.

We found that among patients with and those without brain tumors, 554 (4.89%) and 235 (2.08%) individuals, respectively, were identified as having a prior migraine diagnosis.

Compared to unaffected controls, patients with brain tumors experienced an independent 2.45-fold increased risk of having a prior migraine diagnosis.

The risks were even higher among men (odds ratio (OR) = 3.04, 95% confidence interval (CI) = 2.29 ~ 4.04) and after patients who had received a prior migraine diagnosis within 3 years were excluded (OR = 1.91, 95% CI = 1.59 ~ 2.29).

This is the first report demonstrating the occurrence of brain tumors to be associated with a prior migraine history, for both men and women, in a population-based study.

Extended: We found that there was a significant association between brain tumors and migraines regardless of sex.

Compared to unaffected controls, patients with brain tumors experienced a 2.45-fold increased risk of having a prior migraine diagnosis, after the factors of age, sex, monthly income, geographic region, and urbanization level were considered in the conditional logistic regression analyses.

Future studies are required to elucidate the mechanism and possible causal link, if any, connecting migraines to brain tumors, together with the potential effects of migraine treatment on the risks of consequent brain neoplasms.

Introduction

Although brain neoplasms in headache patients are less common, headaches frequently occur (about 33% ~ 71%) in patients with brain tumors [26–28].

Approximately 58.78% of patients with brain neoplasms also reported headaches in a 2-year prospective study, and half of them declared headaches to be their first complaint [29].

As headaches are the most common complaint and are frequently reported as the initial symptom among patients with malignant brain tumors, it was speculated that headaches or migraines should be treated as risk factors for the development of brain tumors or merely be considered as the "first sign" of brain neoplasms.

That large, prospective cohort study found that a headache history was not associated with increased risks of subsequent brain neoplasm occurrence.

Our nationwide, population-based nested case-control study was carried out to investigate the risks of migraine occurrence in preceding years among patients diagnosed with a brain tumor and unaffected matched controls.

Methods

As for selection of cases for this case-control study, we first identified 12,355 patients who had received a first-time diagnosis of a brain tumor (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 191) between January 1, 2006 and December 31, 2013.

11,325 controls (one control per case) were randomly selected and matched with cases in terms of sex, age, monthly income (NT$0 ~ NT$15,840; NT$15,841 ~ NT$25,000; ≥NT$25,001, the government-stipulated minimum wage for full-time employees in Taiwan was NT$15,840, and the average exchange rate in 2017 was US$1 ≈ New Taiwan (NT)$30), geographical location (northern, central, eastern, and southern Taiwan), urbanization level (five levels, with 1 being the most urbanized and 5 the least), and index year.

While for cases, we assigned the year of the index date as the year in which the cases received their first brain tumor diagnosis, for controls, the year of the index date was simply a matched year in which controls had an ambulatory care visit.

Results

The conditional logistic regression analyses (conditioned on sex, age, monthly income, geographical location, and urbanization level) suggested that the odds of prior migraines was 2.45-times greater (95% CI = 2.09 ~ 2.96, $p < 0.001$) for patients with a brain tumor than for controls.

After excluding patients who had received a first-time migraine diagnosis within 1 year prior to the index date, we found a significant association still existed between brain tumors and migraines (OR = 1.99, 95% CI = 1.68–2.34).

The association between brain tumors and migraines remained after excluding patients who had received a first-time migraine diagnosis within 2 (OR = 1.87, 95% CI = 1.57–2.23) or 3 years (OR = 1.91, 95% CI = 1.59–2.29) prior to the index date.

Discussion

In this nested case-control study, we found that among patients with and those without brain tumors, 554 (4.89%) and 235 (2.08%) individuals, respectively, were identified as having a prior migraine diagnosis.

Several methodological strengths of our study should be noted, including the use of a large-scale population-based study to evaluate the risks of brain tumors associated with a prior diagnosis of migraines to fairly exempt our study from selection and non-response biases.

In terms of sex differences, Kurth and others specifically examined apparently healthy women only in a prospective study and reported a null finding of migraines being associated with subsequent brain tumor risks.

Because the healthcare utilization was recorded chronologically in this nested case-controls study, there was no apparent reason to consider that patients with and without malignant brain tumors afterwards would present distinctively on prior healthcare visits for migraine.

Conclusions

Although epidemiologic evidence suggests the association, replication of studies to validate migraines per se as a risk factor for brain neoplasm development is imperative, both scientifically (i.e., to characterize the potential causal link) and clinically (i.e., to direct patient management).

Future studies are required to elucidate the mechanism and possible causal link, if any, connecting migraines to brain tumors, together with the potential effects of migraine treatment on the risks of consequent brain neoplasms.

Acknowledgement

A machine generated summary based on the work of Chen, Chao-Hung; Sheu, Jau-Jiuan; Lin, Yi-Chun; Lin, Herng-Ching. 2018 in The Journal of Headache and Pain.

The prevalence of headache disorders in children and adolescents in Ethiopia: a schools-based study

DOI: https://doi.org/10.1186/s10194-020-01179-2

Abstract-Summary

The Global Burden of Disease (GBD) study establishes headache as the second-highest cause of disability worldwide.

Because most headache data in GBD are from adults, leading to underestimation of headache-attributed burden, a global schools-based programme within the Global Campaign against Headache is contributing data from children (7–11 years) and adolescents (12–17 years).

Gender- and age-adjusted 1-year prevalence of headache was 72.8% (migraine: 38.6%; tension-type headache: 19.9%; UdH: 12.3%; all headache on ≥15 days/month: 1.2%; probable medication-overuse headache: 0.2%).

Headache was more prevalent in females (76.2%) than males (71.0%), a finding reflected only in migraine among the headache types.

Headache was more prevalent among adolescents (77.6%) than children (68.4%), reflected in all types except migraine, although prevalence of UdH fell sharply after age 14 years to 3.9%.

For headache overall, findings matched those in Turkey and Austria, obtained with the same questionnaire, but the high prevalence of migraine, not increasing with age, was surprising.

The study highlighted diagnostic difficulties in young people, especially when poorly educated, with migraine diagnoses driven by improbably high proportions reporting nausea (44.8%) and vomiting (28.0%) as usual symptoms accompanying their headaches.

Headache is very common in children and adolescents in Ethiopia.

Extended: Headache is very common in children and adolescents in Ethiopia—apparently more so than in adults—a finding with major public-health implications for a country in which half the population are aged under 18 years [30].

Introduction

Over multiple iterations between 2000 and 2019, the Global Burden of Disease (GBD) study has demonstrated that headache disorders are a major cause of global ill health, to the extent of being the second highest cause of disability [8–35].

A key objective of the Global Campaign against Headache, under the direction of Lifting The Burden (LTB), is to quantify headache-attributed burden worldwide [36–39].

In children (aged 6–11 years) and adolescents (12–17 years), the same are important, but recent studies have shown, in addition, a prevalent headache disorder characterised by mild pain of short duration (<1 h) [40, 41].

While no published data exist for child and adolescent headache in this country, a population-based national survey on adult headache disorders showed that they were common: 1-year prevalence estimates were 17.7% for migraine (higher than the global mean [35]), 20.6% for TTH, 0.7% for probable MOH (pMOH) and 2.5% for other headache on ≥15 days/month [42].

This study estimated the prevalence and attributed burden of headache disorders in children and adolescents in Ethiopia.

Methods

Enquiry was by self-completed questionnaire administered under supervision to pupils within their school classes.

Information sheets describing the nature and purposes of the survey, and consent forms, were distributed to pupils in the participating schools on the day preceding the survey, and prior consent obtained from or on behalf of each participating child or adolescent (in most sites, teachers signed to signify the consent of children rather than the children themselves, in accordance with the terms of ethics approval).

In each school, all classes including pupils aged 6–11 years and/or 12–17 years were invited to participate.

Pupils who happened to be absent from school on the survey day were not part of the sample, and not, therefore, counted as non-participants.

Results

Adjusted 1-year prevalence estimates were 72.8% for all headache, 38.6% for migraine, 19.9% for TTH, 12.3% for UdH and 1.2% for all headache on ≥15 days/month.

HY was reported by 630 (36.5%) of 1725 participants with headache (one did not respond to this question).

Adolescents reported only marginally more HY than children, although a year-by-year analysis showed a substantial increase (to 42–44%) in those aged 15–17 years (OR: 1.8 [1.4–2.3]; $p < 0.001$).

Headache on ≥15 days/month was, as anticipated, the greatest contributor to HY proportionately (by definition, > 50% was expected), but its overall impact was limited by its relatively low prevalence.

This discrepancy was evident in migraine, TTH and UdH, but, for headache on ≥15 days/month, HY was approximately matched by both predictions.

Discussion

Although we are not presenting headache duration here, reported duration for 64.9% of all headache, including 84.4% of cases diagnosed as probable migraine, was <2 h. In relation to this, we must question our finding of 38.6% migraine prevalence, which we acknowledge to be implausible.

LTB's study of adult headache disorders in Ethiopia estimated 1-year prevalence of migraine at 17.7% (with rather more TTH, at 20.6%) [42].

In children in particular, headache diagnosis is notoriously difficult, dependent as it is on comprehension of language on the one hand (formulation of ICHD criteria into questions that are clear and unambiguous to children is a challenge) and subjective evaluations on the other (over a quarter [26.5%] of cases with reported headache duration of <1 h were diagnosed as probable migraine, the distinction from UdH resting solely on reported headache intensity).

Conclusions

Headache is very common in children and adolescents in Ethiopia—apparently more so than in adults—a finding with major public-health implications for a country in which half the population are aged under 18 years [30].

With no similar study yet from elsewhere in the whole of SSA, or from another low-income country, this finding also contributes to knowledge and understanding of child and adolescent headache globally.

Acknowledgement

A machine generated summary based on the work of Zewde, Yared Zenebe; Zebenigus, Mehila; Demissie, Hanna; Tekle-Haimanot, Redda; Uluduz, Derya; Şaşmaz, Tayyar; Bozdag, Fatma; Steiner, Timothy J. 2020 in The Journal of Headache and Pain.

The prevalence of headache disorders in children and adolescents in Mongolia: a nationwide schools-based study

DOI: https://doi.org/10.1186/s10194-020-01175-6

Abstract-Summary

The Global Campaign against Headache collects data from children (7–11 years) and adolescents (12–17 years) both to inform health and education policies and to contribute to the Global Burden of Disease (GBD) study.

This survey in Mongolia was part of this global enquiry.

Observed lifetime prevalence of headache was 81.0%.

Gender- and age-adjusted 1-year prevalence was 59.4% (migraine: 27.3%; tension-type headache [TTH]: 16.1%; UdH: 6.6%; all headache on ≥15 days/month: 4.2%; probable medication-overuse headache: 0.7%).

All headache types except UdH were more prevalent among females than males, and all were more prevalent among adolescents than children, although UdH represented a higher proportion of all headache in children (13.0%) than in adolescents (10.0%).

At least in adolescents, headache in Mongolia is no less common than in adults.

The clear difference from similar studies in other countries was a lower prevalence of UdH, perhaps a consequence of reporting bias in a non-troublesome headache (mild and short-lasting by definition).

This study informs policy in Mongolia and, with no similar study yet from elsewhere in Western Pacific Region, makes an important contribution to the global enquiry.

Extended: At least in adolescents, headache is no less common than it is in adults in Mongolia, nor in this age group than in other countries.

Introduction

Studies in children and adolescents have been relatively few, with the prevalence of headache disorders much less well measured.

LTB, in collaboration with the International Headache Society (IHS), is now undertaking a global programme of schools-based studies using a standardised protocol [43] to collect data from children aged 6–11 years and adolescents aged 12–17 years in countries in all world regions.

The study focuses on the headache disorders with public-health importance.

As adding to knowledge and understanding of the global burden of headache, an important purpose of this study is to inform local health and educational policies.

Methods

We followed the generic protocol for the global programme [43], conducting a cross-sectional survey in schools selected to be nationally representative.

A structured questionnaire was completed by pupils under supervision within their school classes.

Information sheets describing the nature and purposes of the survey were distributed to pupils in the participating schools to take home to parents or guardians.

Pupils who were absent from school on the survey day were not counted as non-participants since they were not available for inclusion.

We categorized schools by their locality (urban, semi-rural or rural), by pupils' home income (teachers' estimates of the proportions of pupils coming from low-income homes: less than one quarter ["higher income"], one quarter to one half ["middle income"] or more than half ["lower income"]), and by home proximity (teachers' estimates of the proportions of pupils travelling for ≥1 h/day to attend: less than one quarter ["mostly close"] or more than one quarter ["many distant"]).

Results

Headache ever was reported by 3456 participants (observed lifetime prevalence: 81.0%; 95% CI: 79.8–82.2%).

Nausea and vomiting, both specific to migraine, were reported by 48.8% and 14.5% respectively of participants with headache.

HY was reported by 679 participants, 26.0% of 2614 with headache (three did not respond to this question) and 15.9% of the total sample.

Females (30.3%) reported HY substantially more than males (20.7%; $p < 0.001$), but adolescents (27.0%) only marginally more than children (24.3%; $p > 0.05$).

Headache on ≥15 days/month, including pMOH, was, proportionately, by far the greatest contributor to HY (≥70%), which was expected since, by definition in these disorders, it must be >50%.

For pMOH, HY was closely matched by both predictions; for other headache on ≥15 days/month, predictions were reasonably approximated.

Discussion

As similar studies have found in European [40, 44] and African Regions [45], headache had been experienced by most of these young participants (reported lifetime prevalence 81.0%).

By the same token, the prevalence of UdH as a proportion of all reported headache is expected to decline with increasing age, as was seen in Turkey [40], Lithuania [44] and Austria [41], and as it did here, from 13.0% in children to 10.0% in adolescents.

Most telling in this study was a prevalence of headache on ≥15 days/month of 10.7%.

While reported headache days in the preceding one and four weeks were perfectly feasible for migraine, TTH and UdH, the 1-day prevalence estimates that these gave rise to predicted less HY for each of these than was actually reported (by factors of 1.25–1.5 and about 2 for the 1-week and 4-week estimates respectively).

Conclusions

The findings of this study are available to inform educational and health policies in Mongolia.

With no similar study yet from elsewhere in the whole of Western Pacific Region, they also make an important contribution to LTB's global enquiry into child and

adolescent headache, a major fact-finding component of the Global Campaign against Headache [36, 37].

Acknowledgement
A machine generated summary based on the work of Luvsannorov, Otgonbayar; Anisbayar, Tsengunmaa; Davaasuren, Munkhzul; Baatar, Otgonzaya; Batmagnai, Khaliunaa; Tumurbaatar, Khulan; Enkhbaatar, Sarantuya; Uluduz, Derya; Şaşmaz, Tayyar; Solmaz, Elif Tuğçe; Steiner, Timothy J. 2020 in The Journal of Headache and Pain.

Primary headache disorders among the adult population of Mongolia: prevalences and associations from a population-based survey

DOI: https://doi.org/10.1186/s10194-019-1061-5

Abstract-Summary
In the ongoing Global Campaign endeavour to improve knowledge and awareness of headache prevalence worldwide, Mongolia is a country of interest.

It sits between Russia and China, in which prevalence is, respectively, much higher and much lower than the estimated global mean.

The crude 1-year prevalence of any headache was 66.1% (95% CI: 64.0–68.2%), with a strong female preponderance (OR: 2.2; $p < 0.0001$).

Age-and gender-adjusted prevalences were: migraine 23.1% (for females, OR = 2.2; $p < 0.0001$); tension-type headache (TTH) 29.1% (no gender difference); probable medication-overuse headache (pMOH) 5.7% (trending towards higher in females); other headache on ≥15 days/month 5.0% (for females, OR = 2.2; $p = 0.0008$).

Any headache yesterday was reported by 410 (20.1%; for females, OR = 2.4; $p < 0.0001$).

Only pMOH showed a strong association with age, peaking in middle years with a five-fold increase in prevalence.

Migraine showed a consistent association with educational level, while pMOH showed the reverse, and was also more common among other groups than among participants who were single (never married).

Migraine was less common among rural participants than urban (OR: 0.80; $p = 0.0326$), while pMOH again showed the reverse (OR: 2.4; $p < 0.0001$).

PMOH (but not migraine or TTH) was significantly associated with obesity (OR: 1.8; $p = 0.0214$).

Headache disorders are common in Mongolia, with, most notably, a very high prevalence of headache on ≥15 days/month corroborated by the high prevalence of headache yesterday.

Extended: The crude 1-year prevalence of any headache in the study population was 66.1% (95% CI: 64.0–68.2%), with a strong female preponderance (73.3% [70.7–75.7%] versus 55.4% [51.9–58.7%] in males; OR: 2.2; $p < 0.0001$).

The crude 1-year prevalence of migraine was 24.1% (n = 492), 8.7% (n = 178) definite and 15.4% (n = 314) probable.

The crude 1-year prevalence of TTH was 29.2% (n = 596), 20.7% (n = 423) definite and 8.5% (n = 173) probable.

Migraine showed a consistent association with educational level, while pMOH showed the reverse (more common in the less well educated), this perhaps being reflected in its higher prevalence among the unemployed.

Migraine was less common among the latter (OR: 0.80; $p = 0.0326$).

Introduction

Headache disorders are now acknowledged as the most prevalent cause of public ill health, affecting people in all countries, and as the second highest cause of disability worldwide [46–48].

GBD has been increasingly well informed during these years, notably by the population-based studies supported in countries around the world by Lifting The Burden (LTB) [36–49].

These had highly disparate findings: whereas prevalences were high in Russia for migraine (20.8%), TTH (30.8%) and, especially, headache on ≥15 days/month (10.5%), in China these were notably below global averages (9.3%, 10.8% and 1.0% respectively—even though headache disorders were still a substantial cause of public ill health here).

We focused on the headache disorders of public-health importance (migraine, TTH, medication-overuse headache [MOH] and other headache occurring on ≥15 days/month), the purposes being two-fold: to add to the global map of headache, and, more importantly, to inform public-health policy in the country.

Materials and methods

The study was a cross-sectional, population-based survey among randomly-selected Mongolian adults (aged 18–65 years) conducted in accordance with published methodology [50, 51].

Survey it included, for all participants, demographic enquiry and a headache screening question ("Have you had headache during the last year?").

Although we did not measure the altitude of each household, we had altitude data for each of the survey areas (see "Sampling and selection" above), according to which we categorized this variable as <1000 m, 1000–2000 m or > 2000 m. We took waist measurement (ignoring those known to be pregnant) and recorded self-reported height and weight, calculating body-mass index (BMI) as (weight in Kg)/(height in m)^2.

Participants reporting headache on ≥15 days/month were first separated, and described as a distinct group, with those also reporting regular use of acute headache medication on >15 days/month (triptans and combination analgesics being used rarely in Mongolia) considered to have probable MOH (pMOH).

Results

The crude 1-year prevalence of any headache in the study population was 66.1% (95% CI: 64.0–68.2%), with a strong female preponderance (73.3% [70.7–75.7%] versus 55.4% [51.9–58.7%] in males; OR: 2.2; $p < 0.0001$).

The crude 1-year prevalence of migraine was 24.1% (n = 492), 8.7% (n = 178) definite and 15.4% (n = 314) probable.

The age- and gender-adjusted prevalence of migraine was 23.1%.

The crude 1-year prevalence of TTH was 29.2% (n = 596), 20.7% (n = 423) definite and 8.5% (n = 173) probable.

The crude prevalence of other headache on ≥15 days/month was 5.3% (n = 108), higher among females (6.7%) than males (3.2%; OR: 2.2; $p = 0.0008$).

Discussion

Migraine was substantially more common among females than males, with age- and gender-adjusted 1-year prevalence of 23.1%.

Headache on ≥15 days/month (age- and gender-adjusted prevalence 10.7%) was also more common in females than males.

Over half of cases (5.7%) were pMOH, which showed a strong association with age, peaking in middle years with a five-fold increase in prevalence.

Migraine showed a consistent association with educational level, while pMOH showed the reverse (more common in the less well educated), this perhaps being reflected in its higher prevalence among the unemployed.

While headache disorders were common, the most noteworthy finding was the very high prevalence of headache on ≥15 days/month, corroborated by the high prevalence of headache yesterday (20.1%), which also showed a strong female association.

In Nepal, an LTB-supported study (using the same methodology) found a very strong relationship between migraine prevalence (and indices of severity) and altitude up to 2000 m [52, 53], which is not reflected here.

Conclusion

The prevalence of headache disorders among the adult population of Mongolia is high, with a very similar picture to neighbouring Russia and in excess of global means.

Headache on ≥15 days/month is very common, as is pMOH, a main contributor.

This new evidence adds to knowledge of the global prevalence of headache.

Acknowledgement

A machine generated summary based on the work of Luvsannorov, Otgonbayar; Tsenddorj, Byambasuren; Baldorj, Dorjkhand; Enkhtuya, Selenge; Purev, Delgermaa; Thomas, Hallie; Steiner, Timothy J. 2019 in The Journal of Headache and Pain.

Prevalence and risk factors associated with headache amongst medical staff in South China

DOI: https://doi.org/10.1186/s10194-020-1075-z

Abstract-Summary
A previous study by our team reported the prevalence of primary headache disorders and factors associated with headache among nurses in three hospitals in North China.

Among 645 medical staff, 548 (85%) responded (doctors = 240, nurses = 308).

Among the medical staff, the 1-year prevalence of primary headache disorders was 50%, with 25.9% experiencing migraine and 24.1% experiencing tension-type headache (TTH).

The prevalence of migraine in female doctors was higher than that in female nurses, although this difference was not significant (32.4% vs. 29.8%, p = 0.628).

Multivariate analysis showed that being female and working in other specialties (Emergency Department & Radiology Department) remained independent risk factors for migraine in doctors (OR 2.314 and 3.223).

Working more than 6 night-shifts per month was associated with an increased prevalence of migraine and TTH in doctors; the same was true in nurses for migraine, but not for TTH.

The prevalence of primary headache disorders in both nurses and doctors is higher than that in the general population in South China.

Further, female doctors are more susceptible than female nurses to migraine.

The risk factors relevant to headache that were found in this study should provide an important reference for promoting occupational health in medical staff, especially female doctors in China.

Extended: The prevalence of both migraine and TTH peaked during middle age (30–39 years) in the nurse and doctor groups but were higher in the former group than in the latter (migraine: 31.4% vs. 25.2%, p = 0.168 < 0.05; TTH: 29.1% vs. 24.3%, p = 0.213 < 0.05).

The prevalence of TTH was significantly higher for some nursing roles (nurse: 15.6%, nurse practitioner: 34.0%, p < 0.001), but this was not observed for doctors (resident: 22.5%, attending physician: 26.6%, deputy chief physician or above: 21.3%, p = 1.000 > 0.05).

The prevalence of migraine and total headache did not significantly differ with title for either doctors or nurses.

Background
A population-based study in China showed that the 1-year prevalence of primary headache disorders was 23.8% [4], which appears to be much lower than that in other countries and regions.

European regional studies showed that 53%–75%of people experienced headache disorders, while the 1-year headache prevalence was 45% in Ethiopia and 62% in Zambia [46].

In North China, we found that the prevalence of primary headache disorders in nurses was significantly higher than that in the general population (45.3% vs. 23.8%) [54].

We sought to provide recent statistics on the prevalence of primary headache disorders in medical staff in South China.

Our aims were to update prior prevalence estimates and to identify other factors relevant to headache disorders among medical staff in China, which should be a supplementary extension of "Lifting The Burden" in China.

Methods

In each hospital, we randomly selected eight clinical departments, from which all doctors and nurses were invited to participate the headache survey.

All those reporting headache were interviewed after their questionnaires were reviewed by neurologists.

Neurologists, who had been systematically trained with The International Classification of Headache Disorders, third edition (ICHD-3) tool and the survey, explained the notes for the questionnaire and answered the participant's questions.

Each participant completed the structured questionnaire to gather demographic data, occupation-related factors and headache characteristics over the previous year.

The demographic and headache profile sections of the questionnaire were the same items as used in a Chinese national epidemiology study, and were validated for headache assessment and diagnosis in the general population [4, 54, 55].

All those reporting headache were invited to interviews after their questionnaires were reviewed.

In face-to-face interviews, trained neurologists would confirm the headache diagnosis based on the ICHD-3.

Results

Specialty did not correlate with any type of headaches in doctors (migraine: internal medicine: 20.3%, surgical department: 19.2%, other specialties: 34.5%, $p = 0.786 > 0.05$; TTH: internal medicine: 22.5%, surgical department:27.4%, other specialties: 17.2%, $p = 1.000 > 0.05$) or with TTH in nurses (internal medicine: 26.2%, surgical department: 22.8%, other specialties: 26.1%, $p = 1.000 > 0.05$).

Seniority and work arrangement had no effect on the prevalence of headache, including migraine and TTH, in doctors or nurses.

Among the nurses, marital status and specialty were not identified as risk factors for TTH in the multivariate logistic regression analysis, and age, nationality, education, BMI, seniority, and work arrangement were not identified as risk factors for either type of headache.

Discussion

We found that the 1-year prevalence of primary headache disorders among medical staff in Sanya, South China, was 50% (migraine: 25.9%; TTH: 24.1%), which was

significantly higher than the 23.8% (migraine: 9.3%; TTH: 10.8%) obtained in a population-based study in mainland China [4].

Another study [54] recruited 1102 nurses among which only 10 respondents had two types of primary headache and only 2 were diagnosed with both CDH and MOH, suggesting nursing staff had lower prevalence of MOH and CDH than the general population.

This study is the first to investigate the prevalence of primary headache disorders among doctors in mainland China (45% had primary headache disorder: 21.7% had migraine, and 23.3% had TTH).

A senior job title was significantly associated with a greater prevalence of headache (both TTH and migraine) in nurses, indicating that occupational factors affected the prevalence of headache.

Conclusion
Our study shows that the prevalence of primary headache disorders (including migraine and TTH) in both nurses and doctors is higher than that of the general population in South China.

Acknowledgement
A machine generated summary based on the work of Xie, Wei; Li, Ruibing; He, Mianwang; Cui, Fang; Sun, Tingting; Xiong, Jianmei; Zhao, Dengfa; Na, Weinan; Liu, Ruozhuo; Yu, Shengyuan. 2020 in The Journal of Headache and Pain.

Prevalence and comorbidity of migraine headache: results from the Singapore Mental Health Study 2016

DOI: https://doi.org/10.1007/s00127-019-01755-1

Abstract-Summary
Migraine is a highly prevalent and disabling neurological disorder associated with a wide range of psychiatric comorbidities.

Studies have revealed that those with migraine headache and coexisting psychiatric disorders have poorer treatment outcomes and increased disability.

The study aims to establish the prevalence, correlates, and comorbidities of migraine headache among the multi-ethnic Asian population in Singapore.

The lifetime prevalence for migraine headache in the Singapore general population was 8.2%.

Participants belonging to the older age group (65 years and above versus 18–34 years of age), and those who were economically inactive (versus employed) were less likely to experience migraine headache.

Poisson regression analyses showed that migraine headache was also significantly associated with psychiatric conditions such as major depressive disorder (MDD) (prevalence ratio (PR), 1.80; 95% CI, 1.25–2.58), bipolar disorder (BD)

(PR, 3.55; 95% CI, 2.29–5.51), generalized anxiety disorder (GAD) (PR, 2.04; 95% CI, 1.12–3.69), obsessive compulsive disorder (OCD) (PR, 2.20; 95% CI, 1.49–3.26), and alcohol use disorder (AUD) (PR, 1.93; 95% CI, 1.20–3.08).

Those with migraine headache were significantly associated with poor functioning and disability compared to those without migraine headache.

Our study showed significant associations between migraine headache and psychiatric disorders, as well as with role functioning and disability.

Extended: Studies have revealed that patients with migraine headache and with coexisting psychiatric disorders are associated with poorer treatment outcomes and increased disability as compared to migraine headache without comorbid psychiatric conditions [56–58].

Those with migraine were two times more likely to have major depressive disorder (MDD) and alcohol use disorder (AUD), and three times more likely to have generalized anxiety disorder (GAD) [58].

These findings can help to create awareness and encourage holistic coordinated approaches to the management of migraine in health care settings.

Introduction

Studies have revealed that patients with migraine headache and with coexisting psychiatric disorders are associated with poorer treatment outcomes and increased disability as compared to migraine headache without comorbid psychiatric conditions [56–58].

A population-wide epidemiological study conducted in Singapore—the Singapore Mental Health Study (SMHS 2010)—was the first to establish the lifetime prevalence of migraine headache as 5.6% and that migraine was significantly associated with psychiatric disorders.

The aims of the current article were to (1) establish the prevalence, correlates and comorbidity of migraine headache among the general population of Singapore, (2) examine changes, if any, in the prevalence of migraine since the last survey—SMHS 2010, (3) assess the extent of role disability among individuals with migraine headache, and finally, (4) examine the comorbidity of common psychiatric disorders with migraine headache in this population.

Methods

Singapore is a multi-ethnic country in South-East Asia, with a resident population of 3.8 million [59] of which 74.2% are Chinese, 13.3% are Malays, 9.1% are Indians, and 3.3% belong to other ethnic groups.

The SMHS 2016 was a cross-sectional epidemiological household survey conducted among Singapore citizens and permanent residents, aged 18 years and above who were living in Singapore between 2016 and 2017, and randomly selected from an administrative database.

Participants living outside Singapore, those who were unable to be contacted due to an incomplete or incorrect address, those residents who were incapable of doing an interview due to severe physical and mental conditions, and those who were unable to complete the interview in one of the specified languages were excluded from the survey.

Face-to-face interviews were conducted at the respondents' homes or another preferred location and respondents completed the interviewer—administered questionnaire in English, Chinese, and Malay according to their preference.

Assessments

In accordance with McWilliams et al's methodology, to elucidate the relationship between migraine headache, significant socio-demographic variables and comorbid psychiatric disorders while accounting for other variables that may have independent effects on psychopathology, three series of Poisson regression models were used [60].

In the first Poisson model, prevalence ratios (PRs) for the association between migraine headache and psychiatric disorders were adjusted for socio-demographic variables such as age, gender, ethnicity, education level, and employment status.

The second Poisson regression model was adjusted for the significant socio-demographic variables (such as age, gender, ethnicity, education level, and employment status) and presence of other chronic physical conditions.

The third Poisson regression model was adjusted for the significant socio-demographic variables, other chronic physical conditions, and psychiatric disorders.

The mean score of role functioning and disability among individuals with migraine headache and individuals without migraine headache were assessed using a linear regression model after controlling for significant socio-demographic variables including age, gender, ethnicity, education level, and employment status.

Results

The first model of Poisson regression analysis adjusting for socio-demographic variables shows that those with migraine headache were significantly associated with all psychiatric disorders compared with those without migraine headache.

The second model of Poisson regression used to examine the association, adjusted for significant socio-demographic variables, and the presence of any of the 17 other chronic physical conditions revealed that those with migraine headache remained significantly associated with all psychiatric disorders compared with those not having migraine headache.

The third model of Poisson regression, adjusted for significant socio-demographic variables, 17 chronic physical conditions, and psychiatric disorders, revealed that those with migraine headache remained significantly associated with MDD (PR, 1.60; 95% CI, 1.08–2.37), BD (PR, 2.70; 95% CI, 1.70–4.29), and OCD (PR, 1.72; 95% CI, 1.15–2.55) compared with those not having migraine headache.

Discussion

The increase in the prevalence of migraine could be due to more individuals seeking treatment for headaches and receiving a diagnosis of migraine as compared to the previous study.

Similar findings have been reported in various studies, where individuals with migraine headache were more likely to be female [58, 61, 62].

Ethnicity also appears to play a role in migraine headache; while individuals of Malay ethnicity were more likely than those of Chinese ethnicity to experience

migraine in the current study, these findings are consistent with a previous study conducted in 2010 among Singapore's general population [58] as well as in the clinical population by Tai and others [63].

Our findings are in agreement with the previous population-based studies conducted in China [64], Italy [65], United States [66], and Japan [67] that have found migraine headache prevalence to decrease significantly with increasing age.

Consistent with various research findings, our study also found an association of migraine headache with psychiatric disorders, including MDD, GAD, BD and OCD [58, 61, 68–71].

Conclusions

The present study established that migraine headache is prevalent in Singapore with 1 in 12 people in the population having lifetime migraine headache.

The study found a significant association between migraine headache and psychiatric disorders and established its negative impact on functioning and disability.

Acknowledgement

A machine generated summary based on the work of Jeyagurunathan, Anitha; Abdin, Edimansyah; Vaingankar, Janhavi Ajit; Chua, Boon Yiang; Shafie, Saleha; Chang, Shi Hui Sherilyn; James, Lyn; Tan, Kelvin Bryan; Basu, Sutapa; Chong, Siow Ann; Subramaniam, Mythily. 2019 in Social Psychiatry and Psychiatric Epidemiology.

Prevalence of migraine in Upper Egypt

DOI: https://doi.org/10.1186/s41983-019-0067-x

Abstract-Summary

This study aims to estimate the prevalence of migraine headache among the population of Al-Quseir city (Upper Egypt) and its impact on the patients' life.

This study is part of a door-to-door survey of major neurological disorders in Al-Quseir city, Red Sea Governorate.

Respondents were identified as suffering from migraine with aura, migraine without aura, and probable migraine as defined by the diagnostic criteria of the International Headache Society (IHS).

Migraine Disability Assessment Scale (MIDAS) questionnaire was used to assess the impact of the disease on the patients' daily life.

We identified 911 patients suffering from migraine.

Among migraine patients, most of the attacks recorded were of moderate to severe intensity (97%) although virtually 66% of migraine patients reported that headache significantly interfered with their daily activities.

Migraine headache has a deleterious impact on the patient's functional and wellbeing.

Extended: This study aims to estimate the prevalence of migraine headache among the population of Al-Quseir city, Red Sea Governorate, Upper Egypt, and to determine migraine-related disability and treatment gap.

This study is part of a door-to-door survey of major neurological disorders that was conducted in Al-Quseir city (Red Sea Governerate) over a period of about 2 ½ years (July 1, 2009, to January 31, 2012).

Introduction

Migraine is most prevalent during the peak productive years and has a negative influence on the quality of life.

Despite high levels of temporal disability, many migraineurs have never consulted a physician for the problem, which in turn has introduced selection bias in migraine studies based on patients who seek treatment rather than persons from the general population [72].

Although numerous studies of migraine prevalence have been published, reviews of the epidemiological literature have shown a large variation in the prevalence rates (ranging from 1.

This study aims to estimate the prevalence of migraine headache among the population of Al-Quseir city, Red Sea Governorate, Upper Egypt, and to determine migraine-related disability and treatment gap.

Population and Methods

This study is part of a door-to-door survey of major neurological disorders that was conducted in Al-Quseir city (Red Sea Governerate) over a period of about 2 ½ years (July 1, 2009, to January 31, 2012).

This project was carried out on eligible inhabitants who had been living in Al-Quseir city, for at least 6 months at the time of the study.

This study was approved by the Local Ethics Committee of Assiut University and Ministry of Health (Red Sea Area Health Service) prior to commencement.

The study area, Al-Quseir city, is a representative city of those lying on Red Sea.

Al-Quseir city is the second city in the Red Sea Governorate as regards the number of population [73].

The intensity of attacks was recorded using three grades (mild, moderate, and severe) according to the International Classification of Headache Society 2004 [74].

Results

From the total number of 33,285 persons, those were screened through door to door, we identified 911 patients suffering from migraine (650 females and 261 males).

Regarding prophylactic treatment in between attacks, it was found that the treatment gap among migraineurs was 91.5%, i.e., most detected migraineurs (91.5%) were receiving no prophylactic treatment.

Discussion

Although, a door-to-door approach in estimating the prevalence of migraine is difficult and time consuming, it is more accurate than hospital-based studies as the majority of patients do not seek medical advice for self-limited paroxysmal disorders [75, 76].

Migraine prevalence in the current study is near the global data of WHO estimates which mentioned that migraine appears somewhat less prevalent, but still common, in Asia (3% of men and 10% of women) and in Africa (3–7% in community-based studies) [77].

These results are partially consistent with most studies on migraine prevalence, which have reported variation among different age groups, with prevalence figures following an inverted U-shaped distribution, increasing from age 15 to 18, peaking during the third and early fourth decades of life and declining thereafter [78, 79].

This heavy burden of migraine disability, besides the very wide treatment gap, might throw some light on this major health problem and necessitates more public awareness and the need for prophylactic treatment.

Conclusion

The lifetime prevalence of migraine in Al-Quseir was 3.38/100 with male prevalence of 1.95/100 and female prevalence of 4.8/100.

The highest prevalence figures were found during early adult life (18–40 years) among both genders reaching a total prevalence of 4.77/100 (2.89/100 for male and 6.53/100 for female).

Acknowledgement

A machine generated summary based on the work of El-Tallawy, Hamdy N.; Farghaly, Wafaa M.; Abdelhamed, Mohamed A.; Badry, Reda; Rageh, Tarek A.; Soliman, Wael T.; Abdulghani, Khaled O.; Hassan, Mahmoud; Sobhy, Sayed; Shehata, Ghaydaa A. 2019 in The Egyptian Journal of Neurology, Psychiatry and Neurosurgery.

Migraine prevalence, clinical characteristics, and health care-seeking practice in a sample of medical students in Egypt

DOI: https://doi.org/10.1186/s41983-021-00282-8

Abstract-Summary

To assess the prevalence, characteristics, and degree of disability of migraine in a sample of Egyptian medical students and to study their health care-seeking practice when having migraine A descriptive cross-sectional, questionnaire-based study included 631 undergraduate medical students enrolled in the Faculty of Medicine.

Participants' sociodemographic data, migraine prevalence, characteristic, migraine disability, and health care-seeking practice were evaluated.

By using the MIDAS test in the questionnaire, we assessed the impact of migraine headache on the daily activities of the students.

Prevalence of migraine in medical students was found to be 17.9% causing moderate disability.

Migraine was significantly more prevalent and caused more disability among female students compared to males (p value 0.001 and 0.001).

Migraine is highly prevalent among medical students with predominant female prevalence and has a negative impact on their academic performance and other activities.

Extended: Migraine is highly prevalent among medical students with predominant female prevalence.

Introduction

Migraine was ranked as the third most prevalent disorder and seventh highest specific cause of disability worldwide in the Global Burden of Disease Survey, 2010 [80].

The prevalence of migraine is generally highest in the most productive years of life.

In the adult population, females have higher prevalence of migraine compered to males [81].

The life of medical students usually has multiple triggers for migraine, particularly stress and irregular sleep.

The aim of this work was to assess the prevalence, characteristics, and degree of disability of migraine among medical students in the Faculty of Medicine, and to study the health care-seeking practice of medical students when having migraine.

Methods

This study is a descriptive cross-sectional study among undergraduate medical students enrolled in the Faculty of Medicine, from first to sixth grade during the 2017/2018 academic year.

The questionnaire was designed in English and contained four main sections: section 1, demographic characteristics of the students (age, sex, residence, grade, marital status, and family history); section 2, candidates were asked about the following: frequency of headache attacks during the last 3 months, duration of the single attack in hours.

Before study implementation, a pilot test for the questionnaire form was done among ten potential participants from each grade.

After data collection, each questionnaire was duly studied, and the diagnosis of different types of headache, especially migraine and its subtypes, was made according to the International Classification of Headache Disorders, third Edition (beta version) as follows: migraine without aura, migraine with aura, chronic migraine, probable migraine [80].

Results

According to ICHD 3, the medical students who had migraine in the last 3 months were 113 (17.9%), mostly of episodic type (88.5%).

Migraine headache was described by medical students by being of moderate intensity in nearly three fourths (76.0%) of migrainous students, occurring with frequency of 5–9 episodes every 3 months in more than one third of them (41.9%).

Students who had migraine described their migraine headache as being unilateral in nearly half (44.2%) of them, throbbing in character and increases with daily activity in three fourths of them (77% and 75.2% respectively).

Married medical students reported higher prevalence of migraine than single students (p value 0.030).

Medical students who had family history of headache were having statistically significant higher prevalence of migraine than their classmates with negative family history (p value <0.001).

Discussion

Migraine prevalence among medical students in this study was higher compared to migraine prevalence in the Egyptian general population which was 10.5% in Kandil and colleagues, a study conducted in Assiut Governorate, Egypt [82].

Other studies have revealed less positive family history of headache prevalence among medical students with migraine, whereas the prevalence was 20.6% in the study conducted by Ghorbani and colleagues [83].

High proportions of subjects with both migraine with and without aura may be expected in headache-prone populations as medical students reported in several previous clinical studies [84–86].

Our medical students with migraine had experienced mean frequency of attacks 5.96 per month which is higher than previous studies.

Regarding headache characteristics, 94.6% of our medical students with migraine had moderate to severe intensity of their attacks which is higher than that found in other studies [87, 88].

Conclusions

Migraine is highly prevalent among medical students with predominant female prevalence.

The Faculty of Medicine should conduct campaigns among students to raise their awareness about the high prevalence of migraine, diagnosis, and its impact on their academic performance.

Stress management programs should be developed so that students can learn the correct methods of stress alleviation which in turn will lessen the impact of migraine on their academic performance and other activities.

Limitations of the Study

The main limitation of the study is that it is a single center study.

Although the study included a large number of students, but still it is not representative of medical students in Egypt.

Acknowledgement

A machine generated summary based on the work of Oraby, Mohammed I.; Soliman, Rasha H.; Mahmoud, Mustafa A.; Elfar, Eman; Abd ElMonem, Noha A. 2021 in The Egyptian Journal of Neurology, Psychiatry and Neurosurgery.

Primary headache disorders in the adult general population of Pakistan—a cross sectional nationwide prevalence survey

DOI: https://doi.org/10.1186/s10194-017-0734-1

Abstract-Summary

The large geographical gaps in our knowledge of the prevalence and burden of headache disorders include almost all of Eastern Mediterranean Region (EMR).

One adult member (18–65 years) of each household, also randomly selected, was interviewed by a trained non-medical interviewer from the same location using a previously-validated structured questionnaire translated into Urdu, the national language.

We estimated 1-year prevalences of the headache disorders of public-health importance and examined their associations with demographic variables using multivariate analysis.

There were 4223 participants (mean age 34.4 ± 11.0 years; male 1957 [46.3%], female 2266 [53.7%]; urban 1443 [34.2%], rural 2780 [65.8%]).

Headache in the previous year was reported by 3233 (76.6% [95% CI: 75.3–77.8%]).

The age- and gender-adjusted 1-year prevalence of migraine was 22.5% [21.2–23.8%] (male 18.0% [16.8–19.2%], female 26.9% [25.6–28.2%]), of tension-type headache (TTH) 44.6% [43.1–46.1%] (male 51.2% [49.7–52.7%], female 37.9% [36.4–39.4%]), of probable medication-overuse headache 0.7% [0.5–1.0%] (male 0.7% [0.5–1.0%], female 0.8% [0.5–1.1%]) and of other headache on ≥15 days/month 7.4% [6.6–8.2%] (male 4.4% [3.8–5.0%], female 10.4% [9.5–11.3%]).

Migraine was more prevalent in females by a factor of 3:2 although this association barely survived ($p = 0.039$) after correcting for other factors.

All headache and migraine were age-related, peaking in the age group 40–49 years; TTH peaked a decade earlier.

With three quarters of its population affected, headache disorders must be on the public-health agenda of Pakistan.

Extended: Migraine was more prevalent in females in a ratio of 3:2 ($p < 0.001$), pMOH and other headache on ≥15 days/month about two-fold (the latter significantly [$p < 0.001$] but the former not).

Burden data will be reported in a future publication.

Background

Headache disorders affect almost half the world's population, according to a survey of the published literature conducted nine years ago [89].

Tension-type headache (TTH) and migraine are the major contributors in terms of prevalence, being the second and third most common disorders in the world [31].

Large geographical gaps in our knowledge of the prevalence and burden of headache disorders have been evident from the various surveys [31, 89–91].

In the Eastern Mediterranean Region is another large geographical knowledge gap; the countries include Pakistan, with the sixth largest population in the world [92] and characterised by economic and political instability and, in parts, by geographical inaccessibility.

Its two purposes were to contribute to knowledge of the global burden of headache [32] and to provide evidence for national health policy in Pakistan.

Methods

This questionnaire, used in similar studies conducted in other countries [50], included demographic enquiry, screening and diagnostic questions for headache.

Diagnoses were not made by the interviewers, but subsequently by diagnostic algorithm [50], applied to the most bothersome headache if a participant reported more than one type of headache.

In calculating this we assumed a headache prevalence of 50% and applied a confidence level of 99% and confidence interval (CI) of 2%.

We calculated headache prevalences as percentages with 95% CIs.

We performed bivariate analyses, calculating odds ratios (ORs) with 95% CIs, to look for associations between headache types (migraine, TTH or all headache on ≥15 days/month) and demographic variables.

In subsequent multivariate logistic regression analyses, we calculated Exp(B) with 95% CIs taking prevalence of each headache type as the dependent variable and gender, age, marital status, habitation, education level, income, province and BMI as factors.

Results

TTH was by far the most prevalent headache disorder (44.7%), but migraine was also very common, reported by over one fifth (22.9%) of participants.

Migraine was more prevalent in females in a ratio of 3:2 ($p < 0.001$), pMOH and other headache on ≥15 days/month about two-fold (the latter significantly [$p < 0.001$] but the former not).

Participants who were divorced, widowed or separated also had more headache (OR = 1.9), migraine (OR = 1.8) and headache on ≥15 days/month (OR = 2.5), but less TTH (OR = 0.7) than single participants.

Age 40–49 years remained positively associated with migraine, and an association emerged with headache on >15 days/month, while ages 30–49 were positively associated with TTH.

Being poor remained strongly associated with both migraine and headache on ≥15 days/month, but the negative association with TTH did not survive.

Discussion

Very similar findings have emerged from India, a country which shares Pakistan's genetic, environmental and cultural composition: the 1-year prevalence in Karnataka State of all headache was 63.9%, of migraine 25.2% (with a 4:3 female preponderance) and of TTH 35.1% [93].

The prevalence in Pakistan of all causes of headache on ≥15 days/month (8.1%) is approaching three times the estimated global average of 3% [89], but still not outside the range found by similar studies.

Speculatively, the same may have occurred, to a greater degree, with TTH, a disorder perhaps more easily hidden than migraine: in contrast to most studies elsewhere, we found in Pakistan a significantly higher prevalence of TTH in males (51.2%) than in females (37.9%), although this difference, with Exp(B) = 0.8, was also barely significant (p = 0.026) after correction for other factors.

Conclusion

With over three quarters of its population affected, headache disorders must be on the public-health agenda of Pakistan.

Worldwide, these disorders are the third leading cause of disability [91]; information from specific enquiry into the burden attributable to headache disorders in this country is needed to inform health policy and priority-setting, and will be reported soon.

Acknowledgement

A machine generated summary based on the work of Herekar, A. A.; Ahmad, A.; Uqaili, U. L.; Ahmed, B.; Effendi, J.; Alvi, S. Z.; Shahab, M. A.; Javed, U.; Herekar, A. D.; Khanani, Rafiq; Steiner, T. J. 2017 in The Journal of Headache and Pain.

The prevalence of primary headache disorders in Saudi Arabia: a cross-sectional population-based study

DOI: https://doi.org/10.1186/s10194-020-1081-1

Abstract-Summary

The large geographical gaps in our knowledge of the prevalence and burden of headache disorders include most of Eastern Mediterranean Region (EMR).

We surveyed Arabic-speaking adults aged 18–65 years in all 13 regions of KSA.

While previous Global Campaign studies have engaged participants by calling at randomly selected households, the culture of KSA made this unacceptable.

We estimated 1-year prevalences of the headache disorders of public-health importance (migraine, tension-type headache [TTH] and probable medication-overuse headache [pMOH]) and examined their associations with demographic variables.

Gender and age distributions imperfectly matched those of the national population, requiring adjustments for these to prevalence estimates.

Observed 1-year prevalence of all headache was 77.2%, reducing to 65.8% when adjusted.

For headache types, adjusted 1-year prevalences were migraine 25.0%, TTH 34.1%, pMOH 2.0% and other headache on ≥15 days/month 2.3%.

Adjusted 1-day prevalence of any headache was 11.5%.

Migraine was negatively associated with age > 45 years (OR: 0.4; p = 0.0143) while pMOH was most prevalent in those aged 46–55 years (OR: 2.7; p = 0.0415).

Prevalences of migraine and TTH in KSA are considerably higher than global averages (which may be underestimated), and not very different from those in Pakistan.

Extended: We estimated 1-year prevalences, gender- and age-adjusted, of 25.0% for migraine and 34.1% for TTH.

Introduction

Over a decade ago, a systematic review of the published literature found that headache disorders affected almost half the world's population [89].

In various iterations of the Global Burden of Disease (GBD) study, they were shown to be the second and third most common disorders in the world [31] and of clear public-health importance [8, 31, 32, 47–95].

Lifting The Burden (LTB), conducting the Global Campaign against Headache [36, 37, 49–96], has since been supporting a series of population-based studies to fill these gaps [4, 42–100].

Since there were, in 2007, no data on headache from the whole of the Eastern Mediterranean Region (EMR) [89], these studies have included Pakistan [100], an EMR country with the sixth largest population in the world.

We report here a second Global Campaign study from EMR, with prevalence findings of a nationwide cross-sectional population-based survey in the Kingdom of Saudi Arabia (KSA).

All Global Campaign studies so far have followed standardized methodology developed by LTB [51].

Methods

For planning purposes we anticipated a 20% non-participation proportion and a requirement therefore to contact a minimum of 2400 potential respondents (N), drawn from each region in proportion to its population according to the census [101].

Any Arabic-speaking person aged 18–65 years who answered the telephone was a potential participant.

Each eligible person who agreed upon first contact to participate was included in the survey and, whenever willing, interviewed immediately through the cell-phone call.

The questionnaire had four parts: (a) personal and demographic enquiry (including gender, age, marital status, educational level, employment and income from all sources), and (b) headache screening questions, which were addressed to all participants; these were followed in those screening positively by (c) diagnostic questions based on ICHD-II [102] and d) enquiry into burden.

Throughout the period of data collection, for fraud-detection purposes, participants were randomly selected and called again, at the rate of approximately 2/week.

Results

Since gender and age both influence headache prevalence, we adjusted observed values for these.

1789 participants (77.2% [95% CI: 75.5–79.0%]) reported headache in the preceding year.

Gender- and age-adjusted 1-year prevalence was 65.8% [63.9–67.7%].

Headache yesterday [HY] was reported by 254 participants (11.0% [9.7–12.2%]).

For TTH, the age-relationship was rather flat across all ages, with only a small peak among those aged 26–35 years.

For pMOH, with small numbers and wide CIs, reported prevalence increased steadily up to 46–55 years and then declined sharply.

Other headache on ≥15 days/month also declined after 46–55 years, again with small numbers.

HY was reported more as age increased up to 46–55 years, but this was a non-significant trend.

Discussion

The global age-standardised 1-year prevalence estimates for migraine and TTH, from GBD2016 [8] (which has the most detailed headache analyses), are 14.4% and 26.1%.

In Pakistan the age- and gender-adjusted 1-year prevalence of migraine is 22.5% [95% CI: 21.2–23.8%]; in KSA, at 25.0 [23.2–26.8], it is somewhat higher (Fisher's exact test: $p = 0.0238$).

TTH is more prevalent in males in both countries, in Pakistan by about 1.3:1, in KSA by 1.2:1.

There is a large gender-related difference in pMOH between KSA and Pakistan: while this disorder affects only 0.8% of adults in Pakistan [100], and the same proportion of males in KSA, it is reported by 3.4% of females in KSA, making it predominantly a problem among women in this country.

Conclusion

Prevalences in KSA of migraine and TTH, and perhaps of pMOH, are considerably higher than global averages.

Prevalences in KSA are not very different from those in Pakistan, also an EMR country but with many differences otherwise.

Information on the burden attributable to these disorders in KSA, needed to inform health policy and priority-setting, will be reported later.

Acknowledgement

A machine generated summary based on the work of Jumah, Mohammed Al; Khathaami, Ali M. Al; Kojan, Suleman; Hussain, Mohamed; Thomas, Hallie; Steiner, Timothy J. 2020 in The Journal of Headache and Pain.

Survival outcome and mortality rate in patients with migraine: a population-based cohort study

DOI: https://doi.org/10.1186/s10194-018-0889-4

Abstract-Summary
Whether the patients with migraine have an elevated mortality risk in Taiwan is unclear.

Compared with the comparison cohort, the corresponding aHRs for mortality were 0.81 (95% CI = 0.76–0.87), 0.89 (95% CI = 0.80–0.98), and 0.78 (95% CI = 0.72–0.84) in the total migraine, SM, and NM cohorts, respectively.

SM, male sex, comorbid alcohol-related illness, depression, and mental disorders were identified as risk factors for subsequent mortality.

Comorbid alcohol-related illness significantly increased the mortality risk in patients with migraine.

These patients would benefit from controlling their migraines and reducing the subsequent mortality.

Extended: Compared with the comparison cohort, the corresponding adjusted HRs (aHRs; 95% CIs) of the mortality were 0.81 (0.76–0.87), 0.89 (0.80–0.98), and 0.78 (0.72–0.84) for the total migraine, SM, and NM cohorts, respectively.

Compared with the comparison cohort, the average hospitalization duration was 0.66 days longer for the patients ever with SM.

The findings of this study might constructively inform the development and implementation of effective treatment strategies to reduce the migraine burden in Taiwan.

The diagnoses of SM and NM in this study were highly reliable and our results indicate that the sample size was sufficient to statistically demonstrate the mortality risk in patients with migraine in Taiwan.

Our findings provide vital information for clinicians and for assisting global efforts for understanding and treating migraine.

Background
Numerous epidemiological studies conducted in developed Western countries have found that migraines affect approximately 20% of the general population [103, 104].

Researchers have proposed that patients with migraine have a higher risk of mortality due to a high vulnerability to other fatal diseases.

Although numerous studies have examined the markers for the long-term outcomes of migraine, the actual mortality risk in patients with migraine has remained unclear so far [105–107].

Further investigation is required to understand the correlated mortality in patients with migraine to elucidate future treatment strategies for migraine.

Patients with such a condition may experience considerably more disability than patients with a classic, non-status migraine (NM) and thus may require specific pharmacological treatment or adopt psychological strategies to reduce the burden of the disease [108].

Methods
This population-based cohort study used the Longitudinal Health Insurance Database (LHID) provided by the National Health Research Institutes in Taiwan.

The comparison cohort comprised patients without a migraine diagnosis in the LHID.

For each identified patient with migraine, 4 non-migraine participants from the LHID were randomly selected for the comparison cohort and were frequency matched with age (each 5-year span); sex; and comorbidities of depression (ICD-9-CM 296.2, 296.3, 296.82, 300.4, and 311), mental disorders (ICD-9-CM 290–319), insomnia (ICD-9-CM 307.4 and 780.5), alcohol-related illness (ICD-9-CM 291, 303, 305.00, 305.01, 305.02, 305.03, 571.0, 571.1, 571.3, 790.3, and V11.3), and anxiety (ICD-9-CM 300.00); and index date (year).

Univariable and multivariable Cox proportional hazard regression analyses were used to assess the risk of mortality associated with migraine compared with the comparison cohort.

Results
Compared with the comparison cohort, the corresponding adjusted HRs (aHRs; 95% CIs) of the mortality were 0.81 (0.76–0.87), 0.89 (0.80–0.98), and 0.78 (0.72–0.84) for the total migraine, SM, and NM cohorts, respectively.

The aHRs of mortality were 0.68–0.86 and 0.64–0.84 in the total migraine and NM cohorts, respectively.

Discussion
To the risk factors of age and the condition of SM, alcohol-related illness, male sex, depression, and mental disorders were major risk factors for all-cause hospitalization and mortality in patients with migraine.

Among the comorbidities, alcohol-related illness was the strongest risk factor for hospital admission and mortality in patients with migraine.

To cardiovascular risk, this study reveals that alcohol-related illness is another risk factor to cause premature mortality in Taiwanese patients with migraine.

We only analyzed the mortality risks in patients with migraine who died after being treated at inpatient facilities, excluding mortality cases outside a hospital.

The diagnoses of SM and NM in this study were highly reliable and our results indicate that the sample size was sufficient to statistically demonstrate the mortality risk in patients with migraine in Taiwan.

Conclusions
This study revealed that Taiwanese patients with migraine benefit from comprehensive and universal health care for not only controlling their migraines but also reducing subsequent mortality risk.

Our findings provide vital information for clinicians and for assisting global efforts for understanding and treating migraine.

Acknowledgement
A machine generated summary based on the work of Harnod, Tomor; Lin, Cheng-Li; Kao, Chia-Hung. 2018 in The Journal of Headache and Pain.

Major sex differences in migraine prevalence among occupational categories: a cross-sectional study using UK Biobank

DOI: https://doi.org/10.1186/s10194-021-01356-x

Abstract-Summary
Gender-related differences regarding an association of migraine with important occupational characteristics has been hardly studied.

The current study scrutinizes gender-specific differences in the prevalence of migraine across a broad spectrum of occupational categories, shedding also light on associations with important job-related features such as shift work, job satisfaction, and physical activity.

Prevalence ratios of migraineurs compared to healthy controls among different occupational categories and job-related variables were estimated using log-binomial regression analyses.

We detected a differential prevalence pattern of migraine in relation to different job categories between men and women.

In men, migraine appears to be more prevalent in highly physically demanding occupations (PR 1.38, 95% CI [0.93, 2.04]).

Migraine is also more prevalent in jobs that frequently involve shift or night shift work compared to healthy controls.

Our results show that migraine is genderdependently associated with physically demanding jobs and shift working.

Extended: Our results show striking differences between men and women in the prevalence of migraine dependent on occupational categories.

Introduction
Among the modifiable risk factors, work-related stressors have recently been found to be associated with migraine onset [109].

In a prospective cohort study [110] it has been found that a high effort-reward imbalance among women employed in the public sector is associated with an increased risk of a new migraine onset.

Brief review of the literature it emerges that finding possible correlations between migraine pathogenesis and work-related issues is a complex process, since many interconnected factors may increase the risk for the development of this disorder.

This highlights the need for a more precise approach for studying the association between work-related risk factors, sex and migraine, to be able to clarify some diverging results in the literature [111].

The aim of this study is therefore to investigate the gender-specific association between occupational categories and work-related features such as physical activity involved, shift work, job satisfaction and migraine, using the large population-based UK Biobank cohort.

Materials and Methods

In order to investigate the prevalence of migraineurs among the various job categories we used the "Job code at visit" variable, that broadly divides the participants into nine different subgroups, according to the Standard Occupational Classification (SOC2000): managers and senior officials, professional occupations, associate professional and technical occupations, administrative and secretarial occupations, skilled trades occupations, personal service occupations, sales and customer service occupations, process, plant and machine operatives and elementary occupations.

Covariates such as ethnic background, educational status, age, BMI and neuroticism are associated both with the exposure (job and job-related issues) and the outcome (migraine), therefore they were considered confounders.

We performed the calculations for PR and 95% CI using two models: (i) adjusting for sociodemographic confounders such as age, BMI, ethnic background (ii) as model (i) including education level and neuroticism as well [112].

In three cases it was not possible to perform the analysis for the first model: occupational category and heavy manual or physical work for women and shift work for men.

Results

From the data we can see that migraineurs are slightly more prevalent in jobs that involve constant shift or night shift work, and this holds true especially for women.

Migraine results to be more prevalent in men that are more often involved in heavy manual or physical work (fully adjusted PR 1.38, 95% CI [0.93, 2.04]) and in walking or standing (fully adjusted PR 1.41, 95% CI [1.02, 1.95]).

The same feature is shared by women, with higher prevalence of migraine among participants with jobs characterized by frequent walking/standing (fully adjusted PR 1.23, 95% CI [1.02, 1.48]).

Female migraineurs are more prevalent among jobs that involve shift work (fully adjusted PR 1.45, 95% CI [1.14, 1.83]).

Migraine appears to be less prevalent among women moderately happy with their job (fully adjusted PR 0.76, 95% CI [0.52, 1.12]).

Discussion

While other studies focused only on a very particular work sector (e.g. health professionals) [110–113], we considered nine different job categories (according to SOC2000) as well as important job related features such as work-related physical activity, shift work and job satisfaction.

Stratifying by sex we were able to perform more precise analyses, highlighting sex-specific differences on the prevalence pattern of migraine among the various job-related features.

The analyses on the work-related physical activity show that frequent heavy manual physical work is related to higher prevalence of migraine among men, while for women there is no significant difference compared with the healthy controls.

Our analyses show that migraine is more prevalent in jobs characterized by frequent shift and night shift work.

This allowed us to give an estimation of the prevalence of migraine among different work-related groups, but not to assess risk or incidence.

Conclusion
Previous studies showed how particular job-related features exert a differential impact on women and men in terms of migraine risk.

This research shows that migraine is more prevalent in physically demanding occupations, especially in men.

Migraine is also more prevalent in jobs that involve frequently shift or night shift work, and the prevalence is even higher in women.

Acknowledgement
A machine generated summary based on the work of Affatato, Oreste; Miguet, Maud; Schiöth, Helgi B.; Mwinyi, Jessica. 2021 in The Journal of Headache and Pain.

1.2 Personal and Societal Burden

Machine generated keywords: child, migraine patient, adolescent, score, sleep, child adolescent, school, udh, measure, tth, hrqol, gbd, stress, hru, mida.

Migraine remains second among the world's causes of disability, and first among young women: findings from GBD2019

DOI: https://doi.org/10.1186/s10194-020-01208-0

[Section 1]
The approach takes away the spotlight from disabling diseases that do not cause early death—such as headache disorders.

Headache disorders in 2019 ranked 14th among global causes of DALYs (all ages, both genders) [114].

Among females aged 15–49 years, headache disorders (1016.1) were second only to gynaecological diseases (1230.5), with depressive disorders third (890.4).

The level-3 grouping of headache disorders in GBD2019 includes only specific diseases: migraine and tension-type headache (TTH), each with medication-overuse headache (MOH) as a sequela factored in according to the proportion of MOH attributed to it [114].

The authors of the GBD2019 report wrote: "The prominent position of headache disorders in the DALY rankings in the 10–24-year and 25–49-year age groups has received little attention in global health policy debates" [114].

Acknowledgement
A machine generated summary based on the work of Steiner, T. J.; Stovner, L. J.; Jensen, R.; Uluduz, D.; Katsarava, Z.; 2020 in The Journal of Headache and Pain.

Migraine is first cause of disability in under 50s: will health politicians now take notice?

DOI: https://doi.org/10.1186/s10194-018-0846-2

[Section 1]
A strength was its scope of enquiry, simultaneously into migraine, tension-type headache (TTH) and medication-overuse headache (MOH), the three headache disorders of major public-health importance.

In GBD 2016, the decision was made that burden attributed to MOH would be more correctly attributed to the antecedent disorders, in due proportion (73.4% to migraine, 26.6% to TTH, from a meta-analysis of three studies [115–117]).

All three contribute to the disability burden of migraine, and all three contributions should be duly recognised. (We noted earlier that GBD does not consider disability associated with the interictal state of headache disorders [91], although significant interictal burden is reported by many people with migraine [118]).

From GBD 2016 it is more evident than ever that headache disorders have a very large detrimental effect on public health.

If studies contributing to GBD are standardized, future iterations of GBD may not only show the relative importance of headache in global public health but also monitor the benefits of improvements in headache care, new treatments and societal change.

Acknowledgement
A machine generated summary based on the work of Steiner, Timothy J.; Stovner, Lars J.; Vos, Theo; Jensen, R.; Katsarava, Z. 2018 in The Journal of Headache and Pain.

21st Century Headache: Mapping New Territory

DOI: https://doi.org/10.1186/s10194-021-01233-7

Abstract-Summary
Headache prevalence and burden is changing as society evolves, with headache now occurring earlier in life.

Contributing factors, mostly associated with changing life style, such as stress, bad posture, physical inactivity, sleep disturbance, poor diet and excess use of digital technology may be associated with the phenomenon that could be labelled as 'twenty-first century headache'.

The headache-related impact on productivity and absenteeism negatively influences an individual's behaviour and quality of life, and is also associated with a high economic cost.

Since the majority of sufferers opt to self-treat rather than seek medical advice, substantial knowledge on headache prevalence, causation and burden is unknown globally.

The broad use of digital technology to gather real world data on headache triggers, burden and management strategies, in self-treated population will allow these sufferers to access appropriate support and medication, and therefore improve quality of life.

Background

Headache disorders are among the main causes of disability worldwide; however, the majority of sufferers are never professionally diagnosed and instead, turn to over-the-counter (OTC) medications to self-manage symptoms [8].

Predominantly experienced by those aged 15–49 years, headache incidence in school aged children is increasing, indicating that headache disorders are being reported earlier in life than they were before [8, 119].

There is accumulating evidence in recent literature that modern lifestyle in industrial countries may have an effect on headache incidence, prevalence and impact.

Headache Triggers Associated with twenty-first Century Lifestyle

The recently increased use of digital technology is associated with increased risk of obesity, fatigue and headache; thus, headache incidence has been linked to prolonged (>8 h/day) computer use in IT professionals in China and to excessive (>4 h/day) video game use in adolescents in Brazil [120, 121].

Increased smartphone usage has been linked to headache, sleep disturbance, cognitive impairment and fatigue, with call frequency significantly correlated with headache risk [122].

The coronavirus disease 2019 (COVID-19) pandemic has been associated with both increased and decreased headache frequency [123].

To being reported as a symptom of infection, headache frequency and severity increased in uninfected individuals due to psychological stress, social isolation, sleep disruption and poor dietary habits [124, 125].

Headache Impact on Cognitive and Daily Functionality

The cognitive impact of migraine has been well characterised, with multiple studies showing that migraine sufferers experience greater memory deficits during an attack compared with other headache types; however, the evidence for the impact of TTH on cognitive functioning is limited [126, 127].

Headache disorders contribute to distraction and poor concentration that define presenteeism at work; recent studies in Europe showed that only 50% of headache sufferers with presenteeism completed their normal working day [128, 129].

Absenteesim is also a problem: approximately 22% of migraine sufferers and 10% of TTH sufferers take several days per year off work due to headache [130].

The cognitive impact and loss of productivity may also be linked to anxiety, avoidance behaviour, reduced social interactions and lifestyle compromise reported by 16% of migraine sufferers and 20% of TTH sufferers [131, 132].

Changing the Paradigm: Non-Doctor Headache

This population of headache sufferers, that could be referred to as the 'non-doctor treated headache' (NDH) population, relies on OTC medication for symptom relief [133].

There are limited data on the management of headache in the NDH population with respect to headache type, reduction in quality of life, triggers, OTC medication and non-pharmacological management techniques [134].

While randomised controlled trials (RCTs) adequately assess professionally diagnosed and managed headache, the NDH population should be captured by real world evidence studies, a number of which have been successfully undertaken and delivered important insights in headache-related behaviour and experiences [135].

The digital technology can serve as a double-edged sword: while possibly attributing to rising incidence and prevalence of headache, it provides an enormous pool of real world data.

An increasing number of smartphone applications capture and record headache frequency, intensity, triggers, duration and medication choice [136].

Conclusions

Because causal factors seem to evolve with socioeconomic development, it is important to identify the true burden and triggers related to 'twenty-first century headache' in real world settings [8, 119].

Clinical experts and modern analysis techniques, such as artificial intelligence and machine learning, should be engaged in the analysis of these data to help identify NDH-relevant and specific outcome measures that should be further validated in RCTs assessing the impact of twenty-first century headache on cognitive abilities, functionality and society.

Providing new guidelines to trained pharmacists and establishing an educational programme for the general population will empower headache sufferers to manage better their condition and decrease the burden of twenty-first century headache.

Acknowledgement

A machine generated summary based on the work of Goadsby, Peter J.; Lantéri-Minet, Michel; Michel, Martin C.; Peres, Mario; Shibata, Mamoru; Straube, Andreas; Wijeratne, Tissa; Ebel-Bitoun, Caty; Constantin, Luminita; Hitier, Simon. 2021 in The Journal of Headache and Pain.

Burden of Migraine in Patients With Preventive Treatment Failure Attending European Headache Specialist Centers: Real-World Evidence From the BECOME Study

DOI: https://doi.org/10.1007/s40122-021-00331-3

Abstract-Summary

Patients with difficult-to-treat migraine often cycle through different preventive therapies, but real-world prospective evidence describing the burden of migraine in patients with prior preventive treatment failure (PPTF) in Europe is limited.

In BECOME, we aimed to characterize and assess the prevalence and burden of migraine in patients with PPTF attending specialist headache centers in Europe and Israel.

In part 2, patients from part 1 with ≥ 1 PPTF and ≥4 MMD were enrolled, and impact of migraine on patient-reported outcomes, and healthcare resource utilization (HRU) were examined.

In part 1 (n = 20,837), 62.2% of patients reported ≥ 1 PPTF.

In part 2 (n = 2419), 15.3% of patients reported ≥ 4 PPTF.

In part 2, the migraine burden measured by the EuroQoL 5 dimensions 5 level (EQ-5D-5L) questionnaire indicated an impact of at least moderate severity in performing usual activities in 26.5% of patients, pain/discomfort in 51.2%, and 26.1% reported being at least moderately anxious/depressed.

Most patients reported a severe impact on daily activities and disability due to migraine.

In part 2, analysis of HRU showed 21.2% patients visited an emergency department and 8.4% were hospitalized for headache/migraine in the past year.

This study provides real-world evidence of the high personal, social, and HRU burden of migraine in Europe and Israel.

Extended: These findings demonstrate an unmet need for the management of difficult-to-treat migraine.

Digital Features

This article is published with digital features, including a video abstract, to facilitate understanding of the article.

To view digital features for this article go to https://doi.org/10.6084/m9.figshare.16676617.

Introduction

While the burden of migraine in Europe has been previously reported [10–131, 137, 138], the evidence relating to the burden in patients with prior preventive treatment failure (PPTF) is limited.

An acknowledged limitation of these burden studies has been the extent to which migraine has been correctly diagnosed in all cases.

We aimed to describe the disease characteristics, especially in terms of monthly migraine days (MMD) and treatment failures, among patients who visited specialty care centers across Europe and Israel.

We investigated the disease burden and healthcare resource utilization (HRU) among patients who had failed standard of care preventive treatments.

Methods

Part 1 of the study was designed to prospectively assess the prevalence of new and follow-up patient visits to specialist headache centers and to ascertain the healthcare infrastructure of the participating headache specialist care sites.

Other endpoints in part 1 included the proportion of patients visiting headache sites within a 3-month period stratified according to (1) frequency of MMD (<4, 4–7, and 8–14 MMD, or ≥ 15 headache days per month, at least eight of which are migraine days), (2) new versus follow-up visit, (3) inpatient versus outpatient, and (4) medication overuse and medication overuse headache [139].

The burden of migraine was assessed according to 1 PPTF/> 4 PPTFs in the overall group of patients with CM and in subgroups designated as low-frequency CM (LFCM; ≥ 15 monthly headache days [MHD], of which 8–14 are MMD) and high-frequency CM (HFCM; ≥ 15 MHD, of which ≥15 are MMD).

Results

Of the 20,837 patients with migraine examined during the 3 months in part 1 of the study, 74.3% (15,479/20,837) reported more than 4 MMD and 22.9% (4767/20,837) suffered from CM.

Within a given MMD category, the proportion of patients who reported at least moderate problems increased with increasing PPTF.

For the anxiety or depression domains, the proportion of patients who reported at least moderate anxiety or depression tended to increase with increasing MMD, and no consistent association with PPTF was found.

In both the HFEM and HFCM categories, a higher number of PPTFs was associated with a lower proportion of patients reporting anxiety, perhaps reflecting adaptation to the condition in a population likely to have longer-standing disease.

The mean MSQ-RFP score of 59.2 (58.2–60.1) indicated that patients had to cancel or needed help in their social and work-related lives because of migraine symptoms.

Discussion

In part 1 of the study, comprising patients visiting headache centers during a 3-month period, 62.2% of patients reported failure of at least one prior preventive therapy and 74.3% of patients reported ≥4 MMD, representing a high burden of the disease.

In this study, we found high proportions of patients consulting for a follow-up visit (77.0%) and reporting ED visits (21.2%; mean [SD] visits per patient, 3.0 [5.4]) for their migraine and hospitalization due to migraine (8.4%; mean [SD], 1.5 [2.3]) in the previous 12 months.

The specific aim of this study was to assess the burden of migraine in patients with at least one PPTF visiting the specialist centers in Europe and Israel.

Conclusions
The BECOME study demonstrates the high prevalence of PPTF among patients with migraine who visited headache clinics and confirms the significant and increasing HRQoL and societal burden in patients with increasing disease severity due to migraine.

Both PRO and HRU data revealed that the disease burden increases with MMD.

Our results indicate that the number of PPTFs add to the burden of migraine.

Acknowledgement
A machine generated summary based on the work of Pozo-Rosich, Patricia; Lucas, Christian; Watson, David P. B.; Gaul, Charly; Ramsden, Emma; Ritter, Shannon; Martelletti, Paolo; Snellman, Josefin. 2021 in Pain and Therapy.

Global assessment of migraine severity measure: preliminary evidence of construct validity

DOI: https://doi.org/10.1186/s12883-019-1284-8

Abstract-Summary
This study investigated how migraine patients rate the severity of their disease and how these ratings correlate with their socio-demographic, clinical, and psychosocial characteristics.

We obtained a broad range of clinical and patient-reported measures (e.g., patients' ratings of migraine severity using the Global Assessment of Migraine Severity (GAMS), and migraine-related disability, as measured by the Migraine Disability Scale (MIDAS)).

Median regression analysis was used to examine the predictors of patient ratings of migraine severity.

Patients' report of severity on the GAMS was strongly correlated with patients' ratings of MIDAS global severity question, overall MIDAS score, migraine type, PHQ-9 score, and frequency of migraine attacks.

Mediation analyses revealed that MIDAS mediated the effect of depression on patient ratings of migraine severity, accounting for about 32% of the total effect of depression.

Migraine subtype, frequency of migraine, employment status, depression, and migraine-related disability were statistically significant predictors of patient-ratings of migraine severity.

This study highlights the impact of clinical and psychosocial determinants of patient-ratings of migraine severity.

Extended: Median regression analysis was used to model the association between influence of migraine disability assessment, socio-demographic characteristics (sex, age, employment status, education and marital status), self-reported side effects from medication (yes or no), migraine subtype, migraine frequency classification, and self-reported depression and anxiety symptoms (PHQ-9).

Future research will also need to investigate the validity of GAMS in community-dwelling persons with migraine.

A single-item global rating scale of migraine severity may be a rapid and efficient way for clinicians to obtain information about disease severity, but requires validation in future prospective studies.

Background

Migraine represents one-third of all neurological disease burden [140] and is one of the top 15 conditions with the most substantially increased disease burden ranking in the past decade; it is among the top 25 causes of years lived with disability (YLDs)[2].

Several standardized and validated scales have been developed to assess patient-reported or physician-reported migraine severity, a concept closely linked to disability [141–144].

The limitations of longer severity measures are addressed in a brief single item patient-reported measure, the Global Assessment of Migraine Severity (GAMS), developed to assess patients' perception of their disease severity.

The objectives of this current study were to (1) explore how patients with migraine perceive the severity of their disease and its inter-relationship with patients' demographic, clinical, and psychosocial characteristics, and (2) assess how GAMS compares to other measures of migraine severity and disability.

We hypothesize that patients' ratings of migraine severity would be strongly correlated with other validated measures of migraine severity and patients' psychosocial characteristics.

Methods

Fisher's exact test was used to assess the association between patients' ratings on GAMS and sex, marital status, employment status, education, medication side effects, migraine subtype, MIDAS (No/little/mild vs moderate/severe).

The association between patients' ratings on the GAMS and MIDAS, PHQ9, HADS-D, HADS-A, and migraine frequency was assessed using polyserial correlation.

Associations between patients' ratings on the GAMS and binary or ordinal clinical and self-reported characteristics (e.g., frequency of migraine attacks, intensity of migraine pain, migraine subtype, use of psychotropic medications, side-effects from medication, employment status) were assessed using biserial correlations.

Median regression analysis was used to model the association between influence of migraine disability assessment, socio-demographic characteristics (sex, age, employment status, education and marital status), self-reported side effects from medication (yes or no), migraine subtype, migraine frequency classification, and self-reported depression and anxiety symptoms (PHQ-9).

Results

Pearson's chi square test revealed statistically significant univariate associations between patients' ratings of migraine severity, as measured by GAMS, and patients' rating on migraine-related disability, migraine subtype (chronic versus episodic), and employment status (employed versus not employed).

Patients who report more severe migraines are likely to be unemployed individuals who report more disabling, chronic migraine with aura, and endorse clinically elevated levels of depression symptoms.

Mediation analysis revealed that migraine-related disability (measured by MIDAS) partially mediated the effects of depression and employment status on patient-reported GAMS ratings.

Patients with clinically elevated levels of depression symptoms were likely to self-report a 0.63 unit increase on the GAM, after adjusting for the indirect effects through migraine-related disability as measured by MIDAS, as compared to an unadjusted effect of 0.47.

The indirect effects of depression mediated through the MIDAS accounted for 9.5% of the employment status patients' ratings of migraine severity (measured by GAMS).

Discussion

In our headache outpatient clinic, we investigated the validity of GAMS, a brief patient-reported measure of migraine severity in migraine patients, and explored the determinants of patient-ratings of migraine severity in this outpatient cohort.

Our study demonstrates a moderate to strong correlation between patient-ratings of migraine severity and clinical characteristics and validated measures such as MIDAS score, MIDAS migraine severity question, PHQ9, HADS-A, migraine subtype, frequency of migraine attacks.

The novelty of our study finding lies in the use of a single item global rating of migraine severity to identify clinical and psychosocial determinants of patient-reported severity of migraine.

A future prospective longitudinal study to assess the reliability and other psychometric properties of the GAMS in relation to other validated scales such as the Migraine Severity Scale and the Headache Impact Test is warranted.

Patients with chronic migraine were more likely to report a higher severity of headache compared to patients with episodic migraine.

Conclusion

We demonstrate the validity of GAMS as a brief measure of patient-reported migraine severity and identified clinical and psychosocial correlates and/or mediators of patient-reported severity of migraine in a cohort of migraine patients seen in an outpatient Headache clinic.

Acknowledgement

A machine generated summary based on the work of Sajobi, Tolulope T.; Amoozegar, Farnaz; Wang, Meng; Wiebe, Natalie; Fiest, Kirsten M.; Patten, Scott B.; Jette, Nathalie. 2019 in BMC Neurology.

Perceived stress in patients with migraine: a case-control study

DOI: https://doi.org/10.1186/s10194-017-0780-8

Abstract-Summary
Perceived stress is the most common trigger for migraine.

The objective of this study was to examine the clinical significance of perceived stress in migraine patients.

They completed self-reported questionnaires including Perceived Stress Scale (PSS), 12-item Allodynia Symptom Checklist (ASC-12), Migraine Disability Assessment Scale (MIDAS), Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), Epworth Sleepiness Scale (ESS), Insomnia Severity Index (ISI), and Migraine-Specific Quality of Life Questionnaire (MSQ).

Degree of perceived stress in migraine patients was measured and compared to that in healthy controls.

Predictors for perceived stress and their impact on quality of life (QOL) of migraine patients were also determined.

Chronic migraine is a critical factor for perceived stress.

Perceived stress affects QOL of migraine patients.

Background
It has been found that migraine patients have higher levels of perceived stress than healthy controls [145, 146].

Stress can trigger migraine attacks.

About 80% of migraine patients with identifiable triggers have reported that stress is a common trigger [147].

In a Korean hospital-based study, stress is the most common trigger for episodic migraine, followed by sleep deprivation and fatigue [148].

Factors associated with perceived stress in migraine patients have not been reported yet.

If predictors for perceived stress of migraine patients can be identified, a guideline can be developed for clinicians to manage stress adequately.

The second aim of this study was to identify predictors for perceived stress in migraine patients.

Although it is known that migraine and comorbid disorders will reduce QOL of patients, the impact of stress on QOL has not been reported.

Methods
It was measured by the 12-item Allodynia Symptom Checklist (ASC-12) with a cut-off score of >2 to define allodynic patients [149].

Eligible subjects underwent several self-reported questionnaires including the Korean version of Perceived Stress Scale (PSS) [150], Migraine Disability Assessment Scale (MIDAS) [151], Patient Health Questionnaire-9 (PHQ-9) [152], Generalized Anxiety Disorder-7 (GAD-7) [153], Epworth Sleepiness Scale (ESS) [154], Insomnia Severity Index (ISI) [155], and Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQ) [156].

The degree of PSS score in migraine patients was examined and compared to that in controls.

The Korean version of the PHQ-9 has been validated in patients with migraine [152].

The Korean version of the GAD-7 has been validated in patients with migraine [153].

Each ESS item score measures a particular "situational sleep propensity".

The sum of those item scores (i.e., total ESS score) measures the subject's average sleep propensity across those different situations in daily life.

The Korean version of the ISI has been validated in patients with sleep disorders [155].

Results

Although migraine patients and controls had no significance difference in age, gender, employment status, household income, or body mass index, education level in migraine patients was significantly ($p < 0.001$) lower than that in controls.

A total of 208 (91.6%) migraine patients had migraine without aura while 103 (45.4%) patients had CM.

While the mean PSS score adjusted for education was significantly ($p < 0.001$) higher in migraine patients than that in controls, the score adjusted for education, depression, and anxiety in migraine patients was not significantly different from that in controls.

Regarding migraine chronicity, only CM patients had higher ($p < 0.05$) mean PSS scores than controls after controlling for education, depression, and anxiety.

CM, earlier onset of migraine, higher intensity of headache, phonophobia, allodynia, higher scores of MIDAS, PHQ-9, GAD-7, ESS, and ISI were associated with PSS score.

Discussion

Our study revealed that the level of perceived stress was significantly higher in CM patients than that in controls.

While a higher level of perceived stress has been previously reported in migraine patients compared to that in healthy controls in two studies [145, 146], there was no difference in mean PSS score between migraine patients and controls after controlling for depression and anxiety in this study.

This reveals that depression and anxiety are major determinants of perceived stress in migraine patients and controls.

Depression and anxiety are not likely to be unique for perceived stress in patients with migraine.

After investigating the relationship between migraine chronicity and perceived stress, it was found that CM patients had higher levels of perceived stress than controls.

Our data demonstrated that CM appeared to be a migraine-specific factor for perceived stress.

Conclusions
It was found that the level of perceived stress was significantly higher in CM patients than that in controls.

Acknowledgement
A machine generated summary based on the work of Moon, Hye-Jin; Seo, Jong-Geun; Park, Sung-Pa. 2017 in The Journal of Headache and Pain.

The burden attributable to headache disorders in children and adolescents in Lithuania: estimates from a national schools-based study

DOI: https://doi.org/10.1186/s10194-021-01237-3

Abstract-Summary
We recently showed headache to be common in children (aged 7–11 years) and adolescents (aged 12–17) in Lithuania.

We provide evidence from the same study of the headache-attributable burden.

Questionnaires were completed by 2505 pupils (1382 children, 1123 adolescents; participating proportion 67.4%), of whom 1858 reported headache in the preceding year, with mean frequency (±SD) of 3.7 ± 4.5 days/4 weeks and mean duration of 1.6 ± 1.9 h. Mean proportion of time in ictal state, estimated from these, was 0.9% (migraine 1.5%, probable medication-overuse headache [pMOH] 10.9%).

Lost school time was 0.5 ± 1.5 days/4 weeks (migraine 0.7 ± 1.5, pMOH 5.0 ± 7.8) based on recall, but about 50% higher for migraine according to actual absences recorded in association with reported headache on the preceding day.

More days were reported with limited activity (overall 1.2 ± 2.4, migraine 1.5 ± 2.2, pMOH 8.4 ± 8.5) than lost from school.

Emotional impact and quality-of-life scores generally reflected other measures of burden, with pMOH causing greatest detriments, followed by migraine and tension-type headache, and UdH least.

Burdens were greater in adolescents than children as UdH differentiated into adult headache types.

Headache in children and adolescents in Lithuania is mostly associated with modest symptom burden.

The consequential burdens, in particular lost school days, are far from negligible for migraine (which is prevalent) and very heavy for pMOH (which, while uncommon in children, becomes four-fold more prevalent in adolescents).

Extended: Lost school time per affected pupil because of any headache averaged 0.5 days/4 weeks (ie, 0.5 days in 20 [2.5%], assuming a 5-day week).

Lost school time was greater for migraine than for TTH ($p < 0.01$) or UdH ($p < 0.001$), while pMOH cost those affected one quarter (5/20) of their school days.

More days were reported with limited activity than were lost from school (notably, about one in every three for pMOH).

Emotional impact and QoL scores generally reflected other measures of burden.

These findings are of importance not only to health policy but also to educational policy in Lithuania.

Introduction

In our recently published prevalence study, we showed headache to be common in children (aged 7–11 years) and adolescents (aged 12–17) in Lithuania [44], as we have with similar schools-based methodology in Turkey [40], Austria [41], Ethiopia [157] and Mongolia [158].

The prevalence study was part of a global enquiry into child and adolescent headache [43], an ongoing programme conducted by Lifting The Burden (LTB) [36–159] in its endeavour within the Global Campaign against Headache [36–38] to measure the scale and scope of headache-attributed burden worldwide.

From the public-health perspective, while disease prevalence determines the magnitude of disease-attributed burden in a population, it is not of itself very informative.

We present estimates of burden based on the prevalence findings [44] together with evidence of burden collected directly and contemporaneously from the same sample.

Methods

The child and adolescent versions of LTB's Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) structured questionnaire [43] were administered to the pupils in class, and completed under supervision.

Burden enquiry included symptom burden (frequency of headache, and its usual duration and intensity during episodes), symptomatic medication intake (frequency), lost time from schooling and other activities as well as lost parental work time (using adaptations of the Headache-Attributed Lost Time (HALT) index [160]), and selected (headache-relevant) questions from KINDL® [161] addressing concentration, emotional impact and quality of life (QoL) [43]).

We expressed lost school time because of headache in days in the preceding 4 weeks, counting not going to school as a whole day and leaving school early as a half-day.

We counted participants reporting HY and the intensity of it, and those (as proportions) reporting a lost school day because of HY.

We estimated predicted values of lost school yesterday as the product of number affected by headache and mean reported days (divided by 20) lost per pupil over the preceding 4 weeks.

Results

Gender- and age-adjusted 1-year prevalence of any headache was 76.6%, of migraine 21.4%, of tension-type headache (TTH) 25.6%, of UdH 24.0%, of all headache on ≥15 days/month 3.9% and of probable medication-overuse headache (pMOH) 0.8%.

Headache on ≥15 days/month (including pMOH) was, of course, more frequent than the episodic headaches but, among the latter, UdH was less frequent ($p < 0.001$) than migraine or TTH.

Participants with migraine and reporting HY were more likely to have lost school time yesterday than those with other headache types and reporting HY, but numbers were too few for significance (RR = 1.5 [0.9–2.3]; p = 0.1163).

Migraine, pMOH and other headache on ≥15 days/month were not significantly different from each other, but all had greater impact ($p < 0.001$) than TTH.

Discussion

For all headache types, more days were reported with limited activity than lost from school.

The 1.5 days/4 weeks (5.4%) reportedly affected in this way in those with migraine suggests a considerable life diminution, while the 8.4 days/4 weeks (almost 1 day in every three) reported by those with pMOH, and the 4.6 days (one in six) reported by the larger group with other headache on ≥15 days/month, are indicative of major life impairments.

The six questions contributing to this score related principally to concentration, mood, fear of headache and coping with it, so the gradient observed—pMOH having greatest impact, followed by other headache on ≥15 days/month, migraine and TTH, and UdH having significantly the least—was as expected.

Conclusions

Headache, common in children and adolescents, is associated with symptom burdens that may not, for most, be onerous, but the consequential burdens, in particular lost school days, are not insubstantial.

These findings are of importance not only to health policy but also to educational policy in Lithuania.

Acknowledgement

A machine generated summary based on the work of Genc, Diana; Vaičienė-Magistris, Nerija; Zaborskis, Apolinaras; Şaşmaz, Tayyar; Tunç, Aylin Yeniocak; Uluduz, Derya; Wöber, Christian; Wöber-Bingöl, Çiçek; Steiner, Timothy J. 2021 in The Journal of Headache and Pain.

Impact of primary headache disorder on quality of life among school students in Kuwait

DOI: https://doi.org/10.1186/s10194-020-01124-3

Abstract-Summary

Primary headache disorders have being increasingly reported in younger populations.

To assess the burden of primary headache disorder and its impact on the quality of life on school student in Kuwait.

A cross-sectional study was conducted among Kuwaiti primary and middle school students of both genders in randomly selected schools located in two governorates in 2018/2019 academic year.

Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire for children and adolescents was used to assess the impact of primary headaches on the quality of life.

One thousand and ninety-one questionnaires were completed by primary and middle school students of both genders; of whom 466 students (girls 321 (68.88%) were diagnosed with primary headache disorders with mean age 11.98 ± 2.03 years.

Their parents lost a mean of 2 ± 2.03 days of work because of headaches of their children and parents prohibited 5.7% of the students to engage in any activity due to their headaches.

19.4% of students reported they did not want others noticing their headache.

Primary headache disorder can have a significant impact on the quality of life in children.

Implementing strategies to properly manage schoolchildren with primary headaches can have profound effects on their quality of life.

Extended: Once the burden is recognized, efforts can be implemented to improve not only the patients' quality of life in the future leading to positive outcomes over time, but also their parents as it is also noted that their lives are limited with the responsibilities that are associated with taking care of their children [162].

It serves as a ground basis for future research investigations in attempt to implement the best interventions to tackle all the emotional and behavioral issues.

Introduction

Headaches can significantly lead to debilitated cognitive, emotional and recreational functioning in all areas of life ranging from their homes to their scholar activities [163].

Headache disorders are burdensome conditions has been reported in previous papers.

There are at least six main themes that have been associated to the broad concept of burden and impact of primary headache as its prevalence, its overall impact (mostly defined as reduced QoL or disability), impact on work or school activities, impact on family life, interictal burden and disease costs [164].

A research of this kind is conducted to shed light on the burden of such headache disorders.

Methods

We conducted a cross-sectional study with a school-based sample whereby a questionnaire was distributed to primary and middle schoolchildren aged 7–16 years in governmental schools in Kuwait.

Equal numbers of boys and school girls are included in our study.

The survey used Lifting the Burden, Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire that was translated into Arabic [43].

The Child HARDSHIP for children aged 6–11 years and Adolescent HARDSHIP questionnaire for adolescents aged 12–17 years were used in this study.

Data were obtained from the children and adolescents themselves after explanation of the questions by physician of the study team.

Questionnaire distribution and data collection were organized and conducted by physician supervisors during a school class as a paper-pencil version.

To collect study data, well trained physicians conducted face to face interviews using Child and Adolescent HARDSHIP questionnaires.

Results

With respect to severity, majority of students labeled their headaches as 'quite bad', whereas few of students experienced 'very bad' headaches.

Majority of the students (51.5%) experienced a feeling of sadness ranging from sometimes to always, on the other hand, 25% never experienced it.

Most of the students (67.3%) struggled to cope with the headache as (22.4%) never was able to cope, while sometimes 48.1% could manage.

The greater number of the students were comfortable with people noticing their headaches, in contrast to 19.4% who always did not want people to notice it.

Feeling bored was always experienced by 18.1% of the population, however, almost half of the remaining felt it sometimes (43%).50% of the children reported never feeling alone, followed by sometimes in (30.2%).

Feeling different from the other children was witnessed always in (9.7%) of the students, nonetheless, (56.9%) never experienced it.

Discussion

A previously published population-based study in Kuwait estimated that one-year prevalence of primary headache disorders in children and adolescents was 19.4% [165].

Studies that estimate the impact of primary headache in children are scarce.

The burden of headache in children and adolescents in our results is in agreement with earlier results that revealed total scores of 17.8–44 days where pediatric headache patients were totally or partially disabled at home or at school because of their headache [166].

Majority of our cohort used symptomatic medications for headache on average 3.26 days a month, which is in agreement with earlier studies, which reported medication use among children in a variable percentage ranging from 30% to 80% [167, 168].

The extent of headaches can lead to lack of attention and concentration which was reported in our study participants as well as those in other researches [169].

Conclusions

Recognizing the psychosocial effects induced by headaches is vital for the development of the best clinical and holistic care for the patients.

Acknowledgement
A machine generated summary based on the work of Al-Hashel, Jasem Y.; Alroughani, R.; Shuaibi, S.; AlAshqar, A.; AlHamdan, F.; AlThufairi, H.; Owayed, S.; Ahmed, Samar F. 2020 in The Journal of Headache and Pain.

Patients' perspective on the burden of migraine in Europe: a cross-sectional analysis of survey data in France, Germany, Italy, Spain, and the United Kingdom

DOI: https://doi.org/10.1186/s10194-018-0907-6

Abstract-Summary
This study aimed to characterize the incremental burden of migraine in individuals who suffer from ≥4 monthly headache days (MHDs) by examining health-related quality of life (HRQoL), impairments to work productivity and daily activities, and healthcare resource utilization (HRU) in the EU5 (France, Germany, Italy, Spain, United Kingdom).

Short-Form 36-Item Health Survey, version 2 (SF-36v2) physical and mental component summary scores (PCS and MCS), Short-form-6D (SF-6D), and EuroQoL (EQ-5D), impairments to work productivity and daily activities (Work Productivity and Activity Impairment Questionnaire (WPAI), and HRU were compared between migraine respondents suffering from ≥4 MHDs (n = 218) and non-migraine controls (n = 218) by propensity score matching using sociodemographic characteristics.

HRQoL was lower in migraine individuals suffering from ≥4 MHDs compared with non-migraine controls, with reduced SF-36v2 PCS (46.00 vs 50.51) and MCS (37.69 vs 44.82), SF-6D health state utility score (0.62 vs 0.71), and EQ-5D score (0.68 vs 0.81) (for all, $p < 0.001$).

Respondents with migraine suffering from ≥4 MHDs also reported higher levels of absenteeism from work (14.43% vs 9.46%; $p = 0.001$), presenteeism (35.52% vs 20.97%), overall work impairment (38.70% vs 23.27%), and activity impairment (44.17% vs 27.75%) than non-migraine controls (for all, $p < 0.001$).

Consistently, migraine subgroups (4–7 MHDs, 8–14 MHDs and CM) had lower HRQoL, greater overall work and activity impairment, and higher HRU compared to non-migraine controls.

Migraine of ≥4 MHDs was associated with poorer HRQoL, greater work productivity loss, and higher HRU compared with non-migraine controls.

Background
Migraine was the sixth leading cause of disability-adjusted life years (DALYs) worldwide for the age group 25 to 39 years in the 2015 Global Burden of Disease (GBD) study [170].

The GBD 2016 study reported migraine as the first leading cause of years lived with disability (YLDs) worldwide in both males and females for the age group 15 to 49 years, demonstrating that the burden is higher in the groups of prime productivity [47].

The primary objective of this study was to characterize the incremental burden of migraine in those experiencing ≥4 MHDs from patients' perspective in terms of HRQoL, work and activity impairment, and HRU compared with non-migraine controls among the EU5.

The secondary objective was to characterize the burden of migraine from the perspective of migraine patients experiencing ≥4 MHDs from the EU5 by frequency of migraine (eg, 4–7, 8–14, and ≥ 15 MHDs) compared with non-migraine controls.

Methods

Of the 16,340 survey respondents who reported experiencing migraine in the past 12 months, a randomly selected subsample of 1680 respondents (10%) completed the migraine module with additional questions on migraine characteristics and of these, 771 respondents reported a physician-diagnosed migraine.

The study sample (respondents who self-reported a physician-diagnosis of migraine) who completed the migraine module and indicated that they experienced migraines of at least 4 MHDs were matched by propensity scores to those without migraines (controls) using sociodemographic characteristics (see below).

As the objective of the study was to estimate the incremental burden associated with migraine, the propensity score of respondents with migraine was compared with that of those without migraine (controls) using demographic and comorbidities data.

This procedure was conducted separately within each country and for those with 4–7 EM, 8–14 EM, and CM to limit the risk that respondents differ from controls on matching characteristics within the smaller migraine subgroups.

Results

6 months before completion of questionnaire, the mean number of total HCP visits (8.5 vs 5.1; $p < 0.001$) and ED visits (0.46 vs 0.21; $p = 0.011$) reported by the migraine sample were significantly higher than non-migraine controls.

A significantly higher proportion of migraine respondents compared with non-migraine controls had at least one visit to a general/family practitioner (77.1% vs 67.4%; $p = 0.025$), neurologist (13.8% vs 3.7%; $p < 0.001$), and psychiatrist (13.3% vs. 3.2%; $p < 0.001$) in the prior 6 months.

Discussion

The analysis showed that after propensity score matching of the subgroups based on demographic and health characteristics, those suffering from migraine of at least 4 MHDs had significantly lower HRQoL, increased work and activity impairment, and higher HRU than their non-migraine matched controls.

The present study showed higher levels of absenteeism (1.5-fold), presenteeism (1.7-fold), work productivity impairment (1.7-fold), and activity impairment

(1.6-fold) in those suffering from at least 4 MHDs compared with non-migraine matched controls.

These findings are consistent with previous studies in Europe and the US conducted in the overall migraine population where ED visits, hospitalizations, and medicines are among the major cost drivers, while the presence of certain symptoms and/or comorbidities leads to further increase in direct costs [10, 171, 172]; as the frequency and severity of migraine increased, the HRU and economic impact to the healthcare system also increased.

Conclusions

The findings of the current study reveal that there is an incremental burden due to migraine on HRQoL (mental, physical, and health status), work productivity (both presenteeism and absenteeism), and the utilization of healthcare resources among those who suffer from migraine ≥4 MHDs in comparison to the matched non-migraine controls in the EU5.

Migraine is undertreated as the patients did not have access to appropriate healthcare, suggesting that effective management and preventive treatments are needed to lessen the frequency and burden of migraine.

Acknowledgement

A machine generated summary based on the work of Vo, Pamela; Fang, Juanzhi; Bilitou, Aikaterini; Laflamme, Annik K.; Gupta, Shaloo. 2018 in The Journal of Headache and Pain.

My migraine voice survey: a global study of disease burden among individuals with migraine for whom preventive treatments have failed

DOI: https://doi.org/10.1186/s10194-018-0946-z

Abstract-Summary

My Migraine Voice is a large global cross-sectional study aimed at understanding the full burden and impact of migraine directly from patients suffering from ≥4 monthly migraine days (MMDs) with a history of prophylactic treatment failure.

This study was conducted worldwide (31 countries across North and South Americas, Europe, the Middle East and Northern Africa, and the Asia-Pacific region) using an online survey administered to adults with migraine who reported ≥4 MMDs in the 3 months preceding survey administration, with pre-specified criteria of 90% having used preventive migraine treatment (80% with history of ≥1 treatment failure).

Prophylactic treatment failure was defined as a reported change in preventive medication by individuals with migraine for any reason, at least once.

Seventy-four percent of the participants reported spending time in darkness/isolation due to migraine (average: 19 h/month).

While 85% of all respondents reported negative aspects of living with migraine (feeling helpless, depressed, not understood), sleeping difficulties (83%), and fear of the next attack (55%), 57% shared ≥1 positive aspect (learning to cope, becoming a stronger person).

The burden of migraine is substantial among this cohort of individuals with at least 4 migraine days per month and for whom at least 1 preventive migraine treatment had failed.

Respondents reported some positive aspects in their migraine journey; the greater resilience and strength brought on by coping with migraine suggests that if future treatments could address existing unmet needs, these individuals with migraine will be able to maximize their contribution to society.

Extended: My Migraine Voice adds to the existing literature since it includes a large number of countries, involves people with migraine meeting the ICHD-3 criteria, and assesses migraine burden during premonitory, headache, and postdrome phases of the migraine attack, thereby allowing for a comprehensive and truly global assessment of migraine burden.

The greater resilience and strength brought on by coping with migraine suggests that if future treatments could address their existing unmet needs, these individuals with migraine will be able to maximize their contribution to society.

Background

The current understanding of migraine burden among individuals with the highest unmet needs, specifically those experiencing ≥4 monthly migraine days (MMDs) and prior prophylaxis failure, is limited.

Understanding the burden of disease in individuals with ≥4 MMDs is very important to enable physicians and/or others involved in migraine management to make well-informed decisions on appropriate preventive migraine care for these people.

No detailed assessment of the current treatment pathway, impact on work productivity, or burden associated with premonitory and postdromal phases of migraine is available in individuals experiencing ≥4 MMDs who have had previous prophylactic treatments that failed and continue to experience frequent migraines.

The objectives of My Migraine Voice were to assess migraine characteristics and describe the current real-world burden and impact of living with migraine from clinical, personal, and economic perspectives among adults with migraine experiencing ≥4 MMDs.

Methods

This was a large, cross-sectional, multi-country online survey of adult participants (≥18 years of age) with migraine.

Screening questions to determine eligibility included a description of migraine based on the International Classification of Headache Disorders third edition (ICHD-3) criteria followed by a series of migraine symptom and characteristic questions to qualify that participants were experiencing migraine.

Prespecified quotas were applied to people reporting a history of taking a prophylactic medication to prevent their migraine: 90% of participants reported current

or previous use of preventive migraine medication, of which 80% switched preventive treatment, and the remaining 10% were preventive treatment-naïve.

Because of limited published information on the burden before and after the migraine attack, the survey included questions on the migraine phases.

A validated questionnaire was included in the survey to assess the impact of migraine on work productivity and daily activities among employed respondents.

Results

Migraine was also reported to cause sleeplessness by 83% of all respondents on average (86% for those with ≥2 TFs).

Of all survey respondents, 70% reported that migraine has affected their professional life, which rose to 75% in the ≥2 TFs subgroup and was significantly higher than those with no TF (60%) ($p < 0.05$).

A majority of respondents in employment (60%) reported missing ≥1 day of work in the last month due to migraine, with an average of 4.6 working days being missed in the last month, which is consistent with the average of 4.5 working days missed due to migraine (absenteeism) measured by the WPAI questionnaire.

Paid sick days reported by respondents in employment in the last month were on average 2.4 days: 2.7 days in the ≥2 TFs subgroup vs 1.7 days in those with 1 TF ($p < 0.05$).

Discussion

This large worldwide study of 11,266 participants constitutes the largest survey to date conducted in individuals with migraine suffering from ≥4 MMDs and focused mostly on those who previously experienced failure of migraine prevention treatments.

This study describes the personal, social, humanistic, and economic burden of migraine in detail, and for the first time, it allows quantifying the burden during different phases of the migraine attack for individuals suffering from ≥4 MMDs with a history of prophylactic treatment.

Despite the limitations above, this study strikes a balance between the sample size needed to obtain a higher-resolution description about the burden of migraine imposed on affected individuals with the highest unmet need (≥4 MMDs) and potential caveats in generalizing its findings to all people with migraine (irrespective of disease severity) resulting from the above-mentioned limitations.

Conclusions

Despite challenges posed by migraine, only 9% reported receiving disability allowance due to their migraine.

Acknowledgement

A machine generated summary based on the work of Martelletti, Paolo; Schwedt, Todd J.; Lanteri-Minet, Michel; Quintana, Rebeca; Carboni, Veruska; Diener, Hans-Christoph; Ruiz de la Torre, Elena; Craven, Audrey; Rasmussen, Annette Vangaa; Evans, Simon; Laflamme, Annik K.; Fink, Rachel; Walsh, Donna; Dumas, Paula; Vo, Pamela. 2018 in The Journal of Headache and Pain.

Burden and attitude to resistant and refractory migraine: a survey from the European Headache Federation with the endorsement of the European Migraine & Headache Alliance

DOI: https://doi.org/10.1186/s10194-021-01252-4

Abstract-Summary

To overcome those issues, the European Headache Federation (EHF) issued a Consensus document to propose criteria to approach difficult-to-treat migraine patients in a standardized way.

The Consensus proposed well-defined criteria for resistant migraine (i.e., patients who do not respond to some treatment but who have residual therapeutic opportunities) and refractory migraine (i.e., patients who still have debilitating migraine despite maximal treatment efforts).

The aim of this study was to better understand the perceived impact of resistant and refractory migraine and the attitude of physicians involved in migraine care toward those conditions.

A relevant proportion of participants reported that patients with resistant and refractory migraine were frequently seen in their clinical practice (49.5% for resistant and 28.9% for refractory migraine); percentages were higher when considering only those working in specialized headache centers (75% and 46% respectively).

Many physicians reported low or moderate confidence in managing resistant (8.1% and 43.3%, respectively) and refractory (20.7% and 48.4%, respectively) migraine patients; confidence in treating resistant and refractory migraine patients was different according to the level of care and to the number of patients visited per week.

Patients with resistant and refractory migraine were infrequently referred to more specialized centers (12% and 19%, respectively); also in this case, figures were different according to the level of care.

There is the need of more evidence regarding the management of those patients and clear guidance referring to the organization of care and available opportunities.

Extended: Underlying mechanisms in migraine are far from being entirely clear and there hope that the ongoing future research may shade light on novel targets which may allow the development of new drugs.

Background

New migraine treatments, both acute and preventative, such as lasmiditan, monoclonal antibodies (mAbs) targeting the calcitonin gene-related peptide (CGRP) pathway, and gepants are changing the landscape of migraine treatment offering new opportunities and challenges [173–177].

In details, the new definitions of the difficult to treat migraine included non-response to acute and preventative medications.

Further, patients who tried three different classes of migraine preventative and still suffer eight debilitating migraine days classify for resistant migraine.

In order to be defined as refractory, failure to all available classes of migraine preventatives, including mAbs targeting the CGRP pathway, is required.

Methods

We conducted a web-questionnaire-based cross-sectional international study involving headache physicians.

All physicians involved in the care of patients with headache, without any restriction referring to country of residency, specialization, and years of experience in headache care were entitled to fill the questionnaire.

Work settings categories were defined, according to EHF definitions of the level of care [178], as follows: (1) first level of care—General primary care defined as first-line headache service (accessible first contact for most people with headache); (2) second level of care - Special-interest headache care defined as ambulatory care delivered by physicians with a special interest in headache; (3) third level of care—Headache Specialists Centers defined as advanced multidisciplinary care delivered by headache specialists in hospital-based centers.

The questionnaire was not anonymous, and participants were requested to provide consent to be listed as contributors to the study.

Results

Resistant migraine was frequently encountered in clinical practice.

137/277 (49.5%) participants reported that they manage very frequently patients with resistant migraine, 100 (36.1%) participants reported that they manage occasionally those patients, and 40 (14.4%) reported that they manage rarely those patients.

80/277 (28.9%) participants reported that they manage very frequently patients with refractory migraine, 110 (39.7%) reported that they manage occasionally those patients, and 86 (31.0%) reported that they manage rarely those patients.

245/277 (88.4%) respondents reported that patients with resistant migraine were treated in their own center, while 32 (11.6%) reported that patients were referred to a more specialized center.

Referring to the ideal setting of care, 22 (6%) respondents considered that resistant migraine should be managed in general primary care, 162 (43%) in special interest headache care, and 191 (51%) in specialized headache centers.

Discussion

Resistant and refractory migraine are particularly common in tertiary level headache centers, where 75% and 46%, respectively, of the physicians use to see very frequently those patients.

Even in tertiary level headache centers, only 39% of physicians reported high confidence in managing patients with refractory migraine.

Physicians with more experience (i.e., more patients visited per week and more years in practice) reported more often a high confidence in treating both resistant

and refractory migraine, further highlighting the lack of standardized guidelines and the consequent physicians' trend to mainly rely on their expertise.

We found a low referral to more advanced levels of care for patients with resistant and refractory migraine, despite a relevant proportion of physicians operating in the two more basic levels of care expressed from low to moderate confidence in treating those patients.

Conclusions
Resistant and refractory migraine are conditions which are perceived as common in the clinical practice of those involved in the care of patients with migraine and working in dedicated headache care or centers.

It would be important to set up organized systems for referral of the difficult-to-treat patients from general primary care/neurology and eventually from special interest headache care to tertiary headache centers and to provide guidance on migraine care in situations where the positive clinical response if difficult to achieve.

Further research is also needed to clarify the mechanisms which contribute to drug refractoriness in migraine, to understand the role of comorbidities and the therapeutic opportunities arising from combination drugs.

Acknowledgement
A machine generated summary based on the work of Sacco, Simona; Lampl, Christian; Maassen van den Brink, Antoinette; Caponnetto, Valeria; Braschinsky, Mark; Ducros, Anne; Little, Patrick; Pozo-Rosich, Patricia; Reuter, Uwe; Ruiz de la Torre, Elena; Sanchez Del Rio, Margarita; Sinclair, Alexandra J.; Martelletti, Paolo; Katsarava, Zaza; 2021 in The Journal of Headache and Pain.

Burden of migraine among japanese patients: a cross-sectional National Health and Wellness Survey

DOI: https://doi.org/10.1186/s10194-020-01180-9

Abstract-Summary
This study aimed at estimating the disease burden of migraine in Japan and identifying factors associated with the burden using the 2017 National Health and Wellness Survey.

Migraine patients were defined by ICHD-3 like criteria with ≥4 monthly headache days (MHDs), and non-migraine respondents were selected using 1:4 propensity score matching.

Multivariate analyses were conducted to compare Health-related Quality of Life (HRQoL), work productivity and activity impairment (WPAI), healthcare resource utilization (HRU) and costs between the two groups, and to identify factors associated with these outcomes in migraine patients.

In 30,001 respondents, 378 migraine patients were identified.

Migraine patients had higher absenteeism (6.4% vs. 2.2%), presenteeism (40.2% vs. 22.5%), total work productivity impairment (44.3% vs. 24.5%), total activity impairment (45.0% vs. 23.9%), indirect costs (1,492,520 JPY vs. 808,320 JPY) and more visits to healthcare providers in the past 6 months (7.23 vs. 3.96) ($p < 0.001$).

Japanese migraine patients experience an incremental burden.

Extended: Migraine patients were defined by ICHD-3 like criteria, among respondents who self-reported experienced migraine in the past 12 months.

Background

This includes measuring the burden of disease by use of patient reported outcome tools such as health-related quality of life (HRQoL), the impact of illness on work productivity and the associated economic burden [179].

Japanese studies have shown that 32% of migraine patients reported severe to moderate impairment to social activities including cancellation of work and daily appointments [180].

The primary objective of this study was to estimate the humanistic and economic burden of migraine by comparison of HRQoL, work productivity and activity impairment (WPAI), and healthcare resource utilization (HRU) in individuals with migraine classified according to the International Classification of Headache Disorders third edition (ICHD-3) [20] like criteria and having at least 4 monthly headache days (MHDs).

The secondary objective was to examine the relationship between the humanistic and economic burden of migraine and sociodemographic factors, disease characteristics and comorbidities among Japanese migraine patients.

Methods

Migraine patients were defined by ICHD-3 like criteria, among respondents who self-reported experienced migraine in the past 12 months.

Migraine-specific questions were asked to all respondents who experienced migraine, which included: symptoms experienced due to migraine, number of years experiencing migraine, diagnosing physician, number of migraines in the past 30 days and in the past 6 months, number of headache days in the past 30 days, days of missed work due to migraine in the past 6 months, days of missed household activities due to migraine in the past 6 months, use of prescription medication to treat or prevent migraine.

Comparisons between migraine patients and non-migraine respondents were performed using chi-square tests for categorical variables and one-way analysis of variance (ANOVA) for continuous variables, for demographic and general health characteristics, to understand the baseline differences between the two groups.

HRQoL, WPAI, HRU and costs were compared between migraine patients and matched non-migraine respondents.

Results

After adjusting for age, gender, CCI, marital status, education, household income, region, insurance type, employment status, BMI, smoking status, alcohol use and exercise behavior, migraine patients had significantly lower PCS (45.17 vs. 49.89),

MCS (42.28 vs. 47.71), RCS (37.91 vs. 44.19) and SF-6D index (0.64 vs. 0.74) than matched non-migraine respondents (all $p < 0.001$).

After adjusting for the same covariates as mentioned above, migraine patients had significantly higher absenteeism (6.4% vs. 2.2%), presenteeism (40.2% vs. 22.5%), total work productivity impairment (44.3% vs. 24.5%) and total activity impairment (45.0% vs. 23.9%) than matched non-migraine respondents (all $p < 0.001$).

After adjusting for the same covariates, it was estimated that migraine patients incurred significantly more annual indirect cost (1,492,520 JPY vs. 808,320 JPY) compared to matched non-migraine respondents.

Discussion

We found that Japanese patients with migraine (with or without aura and with at least 4 MHDs) experienced significantly higher humanistic and economic burden in terms of decreased HRQoL, and increased WPAI, HRU and indirect costs, compared to matched non-migraine respondents.

No statistically significant difference in direct costs between migraine patients and non-migraine respondents was observed in this study.

Indirect costs were significantly lower among non-migraine respondents, indicating that the poorer QoL and work productivity among migraine patients have a costly impact on the Japanese society.

A retrospective, observational cohort study in the US identified that migraine patients incurred significantly higher indirect cost due to higher productivity loss, as well as direct cost due to higher level of healthcare utilization, compared to matched patients without migraine [181].

Conclusions

Increased number of MHDs among Japanese migraine patients were associated with worse HRQoL and increased HRU.

This demonstrates that better care is needed for Japanese migraine patients.

Acknowledgement

A machine generated summary based on the work of Kikui, Shoji; Chen, Yirong; Todaka, Hiroshi; Asao, Keiko; Adachi, Kenji; Takeshima, Takao. 2020 in The Journal of Headache and Pain.

Burden of Migraine in Europe Using Self-Reported Digital Diary Data from the Migraine Buddy© Application

DOI: https://doi.org/10.1007/s40120-018-0113-0

Abstract-Summary

This study described the burden of migraine as reported by individuals with migraine in the real world using a mobile application.

Data were analyzed descriptively for the most recent 28-day period reported by users (n = 3900) during the study period (June 2015–July 2016) who were randomly selected on the basis of data completeness (completion rates >70%) and stratified by migraine headache days/month: 4–7 episodic migraine (EM; n = 1500), 8–14 EM (n = 1500), and chronic migraine (≥15; CM; n = 900).

More than 95% of users reported that migraine negatively affected their daily activities during at least one migraine attack.

44.8% CM, 40.9% 8–14 EM, and 34.7% of 4–7 EM sufferers, respectively, reported anxiety and/or depression symptoms during migraine attacks.

Employed respondents (n = 3106) reported an average of 2.3 workdays missed per month and that at least one in four migraines led to work absenteeism; these migraines were commonly reported to have at least moderate to severe levels of pain, corresponding to the inability of persons to perform some or even any activities.

This study, leveraging patient-reported data collected through a mobile application, demonstrates the high burden and impact of migraine on health-related quality of life, work productivity, and overall well-being of individuals suffering from migraines.

Introduction

Migraines are most often treated with acute therapies, which are used to relieve the pain and associated symptoms of a migraine attack at the time it occurs.

It is recommended for patients in whom acute therapy is either ineffective or contraindicated, in patients with high frequency and severity of migraine, or in patients who suffer significant disability due to aura and other associated symptoms [182, 183]; however, prophylactic treatment is generally underutilized [172, 184].

The objective of the present study was to describe the burden of migraine in terms of impact, symptoms, triggers, and other migraine characteristics as perceived by migraine sufferers in a real-world setting using a self-reported smartphone application (app), Migraine Buddy©.

This study aimed to assess the burden of migraines in terms of affected daily activities, medication usage, and impact of anxiety and depression in patients who suffer from at least four monthly migraine days (MMDs); evaluate the impact of migraine on work productivity; and describe the characteristics of migraine attacks (pain level, duration, symptoms, triggers) experienced by this population of interest.

Methodology

Migraine Buddy is a free smartphone app used to collect self-reported migraine data.

The study used anonymized self-reported data from 3900 randomly selected adult Migraine Buddy users, recorded during the 13-month period from June 1, 2015 through July 3, 2016.

Data from individuals who were at least 18 years of age, had agreed to participate in the study, and had more than 70% completeness rates in their migraine records were included in the study sample.

The variables examined in the study included the following: demographic characteristics (age, gender); migraine characteristics (triggers, auras, symptoms, pain location and intensity, start time and duration of migraine); migraine burden

(location of onset, impact on activities such as social, home, work, medication use, or other relief methods); impact of migraine on work productivity [employment status, workdays missed (absenteeism)]; anxiety and depression; and the number of medications used to treat migraine.

Results

The most commonly self-reported migraine symptoms were related to pain/body (91.7% of users), mood and cognition (87.3%, which included nausea, anxiety, confusion, blurred vision, moodiness, or giddiness), and environment [such as ringing in ears (tinnitus), sensitivity to light, noise, or smell; 85.5%] (each user could specify more than one symptom per record and therefore numbers do not add up to 100%).

Among employed users, migraines were commonly reported to have at least moderate to severe levels of pain (63% of migraine records), and 83% of respondents self-reported moderate pain in at least one of their absenteeism-related migraines.

The most commonly reported symptoms recorded by migraine sufferers in work absenteeism-related migraines were body pain (73%), mood and cognition (69%), environmental handicap (65%), depression (24%), and/or sleep alterations (13%).

Discussion

Migraine can have a considerable impact on the lives of affected individuals as seen in this sizeable international study, based on self-reported data from individuals suffering from at least four MMDs using a digital phone app.

This is an innovative study utilizing the self-report data from the biggest digital app specific for migraine that allows users to voluntarily record and monitor their migraines as they are occurring and understand their own symptoms, triggers, and migraine characteristics; this has the potential for patients and their caregivers or physicians to better manage their disease but also for the wider scientific community to understand the migraine burden, especially in people of their prime working and reproductive years.

As these data are obtained through a mobile phone app, there is potential bias as the study includes data as reported by users, and no physician diagnosis is used to confirm whether the responder indeed suffers from migraine and the frequency of attacks.

Conclusions

The large dataset analyzed retrospectively from 3900 users of a popular migraine application has provided results that are comparable and consistent with previous studies published on the burden of migraine in Europe and the rest of the world [131, 185].

Acknowledgement

A machine generated summary based on the work of Vo, Pamela; Paris, Nicolas; Bilitou, Aikaterini; Valena, Tomas; Fang, Juanzhi; Naujoks, Christel; Cameron, Ann; de Reydet de Vulpillieres, Frederic; Cadiou, Francois. 2018 in Neurology and Therapy.

Burden of migraine in a Kuwaiti population: a door-to-door survey

DOI: https://doi.org/10.1186/s10194-017-0814-2

Abstract-Summary
Migraine prevalence and disability imprints on Kuwaiti population are underreported.

We aimed to measure the prevalence of migraine and to assess its burden in Kuwait.

A total of 15,523 subjects were identified; of whom 3588 (23%) were diagnosed as episodic migraine and 845 (5.4%) as chronic headache.

Prevalence of episodic migraine was 31.71% in female versus 14.88% in males ($p < 0.01$) with a mean age of 34.56 ± 10.17 years.

Tension type headache and sinus-related headaches were diagnosed in 8.9% and 2.1% of migraine subjects respectively.

The majority (94.6%) of migraine subjects used symptomatic drugs for headache attacks, whereas 39.9% were taking preventive medication.

In the preceding 3 months to the survey, subjects with episodic migraine had lost a mean of 1.97 days from their paid work or school attendance compared to 6.62 days in chronic headache sufferers ($p < 0.001$).

Subjects with episodic migraine lost a mean of 1.40 days from household work compared to 5.35 days in subjects with chronic headache ($p < 0.001$).

Participants with episodic migraine and chronic headache missed a mean of 2.81 and 3.85 days on social occasions, in the preceding 3 months ($p < 0.001$).

Migraine in Kuwait is highly prevalent and it has a significant impact on activity of daily living, schooling/ employment and social occasions of patients.

Background
Global Burden of Disease Survey (GBD) 2010 [31] estimated that the global prevalence of migraine is approximately 15% and migraine was ranked as third most common diseases in the world behind dental caries and Tension type headache (TTH).

Migraine prevalence in Saudi Arabia, Qatar and Oman, is within the estimated worldwide prevalence range of 0.7–21.9% [186].

The lifetime migraine prevalence in the three Gulf countries was lower than in European studies, which report a range of 12–28% [104].

Our study aimed to assess the prevalence of migraine and its burden in Kuwait through a comprehensive approach utilizing a door-to-door survey.

We further report on the prevalence of episodic migraine stratified by age and gender, characters of migraine in addition to its burden, which was not shown in our previous published paper [187].

Methods

Kuwaiti adults aged 18–65 years who were living in Kuwait for the last 6-month were identified.

One adult member of each household was randomly selected after obtaining an informed consent.

The survey used several questionnaires such as Lifting The Burden (LTB) [38], Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire [37, 188] which were all translated into Arabic.

Written informed consent was obtained from all the participants and they were free to decline participation at any time during the interviews.

Collected data was analyzed to assess 1-year prevalence for migraine headache as percentages with 95% confidence intervals (CIs).

Prevalence of migraine was stratified by gender and age.

Categorical variables were described in terms of frequency and proportions (%, with 95% CIs where appropriate), continuous variables in terms of means and standard deviations (SDs).

Results

The majority (94.6%) of migraine subjects used symptomatic drugs for their headache attacks during the past month, whereas 39.9% were taking preventive medication at the time of the survey.

Subjects with episodic migraine had lost a mean of 1.97 days from their paid work or school attendance, versus 6.62 lost days in patients with chronic headache ($p < 0.001$).

Subjects with episodic migraine lost a mean of 1.40 days from their household work versus 5.35 lost days in subjects with chronic headache ($p < 0.001$) in the preceding 3 months of the survey.

Regarding social and family activities, subjects with episodic migraine and chronic headache missed mean of 2.81 and 3.85 days in the preceding 3 months of the survey ($p < 0.001$).

Discussion

The 1-year prevalence of migraine in our study was 23%, which was higher than previous studies conducted in Arab Gulf countries (Qatar 7.9% [189] and in Oman 10.1% [190]).

More than 38% of migraine subjects were younger than 30 years of age and approximately 68% were in the age group between 18 to 50 years of age similar to previous published studies [98, 100, 191].

Prevalence of migraine in females is high in the 18–30 age group and middle age group (31–40 years) but sharply declined in the postmenopausal age group (51–65 years), which is similar to previous reports [98, 192].

We reported that subjects with episodic migraine lost an average 1.8 days from their paid work in the preceding 3 months to the survey, which was nearly similar to an Italian study of 2.3 lost days [193] and Eurolight project that reported mean lost workdays about 1 day/ month [131].

This study is the first and largest population-based survey in Kuwait to estimate the prevalence of migraine headache, and the first to measure migraine-attributed burden.

Conclusions
Migraine is prevalent in Kuwait and has a significant socioeconomic burden especially in its chronic form.

Improving the public awareness of migraine through health education of primary care providers and public media may reduce the misdiagnosis and subsequently result in better quality of life and reduce the economic burden.

Acknowledgement
A machine generated summary based on the work of Al-Hashel, Jasem Yousef; Ahmed, Samar Farouk; Alroughani, Raed. 2017 in The Journal of Headache and Pain.

Burden of migraine in Finland: health care resource use, sick-leaves and comorbidities in occupational health care

DOI: https://doi.org/10.1186/s10194-019-0964-5

Abstract-Summary
Electronic medical records were assessed for overall and migraine related health care visits, sick-leaves and comorbidities.

Prophylactic medication was prescribed to 13% of migraine patients and exclusively acute medication to 37%.

Although migraine related visits and sick-leave days were significantly lower than overall visits or sick-leave days, both increased by prophylactic treatment line.

The number of visits rose from 13.8 to 26.2 and sick-leave days from 16.8 to 30.4 per patient-year, in those without prophylaxis vs. ≥3 prophylactic treatments.

Migraine patients had 1.7-fold increase in visits and 1.8-fold increase in sick leave days on average per patient-year, when compared to the control population.

Depression and anxiety were 1.8-fold more common among patients with migraine, and the frequency also increase by treatment line.

Migraine burden increased by each failed treatment line and was associated with increased comorbidity.

Migraine patients had significantly higher extent of visits and sick-leave days as well as extent of comorbidities when compared to their age- and gender-matched counterparts.

Extended: Electronic medical records (EMR) of a private health care provider Terveystalo were utilized in this retrospective register-based study.

Introduction

Regardless of monthly migraine days, chronification of migraine is associated with substantially increasing individual and social burden.

The burden of migraine has been elucidated in multiple surveys and studies [10, 138, 172, 193–198] and recently Silberstein and others showed that disease disability, health care resource use (HCRU), and direct costs increase concomitantly with increasing number of headache days [199].

None of the current prophylactic treatments have originally been developed for migraine, and their specific mechanisms of action in migraine are not known.

The attention has recently thus turned into revealing the true impact of migraine disease burden also for patients in the need or failing prophylactic treatments [195, 200].

Several surveys and studies have been conducted on the burden of migraine, and some of them also using data from Finland [194, 201, 202].

The main aim of the present study was to examine the burden of migraine and evaluate HCRU, sick-leaves and comorbidities among migraine patients compared to a control population in occupational health care setting.

Methods

17,623 of the patients had migraine according to ICD-10 code (G43*, on a three-character level) and were included in the primary cohort.

Each patient was followed from the first G43* diagnosis in the EMR, or from the first fulfilment for any of the criteria for the extended cohort, until 31st December 2017.

Patients in the primary cohort were divided into groups based on medication prescribed at the health care provider.

In the health care provider's register on 31st December 2017, the point prevalence for migraine was calculated by gender in 5-year age groups in the primary and extended cohorts.

To assess the impact of migraine in subjects with high HCRU, migraine patients were divided into quartiles based on either overall visits or sick-leaves in patient-years.

For each patient, the total number of visits and sick-leave days were defined and divided by the total patient-wise follow-up time, where after the cohort was divided into quartiles.

Results

This was reflected both in total visits (prophylactic vs. acute vs. no prescription: 18.4 vs. 15.0 vs. 12.9 visits per patient-year, $p < 0.001$) and migraine specific visits (2.4 vs. 1.3 vs. 0.8 per patient-year, $p < 0.001$), as well as in total sick leave days (22.5 vs. 17.4 vs. 16.4 per patient-year, $p < 0.001$) and migraine specific sick leave days (2.1 vs. 0.7.

A 2.1-fold increase in migraine related sick leave days was found in subject with botulinum toxin prescriptions.

A comparable increase in sick-leave days was observed: overall sick leave days (no prophylactic prescriptions, vs. ≥3 prophylactic treatments: 16.8 vs. 30.4 sick leave days per patient-year) and disease specific sick leave days (no prophylactic prescriptions, vs. ≥3 prophylactic treatments: 0.6 vs. 6.7 per patient-year).

Discussion

In this extensive registry-based retrospective study using EMRs of Finland's largest private occupational health care provider, 17,623 migraine patients with G43-diagnosis were identified.

Botulinum toxin treatment was associated with 11.9 migraine related sick-leave days per patient-year, also in line with approximately 10 days previously reported [203].

The effect of prophylactic treatment lines on disease burden has been poorly investigated and the incremental increase of all-cause sick-leaves and visits per additional prophylactic treatment line, underlines that migraine related disease burden cannot solely be assessed by migraine related visits or sick-leaves, but should be considered in a larger perspective.

This study also investigated the migraine burden per se compared to age and gender matched controls, where all-cause sick-leaves were 1.8 and visits 1.7 more frequent in the migraine population than in the controls per patient-year.

Conclusions

Migraine patients show a substantially higher extent of comorbidities, sick-leave days and health care visits compared to their age- and gender-matched counterparts.

Unresponsive or undertreated migraine, evidenced by an increase in failed treatment lines, increases morbidity and inevitably leads to productivity losses that pose an increased burden on the health care system and society.

Acknowledgement

A machine generated summary based on the work of Korolainen, Minna A.; Kurki, Samu; Lassenius, Mariann I.; Toppila, Iiro; Costa-Scharplatz, Madlaina; Purmonen, Timo; Nissilä, Markku. 2019 in The Journal of Headache and Pain.

The burden of headache disorders in Ethiopia: national estimates from a population-based door-to-door survey

DOI: https://doi.org/10.1186/s10194-017-0765-7

Abstract-Summary

Headache disorders are the third-highest cause of disability worldwide, with migraine and medication-overuse headache (MOH) the major contributors.

In Ethiopia we have shown these disorders to be highly prevalent: migraine 17.7%, TTH 20.6%, probable MOH (pMOH) 0.7%, any headache yesterday (HY) 6.4%.

To inform local health policy, we now estimate disability and other burdens attributable to headache in this country.

We interviewed one member (18–65 years old) of each household using the HARDSHIP structured questionnaire.

We estimated disability using disability weights (DWs) from the Global Burden of Disease 2013 study.

People with migraine spent 11.7% of their time in the ictal state (DW: 0.441); they were therefore 5.2% disabled overall.

People with pMOH spent 60.2% of time with headache (DW: 0.223), and were 13.4% disabled.

Average proportions of per-person lost productive time were, for migraine, 4.5% from paid work, 5.3% from household work; for pMOH they were 29.2% and 16.0%.

There were highly-disabled minorities, and large gender differences, males losing more paid workdays, females more household workdays.

Across the population aged 18–65 years (effectively the working population), disability from headache was 1.4%, with 1.6% of workdays lost (half from migraine).

Ethiopia is a low-income country, and cannot afford these losses—including, perhaps, 1.6% of GDP.

WHO has recommended structured headache services with their basis in primary care as the most efficient, effective, affordable and equitable solution, potentially cost-saving.

Extended: Headache disorders are not only common in Ethiopia but also heavily burdensome.

People with pMOH are only 0.7% of the adult population but, as might be expected, carry much more individual disability: 60.2% of their time was spent in the ictal state, a huge loss of healthy time, with headache rated severe (2.95 on the scale 1–3) and a disability burden of 13.4%.

People with pMOH in Zambia were 8.3% disabled and lost 7.4% of paid workdays and 5.0% of household workdays [204].

WHO has recommended structured headache services with their basis in primary care as the most efficient, effective, affordable and equitable solution [205], and the model proposed by LTB for Europe [178], which is highly adaptable, could be reworked to match the health-care infrastructure of Ethiopia.

Background

The Global Campaign against Headache is conducted by Lifting The Burden (LTB), a UK-registered non-governmental organization in official relations with the World Health Organization (WHO) [38].

At its launch in 2004, our knowledge of both the scope and scale of the burdens attributable to headache was extraordinarily imprecise; from very large areas of the world, there were almost no reliable data [89].

Findings from these studies have informed various iterations of the Global Burden of Disease (GBD) study [31–94], while providing country policy-makers with local knowledge to guide priority-setting in health care.

Expressly as a needs-assessment to inform national health policy, we present data from the same survey on the burdens attributable to headache in Ethiopia.

Few studies of headache burden are yet available from sub-Saharan Africa (SSA), but this survey follows, and mirrors, a similar one conducted by LTB in Zambia [204].

Methods

The timeframes for burden enquiry were the preceding 3 months and preceding day, the latter addressed to those responding positively to "Did you have a headache yesterday?"

We recorded headache frequency in days affected per month, and usual duration of headache in hours.

We assumed headache frequency in days per month was equal to attack frequency per month unless reported headache duration was >24 h; when this was the case, we applied a correction factor to avoid over-counting.

We derived average time per month spent in the ictal state of each headache type as the product of attack frequency and duration, and expressed it as a proportion of all time (dividing by [30*24]).

We calculated headache-attributed disability at individual level as the product of time in ictal state and the disability weight (DW) from GBD2013 [206] for the disorder in question.

Results

For migraine, headache was reported on an average of 3.3 ± 2.6 days/month, with mean intensity of 2.6 ± 0.5 (moderate to severe pain).

Headache was reported on an average of 2.4 ± 2.1 days/month, with a mean intensity of 2.4 ± 0.5 (also moderate to severe pain).

The mean proportion of total time spent in the ictal state was 7.3% (100*[1.5*34.9]/[30*24]%) and the disability level (mean disability attributed to TTH per adult with the disorder) was 0.27% (0.037*7.3%).

These numbers disguised large gender differences associated with working practices in Ethiopia: males with migraine lost 4.9 ± 7.0 days from paid work and 2.2 ± 6.1 days from household work, females 1.9 ± 5.0 ($p < 0.0001$; t-test, 2-sided) and 6.1 ± 8.9 ($p < 0.0001$) respectively.

Discussion

People with pMOH are only 0.7% of the adult population but, as might be expected, carry much more individual disability: 60.2% of their time was spent in the ictal state, a huge loss of healthy time, with headache rated severe (2.95 on the scale 1–3) and a disability burden of 13.4%.

At population level (among those aged 18–65 years), we estimated disability from migraine at 0.92%, with 0.80% of paid workdays lost, from pMOH at 0.09%, with 0.20% of paid workdays lost, and from other headache on ≥15 days/month at 0.30%, with 0.22% of paid workdays lost.

In Zambia but not Ethiopia, lost paid worktime exceeded the underlying estimated disability level, which again may reflect the poverty of Ethiopia (people cannot afford to miss paid work).

In Zambia, estimated disability from migraine in the entire working population was 0.98%, in Ethiopia very similar (0.92%); but in Zambia, 1.4% of all workdays were lost to migraine, in Ethiopia only 0.80%.

Conclusions: What is to be Done?
At population level, Ethiopia may lose 1.6% of its GDP to headache, but the country has many other health-care problems.

Communicable diseases (including HIV) and malnutrition, along with lack of access to clean water for nearly half the population [207], are high among the causes of ill-health.

Health politicians need to sit down with experts and discuss what must be done to alleviate the headache burden, and how, not just because people in Ethiopia lose much of their health and quality of life to headache but also with the expectation of cost-saving nationally [205].

WHO has recommended structured headache services with their basis in primary care as the most efficient, effective, affordable and equitable solution [205], and the model proposed by LTB for Europe [178], which is highly adaptable, could be reworked to match the health-care infrastructure of Ethiopia.

Acknowledgement
A machine generated summary based on the work of Zebenigus, Mehila; Tekle-Haimanot, Redda; Worku, Dawit K; Thomas, Hallie; Steiner, Timothy J. 2017 in The Journal of Headache and Pain.

The burden of headache disorders in the Eastern Mediterranean Region, 1990–2016: findings from the Global Burden of Disease study 2016

DOI: https://doi.org/10.1186/s10194-019-0990-3

Abstract-Summary
Using the findings of the Global Burden of Disease Study (GBD), we report the burden of primary headache disorders in the Eastern Mediterranean Region (EMR) from 1990 to 2016.

Years lived with disability (YLDs) were calculated by multiplying prevalence and disability weight (DW) of migraine and tension-type headache (TTH).

During the same period, age-standardised YLD rates of migraine and TTH in EMR increased by 0.7% and 2.5%, respectively, in comparison to a small decrease in the global rates (0.2% decrease in migraine and TTH).

The age-standardised YLD rates of both headache disorders were higher in women with female to male ratio of 1.69 for migraine and 1.38 for TTH.

All countries of the EMR except for Somalia and Djibouti had higher age-standardised YLD rates for migraine and TTH in compare to the global rates.

Libya and Saudi Arabia had the highest increase in age-standardised YLD rates of migraine and TTH, respectively.

The findings of this study show that primary headache disorders are a major and a growing cause of disability in EMR.

Extended: During the same period, the relative contribution of migraine YLDs and TTH YLDs to the overall YLDs in EMR increased from 6.0% (95% UI 4.3–7.8) to 6.7% (95% UI 4.9–8.5) and from 1.00% (95% UI 0.75–1.30) to 1.16% (95% UI 0.86–1.49), respectively.

During the same period, age-standardised YLD rates of migraine remained generally unchanged in EMR countries.

Introduction

GBD 2016, provided more accurate estimations of prevalence and burden of headache by countries, regions, and super regions [34].

According to GBD 2016, prevalence of headache disorders was variable across different geographic regions.

Although prevalence of headache is an important epidemiologic measure, the burden of disability related to headache, as measured by YLD, is more informative for health policy making.

GBD 2016 emphasized that primary headache disorders are an important health priority.

Estimating the burden of headache is the first step to implement further measures to reduce its burden such as educating health care providers, developing primary care management, and allocating resources.

We reported the prevalence and burden of primary headache disorders (including migraine and TTH) in Eastern Mediterranean Region (EMR) countries from 1990 to 2016 using data and methods of the Global Burden of Diseases, Injuries, and Risk Factors Study 2016.

Methods

The Global Burden of Diseases, Injuries, and Risk Factors Study 2016 (GBD 2016) is a standardised analytical method that used all eligible sources to estimate the epidemiological data, including prevalence, mortality, years of life lost (YLL), YLDs, and disability-adjusted life years (DALYs), for 328 causes by sex, age, and location from 1990 to 2016.

In the previous GBD iteration (GBD 2015), in addition to migraine and TTH, medication overuse headache (MOH) was also included as a separate disorder.

We presented numbers and rates of prevalence and YLDs of migraine and TTH in 2016 and the changes from 1990 to 2016 for all EMR countries.

From the EMR, data sources from Iran [208–210], Pakistan [100], Tunisia [211], and UAE [212] for migraine, and data sources from Iran [208, 210, 213], Pakistan [100], and Qatar [214] for TTH were used in GBD 2016; however, data inputs from all over the world were used to model the burden of migraine and TTH in EMR countries.

Results

In the EMR, female to male ratio of age-standardised YLDs were 1.69 for migraine and 1.38 for TTH.

From 1990 to 2016, age-standardised YLD rates of migraine and TTH remained generally unchanged.

Comparing the overall all-age YLD rates of migraine and TTH combined, Kuwait had the highest and Djibouti had the lowest YLD rates.

During the same period, age-standardised YLD rates of migraine remained generally unchanged in EMR countries.

The ratio of observed to expected age-standardised YLD rate for migraine ranged from 0.82 in Djibouti to 1.31 in Palestine.

Similar to migraine, age-standardised YLD rates of TTH showed an overall consistency between 1990 and 2016 in EMR countries.

Observed to expected age-standardised YLD rate ratio for TTH ranged from 0.85 in Djibouti to 1.42 in Iran.

Discussion

Our study provides a comprehensive assessment of the values and trends of prevalence and burden of primary headache disorders in EMR countries and their trends from 1990 to 2016.

Risk factors for progression of episodic migraine to chronic migraine can explain a part of the higher burden of headache in the EMR.

Given the limited data sources from the EMR countries, the role of risk factors of chronic migraine in higher burden of headache in the EMR should be interpreted cautiously.

The significant and increasing non-fatal burden of headache inform policy makers and health care providers of EMR countries that primary headache should be a health care priority, and intervention strategies focusing on improvement of diagnosis and treatment of headache must be implemented.

Although we estimated prevalence and YLDs of the primary headache disorders with considerable burden (including migraine, TTH, and MOH—as a sequel of the first two syndromes), we could not include all primary headache disorders classified in ICD-10 classification [215].

Conclusion

Findings from this study show that primary headache disorders are a large cause of disability in the EMR.

Our findings inform policy makers of the EMR countries that headache is a health care priority, and preventive and management interventions must be implemented to address the growing burden of headache in this region.

More studies are needed to provide more accurate data on the prevalence and severity of primary headache disorders in EMR as well as more efficient preventive and management methods to reduce the burden of headache.

Acknowledgement
A machine generated summary based on the work of Vosoughi, Kia; Stovner, Lars Jacob; Steiner, Timothy J.; Moradi-Lakeh, Maziar; Fereshtehnejad, Seyed-Mohammad; Farzadfar, Farshad; Heydarpour, Pouria; Malekzadeh, Reza; Naghavi, Mohsen; Sahraian, Mohammad Ali; Sepanlou, Sadaf G.; Tehrani-Banihashemi, Arash; Majdzadeh, Reza; Feigin, Valery L.; Vos, Theo; Mokdad, Ali H.; Murray, Christopher J. L. 2019 in The Journal of Headache and Pain.

Prevalence and burden of headache in children and adolescents in Austria—a nationwide study in a representative sample of pupils aged 10–18 years

DOI: https://doi.org/10.1186/s10194-019-1050-8

Abstract-Summary
Headache disorders are highly prevalent worldwide, but not so well investigated in children and adolescents as in adults: few studies have included representative nationwide samples.

In a representative sample of children and adolescents in Austria, we estimated the prevalence and attributable burden of headache disorders, including the new diagnostic category of "undifferentiated headache" (UdH) defined as mild headache lasting less than 1 h.

Within the context of a broader national mental health survey, children and adolescents aged 10–18 years were recruited from purposively selected schools.

Prevalence and attributable burden of all headache, UdH, migraine (definite plus probable), tension-type headache (TTH: definite plus probable) and headache on ≥15 days/month (H15+) were assessed using the Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire for children and adolescents.

The 1-year prevalence of headache was 75.7%, increasing with age and higher in girls (82.1%) than in boys (67.7%; $p < 0.001$).

UdH, migraine, TTH and H15+ were reported by 26.1%, 24.2%, 21.6% and 3.0% of participants.

HrQoL was reduced for all headache types except UdH. Participants in single parent or patchwork families had a higher probability of migraine (respectively, OR 1.5, $p < 0.001$; OR 1.5, $p < 0.01$).

Headache disorders are both very common and highly burdensome in children and adolescents in Austria.

This study contributes to the global atlas of headache disorders in these age groups, and corroborates and adds knowledge of the new yet common and important diagnostic category of UdH. The findings call for action in national and international health policies, and for further epidemiological research.

Extended: Headache disorders are very common in children and adolescents in Austria, as they are in other countries worldwide.

Background

Two reviews have estimated the overall mean prevalence of headache in children and adolescents at 54.4–58.4%, with 7.7–9.1% migraine [216, 217].

While a few earlier epidemiological studies had reported unclassifiable headaches, with an average prevalence of about 20% [40, 218, 219], most were silent on what appears to be a substantial proportion of affected children and adolescents.

The authors recommended inclusion of UdH in epidemiological studies not only to report the whole spectrum of headache disorders but also to give a full account of headache-attributed burden.

To redress this, and to contribute to the global atlas of headache disorders in children and adolescents, we performed this epidemiological study in a representative national sample of children and adolescents in Austria.

This study assessed prevalence and burden of, and use of acute medication for, headache overall and each of the common specific headache disorders.

Methods

Burden questions referred to the numbers of days missed from school, leaving school early or with impaired everyday activities due to headache, within the previous 4 weeks.

To participants reporting headache on <15 days/month we applied diagnostic criteria, in order, for definite migraine, definite TTH, probable migraine and probable TTH.

We enquired into gender, school grade, socioeconomic status (SES) of the family, migration background, family constellation and place of residence.

Prevalence estimates (%) for any headache and for each headache type were calculated for the total sample and for each gender and school grade.

In these regression models, all sociodemographic variables (gender, school grade, SES, family constellation, place of residence and migration background) were entered simultaneously, and only main effects were analyzed.

We analyzed impact of headache type on HrQoL, school attendance, school performance and everyday activities, as well as differences regarding medication use, using general linear models.

Results

Some of these sociodemographic characteristics were more associated with specific headache types.

With regard to overall model fit, the sociodemographic characteristics included in the logistic regression models significantly predicted headache type (in all cases, $p < 0.001$), whereas the explained variance was low (Nagelkerke $R^2 = 0.018$ to 0.037).

Higher school grades were associated with migraine and TTH; older participants had a higher probability of these headache types.

During the preceding 4 weeks, 15.6% of participants with headache missed at least one whole school day because of headache, while 11.7% left school early at least once; 41.9% reported at least 1 day on which they were unable to do other activities they had wanted to.

HrQoL scores were reduced in participants with any headache compared with those with no headache on overall KIDSCREEN-10 score and on scores for self-perception, parent-relations and home life, and school environment (all $p < 0.001$).

Discussion

Headache prevalence was higher than reported in earlier reviews [216, 217], but comparable to those from a nationwide study in Turkey also applying the Child and Adolescent HARDSHIP questionnaire (bearing in mind that the Turkish study included 6–18-year-olds) [40].

Although the proportions reporting missed daily activities, school days or lessons were lowest in UdH compared with other headache types, they were still noteworthy (27%, 11%, 8%), clear evidence that the burden of headache is substantially underestimated if UdH is not included.

Among children and adolescents, headache prevalence has, with similar consistency, been reported to increase with age [216, 218, 220, 221].

We found the same, overall and for all headache types except for H15+ and, of course, UdH. Children and adolescents with divorced parents and those living with a single parent have earlier reported higher prevalences of headache [222–224].

One study showed a correlation between migration background of the family and prevalence of headache in children [225].

As UdH is expected to be an immature form of headache with a higher prevalence in younger children, the prevalence of UdH might increase with the inclusion of younger children.

Conclusion

Headache disorders are very common in children and adolescents in Austria, as they are in other countries worldwide.

This study confirms that UdH, a new diagnostic category, is very common in children and adolescents, while supporting the hypothesis that UdH may be a precursor or immature form of migraine or TTH.

Our results contribute to the global atlas of headache disorders in children and adolescents, and reconfirm that headache disorders are highly relevant to health policy.

Acknowledgement

A machine generated summary based on the work of Philipp, Julia; Zeiler, Michael; Wöber, Christian; Wagner, Gudrun; Karwautz, Andreas F. K.; Steiner, Timothy J.; Wöber-Bingöl, Çiçek. 2019 in The Journal of Headache and Pain.

Migraine: a major debilitating chronic non-communicable disease in Brazil, evidence from two national surveys

DOI: https://doi.org/10.1186/s10194-019-1036-6

Abstract-Summary
Even though migraine and other primary headache disorders are common and debilitating, major health surveys in Brazil have not included them.

We repair this omission by combining data on non-communicable diseases (NCDs) in the Brazilian National Health Survey (PNS) 2013 with epidemiological data on migraine prevalence and severity in Brazil.

The purpose is to rank migraine and its impact on public healthh among NCDs in order to support public-health policy toward better care for migraine in Brazil.

Migraine ranked second in prevalence among the NCDs, and as the highest cause of disability among adults in Brazil.

On this evidence, migraine should be included in the next health surveys in Brazil.

Introduction
Chronic non-communicable diseases (NCDs) are a principal concern in public health.

Among NCDs, neuropsychiatric (neurological and mental health) disorders have been identified as the single largest group of contributors to public ill health [34, 226], while pain conditions also play a important role [227].

Brazil has implemented public-health policies to reduce the burden of NCDs, but the targets are restricted to hypertension, diabetes, cardiovascular diseases (including stroke) and mental health disorders.

These policies are driven by NCD surveillance: the National Health Survey (PNS-Pesquisa Nacional de Saúde) in 2013 gathered information on distribution and magnitude of these selected NCDs, and identified risk factors and the social, economic and environmental associations [228].

PNS, the most comprehensive survey on health and its determinants ever held in the country, did not encompass headache disorders [228], and public-health policies based on PNS do not target them.

The purpose was to rank migraine and its attributed disability among NCDs, so supporting public-health policy toward better care for migraine in Brazil.

Methods
PNS was approved by the National Research Ethics Committee, under protocol number 328.159, on 26 June, 2013.

Previous publications showed the validity of a self-reported history of doctor diagnosed NCD in other surveys [229, 230] and in PNS [231, 232].

PNS captured proportions (%) and total numbers of participants, 18 years or older, who reported positively to each.

The estimated number of 1,537 was inflated by 2.5 design effect, to yield N = 3,843 subjects to be interviewed [233–235].

Trained lay interviewers followed a structured questionnaire validated for the diagnosis of primary headache disorders according to the International Classification of Headache Disorders (ICHD-II) [236].

Impact on health was established using MIDAS (Migraine Disability Assessment Scale), which estimates lost productive time [237].

Those with MIDAS scores ≥10 were expected to be candidates for migraine prevention (having at least 3 attacks per month), and considered disabled.

Results

In terms of population prevalence and absolute number with high or very high disability, spine disorders (meaning back pain, neck pain, low back pain or sciatica, vertebrae or disc problems) far exceeded all other NCDs: prevalence 3.03%, 4.4 million affected.

Migraine, however, clearly exceeded spine disorders: 3.75%, and 5.5 million disabled.

Migraine had been included as a NCD in PNS, and the same prevalences found as in BHES, it would have ranked as the most common NCD.

MIDAS grade IV described impact equivalent to disability rated by participants in PNS as high or very high, migraine would have ranked second in Brazil.

If MIDAS ≥10 was indicative of high disability, migraine would have ranked first.

An estimated 5.5 million people in Brazil (or 9.5 million if probable migraine is included, as it should be [51]) are apparently in need of migraine preventative therapy.

Discussion

Migraine is among the most prevalent NCDs in Brazil, and the most disabling in terms of numbers reporting impact equated with severe disability.

Probable migraine has often been neglected in epidemiological studies but, at least in those concerned with public health, it should not be [51].

Although the methodology used here was imperfect, combining data from two very different surveys and extrapolating numbers, the findings mirror those obtained in the Global Burden of Disease (GBD) studies: migraine is among the most prevalent disorders worldwide, and the second most disabling behind low back pain [34, 47].

Other studies showed high numbers of probable migraine prevalence in different populations [238–240], therefore, a high global burden of migraine is trully substantial in Brazil.

Quite clearly, migraine and other headache disorders should be prioritized in health-care policies.

For better estimates to inform policy, migraine should be included in the next health surveys in Brazil.

Conclusion

Migraine is the second most common NCD in Brazil, and the most disabling NCD.

Migraine should be part of the next health surveys in Brazil, to inform public-health strategies promoting better diagnosis and treatment.

Acknowledgement
A machine generated summary based on the work of Peres, Mario Fernando Prieto; Queiroz, Luiz Paulo; Rocha-Filho, Pedro Sampaio; Sarmento, Machado; Katsarava, Zaza; Steiner, Timothy J. 2019 in The Journal of Headache and Pain.

Undifferentiated headache: broadening the approach to headache in children and adolescents, with supporting evidence from a nationwide school-based cross-sectional survey in Turkey

DOI: https://doi.org/10.1186/s10194-018-0847-1

Abstract-Summary
A new approach to these is needed: here we introduce, and investigate, a diagnostic category termed "undifferentiated headache" (UdH), defined in young people as recurrent mild-intensity headache of < 1 h's duration.

The 1-year prevalence of UdH was 29.2%, of migraine (definite and probable) 26.7%, and of tension-type headache (TTH) (definite and probable) 12.9%.

UdH differed with respect to almost all headache features and associated symptoms from both migraine and TTH.

Burden of headache and use of acute medication were lower in UdH than in migraine and TTH.

Headache yesterday was less common in UdH than migraine (OR 0.32; 95% CI 0.28–0.37) and TTH (OR 0.64; 95% CI 0.56–0.77).

Quality of life (QoL) was better in UdH (33.6 ± 5.2) than in migraine (30.3 ± 5.6; $p < 0.001$) and TTH (32.4 ± 5.3; $p < 0.001$), but worse than in pupils without headache (35.7 ± 4.7; $p < 0.001$).

This large nationwide study in Turkey of pupils aged 6–17 years has shown that many children and adolescents have a headache type that does not conform to existing accepted diagnostic criteria.

UdH differs in almost all measurable respects from both migraine and TTH.

Although characterised by mild headaches lasting < 1 h, UdH is associated with significant adverse impact on QoL. Longitudinal cohort studies are needed to evaluate the prognosis of UdH but, meanwhile, recognition of UdH and its distinction from migraine and TTH has implications for epidemiological studies, public-health policy and routine clinical practice.

Extended: Although characterised by mild headaches lasting <1 h, UdH was associated with significant burden, including adverse impact on QoL. Crucially, UdH was common, affecting almost 30% of the pupils.

Background
In the Global Burden of Disease Study 2010 (GBD2010) [31], tension-type headache (TTH) and migraine were revealed as second and third most prevalent disorders in the world.

In children (6–11 years) and adolescents (12–17 years), the prevalence of headache disorders is not well established and the burdens attributable to them are poorly characterised.

The ICHD diagnostic criteria for migraine in adults specify recurrent moderate-to-severe headache of 4–72 h' duration, with a range of specific characteristics (unilaterality, pulsating quality, aggravation by physical activity) and accompanying symptoms (photophobia and phonophobia; nausea and/or vomiting) [20].

In our pilot school-based prevalence survey conducted in Turkey and Austria, mild headache of <1 h's duration was reported by a large proportion (37.2%) of participants aged 6–17 years, often with migraine-like features [43].

We investigate whether a new approach is required in children and adolescents, recognising that the characteristics of adult migraine (and perhaps TTH) may be undeveloped in 6–17 year-olds.

Methods

Conducted nationwide in selected schools, it employed a self-completed structured questionnaire administered to entire classes.

Questions were included on demographics, headache occurrence, ICHD-3 beta diagnostic criteria (no different, with respect to migraine and TTH, from those of ICHD-3 [20]), burden attributable to headache, and QoL. A short questionnaire completed by the mediator recorded details about the school and its local environment.

A further very brief questionnaire also completed by the mediator documented non-participation.

Diagnoses were made using the HARDSHIP algorithm [50], but we modified the process to include UdH. First, we applied the criteria for UdH (duration <1 h, intensity mild).

Among remaining participants, we separated those reporting headache on ≥15 days/month, diagnosing probable MOH (pMOH) when acute medication was reportedly used on ≥15 days/month or, otherwise, "other headache on ≥15 days/month" (these cases were not included in this analysis).

Results

We found the following 1-year prevalences: UdH 29.2%; migraine 26.7% (7.3% definite, 19.4% probable); TTH 12.9% (definite 6.7%, probable 6.2%); pMOH 0.9%; other headache on ≥15 days/month 3.4%; unclassifiable headache 0.5%.

With concern for possible interest bias among responders, we also calculated prevalences with reference to the target sample of 7889 pupils: UdH 26.2%; migraine 23.9% (definite 6.5%, probable 17.4%); TTH 11.6% (definite 6.2%, probable 5.4%); pMOH 0.8%; other headache on ≥15 days/month 3.0%; unclassifiable headache 0.5%.

The proportions of pupils with UdH fulfilling none, one or two of criteria C and D for migraine without aura were 20.7%, 45.7% and 33.5%.

Discussion

The findings of our study reflect this, and support the concept of UdH as a more appropriate diagnosis among these age groups than probable migraine or probable TTH.

In previous epidemiological studies of headache in children and adolescents, we were interested in whether authors classified headache in every participant who screened positively for headache or, instead, selectively reported cases fulfilling any specific set of ICHD diagnostic criteria.

Only five of the 59 studies reliably reported headache that was not classifiable by ICHD criteria [218, 241–244], with prevalences of 2.9–35.5% (mean 18.3 ± 14.1) but with participation proportions ranging between 54.0% and 98.3% (mean 76.2 ± 19.8).

There are implications in our proposal both for ICHD and for future epidemiological studies in these age groups, which may need to recognise UdH. There are also clinical implications if UdH, while clearly distinct from migraine, is in fact a precursor or immature form of it.

Conclusion
It differs measurably with respect to almost all headache features and associated symptoms from both migraine and TTH and has significant adverse impact on QoL. This new diagnostic category in these age groups offers an alternative to jamming an evolving headache disorder that is neither clearly migraine nor clearly TTH into either of these diagnoses.

Future longitudinal studies will show whether UdH represents those headaches that are in a shifting state between migraine and TTH before maturing by adulthood into one or the other.

Differentiating UdH from migraine and TTH therefore has implications not only for epidemiology but also in routine clinical practice, since patients diagnosed with UdH call for closer follow-up with regard to their headache characteristics and associated symptoms, and a different therapeutic approach.

Acknowledgement
A machine generated summary based on the work of Wöber, Christian; Wöber-Bingöl, Çiçek; Uluduz, Derya; Aslan, Tuna Stefan; Uygunoglu, Uğur; Tüfekçi, Ahmet; Alp, Selen Ilhan; Duman, Taşkın; Sürgün, Fidan; Emir, Gülser Karadaban; Demir, Caner Feyzi; Balgetir, Ferhat; Özdemir, Yeliz Bahar; Auer, Tanja; Siva, Aksel; Steiner, Timothy J. 2018 in The Journal of Headache and Pain.

Insufficient sleep is prevalent among migraineurs: a population-based study

DOI: https://doi.org/10.1186/s10194-017-0756-8

Abstract-Summary
Although the association between sleep disorders and migraine has been reported, the association between perceived insufficient sleep and migraine has rarely reported.

The aim of this study is to evaluate the association between insufficient sleep and migraine using the data of the Korean Headache-Sleep Study (KHSS).

The prevalence of insufficient sleep among individuals with migraine (45.5%) was significantly higher compared to that among individuals with non-migraine headache (32.9%, $p = 0.004$) or among non-headache (20.4%, $p < 0.001$).

Average sleep time did not differ among migraine, non-migraine headache, and non-headache groups (7.3 ± 1.2 vs. 7.2 ± 1.2 vs. 7.3 ± 1.4, $p = 0.207$).

Multivariable logistic regression analyses demonstrated that migraine had an increased odds ratio (OR) for insufficient sleep after adjusting for sociodemographic variables, short sleep time, insomnia, poor sleep quality, anxiety, and depression (OR = 1.8, 95% confidence interval [CI] = 1.

The prevalence of insufficient sleep was significantly higher among migraineurs compared to that in non-migraine headache or non-headache group.

Extended: The prevalence of short sleep time was not significantly different among individuals with migraine, those with non-migraine headache, and the non-headache (18.2% vs. 19.1% vs. 16.0%, $p = 0.110$).

The prevalence of insufficient sleep was significantly ($p = 0.004$) higher among individuals with migraine compared to that in individuals with non-migraine headache.

The prevalence of insufficient sleep was higher in individuals with migraine compared to that in those with non-migraine headache or non-headache.

Average sleep time was calculated as (weekday sleep time × 5 + weekend sleep time × 2)/7.

Our findings suggest that migraineurs need longer sleep time than individuals with non-migraine or non-headache to have sufficient sleep.

Background

Migraine and sleep disturbance are common complaints in the general population.

Epidemiological and clinic-based studies have demonstrated a close association between migraine and sleep disturbance.

These symptoms are associated with insufficient sleep.

Insufficient sleep is a common problem in the general population [245, 246].

Information on the association between migraine and insufficient sleep is limited.

It provides an opportunity to assess the association between insufficient sleep and migraine.

The objectives of the present study were: (1) to determine the prevalence of insufficient sleep and migraine in a general population-based sample; (2) to examine the average sleep time and sleep need among individuals with migraine, non-migraine headache, and non-headache; and (3) to assess the association between insufficient sleep and migraine using the data of KHSS.

Methods

The KHSS is a nation-wide, cross-sectional survey regarding headache and sleep among Korean adults aged 19 to 69 years.

If a participant reported an experience of headache during the previous year and her/his most severe type headache met all the criteria, she/he was classified as having migraine.

If a participant's average sleep time was ≤6 h in a day, she/he was classified as having short sleep time.

If an individual's PSQI score was 6 or more, she/he was classified as having poor sleep quality.

In univariable analyses, we modelled the ORs for sleep insufficiency without adjusting for covariates.

Model 2 incorporated short sleep time (≤6 h in average sleep time), insomnia, and poor sleep quality (PSQI) to Model 1.

The final model, Model 4, incorporated sociodemographic variables, short sleep time, insomnia, poor sleep quality, anxiety, and depression.

Results

The average sleep time was not significantly different among individuals with migraine, those with non-migraine headache, and non-headache (7.3 ± 1.4 vs. 7.2 ± 1.2 vs. 7.3 ± 1.2 h, $p = 0.207$).

The prevalence of insufficient sleep was significantly ($p = 0.004$) higher among individuals with migraine compared to that in individuals with non-migraine headache.

Among individuals with insufficient sleep, average sleep time was not significantly different among individuals with migraine, those with non-migraine headache, and non-headache (6.6 ± 1.2 vs. 6.5 ± 1.3 vs. 6.6 ± 1.1 h, $p = 0.875$).

Average sleep time of individuals with migraine did not significantly differ from that of individuals with non-migraine headache (7.9 ± 1.2 vs. 7.5 ± 1.2 h, $p = 0.109$).

Discussion

The key findings of this study were: (1) The prevalence of insufficient sleep and migraine were 27.0% and 5.3%, respectively; (2) Although average sleep time was not significantly different according to headache type, sleep need of migraineurs was longer than that of individuals with non-migraine headache or non-headache; (3) The prevalence of insufficient sleep was significantly higher in migraineurs (45.5%) compared to that in those with non-migraine headache (32.9%) or non-headache (20.4%).

We also observed frequent poor sleep quality among migraineurs in the present study.

Migraineurs had more sleep need compared to individuals with non-migraine headache and non-headache.

The prevalence of migraine, anxiety, depression, poor sleep quality and insomnia in the data of KHSS were similar to that in previous population-based studies [247–249]. Therefore, we could assure that we successfully investigated migraine and insufficient sleep in the present study.

Conclusion
Our findings suggest that migraineurs need longer sleep time than individuals with non-migraine or non-headache to have sufficient sleep.

Acknowledgement
A machine generated summary based on the work of Kim, Jiyoung; Cho, Soo-Jin; Kim, Won-Joo; Yang, Kwang Ik; Yun, Chang-Ho; Chu, Min Kyung. 2017 in The Journal of Headache and Pain.

Burden of migraine and unmet needs from the patients' perspective: a survey across 11 specialized headache clinics in Korea

DOI: https://doi.org/10.1186/s10194-021-01250-6

Abstract-Summary
Migraine is a neurological, primary headache disorder affecting more than 1 billion people worldwide, with a multi-faceted burden that can significantly impact the everyday life of a patient, both during and between attacks.

Studies on patient awareness, burden, and clinical management of migraine in Korea are limited and outdated.

A total of 207 patients with episodic or chronic migraine aged between 15 and 76 years, completed a survey designed to cover the following topics: diagnosis, understanding of the disease, treatment experience, disability, and quality of life.

Validated scales such as the Migraine Disability Assessment (MIDAS) questionnaire and Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQv2.1) were used to assess levels of disability and quality of life, respectively, in patients.

High levels of disability and poor quality of life were reported by patients, as assessed by MIDAS and MSQv2.1, respectively, but only 23.7% had regularly taken preventive medication in the past.

Korean patients with migraine experience significant disability and reduced quality of life as a result of the disease and have clear unmet needs in terms of diagnosis, understanding of the disease, and disease management including treatment.

Extended: Migraine is a disabling, neurological disease that can severely impact every aspect of an individual's life, yet is still under-recognized, under-diagnosed, and under-treated [250].

Background
Migraine and the accompanying symptoms can be significantly burdensome to patients, impacting daily functioning ability and quality of life both during and between migraine attacks [131, 138, 164, 251, 252].

A recent study on sex differences in migraine prevalence among Korean patients showed that in women, prevalence is highest in the 30–39 age group followed by 40–49 [253].

Studies in East Asia, including South Korea, have demonstrated that migraine is associated with a significant burden for patients.

There are unmet needs for East Asian patients in relation to diagnosis and treatment, owing in part to lack of the following: sufficient and appropriate diagnosis, disease awareness, and use of prescription medication [254–257].

The available literature on patient awareness, burden, and clinical management of migraine in Korea is limited and outdated.

A survey was designed to comprehensively investigate the more current difficulties and unmet needs that Korean patients face regarding migraine diagnosis, awareness, treatment, and their perceived disability and quality of life.

Materials and Methods

The survey was created in collaboration with Hankook Research Ltd. and included questions on the following in relation to migraine specifically: history and diagnosis, knowledge about migraine, utilization of medical services, disability and quality of life, unmet treatment needs regarding disease management, and experience with preventive and acute medications prior to visiting their current hospital.

Validated scales such as the Migraine Disability Assessment (MIDAS) questionnaire [141] and the Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQv2.1) [156] were used to assess the level of disability and quality of life of patients, respectively.

The MSQv2.1 measures quality of life among migraine patients during the previous 4 weeks [156].

These items include; limitations of patients' performance of normal activities (for RR), interruptions of patients' performance of normal activities (for RP) and impact of migraine on the respondents' emotions, such as frustration or helplessness (for EF).

Higher scale scores indicate better migraine-related quality of life [258].

Results

The vast majority were female, mean age of onset of migraine was 27.7 years, and mean time from first symptoms to diagnosis was 10.1 years.

Representation of these data by MIDAS grade rather than age group revealed that those in MIDAS grades III and IV had reported the highest mean number of hospitals visited (4.4 [SE = 1.3] and 4.1 [SE = 0.4], respectively), compared with those in grades I and II (2.1 [SE = 0.5] and 3.3 [SE = 1.6], respectively).

Patients spent on average 1,432,500 Korean Won a year on medication for migraine, with those over 60 spending notably less than other age groups.

Approximately one-third of patients overall were satisfied with the doctor-patient relationship in previous hospitals, with notably less satisfaction in the 50–59 group compared with other age groups.

Discussion

The results of this recent survey demonstrate that there are significant issues and unmet needs for Korean patients with migraine regarding diagnosis, awareness, and treatment.

The respondent population were patients in specialized headache clinics, which could not be fully representative of those with migraine in the general population.

The diagnostic criteria of migraine in the ICHD appear straightforward and clear, however, due to the diversity of migraine symptoms among patients and among attacks for an individual patient, some physicians are unsure of the diagnosis of migraine.

A study has shown that only 13% of Korean patients with migraine have aura symptoms [259].

As reported in other studies including analyses in Asian countries [137, 255, 260–262], there are clear unmet preventive treatment needs for Korean patients with migraine, particularly for those in most need of them.

Conclusion

The results of our survey confirm the significant burden that Korean patients with migraine experience and the critical unmet needs with regards to diagnosis and treatment.

Patient-centric intervention to reduce the diagnostic lag, increase awareness and understanding of migraine, optimize the use of medical services, enhance doctor-patient relationships and the management of migraine should be implemented to alleviate the burden of migraine.

Acknowledgement

A machine generated summary based on the work of Kim, Byung-Kun; Chu, Min Kyung; Yu, Soo Jin; Dell'Agnello, Grazia; Han, Jeong Hee; Cho, Soo-Jin. 2021 in The Journal of Headache and Pain.

The Headache-Attributed Lost Time (HALT) Indices: measures of burden for clinical management and population-based research

DOI: https://doi.org/10.1186/s10194-018-0837-3

Abstract-Summary

The burden attributable to headache disorders has multiple components: a simple measure summarising them all does not exist.

The Migraine Disability Assessment (MIDAS) instrument has proved useful, estimating productive time lost in the preceding 3 months due to the disabling effect of headache.

We developed adaptations of MIDAS for purposes of the Global Campaign against Headache, embracing epidemiological studies and the provision of clinical management aids.

We reviewed the structure, content, wording and scoring of MIDAS and made revisions, developing the Headache-Attributed Lost Time (HALT) Indices in three versions.

HALT-7/30 was a variant of HALT-30: focusing only on lost work time for population-based studies of headache-attributed burden, it enquired into lost days in the preceding month (30 days) and week (7 days).

Three versions of the HALT Indices serve different purposes as measures of headache-attributed burden, and offer different means of scoring.

In studies using HALT as a population measure, there is no need to reflect the states of individuals, whereas a measure over shorter periods than 3 months is likely to be more reliable through better recall.

Extended: The burden attributable to headache disorders has multiple components: there are many ways in which recurrent or persistent headache can damage life [50].

The Migraine Disability Assessment (MIDAS) instrument developed by Stewart and Lipton [237] has proved extremely useful.

We reviewed the structure, content, wording and scoring of MIDAS and made revisions, having in mind the purposes.

Three versions of the HALT Indices have been developed to serve different purposes as measures of headache-attributed burden (see below).

Background

The burden attributable to headache disorders has multiple components: there are many ways in which recurrent or persistent headache can damage life [50].

Even developing a measure of one aspect of burden that is applicable equally to all of the important headache disorders is a challenge.

It is important to recognise that, despite its name, MIDAS is not truly a measure of disability: unless headache is very severe, people have an element of choice in whether or not to take time out of work or other activities when affected by headache.

Because productive time is an important casualty of headache, its measurement is highly relevant to assessment of burden attributable to headache.

This manuscript describes the development and use of various adaptations to MIDAS: the Headache-Attributed Lost Time (HALT) Indices.

Methods

Over 10 years, this was employed, usually as a module imported into the much larger Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire [50], in published population-based studies in China [4], India [263], Nepal [264], Pakistan [265], Ethiopia [266], Zambia [204], Russia [267], Lithuania [268], Italy [269] and eight other countries of the European Union [131], and in other studies not yet completed or published in Mongolia, Saudi Arabia, Morocco, Peru and Guatemala.

Learning from these studies, we developed alternative versions that might be better adapted both for certain population studies and for purposes of aiding clinical management.

Further studies made use of one or more versions in different settings: estimation of headache-attributed burden in a workforce in Turkey [270, 271], headache service quality evaluation in headache centres around Europe [272, 273] and education of primary-care physicians in headache management in Estonia [274, 275].

Results

In its first five questions, MIDAS enquired into days affected by headache during the preceding 3 months (90 days) [237].

As did MIDAS, the original HALT (which later became known as HALT-90) recorded days affected by headache during the preceding 3 months (90 days) [237, 276].

Of these, HALT-30 kept the same structure, question format and wording except that "3 months" was replaced by "1 month".

HALT-7/30 was a variant of HALT-30: focusing only on lost work time, it enquired into lost days in the preceding month (30 days) and week (7 days).

Discussion

Other purposes for which headache impact might be measured in individuals are found in studies of populations and groups, often conducted as needs assessments to inform health policy and resource allocation [4, 50, 131, 204, 263–271, 277].

In studies of large groups using HALT as a population measure, there is no longer a need to reflect the states of individuals, whereas a measure over shorter periods than 3 months is likely to be more reliable through better recall [50].

HALT-30 quantifies each individual's headache burden over the preceding 30 days.

For population-based studies of headache-attributed burden, including financial cost, HALT-7/30 enquires into lost work days only, in the preceding month (30 days) and week (7 days).

HALT can generate three summed scores from the first four questions, the unit of each being whole days per period of enquiry: (a) lost work time; (b) lost household work time; and c) total lost productive time—the sum of (a) and (b).

Acknowledgement

A machine generated summary based on the work of Steiner, T. J.; Lipton, R. B.; Jumah, M. Al; Al-Khathami, A.; Allena, M.; Andrée, C.; Ayzenberg, I.; Braschinsky, M.; Gil-Gouveia, R.; Gökmen, G.; Gururaj, G.; Herekar, A.; Katsarava, Z.; Kissani, N.; Kulkarni, G.; Lainez, M.; Lampl, C.; Lantéri-Minet, M.; Linde, M.; Luvsannorov, O.; Manandhar, K.; Mbewe, E.; Quispe, G.; Rao, G.; Rastenytė, D.; Risal, A.; de la Torre, E. Ruiz; Schramm, S.; Selekler, M.; Stokes, H.; Brackett, A. C. Stokes; Stovner, L. J.; Tassorelli, C.; Tekle-Haimanot, R.; Vriezen, P.; Yu, S.-Y.; Zebenigus, M. 2018 in The Journal of Headache and Pain.

The effect of maternal migraine headache on their children's quality of life

DOI: https://doi.org/10.1007/s13760-017-0790-y

Abstract-Summary
Migraine is known to affect one's quality of life; not only the person with migraine but also his/her family and social environment are affected by this condition.

Our study aimed to evaluate the effects of maternal migraine on children's quality of life.

The Visual Analog Scale (VAS), Migraine Disability Assessment Scale, Beck Depression Index (BDI) and Beck Anxiety Index (BAI) were used for evaluation of mothers; 3 to 7-year old KINDL and 7- to 17-year-old KINDL-R Quality of Life Scales were used to evaluate the quality of life of children.

To be significant that VAS, BDI and BAI scores of the mothers were negatively correlated with the children's quality of life.

Our study concluded that the presence of migraine-type headache in mothers worsen the relations in school, self-esteem and quality of life in younger children and social relations, relations in school and quality of life in older children.

The maternal age, disease severity, and anxiety and depression symptoms were shown to predict the quality of life in children.

Performing preventive interventions by individually assessing bio-psycho-social elements for the treatment of mothers with migraine will preserve other family member's and especially children's quality of life.

Extended: That mothers with migraine headaches have impaired quality of life and more symptoms of depression and anxiety than the control group.

Introduction
Chronic diseases are among the most influential factors affecting quality of life [278].

In a medium-scaled study conducted in 2016, the severity of an individual's migraine was determined to impact negatively on the quality of life [279].

Difficulties in business life, decline in academic achievement and problems in family relations are accompanied by migraine headaches [280–282].

There is a lack of study in the literature discussing the effects of maternal migraine headaches on children and, in our knowledge, there are no studies that evaluate the effect of maternal migraine headaches on children's quality of life.

The aim of our study was to evaluate the effect of maternal migraine headaches on the offspring's quality of life by comparing it with the children of healthy mothers.

Our hypothesis is that maternal migraine headaches decrease the quality of life of the child.

Materials and Methods

A patient group of 70 mothers diagnosed with migraine, who applied to Sakarya University Training and Research Hospital Neurology Clinic, and their 111 healthy children without migraine or additional comorbid disease were included in this study.

Pain severity of mothers was assessed using the Visual Analog Scale (VAS) score, quality of life was assessed by the Migraine Disability Assessment Scale (MIDAS), and depression and anxiety symptoms were evaluated using the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI).

Quality of life of children was evaluated using 3 to 7-year old Kindle and 7- to 17-year Kindle Quality of Life Scale.

The general purpose quality of life scale "KINDL" for children and adolescents was developed for 4 to 17-year old children.

The KINDL parent form was used for 4 to 7-year old children, and the kid-KINDL-R self-report form was used for 7- to 13-year-old children.

Findings

The mean age of the migraine group was 37.09 ± 6.94 years.

Age of disease onset in the migraine group was 25.5 ± 8.7 years, disease duration was 11.7 ± 9.1 years, duration between the episodes was 5.7 ± 3.2 months, VAS score was 7.4 ± 1.3, and MIDAS score was 50.8 ± 50.4.

Regression analysis showed that maternal BDI and BAI scores were the two variables that predict the quality of life, in children between 3- to7-year-old, and the model was able to explain 30% of cases.

According to the regression analysis, maternal BDI and BAI scores were the two variables that predict the quality of life, in children between 7- to 17-year-old, and the model was able to explain 20% of cases.

Discussion

This study indicated that the presence of migraine headache in mothers probably disrupts younger children's school relations, self-esteem, and quality of life, and may affect older children's social relations, school relations, and their quality of life.

Maternal anxiety and depression symptoms, maternal age, and severity of maternal migraine headaches are the most possible factors that disrupt the children's quality of life.

Only the effect of maternal migraine headaches on children was assessed, because children with headache, recurrent abdominal pain, and chronic comorbid diseases were excluded from the study due to the possible effects on quality of life.

This study may indicate that the quality of life in children with maternal migraine headache is impaired, and this impairment is particularly correlated with the emotional status of the mother, the duration of the disease and the severity of the pain.

Acknowledgement

A machine generated summary based on the work of Güngen, Belma Doğan; Aras, Yesim Güzey; Gül, Sıdıka Sinem; Acar, Türkan; Ayaz, Ayşe Burcu; Alagöz, Aybala Neslihan; Acar, Bilgehan Atılgan. 2017 in Acta Neurologica Belgica.

Quality of life in children and adolescents with migraine: an Austrian monocentric, cross-sectional questionnaire study

DOI: https://doi.org/10.1186/s12887-019-1537-0

Abstract-Summary
Migraine is a disabling primary headache disorder that occurs in about 10% of children and might lead to a lower quality of life.

The objective of this Austrian monocentric study was to identify migraine triggers and the areas, in which children and adolescents with migraine have a lower quality of life than healthy, headache-free children.

In this cross-sectional, questionnaire study, 76 children from ages 8 to 17 years were included.

Participants filled in a questionnaire surveying the areas of physical, socio-economic and school functioning.

In socio-economic functioning, the father's nationality being Austrian might be related to migraine (p.adjust = 0.108).

Children with migraine had a significantly lower quality of life in school functioning (PedsQL 4.0 questionnaire, p.adjust = 0.04) and had significantly less often "good" grades than children without migraine (p.adjust = 0.048).

Children with migraine show a reduced quality of life in the areas of physical, socio-economic and school functioning.

Extended: The recommendations to future researchers would be: (1) to focus on only one area of functioning to carve out key aspects of the variables, (2) to clarify misleading phrases and descriptions, (3) to enlarge the sample size.

Background
Migraine can develop at all ages [283], and affects 7.7–9.1% of children and adolescents [216, 217].

Population based studies have identified a number of physical and emotional triggering factors, which can induce a migraine attack.

Physical factors that can trigger migraine are age [284–286], comorbidities (i.e. atopic disorders [287], food intolerances and allergy [288], obesity [289, 290], sleep disorders (sleep walking, sleep talking, nightmares, bruxism) [291, 292]), caffeine consumption [288, 293], skipping meals [294], alcohol consumption [288], immobility [289], weather [295, 296], noise, menstruation [295] and smoking [289].

School stress is the biggest predicator for migraine [297].

In children with migraine absenteeism is increased, whilst school performance is reduced [297].

Objectives
To substantiate that, in a single-center cohort, Austrian children and adolescents with migraine have a lower quality of life than healthy controls in specific areas of life.

Methods

Participants for this study were recruited in a Viennese pediatric outpatient clinic, the "First Vienna Pediatric Medical Center," and were asked to fill in the questionnaire after giving written consent.

Children and adolescents diagnosed with migraine, 8–17 years of age, being under regular medical treatment at the pediatric outpatient clinic were asked to participate in this study.

Two types of questionnaires were handed out to the participants and asked to be filled in: (1) Questionnaire for children from 8 to 12 years of age, who could accept their parents support in filling in the questionnaire. (2) Questionnaire for adolescents from 13 to 17 years of age, which has some additional, age-typical questions and could be completed independently.

Additional self-designed questions of school functioning included: a. Are there more migraine attacks before or after school tests?

Statistical evaluation was applied to the total number of study participants, as well as the subgroups of migraine, "migraineur" and "non-migraineur".

Results

A significant relationship was found between physical exercise per week and migraine (χ^2 (3) = 8.091, p = 0.045): Migraineurs exercised less often ≥3 times per week than non-migraineurs did (χ^2 (1) = 4.415, p = 0.036, p.adjust = 0.108).

There was no relationship between maternal nationality and migraine (χ^2 (1) = 0.781, p = 0.377), but their might been between paternal nationality and migraine (χ^2 (1) = 4.356, p = 0.037, p.adjust = 0.108): Migraineurs more often had Austrian fathers than non-migraineurs.

This is underlined by the results of the PedsQL 4.0 (school functioning) questionnaire [298] showing a significantly lower score in school functioning of migraineurs than non-migraineurs (U = 468, p = 0.008, p.adjust = 0.04).

Discussion

To identify the impact of the disease on the patients' quality of life with regards to physical and socioeconomic functioning we conducted a monocentric, cross-sectional questionnaire study on children and adolescent migraine patients and compared the results to age and sex-matched healthy non-migraineurs.

Due to the monocentric approach, only 76 pediatric patients were enrolled in this study, which might explain some of the non-significant results being in contrast to reports in literature, such as a possible association of migraine and gender or age [105, 225].

With regard to physical functioning, our migraine patients exercised less often 3 or more times per week than non-migraineurs, which was accompanied by an impaired ability for physical exercising due to migraine in one third of migraineurs and which might be explained by the assumption that exercise might trigger a migraine attack [299, 300].

Conclusion
Migraine triggers and implications of migraine on areas of life are controversially reported on in population-based studies.

Our results implicate that pediatric migraine patients do not only need special medical attendance but support in other areas of life.

Acknowledgement
A machine generated summary based on the work of Koller, Lydia Stella; Diesner, Susanne C.; Voitl, Peter. 2019 in BMC Pediatrics.

Jealousy in women with migraine: a cross-sectional case-control study

DOI: https://doi.org/10.1186/s10194-020-01114-5

Abstract-Summary
Estrogen influences susceptibility to migraine attacks and it has been suggested to affect jealousy in romantic relationships in women.

Jealousy levels and hormonal status were determined based on a cross-sectional, web-based, questionnaire study among female migraine patients and controls.

Participants with a serious and intimate monogamous relationship were included (n = 498) and divided into the following subgroups: menstrual migraine (n = 167), non-menstrual migraine (n = 103), postmenopausal migraine (n = 117), and premenopausal (n = 57) and postmenopausal (n = 54) controls.

The primary outcome was the difference in mean jealousy levels between patients with menstrual migraine, non-menstrual migraine and premenopausal controls.

The difference in jealousy levels between postmenopausal migraine patients and controls was assessed.

Jealousy levels were higher in menstrual migraine patients compared to controls (mean difference ± SE: 3.87 ± 1.09, $p = 0.001$), and non-menstrual migraine patients compared to controls (4.98 ± 1.18, $p < 0.001$).

No difference in jealousy was found between postmenopausal migraine patients and controls (−0.32 ± 1.24, $p = 0.798$).

Background
Sex hormones have a major influence on migraine, appearing from a three times higher migraine prevalence in premenopausal women compared to men, an increase in attack frequency during menopausal transition, and a postmenopausal decrease of symptoms [301–303].

Although the exact pathophysiological underlying mechanism remains unclear, previous research has suggested that fluctuations in estrogen levels, possibly the rate of decrease in estrogen, may affect the susceptibility to migraine attacks in women and/or higher estrogen levels may be implicated in both sexes [302, 304–307].

In the fertile phase, when estrogen levels are high, women tend to report higher jealousy levels compared to other times of the menstrual cycle [308].

We hypothesized that women with migraine, especially those fulfilling the criteria of MM, would have higher jealousy levels compared to women with non-menstrual migraine (non-MM) and premenopausal controls due to a corresponding provoking effect of estrogen in migraine and jealousy.

Methods

Participants received a web-based questionnaire consisting of questions concerning relationship duration, jealousy feelings and thoughts, menstrual cycle status and exogenous sex hormone use.

The covariates age, relationship duration and hormonal status were chosen a-priori based on previous studies.

Although the effect of relationship duration on jealousy levels is inconsistent in previous studies, this covariate was reasoned to be important, and therefore, was included in this study [309, 310].

Age, relationship duration and hormonal status were included as covariates.

In a secondary analysis, we compared the mean total jealousy levels of postmenopausal migraine patients and controls using a generalized linear model, adjusting for age and relationship duration.

The same statistical model was used to compare mean jealousy levels between women using COC and women with a regular menstrual cycle, controlling for age, relationship duration and migraine status.

Results

A pairwise comparison with Bonferroni correction revealed that the mean jealousy levels were higher in patients with MM compared to controls (mean difference ± SE: 3.87 ± 1.09, $p = 0.001$), and in non-MM patients compared to controls (4.98 ± 1.18, $p < 0.001$).

A pairwise comparison with Bonferroni correction revealed that both MM and non-MM groups reported higher levels compared to the premenopausal control group for the reactive jealousy sub-type (mean difference ± SE: 1.89 ± 0.64, $p = 0.010$ and 1.97 ± 0.70, $p = 0.014$, respectively).

Both MM and non-MM groups reported higher anxious jealousy levels compared to premenopausal controls (1.24 ± 0.49, $p = 0.035$ and 1.83 ± 0.53, $p = 0.002$, respectively).

Non-MM patients reported higher mean preventive jealousy scores compared to premenopausal controls (1.18 ± 0.38, $p = 0.005$).

Discussion

Premenopausal women with migraine in a relationship have significantly higher jealousy scores than controls in this study.

Previous research showed estrogen levels to be higher in women with MM compared to controls during most phases of the menstrual cycle, and with only small differences between MM and non-MM patients [305, 306].

The effect of a disabling chronic disease on the quality of life might explain the higher jealousy response within romantic relationships in female migraine patients.

Although postmenopausal women with migraine are limited in social activities, their jealousy response is comparable to that of postmenopausal controls, suggesting that impaired social functioning only partially contributes to the difference in jealousy between younger migraine patients and controls.

Women using combined oral contraceptives reported higher jealousy compared to non-using women with a regular menstrual cycle, which is congruent with previous studies [308, 309].

In a prior study, higher jealousy levels were found in the fertile phase compared to the non-fertile phase of the menstrual cycle.

Conclusions
Future research is needed on establishing the role of estrogen in women with migraine as this may provide important treatment options for this incapacitating disorder.

Acknowledgement
A machine generated summary based on the work of van Casteren, Daphne S.; van Willigenburg, Florine A. C.; MaassenVanDenBrink, Antoinette; Terwindt, Gisela M. 2020 in The Journal of Headache and Pain.

Effect of Migraine Headache on Productivity of Patients According to Migraine Disability Assessment Score: A Cross-Sectional Study

DOI: https://doi.org/10.1007/s40122-019-0130-4

Abstract-Summary
Migraine is the third most common cause of disability under the age of 50.

There are various scoring systems for assessing this disability, one of which is MIDAS; the Migraine Disability Assessment Score.

The objective of our study was to determine the extent of disability among migraine patients, patterns of prophylaxis, and their healthcare-seeking behaviors.

This survey was done in 50 migraine patients at Jinnah postgraduate medical Centre from April to May 2018.

The questionnaire inquired about the demographic information, management of migraine, and effect of this condition on their sleep, and the last part had assessment to know about their functional disability.

Acetaminophen was the most common medication used during a migraine attack, followed by nonsteroidal anti-inflammatory drugs.

The majority of migraine patients were found to have severe disability, which affected their daily work and social activities.

Despite an increase in disability rate due to migraine, people do not seek regular medical care for this type of headache in Pakistan.

Extended: The majority of patients felt that they have developed tolerance.

Despite an increase in disability rate due to migraine, the trend of people towards seeking regular medical care and prophylaxis is low in Pakistan.

Introduction

These factors further promote disability in migraine patients.

The onset of headache was earlier in patients with migraine, who reported a first-degree family history of the disease [311].

Research conducted on medical students of Karachi, Pakistan, revealed that migraine was the most common type of headache among the target population.

Different scoring systems have been suggested, one of which is MIDAS; the Migraine Disability Assessment Score.

The aim of our study was to evaluate migraine-associated disability among the population in Pakistan using the MIDAS questionnaire.

There are limited data available regarding migraine-associated costs and disability in Pakistan and the findings of our work will contribute towards the existing studies.

The purpose of our research is to determine the extent of disability among migraine patients in the region, patterns of prophylaxis, and healthcare-seeking behaviors among the effected group.

Methods

Participants were included after consenting to the study, which was approved by the ethical committee of JPMC.

The questionnaire was comprised of three parts, the first part inquired about demographic information, while the second part consisted of questions regarding the use of medications during the migraine attack, prophylaxis taken, and pattern of visiting health care facility during or after the migraine symptoms.

The subjects were asked about their sleeping habits and the possible effect of migraine on their sleeping patterns was assessed based on the participant's self-interpretation.

The third part of questionnaire had assessment for calculating the MIDAS score, that is, an inability/reduced ability of more than 50% to attend work or school, the inability/reduced ability to do household work, the inability to participate in non-work-related activities (total scores: 0–3 in each headache attack) [141].

Results

Acetaminophen was the most common medication used by the individuals during a migraine attack (48%), followed by nonsteroidal anti-inflammatory drugs (40%).

Many individuals did not take any prophylaxis (46%) and the majority (54%) of subjects admitted using prophylaxis.

β-blockers were the most common prophylaxis used (20%), followed by tricyclic antidepressants (18%).

There was a lower tendency of going to follow-ups with health care among individuals with migraine and only 32% had a follow-up visit with doctors.

Discussion
Individuals suffering from migraine-related disability experience difficulties in maintaining a work and household routine and struggle with socializing activities, which is consistent with the results of our study [312].

Studies have shown that gender has a direct effect on the intensity of migraine attacks.

A study reported a higher prevalence of severe migraine in females as compared to males and females suffered greater migraine-related disabilities [313].

A study conducted in Psychiatry Tertiary Care Hospital in New Delhi revealed that 66.0% of females with migraines scored low on the Female Sexual Function Index, an indication of lower sexuality as compared to the control group (33%) [314].

Our study showed β-blockers as the most common prophylactic used for migraine, however this is different from the finding in another study where the use of anti-depressants was more common [315].

Conclusions
Most of the results in our study are consistent with migraine-related studies conducted in other countries.

Acknowledgement
A machine generated summary based on the work of Jawed, Shafaq; Ali, Waqar; Yaqoob, Uzair; Shah, Shahnaz; Uddin, Syed Mohammad Mazhar; Haq, Aatera. 2019 in Pain and Therapy.

A cross-sectional study on the burden and impact of migraine on work productivity and quality of life in selected workplaces in the Philippines

DOI: https://doi.org/10.1186/s10194-020-01191-6

Abstract-Summary
This study aimed to evaluate the burden and impact of migraine on work productivity in selected workplaces in the Philippines.

Volunteer employees were screened for migraine using the ID-Migraine™ test.

Eligible employees were tested for migraine severity and impact on work productivity using the Migraine Disability Assessment (MIDAS) questionnaire.

Multiple logistic regression was used to identify significant predictors of migraine disability (high—MIDAS Grade III/IV vs. low—MIDAS Grade I/II).

Differences in quality of life scores by migraine disability were measured using multiple linear regression.

Productivity costs lost to migraine disability were calculated as the number of days lost to migraine multiplied by the self-reported wage rate, and costs according to migraine severity were measured using a two-part generalized linear model.

A total of 511 positive migraine screens were included in the final sample.

Females comprised two-thirds of all positive migraine screens and were more likely to have high migraine disability (odds ratio: 1.60, 95% CI: 1.03–2.49) than males.

Those with high migraine disability scored lower on role limitations compared to those with low migraine disability.

Mean annual productivity costs lost due to migraine disability were PHP27 794 (USD556) per person.

Migraine poses a significant threat to work productivity in the Philippines.

Extended: A total of 954 respondents provided consent and attempted to respond to the survey, or a response rate of around 4.1%.

Migraine poses a significant burden to employee productivity in the Philippines, with annualized costs due to migraine costing as much as PHP40 000 (USD826) per person for those with high migraine disability and PHP10 000 (USD200) per person for those with low migraine disability.

Introduction

While several population-level studies on migraine have been conducted in the past few years, there remain countries with little information on the burden of migraine, specifically in the Asia-Pacific region [8].

A systematic review and meta-analysis on chronic migraine found only seven population-level studies in the Asia-Pacific region estimating chronic migraine prevalence to be approximately 6–17 people per 1000 population [316].

The expectation of worry on the next migraine attack is in itself negatively affecting work productivity and quality of life [317].

This implies that migraine poses a significant economic burden and various studies in the past have tried to quantify the economic impacts of migraine.

In a literature search, this was the only published study found to present data on the burden of migraine in the Asia Pacific region.

Given this, the present study assessed the burden and impact of migraine and work productivity and daily activities in selected workplaces in the Philippines.

Methods

To determine predictors of migraine disability, adjusted odds ratios (OR) and their 95% confidence intervals (CI) were calculated for high vs. low migraine disability for the following socio-demographic factors: gender, age, educational attainment, employee rank, and gross monthly income from the company.

Given that not all migraine positive screens reported absenteeism and presenteeism, a two-part model was used to determine the economic costs of migraine between low and high migraine disability: the first part was a logistic regression model that determined the probability of reporting any economic cost of migraine, while the second part was a generalized linear model (GLM) fit with a log link function and gamma (for absenteeism) or Poisson distribution (for presenteeism and

total days and cost lost to migraine), with the function and distribution confirmed using the box-cox test and modified Park test, respectively [318].

Results

Between low and high migraine disability, differences in demographics were apparent in females, where a higher proportion of females was reported among those with high migraine disability (68.2%) than low migraine disability (57.3%, p = 0.029).

One in five (20.4%) reported having undergone laboratory tests in the past three months, one in three (30.3%) reported visiting the hospital emergency room for headache symptoms in the past 12 months, and one in six (17.6%) reported being hospitalized for a migraine emergency in the past 12 months.

Costs significantly differed between migraine disability: monthly costs lost due to migraine for those with low disability averaged around PHP865.1 (USD17) (95% CI: 754.3–975.9) while costs quadrupled for those with high disability at PHP3 440.8 (USD69) (95% CI: 3323.4–3558.3).

Discussion

This study provided a comprehensive view of how migraine affects employees in selected workplaces in the Philippines.

The mean annual cost was at USD500 per employee for those with low migraine disability and USD800 per employee for those with high migraine disability.

Those with high migraine disability were only expected to take a sick leave for about 12 days a year due to migraine.

Since all employees in the sample had generous company-provided private health insurance and medicine allowances, health care utilization rate for migraine was higher than the national health care utilization rate for any type of service, which was 8% based on the 2017 Demographic and Health Survey [319].

Employers must also be educated on the burden and impact of migraine in the workplace, and results from this study may begin that important conversation for the benefit of employees and companies overall.

Conclusion

Migraine poses a significant burden to employee productivity in the Philippines, with annualized costs due to migraine costing as much as PHP40 000 (USD826) per person for those with high migraine disability and PHP10 000 (USD200) per person for those with low migraine disability.

Quality of life was significantly lower among those with high migraine disability than those with low migraine disability across all eight SF-36 domains.

Most medication taken for migraine remain OTC medicines for symptom relief, and further research is needed to gauge willingness of employers to pay for preventive medication for migraine.

Acknowledgement

A machine generated summary based on the work of Haw, Nel Jason; Cabaluna, Ian Theodore; Kaw, Germaine Erika; Cortez, Joanna Feliz; Chua, Maria Pamela; Guce, Kristel. 2020 in The Journal of Headache and Pain.

Reliability and validity of the 6-item Headache Impact Test in chronic migraine from the PROMISE-2 Study

DOI: https://doi.org/10.1007/s11136-020-02668-2

Abstract-Summary
We examined the reliability and validity of the 6-item Headache Impact Test (HIT-6) specifically on patients with chronic migraine (CM) from the PROMISE-2 clinical trial.

The conceptual framework of HIT-6 was evaluated using baseline data from the PROMISE-2 study (NCT02974153; N = 1072).

Using baseline and week 12 data, convergent and discriminant validity of the HIT-6 was evaluated by correlation coefficients.

Sensitivity to change was assessed by evaluating correlations between HIT-6 scores and change scores for other established reference measures.

Known-groups analyses demonstrated that the HIT-6 total score can distinguish between clinically meaningful CM subgroups.

The HIT-6 was successfully calibrated using IRT with data from PROMISE-2.

Results from these analyses were generally consistent with previous literature and provided supportive evidence that the HIT-6 is well suited for measuring the impact of headache and migraine in the CM population.

Extended: The impact of this homogeneity was evident in the screening and baseline HIT-6 scores that resulted in what were likely attenuated estimates of test–retest reliability; we recommend that this be re-examined in a prospective observational study to examine the accuracy of this supposition and provide a more complete understanding of the psychometric soundness of the HIT-6 in the CM population.

Introduction
Previous research has shown associations between CM and increased headache impact and disability as well as decreased health-related quality of life (HRQoL) [320–323].

One of these, the 6-item Headache Impact Test (HIT-6) [142], recommended by the American Headache Society [324], is intended to measure the impact of headache on daily life, with higher scores reflecting greater migraine impact [325].

The HIT-6 measures headache-related impact on six items, including severe headache pain, limitations to usual daily activities, the wish to lie down, fatigue, negative affect, and limitations to concentration.

A substantial body of literature supports the HIT-6 as a precise and reliable PROM for assessing the impact of headache in the general headache population, as well as in patients with migraine [142, 325–329].

Much of the previous research has evaluated the broad headache population, and there is limited work specifically focused on use of the HIT-6 in CM, which is a particularly debilitating condition with features unique from other headache and migraine disorders.

Methods

For the reported item-level analyses (item-level descriptive statistics, latent variable modeling, classical test theory analyses), the ordinal HIT-6 responses were coded as: never = 1, rarely = 2, sometimes = 3, very often = 4, and always = 5.

To be conservative, no imputation for missing data was used in these analyses, meaning that HIT-6 total scores were not to be calculated for any observations with missing item responses.

To assess internal consistency/reliability, classical test theory analyses (i.e., item-total correlations, coefficient alpha, and alpha with item removed) were computed for the HIT-6 using baseline data, along with the IRT-based reliability plot and the IRT-based marginal reliability estimate.

Consistent with the HIT-6 manual [330] and the assumptions underlying coefficient alpha, only HIT-6 observations with complete item responses were used for the internal consistency reliability analyses.

Results

Complete observations for the HIT-6 items were present as both baseline and Week 12 (i.e., if a patient was presented the HIT-6, all items were answered).

Patients in PROMISE-2 had HIT-6 total scores in the severe range at baseline [331].

The observed correlation between frequency of MMDs and the HIT-6 total score at baseline, which was lower than anticipated, may be attributable to the fact CM patients needed to have a relatively high migraine frequency at baseline to meet study inclusion criteria.

The primary exception was that the PGIC correlation (r = 0.57) was noticeably greater than expected (0.10–0.30), indicating that change in the HIT-6 total score may be a more robust assessment of general headache impact on patients than initially expected.

Discussion

Subsequent studies using a variety of headache patient samples found HIT-6 total scores to be associated, as expected, with numerous other migraine-specific PROM scores as well as with general health and HRQoL measures and with objective headache and migraine outcomes [142, 326, 327, 329, 332–336].

In the same study's open-label phase (in which previously placebo-treated patients received active treatment), the HIT-6 total scores retained the demonstrated decrease from baseline but the differences between treatment groups were no longer statistically significant, as would be expected.

The impact of this homogeneity was evident in the screening and baseline HIT-6 scores that resulted in what were likely attenuated estimates of test–retest reliability; we recommend that this be re-examined in a prospective observational study to examine the accuracy of this supposition and provide a more complete understanding of the psychometric soundness of the HIT-6 in the CM population.

Conclusion
This body of work examined the reliability and validity of the HIT-6 in patients with CM using data from the large PROMISE-2 clinical trial.

The short administration time, easy scoring, and interpretability of the HIT-6 make it an excellent tool for use in applied research, clinical trials, and clinical practice settings so that broader patient experience can be assessed.

Acknowledgement
A machine generated summary based on the work of Houts, Carrie R.; McGinley, James S.; Wirth, R. J.; Cady, Roger; Lipton, Richard B. 2020 in Quality of Life Research.

1.3 Economics

Machine generated keywords: cost, erenumab, mmd, productivity, preventive, migraine day, costeffectiveness, qaly, day, headache day, use acute, societal, loss, billion, annual.

Economic Evaluation of Treatments for Migraine: An Assessment of the Generalizability Following a Systematic Review

DOI: https://doi.org/10.1007/s40273-019-00879-1

Abstract-Summary
The aim of this study was to review the economic evaluations on the prophylaxis and treatments for migraine published in the previous 10 years (since 2009) and to perform a critical assessment of their generalizability.

To assess the level of generalizability, we used the checklist implemented by Augustovski and others Studies were classified as: (1) generalizable; (2) transferable; and (3) context specific.

227 articles were identified after running the search string and 11 studies were included in our review.

None of the studies was judged as generalizable and three were judged transferable according to the established criteria.

Our review suggests that no evidence on the economic value of either acute or prophylactic treatments against migraine is generalizable to different jurisdictions.

The majority of studies reporting results about prophylactic treatments were found to be transferable.

Extended: The aim of this study was to review the economic evaluations on the prophylaxis and treatments for EM and CM to assess the level of generalizability of single studies, as an important and transparent support to the decision-making process.

The aim of our study was to assess the generalizability of economic evidence by means of a validated and widely used checklist [337–339].

To assess the level of generalizability of the articles included in this review, the checklist implemented by Augustovski and others [338, 340] was used.

227 articles were identified after running the search string on the selected databases.

Our review suggests that studies assessing the cost effectiveness of prophylactic treatments are more likely to be a useful support for decision makers as three of them were judged transferable [341–343].

Introduction

Healthcare and societal costs associated with migraine amount to US$36 billion per year in the USA.

The evidence arising from the health economic evaluations (HEEs) of the available strategies for the treatment of migraine has been pooled in four systematic reviews of the literature.

Two reviews [344, 345] investigated the cost effectiveness of oral serotonin receptor agonists for the treatment of CM.

A third review [346] was published in 2009 and underlined the methodological challenges arising from the cost-effectiveness analyses conducted on the pharmacotherapies for migraine.

In the last review, [347] conducted in 2012, the focus was on the cost effectiveness of acupuncture in chronic pain, including migraine.

The heterogeneity of different strategies, previously underlined in other reviews, has substantially increased and, perhaps, any attempt to compare the cost effectiveness across different studies is too ambitious.

Methods

During either the selection or the review process, discrepancies between the reviewers were addressed by giving priority to the opinion of the scholar with the most coherent background depending on the type of issue (i.e., concerning discrepancies regarding study design, priority was given to the statistician's opinion).

The selected items were:the clear description of the study setting and the alternatives being compared;the multicentric study design (only for randomized controlled trial-based HEEs);the clinical and cost data referring to the whole study population;the preference data relevant to the study population;the presence of quantitative/qualitative analysis performed to appraise the variability of results from setting to setting;the adoption of a wide study perspective (healthcare payer or societal);a clear justification of the model structure and parameters (only for model-based HEEs);the presence of a stochastic analysis to explore uncertainty (only for model-based HEEs);full reporting of baseline characteristics of the study sample;the

reporting of the epidemiology (if relevant);the reporting source of utility data;a separate reporting of unitary costs and resource consumption amounts.

Results

All studies [341–343, 348–355] reported an ICER, which in seven articles was expressed in terms of cost per QALY.

Each study included in this review considered both clinical and cost data referring to the study population.

Of Slof, [352] (dis)utilities from the Health Utility Index 3 were attributed to patients enrolled in a clinical trial based on their severity.

The migraine populations considered in the study of Lipton and others [351] were 50% CM and 50% EM, plus sub-groups of patients who had previously not responded to prior preventative therapy.

The study of Slof [352] associated severity-related (dis)utilities to patients according to clinical trial results by using the Health Utility Index 3.

The study of Hens and others [348] only reported the costs of a single dose of the triptans included in the model.

Discussion

The study of Asseburg and others [356] evaluates different strategies for acute migraine by using a network meta-analysis, whilst Augustovski and others [338] only provide methodological requirements to assess the generalizability of trial- and model-based economic evaluations.

This choice could be seen as a limit of the study, on the other hand, our choice was based on focusing our analysis more on the quality and generalizability, to provide suitable information for decision makers.

Our main goal was to provide decision makers and researchers with the current developments in the methodological quality of the economic studies in the field of migraine.

The quality of the included articles was good, although none of the studies was judged as generalizable according to the established criteria.

Our review suggests that studies assessing the cost effectiveness of prophylactic treatments are more likely to be a useful support for decision makers as three of them were judged transferable [341–343].

Conclusions

Our review found that no studies reporting evidence on the economic value of either acute or prophylactic treatments for migraine were generalizable to different jurisdictions.

All the studies that were judged as transferable reported results about prophylactic treatments and therefore were likely to have a higher chance of efficiently supporting decision makers of other jurisdictions.

Acknowledgement

A machine generated summary based on the work of Ruggeri, Matteo; Drago, Carlo; Rosiello, Francesco; Orlando, Valentina; Santori, Costanza. 2020 in PharmacoEconomics.

Headache in Resource-Limited Settings

DOI: https://doi.org/10.1007/s11916-017-0651-7

Abstract-Summary
This review summarizes the unmet need of headache burden and management in resource-limited settings.

It provides a general overview of the nuances and peculiarities of headache disorders in resource-limited settings.

The review delivers perspectives and explanations for the emerging burden of both primary and secondary headache disorders.

A critical analysis of headache disorders is made within the context of growing burden non-communicable disorders in low-resource countries.

Challenges are examined and prospective feasible solutions tailored to existing resources are provided to address headache disorders in resource-limited settings.

Many low-resource countries are entering into the third epidemiological transition featuring increasing burden of non-communicable disorders of which headache disorders contribute a significant proportion.

Life expectancy is rising in some resource-restricted countries; this increases prevalence of secondary headache attributed to neurovascular causes.

Many low-resource countries are still burdened with tropical infectious causes of secondary headache.

Many low-resource settings do not have access to generic headache medications such as triptans.

Addressing the increasing burden of headache disorders in resource-limited settings is important to avert accrued disability which in turn lowers productivity and socioeconomic performance in a young booming population.

Introduction: Burden and Peculiarities of Headache Disorders in Resource-Limited Settings

Resource-limited health settings predominantly involve many developing countries in Africa, Asia, Latin America, and the Caribbean [357].

Compared to high-resource regions, understanding the status quo of health problems such as headache needs a different perspective in low-resource settings.

It is important to recognize the disparity that exists within low-resource settings i.e., some of these countries have slightly better health resources compared to others [357].

Demographic and Epidemiologic Transition: Implications for Headache Disorders

These peculiarities have important implications when examining headache disorders in resource-restricted settings as described in the following paragraphs.

Rapid population growth coupled with unfavorable lifestyle changes can give rise to emergence of chronic progressive conditions such as headache disorders [358].

Sleep disruption, lack of exercise, irregular mealtimes, and higher levels of stress accompanying fast-paced urban-like lifestyle changes happening in many resource-restricted settings can lead to more prevalent primary headaches [358].

Levels of physical activity are on the decline in some low-resource settings [359–363].

Unfavorable change in lifestyle has clear health implications, particularly within the context of lifestyle-related disorders such as obesity and hypertension which are also known risk factors for migraine and secondary headache disorders.

Higher levels of stress, poor sleep hygiene, and irregular mealtimes are all features of unfavorable lifestyle which are linked to higher headache frequency and low quality of life [358].

Primary Headache Disorders as Non-Communicable Disorders

There is emerging burden from primary headache disorders in resource-restricted settings [226, 358].

Headache disorders are largely mis−/underdiagnosed and thus mis−/undermanaged in most resource-restricted settings [364].

There exists a vicious cycle in low-resource settings between increasing headache burden, its under−/mismanagement, poor socioeconomic performance, and limited health resources.

Primary headache disorders such as migraine and tension-type headache account for the most prevalent neurological conditions in resource-restricted settings as well as in the rest of the world [226].

Recent community-based studies from resource-restricted settings revealed the prevalence of primary headache disorders to be increasing [226, 358].

In resource-restricted settings, higher level of headache-related YLDs and DALYs are also driven by increasing population and increasing life expectancy [226].

Despite historic accounts that claim headache to be solely a burden of rich countries, recent studies reveal that prevalence between rich- and low-resource settings is similar [358].

Secondary Headache Disorders

The burden of secondary headache disorders in low-resource countries is on the rise because of increasing life expectancy.

Besides, the prevailing tropical causes of secondary headache such as neuroinfections are still rampant and continue to contribute to secondary headache burden in resource-restricted settings.

The aforementioned points indicate that the burden of headache disorders in resource-restricted settings is comparable to a double-edged sword; these settings are laden by both emerging primary headache and endemic secondary headache disorders.

This overlap of burdens has important implications when considering public health policy and management of headache disorders within resource-restricted settings.

Headache Therapy in Resource-Limited Settings

Improving headache training at various health care settings can be useful in resource-restricted settings.

Traditional, non-medicinal, and holistic forms of therapy are preferred as these fit the cosmovision and culture of many in low-resource settings [365].

Considering devices for headache therapy is impossible for most of these resource-restricted settings—for obvious reasons of cost, maintenance, and lack of expertise.

The Millennium Development Goals (MDGs) were designed to combat infectious diseases in low-resource settings and did not address non-communicable disorders [366].

Healthcare systems in low-resource settings (e.g., Africa) are primarily designed to respond to epidemics of infectious diseases and not to a chronic burden like headache that needs a sustained policy and commitment from different sectors [367].

These matters need to be attended so as to address the burden of headache in resource-restricted settings.

Conclusion

The burden of headache disorders in resource-limited settings is due to increase in both primary and secondary headache.

The rise in primary headache is mostly associated with unhealthy lifestyle choices, low socioeconomic status, and increment in non-communicable disorders.

That the exploding population growth in low-resource countries is young makes it vulnerable to higher incidence of primary headache; since primary headache is naturally common in the young age group.

Management policies should emphasize lifestyle approaches such as regular aerobic exercise which lowers primary headache prevalence (e.g., migraine) along with reducing comorbid conditions such as obesity.

The advantage from lifestyle modification is twofold i.e., reducing migraine chronification and lowering risk for secondary headache causes such as stroke.

Acknowledgement

A machine generated summary based on the work of Woldeamanuel, Yohannes W. 2017 in Current Pain and Headache Reports.

The relationship between headache-attributed disability and lost productivity: 2. Empirical evidence from population-based studies in nine disparate countries

DOI: https://doi.org/10.1186/s10194-021-01362-z

Abstract-Summary

Headache disorders are disabling, with major consequences for productivity, yet the literature is silent on the relationship between headache-attributed disability and lost productivity, often erroneously regarding the two as synonymous.

We evaluated the relationship empirically, having earlier found that investment in structured headache services would be cost saving, not merely cost-effective, if reductions in headache-attributed disability led to >20% pro rata recovery of lost productivity.

We assessed relationships in migraine and probable medication-overuse headache (pMOH), the most disabling common headache disorders.

Disability, in the sense used by the Global Burden of Disease study, was measured as the product of pTIS and disability weight for the ictal state.

Lost productivity was measured as lost days (absence or < 50% productivity) from paid work and corresponding losses from household work over the preceding 3 months.

For migraine, in a linear model, we found positive associations with lost paid worktime, significant ($p < 0.05$) in many countries and highly significant ($p < 0.001$) in some despite low values of R^2 (0–0.16) due to high variance.

With lost household worktime and total lost productivity (paid + household), associations were highly significant in almost all countries, although still with low R^2 (0.04–0.22).

Applying the regression equations for each country to the population mean migraine-attributed disability, we found pro rata recoveries of lost productivity in the range 16–56% (>20% in all countries but Pakistan).

Relief of disability through effective treatment of migraine is expected, in most countries, to recover >20% pro rata of lost productivity, above the threshold for investment in structured headache services to be cost saving.

Extended: Headache disorders are the cause of disabling ill health, awareness of which has increased dramatically over the last decade [8, 31, 32, 34, 44, 47–369].

Relief of disability through effective treatment of migraine can be expected, in most countries, to recover, pro rata, > 20% of lost productivity, with country income level not a factor.

This is something for future studies: the data exist.

Background

In an earlier paper, we searched the literature for evidence of the relationship between headache-attributed disability and lost productivity, recognising the importance of this in the contexts of health care and policy [370].

The crucial question was, and still is: "To what extent might alleviation of the symptom burdens of headache disorders—the principal cause of disability—be expected to reduce the lost-productivity burdens?"

Our aim here, therefore, was to evaluate the relationship between headache-attributed disability on the one hand and lost productivity on the other using empirical data.

These data included symptom burden, allowing calculation of impairment, disability (in the sense used within the Global Burden of Disease (GBD) studies [8, 31, 32, 34, 44, 50, 94–368, 370]), and lost productive time from paid work and household chores.

Methods

We defined headache-attributed disability as in the Global Burden of Disease (GBD) studies, expressed at population level in years lived with (or lost to) disability (YLDs) [8, 31, 32, 34, 44, 50, 94–368, 370].

We defined headache-attributed lost productivity in terms of absenteeism from or reduced productivity in paid work and corresponding losses in household work, ignoring, again for simplicity, the economically less important detriment to social participation.

Symptom enquiry relevant to estimation of disability (as defined) included headache frequency (days/month) and usual attack duration (minutes, hours or days).

We calculated time in ictal state (TIS) at individual level as the product of headache frequency (F) and average duration converted into days (D), and expressed this as a percentage of total days (pTIS).

We assessed associations between these: headache-attributed disability or headache-attributed impairment as independent variables and lost productivity as dependent variable for each country and each headache type.

Results

Evident in all, but more in some countries than in others, are numerous data points indicating high reported lost productivity despite low estimated disability.

Disability values are the same in each, with a possible range of 0–22% based on DW = 0.441 [371] since maximum pTIS was 50% (cases of headache on ≥15 days/month were excluded).

The degrees of scatter indicate complexity and involvement of other factors in the relationships.

With maximum pTIS = 100%, the possible range for disability was also 0–22%, based on DW = 0.217 [371].

Numbers were relatively low, but the degrees of scatter, particularly in Pakistan with negative β, again indicate complexity and involvement of other factors in the relationships.

Discussion

It was reported in one of the population studies that lost productivity due to migraine exceeded disability expected from time spent with headache [263], suggesting that the disabling effect of migraine outlasted headache.

Interictal burden, on the other hand, which was ignored in our analyses (and is ignored in the GBD studies), would not be factored into disability estimates based on pTIS, but neither would we expect it to have an effect on lost productivity.

We should note, however, that for both disorders the relationship between disability and lost productivity is complicated and weakened by a welter of interfering external factors, with high variance reflected at population level in low values of R^2.

LTB studies have introduced enquiry into headache yesterday [50] to obviate recall error in assessments of both disability and lost productivity, but the numbers, for now, remain small (1-day prevalence of migraine is low).

Conclusion
Relief of disability through effective treatment of migraine can be expected, in most countries, to recover, pro rata, > 20% of lost productivity, with country income level not a factor.

While any recovery will offset costs of care provision, our earlier analyses indicate that investment in structured headache services will be cost saving, not merely cost-effective, if proportionate recovery of lost productivity is above this level.

It is likely that a stronger relationship exists at individual level, where many of the extraneous factors are constant.

Introducing headache intensity into our analyses, attempting to reflect impairment and a more nuanced assessment of individual health loss, was not useful for reasons explained.

Acknowledgement
A machine generated summary based on the work of Thomas, Hallie; Kothari, Simple Futarmal; Husøy, Andreas; Jensen, Rigmor Højland; Katsarava, Zaza; Tinelli, Michela; Steiner, Timothy J. 2021 in The Journal of Headache and Pain.

The Humanistic and Economic Burden of Migraine in Europe: A Cross-Sectional Survey in Five Countries

DOI: https://doi.org/10.1007/s40120-020-00196-2

Abstract-Summary
Prior studies have estimated the burden of migraine in patients suffering from ≥4 monthly headache days (MHDs), but the burden experienced by migraineurs suffering from one to three (1–3) MHDs is unknown.

The aim of this study was to examine the incremental burden of migraine in terms of health-related quality of life (HRQoL), impairments to work and daily activities, and healthcare resource utilization (HRU) in five European countries (France, Germany, Italy, Spain, and the UK (EU5]), by comparing migraineurs with ≥4 MHDs and migraineurs with 1–3 MHDs.

The Short-Form 12-Item Health Survey Instrument, version-2 physical and mental component summary (PCS and MCS) scores, Short-Form 6-dimensions (SF-6D), EuroQoL 5-dimensions (EQ-5D) and EuroQoL visual analog scale (VAS) scores, impairments to work productivity and daily activities (Work Productivity and Activity Impairment [WPAI] Questionnaire) scores, and HRU were compared between migraineur groups with ≥4 MHDs (4–7, intermediate-frequency episodic migraine; 8–14, high-frequency episodic migraine; ≥15 chronic migraine) and the migraineur subgroup with 1–3 MHDs (low-frequency episodic migraine) using generalized linear modeling after adjusting for covariates.

Migraineurs with ≥15 MHDs had significantly lower HRQoL and increased WPAI scores and HRU than the 1–3 MHDs subgroup.

This study provides evidence supporting the incremental burden of migraine, characterized by poorer HRQoL and increased WPAI scores and greater HRU, among migraineurs experiencing ≥4 MHDs compared with migraineurs experiencing 1–3 MHDs in the EU5.

Introduction

Differences in the burden of migraine between those with episodic migraine and those with chronic migraine have been reported earlier [11, 372], but only limited data are available on the burden of migraine as a function of the frequency of headache days, particularly among those with one to three MHDs (1–3 MHDs).

The burden of migraine experienced by those with intermediate-frequency episodic (4–7 MHDs) migraine, high-frequency episodic (8–14 MHDs) migraine, and chronic (≥ 15 MHDs) migraine compared with those experiencing low-frequency (1–3 MHDs) migraine in the EU5 has not been reported earlier.

The objective of this study was to characterize this additional burden of migraine with increased MHDs among migraineurs experiencing ≥4 MHDS (4–7, 8–14, and ≥ 15 MHDs) compared with those experiencing 1–3 MHDs, in terms of HRQoL, WPAI, and HRU in the EU5.

Methods

The 2017 NHWS was divided into two components: a base survey component that assessed demographics, diseases experienced and diagnosed, and health outcomes (completed by all respondents) and various disease (e.g., migraine) and non-disease (e.g., vaccination) modules completed by eligible respondents.

The 2017 NHWS included the standard 4-week recall period of the revised Medical Outcomes Study 12-Item Short-Form Health Survey Instrument (SF-12v2), a multipurpose, generic health status instrument comprising 12 questions.

Higher scores indicate better HRQoL. Several studies have used Short Form health surveys to estimate the health status of migraineurs, thus validating the instrument [11].

The EuroQol 5 dimensions (EQ-5D) index score is a preference-based measure of health, ranging on a theoretical scale from 0 to 1 (with1 being equal to full health and 0 being equal [in terms of preference] to death).

Results

A significantly higher number of visits to HCPs and neurologists (for both, $p < 0.001$) were observed in all of the ≥4 MHDs subgroups compared with the 1–3 MHDs subgroup.

Employed migraineurs in the 4–7 and 8–14 MHDs subgroups showed significantly greater activity impairment compared with those in the 1–3 MHDs subgroup ($p < 0.0001$, for both).

The total number of visits to the neurologist were significantly higher in the 4–7 ($p = 0.001$), 8–14, and ≥ 15 MHDs ($p < 0.0001$, for both) subgroups than in the 1–3 MHDs subgroup.

The numbers of total visits to the ER ($p < 0.001$) and psychologists ($p = 0.004$) were significantly higher in the ≥15 MHDs subgroup compared to the 1–3 MHDs subgroup.

Discussion

A recent study by Vo and others [11] among migraineurs in the EU5 reported that migraineurs with ≥4 MHDs, particularly chronic migraineurs (> 15 MHDs), had lower HRQoL, decreased work productivity, and increased activity impairment, and greater HRU compared to non-migraine controls.

Although the previous study showed an increased burden in migraineurs with ≥4 MHDs (particularly among those with 8–14 and ≥ 15 MHDs) compared with non-migraine controls using a smaller sample size [11], the current study uses a larger sample size and reveals that there is an incremental burden due to migraine in all of the subgroups, including the 4–7 MHDs subgroup, but compared with 1–3 MHDs group.

The findings from the current study suggest that when compared with low-frequency episodic migraine (1–3 MHDs), intermediate-frequency episodic, high-frequency episodic, and chronic migraine (≥ 4 MHDs) impose a greater burden on the individual and the healthcare system.

Conclusion

Although respondents experiencing 1–3 MHDs were found to be more prevalent than those experiencing ≥4 MHDs (i.e., 4–7, 8–14, and ≥ 15 MHDs), the incremental burden due to migraine in terms of reduced HRQoL, greater work productivity loss and activity impairment, and increased HRU was higher among those in the ≥4 MHDs subgroups than among those in the ≤3 MHDs subgroup in the EU5.

The findings from this study suggest that respondents experiencing ≥4 MHDs, chronic migraineurs (≥ 15 MHDs) in particular, should be treated more effectively to reduce migraine frequency and lessen the burden of migraine in the EU5.

Acknowledgement

A machine generated summary based on the work of Doane, Michael J.; Gupta, Shaloo; Fang, Juanzhi; Laflamme, Annik K.; Vo, Pamela. 2020 in Neurology and Therapy.

Cost of chronic and episodic migraine patients in continuous treatment for two years in a tertiary level headache Centre

DOI: https://doi.org/10.1186/s10194-019-1068-y

Abstract-Summary

Available data suggest that migraine is world widely associated with a high economic burden, but there is great variability in estimated costs that depends on the geographical, methodological and temporal differences between the studies.

The purpose of this study was to quantify the annual direct cost of episodic migraine (EM) and chronic migraine (CM), both for the patient and for the National Health System (NHS), using data from subjects who attended an Italian tertiary headache centre.

Our sample consisted of 548 patients (85.4% women and 14.6% men): 65.5% had CM and 34.5% had EM.

The average annual expenditure per patient was €1482.

The main item of expenditure were medications that represented 86.8% (€1286), followed by specialist visits (10.2%), hospitalizations for (1.9%), diagnostic tests for (1%) and ED visits for (0.1%).

Costs were significantly higher for women than men (€1517 vs. €1274, $p = 0.013$) and increased with age ($p = 0.002$).

The annual direct cost of CM was 4.8-fold higher than that of EM (€2037 vs. €427, $p = 0.001$).

Our results provide a valuable estimate of the annual direct cost of CM and EM patients in the specific setting of a tertiary headache centre and confirm the high economic impact of migraine on both the NHS and patients.

Extended: The purpose of this study was to quantify and compare the annual direct cost of EM and CM, both for the patient and for the National Health System (NHS), using the data of subjects attending an Italian tertiary level headache centre.

The average annual expenditure per patient was €1482 and the variability of expenditure per patient was high, the spending range of was between €51 and €3644, with an inter-quartile difference of €1666 (€511 - €2177) and a coefficient of variation (standard deviation on the arithmetic mean) of the 58.3%.

The main item of expenditure was represented by medications that represented 86.8% (€1286), followed by specialist visits for 10.2% (€153), hospitalizations for 1.9% (€28), diagnostic tests for 1% (€15) and ED visits for 0.1% (€1).

We believe that the methodology used in our study is a step forward compared to the annualization of data based on self-administered questionnaires for the previous 3–4 months.

Governments and decision makers should strongly support these investigations to reveal the true economic and social impact of migraine, particularly when it is chronic.

Introduction

The third edition of the International Classification of Headache Disorders (ICHD-3) sets the threshold for differentiating episodic migraine (EM) from chronic migraine (CM) at 15 days per month in the last 3 months [20].

Migraine also has an important economic burden on patients and society. ".

It is yet not possible to precisely quantify the direct costs of migraine [373].

The available data suggest that CM is widely associated with a higher economic burden than EM, but there is a large variability in estimated costs that depends on the geographical, methodological and temporal differences between the studies [13–172, 374].

The purpose of this study was to quantify and compare the annual direct cost of EM and CM, both for the patient and for the National Health System (NHS), using the data of subjects attending an Italian tertiary level headache centre.

We comparatively evaluated the impact of gender and age on the economic burden of migraine.

Methods

The data used for the current economic analysis come from a retrospective and non-interventional observational analysis of the electronic medical records (EMR) of all subjects with EM and CM (assessed with the ICHD-3 [20]) who consecutively attended our tertiary level headache centre and who were in continuous treatment and underwent follow-up visits in the 2 years prior to 31 January 2019 (data collection date).

The data collected included demographic characteristics, number of specialist visits, number of diagnostic tests (echocardiogram, carotid color doppler, brain / cervical magnetic resonance, brain computed tomography, radiographs, blood tests), number of accesses in the emergency department (ED), days of hospitalization due to the pathology and consumption of medications (acute and preventives).

Demographic and clinical characteristics, number of specialist visits, number of diagnostic tests, number of ED visits, days of hospitalization, and consumption of drugs (reimbursed and not reimbursed by the NHS) were evaluated descriptively.

Results

The diagnostic tests had an average cost per patient of €15, covered by the NHS for 80% (€12).

The mean annual cost for the NHS relating to the hospital management of patients in terms of days of hospitalization was €28 per patient.

As preventive medications, patients with CM used more antidepressants ($p = 0.000$) and anxiolytics ($p < 0.0001$) while EM patients used more nutraceutics ($p < 0.0001$).

Among acute medications, CM patients used more NSAIDs ($p < 0.0001$) and simple analgesics ($p = 0.020$) while patients with EM used more triptans ($p = 0.035$) and combination analgesics ($p < 0.0001$).

The overall mean annual cost of medications was €1286 per patient, of which the 85.1% accounted for preventive treatments.

Discussion

Our study provides a specific quantification of the annual direct cost associated with CM and EM (assessed with the ICHD-3 [20]) based on gender and age of patients in a large population of subjects attending an Italian tertiary level headache centre.

A systematic review used the preliminary data provided by the Eurolight group, and therefore different from those subsequently published for the Eurolight study, and estimated in €222 (in 2009 Euros) the total annual (direct + indirect) cost per patient in Italy (in seven other European countries in the range between €111 and €649) [375].

Our estimate of direct costs is lower (€1482) and this could depend on the different population studied (CM and EM vs. CM and MOH).

Conclusions

Our results provide a valuable estimate of the annual direct cost of patients with CM and EM in the specific setting of a tertiary level headache centre and confirm the high economic impact of migraine on both the NHS and patients.

Patients with CM have had more visits, diagnostic tests and drug use than patients with EM, which led to a direct annual cost of 4.8 times that of EM.

Costs were significantly higher for women than for men and increased with age.

Acknowledgement

A machine generated summary based on the work of Negro, Andrea; Sciattella, Paolo; Rossi, Daniele; Guglielmetti, Martina; Martelletti, Paolo; Mennini, Francesco Saverio. 2019 in The Journal of Headache and Pain.

Economic burden of migraine in Latvia and Lithuania: direct and indirect costs

DOI: https://doi.org/10.1186/s12889-019-7461-2

Abstract-Summary

This study aims at estimating the economic cost of migraine in Latvia and Lithuania, including both direct and indirect costs.

Direct costs encompass the costs of migraine-related health care resource utilization.

Indirect costs are related to productivity loss, the potential or expected earnings lost due to migraine.

The prevalence rate of migraine and the migraine-related health care resource utilization are proxied from the literature, whereas unit cost of medical services and procedures are retrieved from national databases and providers.

For estimating the indirect cost of migraine, we follow the human capital approach.

We find that the mean per-person total cost of migraine is €801 annually in Latvia, and €721 in Lithuania.

In both countries around 30% of total cost is direct cost; cost related to a wide array of migraine-related medical services and interventions.

The total cost of migraine is €112.26 million in Latvia, corresponding to 0.42% of Latvia's GDP.

The total cost of migraine is €149.62 million in Lithuania, corresponding to 0.35% of Lithuania's GDP.

Improvements in care for patients with migraine, such as easier access to structured headache assessment services, wider availability of various procedures and preventive medications would significantly increase direct costs.

This cost increase might be far outweighed by lower migraine-related productivity loss, especially as the prevalence of migraine is the highest in the most productive years of life.

Extended: Direct costs encompass the cost of a wide array of migraine-related medical services and procedures: consultations with doctors, hospitalizations, emergency room visits, diagnostic testing, and medications.

Indirect costs are related to productivity loss caused by reduced labour force participation, absence from work, and reduced productivity while at work.

The prevalence rate is estimated by identifying systematic reviews on migraine prevalence from a systematic review of the literature in PubMed and Scopus.

The prevalence rate of 11.4% estimated by Woldeamanuel and Cowan [358] for Europe involving a sample size of 808,749 participants is used in further analysis as a conservative estimate.

For estimating the direct cost of migraine in Latvia and Lithuania, first migraine-related health care resource utilization is proxied by relying on previous literature.

Background

Migraine sufferers use health care resources more often than individuals without migraine; they visit their general practitioners more frequently, they typically consult a neurologist about their headaches and several diagnostic tests are performed to rule out other causes of migraine symptoms.

Costs associated with migraine-related health care resource utilization are labelled as direct costs.

This study aims at estimating the economic cost of migraine in Latvia and Lithuania.

No study so far has assessed the economic cost of migraine in Latvia, while one study has examined the cost of migraine in Lithuania as part of the Eurolight project [13].

The productivity losses associated with migraine are significant, the indirect cost of migraine is considered to be far more important than direct costs [13, 203, 376].

To estimate indirect cost for employed migraineurs, we consider that the entire annual gross income is lost; this income could have been earned had the individual lived without disabling migraine.

Methods

For estimating the direct cost of migraine in Latvia and Lithuania, first migraine-related health care resource utilization is proxied by relying on previous literature.

We perform a systematic literature review to arrive at a reliable prevalence rate estimate for Latvia and Lithuania; meta-analysis estimates combining the findings of several European studies on migraine prevalence are preferred over single-country estimates.

For estimating the direct cost of migraine in Latvia and Lithuania, first migraine-related health care resource utilization shall be estimated.

A targeted literature review produced a number of valuable studies; in this subsection these studies are reviewed briefly with the aim of identifying the most relevant source to estimate the migraine-related health care resource utilization in Latvia and Lithuania.

Stewart and others [377] report estimates on absenteeism for migraine sufferers participating in the AMPP study in 2005 in the US.

Results

Mean per-person annual costs of migraine is €205.77 in Latvia, and €177.73 in Lithuania.

In Latvia total cost of migraine-related health care resource utilization is €28.83 million, corresponding to 0.11% of Latvia's GDP in 2017 [378].

In Lithuania total cost of migraine-related health care resource utilization is €36.87 million, corresponding to 0.09% of Lithuania's GDP in 2017 [379].

In Lithuania the total productivity loss incurred through unemployed migraine sufferers is €12.51 million, corresponding to 0.03% of Lithuania's GDP in 2017 [379].

Total productivity cost, considering both employed and unemployed migraineurs, is €83.43 million in Latvia, and €112.75 million in Lithuania.

The mean per-person total cost of migraine is €801.37 annually in Latvia, and €721.24 in Lithuania.

Discussion

We document much higher mean per-person annual total cost of migraine in both Baltic countries: €801 in Latvia, and €721 in Lithuania.

For Lithuania, the total cost of migraine reported in this study is in line with the total cost estimate in [13].

Linde and others [13] find that the total cost of migraine in Lithuania is €139.74 million, derived as the product of the per person mean annual cost and the number of migraine sufferers (N = 469,998).

As we have no information from surveys on how much migraine sufferers exactly spend on medications relieving their pain, we relied on a number of assumptions to arrive at a mean per patient medication cost estimate for Latvia and Lithuania.

Unless a survey among migraineurs is carried out, we cannot validate the annual mean per patient medication cost estimate used in this study.

Conclusions
We found that mean per-person total cost of migraine is €801 annually in Latvia, and €721 in Lithuania.

Mean per-person direct cost is €206 in Latvia and €178 in Lithuania.

Mean per-person indirect cost for unemployed migraineurs is €11,111 in Latvia, and €10,085 in Lithuania; this cost is related to reduced workforce participation.

Mean per-person indirect cost for employed migraineurs is €564 in Latvia, and €521 in Lithuania, this cost is related to absenteeism and impairment while at work.

The total cost of migraine is €112.26 million in Latvia, corresponding to 0.42% of Latvia's GDP.

The total cost of migraine is €149.62 million in Lithuania, corresponding to 0.35% of Lithuania's GDP.

Acknowledgement
A machine generated summary based on the work of Lublóy, Ágnes. 2019 in BMC Public Health.

Burden and costs of migraine in a Swedish defined patient population—a questionnaire-based study

DOI: https://doi.org/10.1186/s10194-019-1015-y

Abstract-Summary
Migraine leads to an extensive socio-economic burden in terms of healthcare costs, reduced workforce and quality of life (QoL) but studies of the health-economic consequences in a Swedish context are lacking.

The objective of this study is to map the health-economic consequences of migraine in a defined patient population in terms of healthcare consumption, production loss and QoL in Sweden.

The results are presented in yearly costs per patient and losses in quality adjusted life years (QALYs).

The total cost per patient and year increased with the number of migraine days per month ($p < 0.001$) and varied between approximately €5000 for those with less than 3 migraine days per month and €24,000 per year for those with 21–28 migraine days per month.

The average loss in QALYs per year also increased with the monthly number of migraine days ($p = 0.023$).

Migraine leads to significant societal costs and loss of quality of life.

There appears to be an unmet need and a potential for both cost savings and QoL benefits connected with a reduction in the number of migraine days.

Extended: The results are presented by number of migraine days per month using the following categories; 0, 1–3, 4–5, 6–7, 8–9, 10–14, 15–20 and 21–28 days.

The results are in the upper range of results reported in a previous European study by Bloudek and others 2012, covering data from the UK, France, Germany, Italy and Spain [172], which might be explained by our study almost only including persons with a physician's diagnosis, while Bloudek and others included a large amount of self-diagnosed persons.

Background

Of the disease burden of migraine in Sweden, people with migraine had on average 1.3 migraine episodes per month, which lasted for 19 h on average [380].

Several studies have shown that migraine leads to an extensive socio-economic burden in terms of direct costs, i.e. resources required for health care and treatment [172], indirect costs, i.e. the value of the lost production resulting from migraine-related absenteeism and presenteeism (reduced productivity at work related to migraine) [11, 13] and reduced quality of life (QoL) [11, 381–384].

An earlier European study has reported yearly health care costs related to migraine between € 500 and 3700 per person depending on country and migraine frequency [172].

The average societal cost of migraine in eight European countries has previously been reported to more than € 1200 per person and year where production loss accounted for the main part [13].

The primary objective of this study was to map the health-economic consequences of migraine in a defined patient population in terms of healthcare consumption, production loss and QoL in Sweden based on a survey of people with migraine.

Method

The web-based questionnaire was designed to include questions about age, gender, migraine duration, migraine frequency, diagnoses, number of visits to physicians and visits to other healthcare providers due to migraine, acute drug treatment and preventive drug treatment, sickness absence and QoL. QoL was measured by the generic instrument, Euro-Qol 5 dimensions—5 levels (EQ-5D-5 L) [385], and a disease-specific instrument, HIT-6 (Headache Impact Test) [386].

Depending on the response, the respondent was instructed to recall their last day with/without migraine and again respond to questions on the health status of that day using EQ-5D-5 L. The number of health care visits and the use of preventive drug treatment were asked with a 12 month recall period while acute drug treatment and sickness absence were asked with a 4 week recall period.

The production loss due to long-term work absenteeism was based on the assumption that respondents with migraine and long-term sick-leave would have had the same productivity as the general population (of corresponding age and sex) if they would have been free of migraine.

Results

More than half of respondents had a migraine episode lasting less than 24 h. 52.9% of the respondents reported that last 4 weeks corresponded to an average month regarding migraine frequency, 30.4% reported it as a "better" month than average, and 14.3% that the last month was "worse" than an average month.

The respondents had reported 22 days of sick leave during the last 12 months.

The average total cost per patient and year for respondents with chronic migraine (defined as at least 15 headache days per month, whereof at least 8 days with migraine) was almost three times higher compared to the average total cost per patient and year for respondents with episodic migraine (€21,782 vs. €7598, $p < 0.001$).

The total average loss in QALYs per person and year was 0.10 and significantly higher for respondents with chronic migraine compared to respondents with episodic migraine (0.25 vs. 0.06, $p < 0.001$).

Discussion

This study is retrospective, i.e. respondents reported migraine experience, resource consumption and QoL for a period back in time.

There might also be a risk of bias in the QoL calculation as the reporting of both observable and retrospective EQ-5D might magnify the difference between the ictal and interictal phases, i.e. people might underestimate their QoL at the last attack compared to the current non-migraine day.

In the UK study, people with migraine retrospectively completed EQ-5D for different levels of severity during one single migraine episode resulting in a loss in QoL of 0.21 for mild migraine, 0.34 for moderate migraine and 1.07 for severe migraine.

In the UK study, the respondents assessed their QoL at a time of the migraine episode when feeling the worst.

Respondents reported QoL during a whole migraine episode.

Conclusions

Both costs and loss in quality of life increases with the number of migraine days.

There is potential for both cost savings and quality of life benefits connected with a reduction in the number of headache and migraine days.

Acknowledgement

A machine generated summary based on the work of Hjalte, Frida; Olofsson, Sara; Persson, Ulf; Linde, Mattias. 2019 in The Journal of Headache and Pain.

A universal outcome measure for headache treatments, care-delivery systems and economic analysis

DOI: https://doi.org/10.1186/s10194-021-01269-9

Abstract-Summary

We envisaged a need for a new outcome measure for this purpose, applicable to all forms of treatment, care and care-delivery systems as opposed to comparisons of single-modality treatments.

We noted that pain was the key burdensome symptom of migraine and episodic tension-type headache (TTH), that pain above a certain level was disabling, that it was difficult to put economic value to pain but relatively easy to do this for time, a casualty of headache leading to lost productivity.

We therefore based the measure on time spent in the ictal state (TIS) of migraine or TTH, either as total TIS or proportion of all time.

We expressed impact on health, in units of time, as TIS*DW, where DW was the disability weight for the ictal state supplied by the Global Burden of Disease (GBD) studies.

If the time unit was hours, TIS*DW yielded hours lived with (or lost to) disability (HLDs), in analogy with GBD's years lived with disability (YLDs).

Acute treatments would reduce TIS by shortening attack duration, preventative treatments by reducing attack frequency; health-care systems such as structured headache services would have these effects by delivering these treatments.

For health-care systems, additional gains from provider-training (promoting adherence to guidelines and, therefore, enhancing coverage) and consumer-education (improving adherence to care plans), increasing numbers within populations gaining the benefits of treatments, would be measurable by the same metric.

The new outcome measure expressed in intuitive units of time is applicable to treatments of all modalities and to system-level interventions for multiple headache types, with utility for CEA and for informing health policy.

Extended: Our purposes in this manuscript were first to review the literature for candidate measures in common use that might serve the requirements of economic evaluation; second, subject to findings, to develop a new measure applicable equally to all forms of treatment, care and care-delivery systems for headache regardless of type; and third to demonstrate its broad utility in these applications.

Introduction

The first manuscript in this themed series noted the high ill-health, disability and economic burdens arising from headache disorders worldwide, which persist despite the existence of effective treatments [387].

Lay a difficulty: on what outcome measure(s) might economic evaluation of headache services, as opposed to single-modality treatments such as acute or preventative drugs, be based?

Previous economic evaluations have used both disease-specific clinical outcomes and generic measures [346, 352, 388–393], but choice among the former has been restricted almost exclusively to those used and reported in randomised clinical trials (RCTs), which are rarely designed to support economic evaluation.

Our purposes in this manuscript were first to review the literature for candidate measures in common use that might serve the requirements of economic evaluation; second, subject to findings, to develop a new measure applicable equally to all forms of treatment, care and care-delivery systems for headache regardless of type; and third to demonstrate its broad utility in these applications.

Review of Potential Candidate Measures

We limited it to efficacy measures previously employed in assessing treatments of migraine and/or tension-type headache (TTH), these being the principal headache disorders for which headache services cater [387].

Pain-freedom may be the outcome most desired by people treating either disorder, and the IHS guidelines for clinical trials in migraine recommend PF2 as primary efficacy endpoint [394].

While use of rescue medication is a measure reflecting primary inefficacy, and expresses an important dimension of outcome, it is applicable only to subsets experiencing this: in the trials, about 60% taking ASA for migraine and 85% for TTH did not require rescue.

A disability-based outcome measure could serve all purposes: comparative evaluation of headache treatments of all types, effectiveness assessment of care-delivery systems, and economic analysis.

Development of a New Measure

Acute treatments would diminish (avert) HLDs by shortening attack duration, preventative treatments by reducing attack frequency; health-care systems such as structured headache services [387] would have these effects or would supplement them by delivering or enhancing delivery of these treatments.

Population estimates would involve interpreting SHR24 reports from RCTs (for example [395–397]): acute drugs would reduce pain intensity from disabling levels to non-disabling within 2 h, without recurrence, in the proportion of attacks stipulated by SHR24 as a reported outcome measure.

For multiple attacks over time, HLDs averted would be dtTIS*DW, with the assumption that treatment was taken before or as soon as headache became disabling so that there was no measurable health loss before treatment.

It would not satisfactorily account for serious AEs, which always require separate recording.) For preventative treatments, effects would be expressed in HLDs averted through the same product dtTIS*DW, again reducible, should the purpose require it, by the proportion of treatment discontinuations due to AEs.

Discussion

This presentation has described the conception and delineation of a new universal outcome measure applicable to treatments of all modalities of headache of multiple types (migraine or TTH, but also of other types manifesting as attacks definable in terms of duration and frequency) and expressed in intuitive units of time.

Multiple outcome measures existed already for treatments of migraine and TTH, and several were widely accepted, though not, perhaps, with universal agreement [398, 399].

In the context of economic analysis, with the purpose of valuing interventions of different types relative to each other, existing measures were applied with difficulty.

A second, that acute treatment is initiated before or as soon as pain becomes disabling, is an assumption necessary to establish a time zero for purposes of effect calculation.

Because it discounts mild pain, the measure has a more restricted application to TTH than to migraine: TTH is, usually but not always, a mild-to-moderate headache [400].

Conclusions
We have described the development of a new universal outcome measure expressed in intuitive units of time and applicable to treatments of all modalities of headache of multiple types.

The measure equips economic analysis of interventions, including implementation of structured headache services, for purposes including informing health policy.

Acknowledgement
A machine generated summary based on the work of Steiner, Timothy J; Linde, Mattias; Schnell-Inderst, Petra. 2021 in The Journal of Headache and Pain.

Validation of a self-reported instrument to assess work-related difficulties in patients with migraine: the HEADWORK questionnaire

DOI: https://doi.org/10.1186/s10194-018-0914-7

Abstract-Summary
The degree to which work-related difficulties are recognized in headache research is poor and often carried out with inadequate information such as "reduced ability to work as usual", which do not capture at all the variety of difficulties and the factors that impact over them.

The aim of this paper is to present the validation of the HEADWORK questionnaire, which addresses the amount and severity of difficulties in work-related tasks and the factors that impact over them.

HEADWORK factor structure was assessed with exploratory and confirmatory factor analysis; internal consistency and construct validity were addressed as well.

Factor analysis retrieved two different scales: "Work-related difficulties", composed of eleven items which explain 67.1% of the total variance, and "Factors contributing to work difficulties", composed of six items which explain 52.1% of the total variance.

HEADWORK is a 17-item, two-scale questionnaire addressing the impact of migraine on work-related difficulties in terms of difficulties in general or specific skills, and the factors contributing to these difficulties, defined as negative impact on work tasks.

Extended: The aim of this paper is to validate this new questionnaire and report its measurement properties.

Future studies are also needed to test the validity of HEADWORK in other headache disorders, such as tension-type headache.

Background

Presenteeism is the main driver of migraine cost and burden: in fact, for each lost workday, patients with EM and CM work three to four days with reduced productivity [401, 402], and the cost associated to presenteeism is higher than that associated to absenteeism [13, 403, 404].

Fourteen topics, that could be referred to difficulties with work-related activities, were transformed into MESH terms and were used to search for relevant publications in which these difficulties were experienced by patients with EM, CM, chronic daily headache or MOH.

The main reason for the paucity of information on this topic is, in our opinion, the lack of patient-reported outcome measures (PROMs) specifically aimed to capture the presence, the severity and the type of work-related difficulties in patients with EM and CM.

Given the paucity of literature data, we ran a qualitative study with the aim of exploring which were the most relevant difficulties experienced by patients with their work activities and which were the factors that contributed most to these difficulties, getting indications directly from employed patients with EM and CM.

Methods

The questionnaire is composed of 14 items that form three scales, namely role-restriction (RR), role-prevention (RP) and emotional function (EF): each scale has a 0–100 score, with lower scores indicating lower health-related QoL. Items refer to different daily activities or social situations, and patients have to rate how frequently migraine determined an impact on these activities, thinking back to the previous 4 weeks, using a 6-point scale from never to always.

We used Pearson's correlation, and expected that HEADWORK scales: (a) were directly correlated with all the other variables (with the exclusion of MSQ scores, and with the estimated average productivity, where an inverse correlation is expected), and with correlation coefficients <.700; (b) had a stronger correlation with the WHODAS-12 than with the MSQ scores, as the construct underlining HEADWORK is the amount and severity of difficulties with work-related activities; (c) had a stronger correlation with the average pain severity and the average work ability than with the variables related to frequency of headache, workdays lost and days worked with reduced productivity.

Results

The second HEADWORK scale, which we named "Factors contributing to work difficulties", is composed of six items with a theoretical range 6–30: actually, it ranged between 6 and 29 and its mean was 15.8 (SD 5.0).

HEADWORK scales were more strongly correlated with the WHODAS-12 than with MIDAS and MSQ scores and also with the average pain severity and the

average work ability rather than with frequency of headache, workdays lost and days worked with reduced productivity.

Consistently with our expectations, females and patients with CM showed higher scores at both HEADWORK scales, than males and EM patients, with medium to large ES.

Contrary to our expectations, people working less than 40 h per week showed higher scores than those working less only at HEADWORK "Factors contributing to work difficulties" scale, with a small ES, while no differences were found for the subscale "Work-related difficulties".

Discussion

Our results showed that the different dimensions regarding the negative influence of migraine on work activities, i.e. the amount and severity of difficulties in work-related tasks and the factors that impact over them, can be measured by two distinct scales.

It will be very interesting to understand what may be the main drivers of HEADWORK scales change, considering the potential role of different variables, such as frequency (which is generally considered as the major outcome measure in headache research—but showed a modest correlation with HEADWORK scores), or severity of headaches, but also presence of treatment-related side effects, particularly such those that may have an important role on work-place activities and productivity, such as somnolence, sedation dizziness or fatigue, and which are relatively common with preventive anti-migraine medications.

Conclusions

We presented the validation of the HEADWORK questionnaire, a brief questionnaire which addresses the impact of migraine on work-related difficulties in terms of presence, and severity, of difficulties in general and specific skills, and it also addresses the factors contributing to these difficulties, defined as negative impact on work tasks.

We propose HEADWORK as a feasible way to produce reliable work-related disability weights in studies evaluating the burden of episodic and chronic migraine in epidemiological and clinical research.

Future studies are also needed to test the validity of HEADWORK in other headache disorders, such as tension-type headache.

Acknowledgement

A machine generated summary based on the work of Raggi, Alberto; Covelli, Venusia; Guastafierro, Erika; Leonardi, Matilde; Scaratti, Chiara; Grazzi, Licia; Bartolini, Marco; Viticchi, Giovanna; Cevoli, Sabina; Pierangeli, Giulia; Tedeschi, Gioacchino; Russo, Antonio; Barbanti, Piero; Aurilia, Cinzia; Lovati, Carlo; Giani, Luca; Frediani, Fabio; Di Fiore, Paola; Bono, Francesco; Rapisarda, Laura; D'Amico, Domenico. 2018 in The Journal of Headache and Pain.

The relationship between headache-attributed disability and lost productivity: 1. A review of the literature

DOI: https://doi.org/10.1186/s10194-021-01264-0

Abstract-Summary
Headache disorders are disabling and have a significant impact on productivity.

We followed PRISMA guidelines in specifying search terms and syntax and in article selection.

We used the term "disability" in the search, accepting any meaning that authors attached to it, but this proved problematic.

In article selection, we included only those that purported to measure disability as so defined and lost productivity.

We included further articles identified from review of the bibliographies of selected articles.

The literature search found 598 studies, of which 21 warranted further review.

Ten applied incompatible definitions of disability and/or lost productivity.

Four reported lost productivity but not disability.

Eight studies reported and measured both but did not assess the association between them or provide the means of doing so.

The literature is silent on the relationship between headache-attributed disability and lost productivity.

Extended: We followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines in specifying search terms and syntax and in article selection.

In article selection, therefore, we defined disability restrictively, only in this sense, notwithstanding our reservations about it expressed earlier.

Eight studies reported and measured both as we defined them, but did not assess association between the two or provide the means of doing so [204, 263, 264, 266, 268, 372–407].

Background
The Global Burden of Disease study (GBD) in its multiple iterations shows that three headache disorders—migraine, tension-type headache (TTH) and medication-overuse headache (MOH), which is a sequela of migraine or TTH—are major contributors to public ill health [8–368].

In GBD2019, the most recent to be analysed, headache disorders were estimated to be responsible for 46.6 million years lived with disability (YLDs) globally (5.4% of all YLDs), with an age-standardized rate of 602.5 YLDs/100,000 person-years [368, 369].

For episodic headache disorders such as migraine and TTH, two essential health states are recognised: ictal (during attacks) and interictal (between attacks) [50, 408].

The ill health associated with headache disorders, and the disability that is its consequence, inevitably lead to lost productivity [50].

The Eurolight project, a survey conducted in ten European countries, estimated societal losses attributable to all headache disorders (direct and indirect costs) at well over €100 billion per year, with more than 90% attributable to lost productivity [409].

Methods

We conducted a systematic review of the English-language literature evaluating the relationship between headache-attributed ill health (expressed as symptom burden or disability) and lost productivity.

We followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines in specifying search terms and syntax and in article selection.

In the initial search, lost productivity was defined to include days of absenteeism from or < 50% productivity in paid or household work (the MIDAS construct [237]), estimated either over the preceding 3 months or in association with headache yesterday [50].

We took the term disability to have any meaning attached to it in the literature, but in the subsequent selection of articles this was problematic.

We included studies that purported to measure disability so defined and lost productivity defined only as above.

All full-text articles found in this process were scrutinised for evidence or comment regarding the relationship between disability and lost productivity.

Results

Ten applied different definitions of headache-attributed disability and/or lost productivity, incompatible with ours [197, 377, 410–417].

Four measured lost productivity according to our definition, but did not report disability [4, 118, 131, 418].

Eight studies reported and measured both as we defined them, but did not assess association between the two or provide the means of doing so [204, 263, 264, 266, 268, 372–407].

The literature was entirely silent with regard to the relationship between headache-attributed disability and lost productivity.

Discussion

Our systematic review of the literature, with the enquiry framed broadly, found not just that it said nothing on the relationship between headache-attributed disability and lost productivity but that this issue of substantial health-economic importance had not even been addressed [90, 118, 131, 408–419].

There is a wealth of empirical evidence of the lost productivity burden of headache and its economic consequences (e.g., [118, 131, 204, 264, 266, 270, 405, 406, 409–419]), to which indirect costs (essentially from lost productivity) are far more contributory than direct health-care costs [409].

If pain intensity were introduced in its place (pTIS * mean intensity) to generate what might be considered a measure of symptom burden—impairment rather than "disability"—the result would arguably be a more nuanced measure of health loss,

which might relate to lost productivity more closely and offer a better way forward in future studies.

Some population studies have found that lost productivity due to headache (in percentage time units) exceeded percentage disability estimated as pTIS * DW [263, 266].

Conclusions
A careful search of the English-language literature found nothing on the relationship between headache-attributed disability and lost productivity.

A prerequisite is to clarify what is meant by "disability".

Acknowledgement
A machine generated summary based on the work of Kothari, Simple Futarmal; Jensen, Rigmor Hølland; Steiner, Timothy J. 2021 in The Journal of Headache and Pain.

Migraine day frequency in migraine prevention: longitudinal modelling approaches

DOI: https://doi.org/10.1186/s12874-019-0664-5

Abstract-Summary
Many clinical trials report outcomes using the frequency of an event over a set period of time, for example, the primary efficacy outcome in most clinical trials of migraine prevention is mean change in the frequency of migraine days (MDs) per 28 days (monthly MDs [MMD]) relative to baseline for active treatment versus placebo.

Parametric models of change in MMD for migraine preventives were assessed using data from erenumab clinical studies.

For each trial, two longitudinal regression models were fitted: negative binomial and beta binomial.

Using the erenumab study data, both the negative binomial and beta-binomial models provided unbiased estimates relative to observed trial data with well-fitting distribution at various time points.

This proposed methodology, which has not been previously applied in migraine, has shown that these models may be suitable for estimating MMD frequency.

Modelling MMD using negative binomial and beta-binomial distributions can be advantageous because these models can capture intra- and inter-patient variability so that trial observations can be modelled parametrically for the purposes of economic evaluation of migraine prevention.

Background
Examining the mean change in MMD frequency across a cohort of patients may not capture the clinically meaningful effects of migraine prevention, such as the

improvement in an individual's ability to perform daily activities or health-related quality of life.

It is considered appropriate for unrestricted count data [420], and because MMD frequency is a count variable, Poisson distribution may be considered an eligible model.

A preliminary analysis, based on cross-sections of the data, has indicated that the beta-binomial is an alternative distribution that could be used to model MMD frequency data and has been shown to provide comparable fits to the negative binomial models [421].

Longitudinal negative binomial and beta-binomial regression models that accommodate over-dispersed data have not been used previously in the assessment of MMD frequency.

Methods

Three longitudinal regression models were evaluated for their ability to estimate the frequency distribution of MMD: multilevel/hierarchical negative binomial regression (with constant dispersion parameter over time), multilevel beta-binomial regression (with constant ICC over time) and the multilevel Poisson model.

The α and β parameters of the beta-binomial distribution can be calculated from the mean and ICC, which represents the strength of the correlation between days for the same patient, i.e. daily outcomes are likely to be similar for the same patient.

The beta-binomial probability function is specified as follows: Where: k is the number of MDs P (Y = k) is the probability of patients experiencing τ MDs N is the number of days in the cycle (28 days) B () is the beta function α and β are the parameters of the underlying beta distribution.

This approach allows the regression models to estimate both the change in MMD frequency over time and the dispersion parameters required to reproduce the distribution of patient-level MMD frequency.

Results

The predicted distributions show a good fit to the actual observations in the EM and CM study; the RMSE estimates were 0.075 and 0.082 for negative binomial regression, 0.102 and 0.081 for beta-binomial regression and 0.142 and 0.152 for Poisson regression for EM and CM studies respectively.

The MAE estimates were 0.246 and 0.330 for negative binomial regression, 0.336 and 0.339 for beta-binomial regression, and 0.466 and 0.654 for Poisson regression for EM and CM studies respectively.

For the EM study, the negative binomial mean MMD for weeks 0, 4, 12 and 24 were 8.261, 7.199, 6.434 and 6.421, respectively.

For the CM study, the negative binomial mean MMD for weeks 0, 4, 8 and 12 were 18.111, 15.418, 14.538 and 13.997, respectively.

Discussion

The approaches described here allows the distribution of individual patients by MMD to be modelled using only the clinical endpoint of the studies - the mean change from baseline in MMD compared with placebo at a single time point.

The Poisson and negative binomial distributions have been used in previous studies to model count data [422–424] and have also been used to approximate headache day frequency data in published migraine studies [425, 426].

Modelling data as continuous events rather than categorising data has many advantages, including the reduction of bias and more accurately estimating the extent of variation in outcomes between groups [427]. This analysis takes the approach of modelling migraine frequency as a continuous outcome and addresses a key limitation of previous modelling approaches which define health states by categorical event frequency or response status.

The proposed approach also provides a greater capability to model indirect comparisons than previous models, as the published endpoints of clinical studies (i.e. mean change in MMD) can be used to estimate the distributions of patients, assuming the patient-level variation is similar across cohorts.

Conclusions
Modelling MMD with regression models that can accommodate overdispersion in a longitudinal framework is a statistically valid method to estimate the variation in MMD, both within and between individual patients.

This approach, which estimates the distribution of patients by MMD, allows outcomes (such as health-related quality of life or pain medication use) to be directly quantified and linked to MD frequency.

Acknowledgement
A machine generated summary based on the work of Di Tanna, Gian Luca; Porter, Joshua K.; Lipton, Richard B.; Brennan, Alan; Palmer, Stephen; Hatswell, Anthony J.; Sapra, Sandhya; Villa, Guillermo. 2019 in BMC Medical Research Methodology.

Disability, quality of life, productivity impairment and employer costs of migraine in the workplace

DOI: https://doi.org/10.1186/s10194-021-01243-5

Abstract-Summary
There is a paucity of evidence on the impact of migraine and other headache disorders and the cost and productivity losses in the workplace.

The number of days when productivity at work was reduced by half or more because of headache was significantly higher in migraine compared to TTH.

The economic loss due to absenteeism for migraine was calculated to be $ 238.3US$/year/person for day-off and 90.2US$/year/person for half-day off using migraine disability assessment score (MIDAS).

The economic loss due to presenteeism for migraine was calculated to be $ 375.4US$/year/person using MIDAS and 2217US$/year/person using work productivity and activity impairment questionnaire (WPAI).

Estimated cost of productivity loss associated with presenteeism using WPAI was calculated at 21.3 billion US$/year in Japan as a whole.

This study revealed a high prevalence and disease burden among employees with migraine that is associated with substantial losses in productivity and employer cost.

These results support the development and implementation of workplace programs to improve migraine management in the workplace and reduce the burden and costs associated with lost workplace productivity.

Extended: The number of day-off multiplied by the daily wage and the number of half-days off multiplied by 50% of the daily wage, and these were converted to annual amounts.

The economic loss due to absenteeism and presenteeism caused by headache was calculated using the age-specific wage in the IT industry according to the Basic Survey on Wage Structure in 2018 by the Ministry of Health, Labor and Welfare, since this survey was conducted in 2018 [428].

The economic loss due to presenteeism was calculated by multiplying the number of the days when work productivity was reduced to less than half from MIDAS by wage multiplied by 0.5 and converted to annual amount.

We believe that quantitative assessment of the reduction in work productivity and presenteeism due to headache should be possible in this homogeneous population.

Introduction

Headache disorders are a public health concern due to their high prevalence, disability and financial cost to society [429].

The World Health Organization estimates that the three most prevalent neurologic disorders worldwide are tension-type headache (1.5 billion), migraine (958.8 million) and medication overuse headache (58.5 million) [226].

Despite the prevalence and disability associated with migraine, many may be suffering in silence at work, resulting in loss of significant productivity in Asian countries with growing economies [430].

To initiate a public health approach to headache disorders, we deployed a research survey on prevalence rates and disease burden associated with headache in the workplace.

Workers of IT companies have been engaging in intellectual and cognitively challenging work and are considered to be a suitable population for our initial study on the impact on work productivity as a result of headache disorders.

Methods

To estimate the economic loss due to headache, we calculated the number of days of headache, moderate or severe headache, the days off work due to headache, the half-days off work due to headache, and when work efficiency was reduced to less than half due to headache, using MIDAS.

The economic loss due to absenteeism and presenteeism caused by headache was calculated using the age-specific wage in the IT industry according to the Basic Survey on Wage Structure in 2018 by the Ministry of Health, Labor and Welfare, since this survey was conducted in 2018 [428].

The economic loss due to presenteeism was calculated by multiplying the number of the days when work productivity was reduced to less than half from MIDAS by wage multiplied by 0.5 and converted to annual amount.

When calculating the amount of economic loss due to presenteeism from WPAI data, we assumed that the degree of work efficiency decline was the same on days with headaches.

Results

Statistically, the mean age of M and HA was significantly younger than TTH ($p < 0.001$, one-way ANOVA followed by Bonferroni's post hoc test).

BMI of M was significantly lower than TTH ($p = 0.049$, one-way ANOVA followed by Bonferroni's post hoc test).

GH was significantly lower in M/TTH than NHA and in M than TTH and NHA ($p < 0.05$, one-way ANOVA followed by Bonferroni's post hoc test).

M, M/TTH and HA showed significantly higher values compared to TTH for lack of understanding of headaches in the workplace, impaired relationships due to headaches and burdening bosses and colleagues with headaches ($p < 0.01$, one-way ANOVA followed by Bonferroni's post hoc test).

M and M/TTH showed significantly higher values compared to TTH and HA to lose their energy to work and not to concentrate on work due to headache ($p < 0.01$, one-way ANOVA followed by Bonferroni's post hoc test).

Discussion

This study revealed a high prevalence and disease burden among employees with migraine that is associated with substantial losses in productivity and employer cost.

Amongst the 2458 respondents (98.5% of those surveyed) 17% had migraine, and compared to individuals with no headache or tension-type headache, people with migraine had significantly more missed workdays, and experienced a greater impact on work productivity, physical and mental health and economic cost to the employer.

Using economic loss due to migraine and working population data from the Statistics Bureau of Japan, the annual economic loss due to presenteeism is US $3.3 billion, calculated from the number of days when work efficiency has fallen to less than half due to headaches using MIDAS.

This suggests that migraine may have an impact on work efficiency and economic losses even on days without headache.

Conclusions

This employee population survey revealed a high prevalence and disease burden of migraine that is associated with substantial losses in productivity and employer cost.

These results support the development and implementation of workplace programs to improve migraine management in the workplace and reduce the burden and costs associated with lost workplace productivity.

Acknowledgement
A machine generated summary based on the work of Shimizu, Toshihiko; Sakai, Fumihiko; Miyake, Hitoshi; Sone, Tomofumi; Sato, Mitsuhiro; Tanabe, Satoshi; Azuma, Yasuhiro; Dodick, David W. 2021 in The Journal of Headache and Pain.

Migraine treatment and healthcare costs: retrospective analysis of the China Health Insurance Research Association (CHIRA) database

DOI: https://doi.org/10.1186/s10194-020-01117-2

Abstract-Summary
Information on prescribing patterns and treatment costs of migraine in China is limited.

This retrospective analysis of the China Health Insurance Research Association (CHIRA) medical insurance claims database in 2016 to 2017 evaluated treatment patterns, direct medical costs, and healthcare resource utilization among adults with migraine in mainland China.

Of 108,375 patients with headache-related outpatient visits, 10,652 were adults with migraine (mean age 51.4 years, 55.4% female).

Migraine patients were prescribed acute medication (26.4%), preventive medication (15.0%), and Chinese patent and herbal medicines (24.5% and 11.7%, respectively).

Medication costs for traditional Chinese medicine (22.4 USD per patient) were higher than for Western medicine (13.5 USD).

Among migraine patients in China, NSAIDs were commonly prescribed as acute medication, while utilization of migraine-specific triptans and preventive medications was low.

Extended: This retrospective analysis of the China Health Insurance Research Association (CHIRA) nationwide medical insurance claims data aimed to understand the treatment patterns, direct medical costs, and healthcare resource utilization among adult patients with migraine in mainland China.

The findings indicate an economic burden associated with the diagnosis and treatment of migraine in China, and possible unmet needs for effective migraine-specific acute treatment as well as preventive medication.

Background
Migraine treatment guidelines for China are consistent with those for Europe and the United States (US) in supporting a stratified approach to acute (abortive) treatment, whereby medication choice is based on attack severity and symptoms, the

efficacy and side effect profile of the drug, and the patient's previous response to acute treatment [50, 90, 118, 131, 142, 183–432].

Although there is substantial evidence for the economic burden of migraine in the US and Europe, this information cannot be generalized to China because of the differences in diagnosis and treatment practices, availability of prescription medication, and use of traditional Chinese medicine alongside Western medicine.

A population-based survey in China in 2009 estimated the total annual direct costs of migraine diagnosis and treatment to be 58.0 billion Chinese yuan renminbi (CNY) (8.4 billion US dollars [USD]) [4].

Methods

The CHIRA database is a medical insurance management information system initiated in 2007 that contains nationwide consecutive inpatient and outpatient visit claims data of urban basic medical insurance in China.

All outpatient visit and healthcare use information for the diagnosis and treatment of headache in 2016 and 2017 was extracted from the CHIRA database.

Adult patients (≥18 years) were selected who had a primary diagnosis of migraine, identified by International Statistical Classification of Diseases and Related Health Problems revision 10 (ICD-10) code (ICD-10 G43.0, G43.1, G43.2, G43.3, G43.8, G43.9) and supplemented by searching physician Chinese character descriptions against translations from the World Health Organization Chinese version of ICD-10.

Patient information identified from the CHIRA database included age, gender, comorbidities (predefined as anxiety, major depressive disorder, epilepsy, fremitus, and insomnia), and medical insurance type (Urban Employee Basic Medical Insurance or Urban Residents Basic Medical Insurance).

Medication costs were calculated for prescribed Western medicine and for Chinese patent or herbal medicine.

Results

The majority (68.8%) of patients receiving acute medication were prescribed non-aspirin NSAIDs, with ibuprofen being the most common (36.5%).

Other classes of acute medication were each prescribed to ≤8.0% of patients receiving acute medication, including opioids (7.1%) and ergot alkaloids (6.1%).

Only 3.3% of patients receiving acute medication were prescribed a triptan.

Other classes were each prescribed to less than 4% of the patients receiving preventive medication.

The proportions of patients prescribed Chinese patent or herbal medicine were comparable with those prescribed Western acute (26.4%) or preventive (15.0%) medications.

Discussion

This is the first study to describe the treatment patterns and costs of migraine treatment in urban mainland China using a retrospective analysis of the large CHIRA medical insurance claims database.

Only 26.4% of patients were prescribed acute medication, which contrasts with higher rates (73%) from Japanese insurance claims data [433]; this may reflect

cultural differences in prescribing patterns or greater reliance on over-the-counter rather than prescription acute medications in China.

Although the Level A evidence supporting triptan use is recognized in Chinese as well as international treatment guidelines [50, 90, 118, 131, 142, 183–432], the rate of triptan prescribing in this study was low; of patients receiving acute medication, only 3.3% were prescribed triptans.

Although we cannot determine whether the 7.1% of patients who were prescribed opioids in our study were non-responders to other medications, this rate of opioid prescription demonstrates an unmet need for additional migraine-specific acute treatments that lack the safety concerns of opioids.

Conclusions

Prescribing rates for acute medication in China were low compared with the US and Japan.

NSAIDs were the most commonly prescribed acute medication, while there was low utilization of migraine-specific triptans and preventive medications.

The findings indicate an economic burden associated with the diagnosis and treatment of migraine in China, and possible unmet needs for effective migraine-specific acute treatment as well as preventive medication.

Acknowledgement

A machine generated summary based on the work of Yu, Shengyuan; Zhang, Yanlei; Yao, Yuan; Cao, Haijun. 2020 in The Journal of Headache and Pain.

Total health insurance costs in children with a migraine diagnosis compared to a control group

DOI: https://doi.org/10.1186/s10194-021-01349-w

Abstract-Summary

We aimed to assess the migraine-related health care costs in 6 to 11 year old children in Germany.

Using claims data of a large German health insurer (BARMER), overall annual health care costs of 6 to 11 year old children with a diagnosis of migraine in 2017 (n = 2597) were compared to a control group of 6 to 11 year old children without a headache diagnosis between 2013 and 2017 (n = 306,926).

Children with migraine caused considerably higher annual per capita health care costs than children without a headache diagnosis (migraine group: € 1018, control group: € 618).

Excess costs directly related to migraine amounted to € 115.

The remaining excess costs were related to comorbidities, which were more frequent in the migraine group.

6–11 year old children with a migraine diagnosis cause significant direct and comorbidity related excess costs in the German health care system.

Extended: The remaining excess costs in the migraine group are explained by the more frequent comorbidities in the migraine group.

This resulted in the same factor for migraine (1.16) and a slightly lower adjusted excess cost for migraine (€ 108 with 95% CI: 50;168).

Introduction

Several publications analyzed health care costs for adult migraine patients, based on questionnaires [13, 172, 434] or secondary (health insurance) data [181, 435, 436].

Although migraine often starts already in primary school age [437], data on migraine related costs in children is scarce.

A large health care data analysis from the US on children aged 2–17 years with headache found annual per capita excess costs of US$ 687 based on 779 children with headache [438].

Estimation of migraine related health care costs for children using secondary (health care) data faces some specific challenges.

Identification of migraine related treatment costs can only be achieved by advanced analysis of health insurance data.

Our analysis of secondary health care data with 309,523 children in total allows an elegant and (due to our large dataset) reliable estimation of both direct and comorbidity related health care costs for migraine in Germany.

Material and Methods

Using ATC codes, we determined three groups of possibly headache/migraine related drugs and calculated costs of painkillers (including triptans), antiemetic drugs and headache preventive drugs.

We calculated the proportion of girls, the mean age and the mean number of different ICD-10 chapters with comorbidities in control and migraine group.

Frequencies and relative risks of comorbidities by ICD-10 chapters in control and migraine group were determined.

This model allows to disentangle the estimated excess costs to directly migraine-related costs and costs associated to the higher frequency of comorbidities in the migraine group.

We modeled likewise the adjusted disease-related costs for each of the preselected comorbidity chapters and calculated the impact of these comorbidity chapters on cost differences between the migraine and control groups.

To assess the impact of a recent migraine diagnosis on costs, we additionally calculated the comorbidity model for total costs for incident migraine cases only.

Results

Total per capita costs were € 400 higher in the migraine compared to the control group.

After adjustment for comorbidities the migraine related excess costs were reduced to € 115.

In the migraine group, 44% of the children had a diagnosis from this chapter, thus, the average cost of comorbidities from this chapter per child was 0.44* € 807 = € 355, compared to 0.31* € 807 = € 250 in the control group.

€ 105 of the total excess costs in the migraine group were due to the higher proportion of children with a comorbidity from the "Mental and behavioural disorders" chapter.

Comorbidities from the chapters "Mental and behavioural disorders", "Codes for special purposes" and "Diseases of the eye and adnexa" explained most of the cost difference between migraine and control group.

Discussion

Main results of the present study are: A diagnosis of migraine in 6–11 year old children was associated with an average of € 400 per capita excess health care costs per year, of which € 115 (29%) were directly related to migraine.

The remaining 71% of excess costs were related to comorbidities, which were more frequent in children with migraine.

The annual per capita excess costs in the migraine group were largely generated by primary care physician and specialist visits (€ 211 in total, corresponding to 53%, of which € 70 were directly migraine-related), with visits to the paediatrician and general practitioner accounting for the largest part.

These amounted to € 19 or 5% of the total excess costs in the migraine group.

Conclusion

Direct health care costs for children were principally caused by visits to primary care physicians and specialists.

A large proportion of the costs turned out not to be directly related to migraine, but rather to the treatment of comorbidities associated with migraine, which therefore should be a focus of future research and treatment strategies.

The fact that the largest proportion of migraine-related costs in children stemmed from visits to paediatricians and general practitioners shows that these are the most promising targets for implementation of migraine prevention strategies in children.

Acknowledgement

A machine generated summary based on the work of Obermeier, Viola; Murawski, Monika; Heinen, Florian; Landgraf, Mirjam N.; Straube, Andreas; von Kries, Rüdiger; Ruscheweyh, Ruth. 2021 in The Journal of Headache and Pain.

Economic consequences of migraine in Sweden and Implications for the cost-effectiveness of onabotulinumtoxinA (Botox) for chronic migraine in Sweden and Norway

DOI: https://doi.org/10.1186/s10194-020-01162-x

Abstract-Summary

This study aimed to describe the economic consequences of migraine in Sweden using cost of illness survey data and, based on this data, assess the cost-effectiveness

of onabotulinumtoxinA (Botox) for the treatment of chronic migraine in Sweden and Norway.

Resulting costs were estimated as annual averages over subgroups of average monthly headache days.

Some results were used to inform a Markov cost-effectiveness chronic migraine model.

Results from the cost of illness analysis (n = 454) indicated a clear correlation between decreased QoL and increased costs with increasing monthly headache days.

Total annual costs ranged from EUR 6221 in patients with 0–4 headache days per month, to EUR 57,832 in patients with 25–31.

The cost-effectiveness analyses indicated that in Sweden, Botox was associated with 0.223 additional QALYs at an additional cost of EUR 4126 compared to placebo, resulting in an incremental cost-effectiveness ratio (ICER) of EUR 18,506.

In Norway, Botox was associated with 0.216 additional QALYs at an additional cost of EUR 4301 compared to placebo, resulting in an ICER of EUR 19,954.

In people with migraine, an increase in monthly headache days is clearly related to lower QoL and higher costs, indicating considerable potential costs-savings in reducing the number of headache days.

Botox reduces headache days and is a cost-effective treatment for chronic migraine in Sweden and Norway.

Extended: In Norway, Botox is reimbursed for CM in patients who previously tried a beta-blocker (propranolol, metoprolol or atenolol) and topiramate.

In Norway, Botox treatment was associated with 5.480 QALYs and a cost of EUR 11,501 per patient over a 10-year time horizon.

When considering indirect costs, Botox is dominating, i.e. Botox provide additional outcome at a lower cost.

Background

A Swedish survey study found that increased monthly migraine days are associated with significant QoL losses and cost increases, with productivity losses comprising the vast majority (80%) of the total [439].

Pharmaceutical treatments for migraine in Sweden and Norway include acute medications for symptom relief during migraine attacks and prophylactic medications intended to prevent and reduce severity of future attacks.

Botox is indicated in both Sweden and Norway for symptom relief in adults fulfilling criteria for chronic migraine (CM) in patients who have responded inadequately or are intolerant of prophylactic migraine medications [440].

In Sweden, erenumab and fremanezumab are reimbursed in patients with CM who have responded insufficiently or are intolerant to at least two prophylactic migraine treatments.

In Norway, erenumab, fremanezumab and galcanezumab are reimbursed for CM in patients who have responded insufficiently or are intolerant to at least three different classes of prophylactic migraine treatments.

Methods

Thirdly, the primary endpoint in the pivotal trials for Botox in patients with CM was the number of headache days per month.

This was a conservative approach, as placebo patients in the trials saw considerable reductions in number of headache days, which is unlikely to be observed in best supportive care in a real-world setting.

In the base case scenario, patients who did not see a ≥ 30% reduction in headache days within the first two cycles (24 weeks) were assumed to discontinue treatment and remain in the "no treatment" health states on placebo transition probabilities for the remainder of the simulation.

The model contains transition probabilities calculated from the clinical trial database for several different patient populations, defined by the number of previously tried oral prophylactics and including or excluding patients overusing acute medications.

Results

Average annual indirect costs ranged from EUR 5105 in the 0–4 headache days group to EUR 52,521 in the 25–31 headache days group.

In Sweden, Botox treatment was associated with 5.711 quality adjusted life years (QALYs) and a cost of EUR 20,700 per patient over a 10-year time horizon.

Botox was associated with 0.223 additional QALYs at an additional cost of EUR 4126 as compared to placebo, resulting in an incremental cost-effectiveness ratio (ICER) of EUR 18,506.

In Norway, Botox treatment was associated with 5.480 QALYs and a cost of EUR 11,501 per patient over a 10-year time horizon.

In Sweden, the probabilistic incremental cost was EUR 4081 with corresponding incremental QALYs of 0.220, resulting in a probabilistic ICER of 18,556.

In Norway, the probabilistic incremental cost was EUR 4270 with corresponding incremental QALYs of 0.215, resulting in a probabilistic ICER of EUR 19,872.

Discussion

A 2013 UK study assessed the CE of Botox in adults in CM compared to placebo, and estimated an ICER of GBP 15,028, assuming a 2-year time horizon and not including indirect costs.

In 2014, an Italian study comparing Botox to placebo in patients with CM estimated an ICER of EUR 9407, assuming a 2-year time horizon and not including indirect costs.

When attempting to mirror the CGRP analyses as closely as possible (patients with ≥3 previous treatments, 10-year time horizon, 30% stopping rule and using utility values mapped from MSQ to EQ-5D) the difference in QALYs for Botox vs placebo were 0.209 and with a corresponding ICER of EUR 16,625 in Sweden and 0.203 QALY difference with a corresponding ICER of 18,462 in Norway.

Conclusions
In people with migraine the number of average monthly headache days is clearly related to lower QoL and higher costs, indicating considerable potential costs-savings in reducing the number of headache days.

The CE results indicate that considering a 10-year time horizon, Botox is a cost-effective treatment option for migraine in Sweden and Norway.

When considering indirect costs, Botox is dominating, i.e. Botox provide additional outcome at a lower cost.

Acknowledgement
A machine generated summary based on the work of Hansson-Hedblom, Amanda; Axelsson, Isabelle; Jacobson, Lena; Tedroff, Joakim; Borgström, Fredrik. 2020 in The Journal of Headache and Pain.

My Migraine Voice survey: disease impact on healthcare resource utilization, personal and working life in Finland

DOI: https://doi.org/10.1186/s10194-020-01185-4

Abstract-Summary
A global My Migraine Voice survey was conducted in 31 countries among 11,266 adults who suffered from ≥4 monthly migraine days (MMD).

Comorbidities, migraine-related emotional burden and impact on daily living and work productivity and activity impairment (WPAI) were assessed.

Subgroup analysis on healthcare resource utilization (HCRU) due to migraine was assessed by visits to healthcare practitioners (HCPs) during the past 6 months and by hospitalizations and emergency room (ER) visits during the past 12 months.

The association between HCRU and MMD and number of comorbidities was assessed using negative binomial regression analysis.

Chronic migraine (CM, MMD ≥ 15) was reported in 19.5% of the respondents.

The negative impact on daily functioning and emotional burden increased significantly by migraine frequency.

Mean number of comorbidities was 2.4, and mean number of HCP visits during the previous 6 months was 5.9.

Increase in migraine frequency and comorbidities was associated with higher HCRU.

Over previous month, the mean number of missed working days for all respondents was 2.8 days of which 54% were paid sick leave days, and in CM up to 6.0 days and 30%, respectively.

The emotional and functional burden was high, and the societal burden increased by frequency and severity of migraine, as shown by higher HCRU and reduced work productivity.

Extended: Increase in migraine frequency was associated with greater productivity loss and use of healthcare resources as well as the effects conveyed to personal and societal level.

We assume that our findings can be generalised to most individuals having either episodic or chronic migraine.

Background

EM is defined as fewer than 15 monthly migraine days (MMD), and CM as 15 or more days with headache, of which ≥8 are considered migraine days.

The classification has been challenged by a recent study arguing that patients suffering from high frequency migraine (MMD ≥8) should be considered to have CM [441].

Regardless of EM or CM, the disability and burden of migraine increases along with increasing headache frequency [199, 320], and increasing number of migraine days equally enhances the risk for chronification of migraine [442].

Surveys across European and other countries have shown the impact of migraine on work, healthcare resource utilization (HCRU) and QoL, among other domains [10, 44, 50, 138–267, 374, 443, 444].

In order to further understand the burden of migraine in a Finnish sub cohort, disease severity was assessed as MMD frequency and impact of reported comorbidities.

Methods

Detailed outcome parameters assessed in the survey including sociodemographic factors, impact on working productivity and healthcare utilization is described in detail in a report by Martelletti and others [195] For the purposes of this study, information was included for age, gender, family and employment status.

Information on healthcare resource utilization based on reported number of migraine-related visits to health care practitioners (HCP) in the past 6 months as well as emergency room (ER) visits and inpatient days (IPD) in the past 12 months were also included.

The impact of migraine on work productivity and daily activities among employed respondents was evaluated by using the Work Productivity and Activity Impairment (WPAI) questionnaire [445] and complemented with additional work-related questions.

Before the analyses were carried out the participants were categorized into three groups: $4 \leq \text{MMD} < 8$, $8 \leq \text{MMD} < 15$ and $\text{MMD} \geq 15$, according to the reported mean monthly migraine days (MMDs) (determined by the self-reported number of migraine days in the past 3 months and divided by 3).

Results

The number of respondents in subgroups according to the self-reported average number of migraine days experienced in the previous 3 months were 133 (39.3%) for $4 \leq \text{MMD} < 8$ and 139 (41.4%) for $8 \leq \text{MMD} < 15$ corresponding to EM, and 66 (19.5%) for $\text{MMD} \geq 15$ corresponding to CM [80].

The mean age was 44 years, the majority were female (93%), had children (66%) and reported a family history of migraine (86%), with no significant difference between the subgroups.

Users in all subgroups reported improved control over migraines in total of 39.2% and improved quality of life in 48.8%.

Mainly individuals in MMD $\geq$ 15 group reported having lost their job due to migraine (27%, $p < 0.001$).

Fifty-three percent of the survey participants reported impairment in daily activities including homework, shopping and hobbies, and the outcome tended to differ between the subgroups ($p = 0.06$).

Discussion

Our main results drawn from the Finnish subset of global My Migraine Voice survey data showed a tendency towards worse outcomes in a wide set of domains assessing migraine burden, consistent with increase in migraine frequency detected by MMDs.

These studies, the global My Migraine Voice survey and other observations [138, 444, 446] indicate that individuals with episodic or chronic migraine report worse health status and negative impact on activities and working life.

In our data, the common WPAI domains assessing indirectly the economic burden of migraine showed that over half of the respondents reported overall work impairment (absenteeism and presenteeism), and the results corroborate the reported loss in overall work productivity in other studies [10–444].

Our results on increasing HCP visits, inpatient days and ER visits by both severity of migraine and comorbidities are consistent with these studies.

Other comorbidities frequently related to migraine are painful musculoskeletal disorders reported in a Finnish study among working aged suffering from migraine [447].

Conclusion

The cohort characterized a population where migraine exhibited the strongest effect both on working and personal life.

Increase in migraine frequency was associated with greater productivity loss and use of healthcare resources as well as the effects conveyed to personal and societal level.

The results point to the need to lessen this burden and to consider more active use of effective prophylactic treatments.

Acknowledgement

A machine generated summary based on the work of Sumelahti, Marja-Liisa; Sumanen, Markku; Sumanen, Merika S.; Tuominen, Samuli; Vikkula, Johanna; Honkala, Sanna M.; Rosqvist, Stina; Korolainen, Minna A. 2020 in The Journal of Headache and Pain.

Impact of migraine on workplace productivity and monetary loss: a study of employees in banking sector in Malaysia

DOI: https://doi.org/10.1186/s10194-020-01144-z

Abstract-Summary

Productivity and monetary loss due to migraine in the workplace may be substantial.

This study aimed to determine the impact of migraine on productivity and monetary lost among employees in the banking sectors, in a multiethnic middle income country.

Migraine-related disability (MIDAS) and headache frequency were recorded.

Impact of migraine on work productivity and activities were evaluated using the Work Productivity and Activity Impairment (WPAI) questionnaire.

The mean percent productivity loss at work (presenteeism) was almost 20-fold higher than the mean percent work time missed due to migraine (absenteeism) (39.1% versus 1.9%).

The mean percent productivity loss in regular activity (activity impairment) and overall work productivity loss (work impairment) was 38.4% and 39.9%, respectively.

Highest monetary loss related to presenteeism was reported in migraineurs with frequency of headache of above 3 days (MYR 25,691.2) (US$6176), whereas highest monetary loss related to absenteeism was reported in migraineurs with MIDAS grade IV (MYR 12,369.1) (US$2973).

The significant impact of migraine on work productivity and regular activity, appears to lead to substantial monetary loss attributed to not only absenteeism, but more importantly to presenteeism.

This study also highlights the unmet needs in migraine management among employees in the banking sector.

Extended: Another limitation is that the study's sample size was small and therefore, findings should be validated by studies on a greater number of participants.

Introduction

In the U.S., annual migraine-related costs for every 1000 employees are estimated to be US$84,000, of which one-third is attributable to lost work time.

The prevalence of migraine among workers in the banking sector in Asia country has never been reported.

The banking sector is therefore particularly worthy of investigation [448] as the extent to which migraine impacts the health of workers in the banking industry remains unknown.

In the United States, estimated migraine-related absenteeism and presenteeism costs among the banking industry workers were $21.5 million and $24.4 million, respectively [449].

The economic impact of migraines on workers in the banking industry in Asia is unknown.

The investigation aimed to determine the impact of migraine on (1) work productivity and activity impairment and (2) costs lost attributed to absenteeism and presenteeism.

Methods

The impact of migraine on work productivity and regular activities during the last 1 month was assessed using the Work Productivity and Activity Impairment (WPAI) questionnaire.

Percent work time missed due to migraine (absenteeism) = [Hours of work missed due to migraine in last 1 month/(Hours of work missed due to migraine in last 1 month + Hours actually worked in the last 1 month)] * 100 Percent impairment while working due to migraine (presenteeism) = Degree of migraine affected work productivity in the last 1 month/10 * 100Subsequently, the cost lost associated with migraine due to absenteeism and presenteeism per year was calculated based on the WPAI results [450].

Estimated monetary value due to absenteeism per year = Individual payroll per person per hour (MYR) * 8 (working hours per day) * (Days of work missed due to migraine in the past three months) * 4 (For changing into the costs per a year).

Results

Participants with MIDAS grade IV reported 3.9% (SD = 6.8) absenteeism.

Higher absenteeism was also observed among participants who reported having above three migraine days per month (2.8%) compared to those of 0–3 EM (1.8%) (Mann-Whitney U = 11,827.5, p = 0.002, Z = − 3.043).

Migraineurs with above three migraine days per month reported significantly higher presenteeism (49.5%, SD = 27.2) than those of 0–3 EM (Mann-Whitney U = 11,659.0, p = 0.004, Z = − 2.877).

Days of work missed due to migraine in the last 3 months for overall participants was 1.2 (SD = 3.9).

The estimated monetary loss due to absenteeism increased three-fold in participants with MIDAS grade III (MYR4,900.7) [SD = 11,085.3] (US$1178) compared to those with MIDAS grade II (MYR1,575.9) [SD = 1823.4] (US$379).

Discussion

This finding provides important information on the level of disability and frequency of migraine among employees in the banking sector and, as well, highlights the potential significant disease burden of migraine among groups with higher migraine disability and headache frequency.

The level of migraine disability, headache frequency and their associated employees' absenteeism found in the study highlights the importance for targeted interventions to reduce the burden of migraine on absenteeism.

The finding of 3.5-fold higher monetary loss due to presenteeism compared to absenteeism is consistent with other studies on the economic impact of migraine [11, 13, 44, 50, 90, 118, 131–443].

The remarkably higher average monetary loss due to presenteeism among individuals with MIDAS grade IV (MYR 12,400 per year; US$3000), and in individuals with over three migraine days per month (MYR 25,000; USD6,000) provide insights into the high burden of presenteeism to organizations and underscore the importance of policies to manage presenteeism .

Further, a small proportion of migraine sufferers with high disability and headache frequency who do not seek treatment but merely use over-the-counter medication.

Conclusion

This study found a high burden of migraine among (bank) employees who responded to the survey and evidence of a considerable proportion of migraineurs with high disability and headache frequency who were under-diagnosed and hence undertreated.

The results provide a cost benchmark for organizations to assess potential savings from interventions to reduce migraine and encourage appropriate treatment-seeking among the employees.

It also appears that currently, there is substantial unmet needs in migraine management among employees in the banking sector in our settings.

Acknowledgement

A machine generated summary based on the work of Wong, Li Ping; Alias, Haridah; Bhoo-Pathy, Nirmala; Chung, Ivy; Chong, Yew Ching; Kalra, Sonesh; Shah, Zia U Bahkt Sultan. 2020 in The Journal of Headache and Pain.

Migraine Characteristics, Comorbidities, Healthcare Resource Utilization, and Associated Costs of Early Users of Erenumab in the USA: A Retrospective Cohort Study Using Administrative Claims Data

DOI: https://doi.org/10.1007/s40122-021-00319-z

Abstract-Summary

The objective of this study was to provide descriptive information on real-world use of erenumab including patient profile and treatment patterns.

We completed a retrospective review of US data (through May 2019) from the IBM MarketScan® Early View Databases, identifying adult patients newly treated with erenumab with a migraine claim in the year prior to first erenumab claim (index) and at least 1 year of continuous pre-index medical and pharmacy insurance coverage, to assess pre- and post-erenumab migraine characteristics, comorbidities, healthcare resource utilization, and associated costs.

The average (SD) age was 46 (12) years, 85% of patients were female, and 64% had at least one claim for chronic migraine; 70% of erenumab users had an initial

dose of 70 mg; 77% of patients in the 6-month follow-up sample (n = 4437) remained on their initial erenumab dose.

In the post-erenumab period, claims for comorbidities of non-migraine headaches and anxiety were reduced and there was a shift to decreased use of acute and preventive medications.

Reductions in overall use and associated cost of healthcare resources such as inpatient hospitalization and outpatient office visits were minimal, with slightly more pronounced reductions in the subgroup of patients that were persistent to erenumab.

We observed reductions in claims for important migraine characteristics, comorbidities, and a shift to decreased use of acute and preventive migraine medications—observations indicative of the real-world effectiveness of erenumab.

Extended: We completed a sensitivity analysis excluding patients prescribed non-erenumab CGRP pathway antagonists from the analysis and noted similar patterns of change as the primary analysis for both acute and preventive medications.

We completed a retrospective, claims-based analysis designed to understand the real-world impact of erenumab as a migraine preventive including changes in migraine characteristics, comorbidities, healthcare resource utilization, and associated costs.

The average (SD) age at first erenumab claim for the full study population was 46.5 (12.1) years and 85.4% of users were women.

Introduction

A recent retrospective analysis of claims for 8707 patients showed persistence of 25% after the first 6 months of treatment declining to 14% by 12 months, for the 14 most common medications used for migraine prevention [451].

These low rates of persistence may lead to increased burden of migraine as healthcare resource utilization has been shown to be greater among individuals who failed multiple migraine preventive therapies [452].

More effective and tolerable preventive treatments may promote wider use with the potential to reduce the burden of migraine to individuals and society.

Erenumab (erenumab-aooe in the USA) was approved in the USA by the Food and Drug Administration (FDA) on 17 May 2018 for the preventive treatment of migraine in adults.

We conducted a claims-based, retrospective observational study to examine the impact of erenumab treatment as a migraine preventive on migraine characteristics, comorbidities, healthcare resource utilization, and associated costs.

Methods

In a sample of patients with 6-month follow-up data, pre- and post-erenumab migraine characteristics, comorbidities, treatment characteristics, healthcare resource utilization, and associated costs in US dollars ($) were described 6 months pre- and post-index.

Healthcare utilization was measured as prescription of medications used for the acute and preventive treatment of migraine, emergency room visits (service place code 23), outpatients care (service place code 22 [outpatient hospital] or 11 [office]),

in-patient hospitalizations (service code 21) and inpatient length of hospital stay, brain imaging studies (Current Procedural Terminology [CPT] code or HCPCS code for an imaging procedure [e.g., CT Head 70,450–70,492, MRI Head 70,336, 76,390, 70,540–70,559] containing HCPCS modifier code 26 to avoid double counting) and their associated costs for 6 months prior to and 6 months after the first claim of erenumab.

Results

In the post-index period, reductions in costs were slightly higher for persistent patients (− $218, $1245 post versus $1463 pre) than non-persistent patients (− $105, $916 post versus $1021 pre).

With these changes, the average costs for preventive medication decreased slightly between pre- and post-erenumab periods with slightly higher reductions for persistent than non-persistent patients; − $226 ($1120 post versus $1346 pre) for persistent patients and − $176 ($1127 post versus $1303 pre) for non-persistent patients.

Aligned to overall reductions in the use of acute and preventive medications in the pre-index period, total costs for acute and preventive medications were reduced with slightly higher reductions in costs for persistent (− $444, $2365 post versus $2809 pre) versus non-persistent (− $281, $2043 post versus $2324 pre) patients.

Discussion

A preliminary review of changes in acute migraine-specific medications pre- and post-erenumab initiation using pharmacy data also observed reductions in acute medication use post-erenumab [453].

Using a combined electronic health record and claims database, Tepper and colleagues [454] observed significant reductions in migraine-specific acute medication use and healthcare resource utilization.

Reporting interim results from a retrospective chart-review study with select US headache centers and focusing on clinical versus medication use outcomes, Faust and colleagues [455] observed reductions in the mean number of migraine/headache days per month and the average duration of migraine/headache attacks, but also noted the continued use of a polypharmacy approach to management in their chronic migraine population.

Although there was an overall reduction in the use of acute medications, preventive medications, and healthcare resource utilization for migraine in the 6-month post-erenumab period, it is important to consider the differences observed between persistent and non-persistent patients.

For acute medications, the higher use of more expensive triptans in the post-erenumab period by erenumab-persistent patients was aligned with a small increase in associated costs.

Conclusion

In this claims-based, retrospective observational study we observed reductions in claims for important migraine characteristics, comorbidities, and a shift to decreased use of acute and preventive migraine medications in the post-erenumab follow-up period—observations indicative of the real-world effectiveness of erenumab.

Further examination is required as persistence to erenumab, which may be influenced by dose change, appears to be an important factor in changes to healthcare resource utilization and costs.

Acknowledgement
A machine generated summary based on the work of Chandler, David; Szekely, Christine; Aggarwal, Shivani; Cyprien, Lori; Bensink, Mark. 2021 in Pain and Therapy.

Care Among Migraine Patients in a Commercially Insured Population

DOI: https://doi.org/10.1007/s40120-020-00179-3

Abstract-Summary
Migraine management is characterized by the poor use of preventive therapy and the overuse of acute medications.

The aim of this study was to describe treatment patterns and healthcare utilization of newly diagnosed migraine patients.

This was a retrospective observation study of newly diagnosed migraine patients (no indication of migraine in the past year) identified in the IBM MarketScan Commercial Claims and Encounters database from 1 January 2010 to 30 June 2014.

Patients generally used acute and preventive therapies to manage migraine attacks, with most patients using preventive therapy (59.1%).

Most of the patients who discontinued preventative therapy also used an acute treatment to manage migraine attacks after discontinuation (77.6%), generally in the year following discontinuation (68.4%).

Patients on acute therapies were found to use triptans excessively (1.6%) and other non-migraine-specific acute medications for treatment (7.1%).

Newly diagnosed migraine patients are not being properly treated, as indicated by their excessive use of acute therapies and short time on preventive treatment before discontinuation of that treatment.

Further study of the reasons why patients discontinue preventive therapy (adverse events, no response, etc) and continue to excessively use acute treatments once their treatment regimen has been established is needed.

Introduction
A study of migraine patients in a tertiary headache center reported that those who used both acute and preventive treatment regimens had a marked reduction in the Migraine Disability Assessment Score (MIDAS) after starting treatment, indicating an improvement in their quality of life [456].

The literature highlights poor use of migraine therapy (poor preventive therapy use and overuse of acute therapies) and shows that when properly treated, migraine

patients have an improved quality of life that includes reduced healthcare costs and HRU.

The aim of this study was to expand the body of information currently available on healthcare utilization by migraine patients and on the treatment received by these patients by evaluating potential quality of care indicators for newly diagnosed migraine patients with a focus on treatment (preventive and acute) and HRU in a commercially insured claims dataset.

Methods

All reported outcomes were measured during the variable-length follow-up period, which was defined as the time from the index date until the earliest of IP death, end of continuous enrollment or 30 June 2015 (end of study).

The following measures of acute migraine treatment were described: patients with any use, who also used preventive treatment, had an opioid or barbiturate as first-line acute treatment and showed excessive use of acute treatment.

Additional measures among patients who discontinued preventive treatment included those who used acute medication after discontinuing preventive treatment at any time after discontinuation and within the first year, those who restarted preventive treatment after discontinuing, and time from discontinuation to end of follow-up.

Continuous measures were reported as per patient per month (PPPM) to account for the variable-length follow-up period.

Results

Of those who had a migraine-related office/neurologist visit after a migraine-related ER visit, less than half made an office (36.5%) or neurologist (30.2%) visit within 2 weeks; on average, these visits occurred >100 days after a migraine-related ER visit (office visits 111.0 ± 206.2 days; neurologist visits 132.7 ± 236.9 days).

More than half of the study patients used preventive medication (59.1%) and started treatment within 0.7 months (median) of their diagnosis.

Patients starting on a second preventive treatment stayed on that treatment for a median of 3.0 months, and 45.0% subsequently started a third preventive treatment.

About one-half (48.8%) of patients who discontinued preventive therapy never started another preventive therapy during the median post-discontinuation follow-up time of 26.5 months.

The use of opioids or barbiturates as the first acute migraine therapy was observed in 34.1% of all acute therapy users and in 29.5% of acute therapy-only users.

Discussion

The results of this study describe patterns of healthcare utilization and treatment among newly diagnosed migraine patients in a commercially insured dataset.

The use of acute and preventive treatment was higher in our patient population than reported previously [457], but the patient population in this prior study comprised of established migraine patients whereas only newly diagnosed migraine patients were enrolled in our study.

Migraine management requires time, and a higher use of both preventive and acute treatments in newly diagnosed migraine patients within the first years of diagnosis is expected [458, 459].

Observed utilization differences could be due to differences in migraine severity, differing time periods observed and data used; in addition, newly diagnosed patients may use more healthcare resources than established patients to obtain a treatment regimen [460–462].

The evaluation of a link between utilization and treatment patterns with migraine severity among new migraine patients using survey or medical chart data is a worthwhile future study.

Conclusions
This analysis of treatment patterns of newly diagnosed migraine patients suggests poor migraine management characterized by inadequate preventive treatment persistence, initial treatment with opioids and barbiturates instead of less potent acute medications and excessive use of acute medications (particularly opioids and barbiturates).

Additional studies evaluating treatment patterns and HRU, particularly new referrals to neurologists or other headache specialists, among newly diagnosed migraine patients is warranted to further understand migraine management among those newly diagnosed and provide insight into improving initial management strategies among migraine patients.

Acknowledgement
A machine generated summary based on the work of Bonafede, Machaon; McMorrow, Donna; Noxon, Virginia; Desai, Pooja; Sapra, Sandhya; Silberstein, Stephen. 2020 in Neurology and Therapy.

Cost-Effectiveness of Erenumab for the Preventive Treatment of Migraine in Patients with Prior Treatment Failures in Sweden

DOI: https://doi.org/10.1007/s40273-020-00996-2

Abstract-Summary
The aim of the study was to determine the cost effectiveness of erenumab for the preventive treatment of migraine.

A hybrid decision-tree plus Markov model was developed to evaluate the cost effectiveness of erenumab as a migraine treatment compared with best supportive care only for patients experiencing at least 4 monthly migraine days for whom at least two prior preventive treatments had failed.

The primary outcomes were costs, migraine days, and quality-adjusted life-years (QALYs).

The analysis was conducted from Swedish societal and healthcare system perspectives based on total migraine, chronic migraine and episodic migraine

populations, using a discount rate of 3% applied to both costs and health benefits and using year 2019 values.

In the base-case deterministic analyses, erenumab treatment resulted in ICERs of Swedish krona (SEK) 34,696 (€3310) and SEK301,565 (€28,769) per QALY gained in the total migraine and episodic migraine populations, respectively.

In the total migraine population, the use of erenumab resulted in a net benefit to society of SEK81,739 (€7773) per patient, assuming a willingness-to-pay threshold of SEK300,000 (€28,528) per QALY.

Our analysis suggests that erenumab is a cost-effective treatment for migraine with a willingness-to-pay threshold of SEK300,000 per QALY.

Extended: In the base-case analysis, there was no distinction between these patients in terms of their clinical trajectory in the model.

Given current evidence and understanding, we believe the present analysis represents a robust assessment of the CE of erenumab.

Introduction

The Swedish Headache Society recommends preventive treatment should be offered to patients who experience frequent attacks (three or more disabling migraine attacks per month) or if the effect of acute medication is insufficient [463].

The goal of preventive treatment is a 50% reduction in the number of headache days, and re-evaluation of the patient is recommended every 3–6 months.

Alleviation of migraine reduces these costs, making successful treatment of migraine a societal investment.

The use of erenumab at a dose of 140 mg is supported by post hoc analysis of data from pivotal studies in EM and CM, in patients with at least one prior treatment failure, demonstrating a reduction in the number of MMDs versus placebo in the overall population [464, 465].

The purpose of this study is to inform healthcare decision making by assessing the cost effectiveness of erenumab versus best supportive care (BSC) in the preventive treatment of migraine in Sweden for patients for whom two or more preventive treatments have failed.

Methods

An economic model with a decision-tree plus Markov structure was developed to assess the cost effectiveness of erenumab as a migraine treatment compared with BSC for patients with at least 4 MMDs for whom at least two preventive treatments have failed.

The model structure was predicated on the assumption that quality-adjusted life-years (QALYs) and (non-treatment-related) costs could be estimated based on the MMD frequency experienced by patients.

In both periods of the model, QALYs and (non-treatment-related) costs were accrued based on how patients were modelled to be distributed across MMD frequencies in each state.

The remaining proportion in the model was assumed to return to the ‘on treatment’ state, where patients again were subject to post-assessment negative discontinuation and possibly later re-entered the re-evaluation period.

Results

Mean MMD reduction at 12 weeks was greater in the erenumab 140 mg arm than in the placebo arm (5.49 and 2.20, respectively, for the total migraine population).

Erenumab had a greater proportion of responders (40.77 vs. 13.89% for the total migraine population), and responders had a greater mean MMD reduction (11.69 vs. 10.95 for the total migraine population) compared with placebo + BSC.

In the base case, the ICER for erenumab was SEK34,696 and SEK301,565 per QALY gained for the total migraine and EM populations, respectively.

Under a willingness-to-pay (WTP) threshold of SEK300,000 per QALY, the net monetary benefit of erenumab to society was estimated at SEK81,738, SEK131,255 and − SEK238 per patient for the total migraine, CM and EM populations, respectively, with significant value coming from the utility gained and indirect costs saved.

With the base-case analysis, lower-dose erenumab 70 mg was also cost effective, with a higher ICER.

Discussion

To US-based evaluations, the model structure included a response-based patient pathway representing the treatment guidelines typically considered by European healthcare systems.

An ICER of SEK34,696 per QALY gained was estimated for erenumab 140 mg among a total migraine population with two or more treatment failures over a 10-year time horizon and including indirect costs.

Even without indirect costs, the results show that erenumab should be considered cost effective for patients with migraine for whom two or more prior preventive treatments have failed.

The results were robust to changes in structural assumptions, and no sensitivity analysis generated an ICER over SEK300,000, except when the treatment was used exclusively in patients with EM or when a 24-week time horizon was employed, which would not account for the health benefits for patients who respond to and remain on erenumab treatment.

Conclusion

Consistent with previous research, erenumab resulted in a meaningful reduction in MMD frequency and an increase in QALYs compared with BSC for patients with prior treatment failures.

The health economic evaluation presented suggests that erenumab is cost effective in patients for whom two or more previous preventive treatments have failed, from both a healthcare and a societal perspective in Sweden, with a threshold value of SEK300,000 per QALY gained.

Acknowledgement

A machine generated summary based on the work of Mahon, Ronan; Lang, Andrea; Vo, Pamela; Huels, Jasper; Cooney, Philip; Danyliv, Andriy; Vudumula, Umakanth; Vadapalle, Sreelatha; Maniyar, Farooq; Goadsby, Peter J. 2021 in PharmacoEconomics.

Cost-Effectiveness Analysis of Erenumab Versus OnabotulinumtoxinA for Patients with Chronic Migraine Attacks in Greece

DOI: https://doi.org/10.1007/s40261-019-00827-z

Abstract-Summary

Existing preventive treatments involve the selective use of onabotulinumtoxinA, which aims at migraine morbidity reduction for patients who have failed initial preventive treatment with oral agents.

Erenumab is a new preventive treatment for migraines.

To evaluate the differences in costs and outcomes of the preventive treatment with erenumab versus onabotulinumtoxinA in patients with chronic migraines (CM) in Greece to assess the economic value of this treatment.

We conducted a cost-effectiveness analysis from both the payer and the societal perspective using a decision-tree analytic model.

Indirect costs for the societal perspective analyses included wages lost on workdays.

Our results indicate that treatment of CM with erenumab compared to onabotulinumtoxinA resulted in incremental cost-effectiveness ratios (ICERs) of €218,870 and €231,554 per QALY gained and €620 and €656 per migraine avoided, from the societal and the payer's perspective, respectively.

Using a common cost-effectiveness threshold equal to three times the local gross domestic product (GDP) per capita (€49,000), for the erenumab ICERs to fall below this threshold, the erenumab price would have to be no more than €192 (societal perspective) or €173 (payer perspective).

The prophylactic treatment of CM with erenumab in Greece might be cost effective compared to the existing alternative of onabotulinumtoxinA from both the payer and the societal perspective, but only at a highly discounted price.

Erenumab could be considered a therapeutic option for patients who fail treatment with onabotulinumtoxinA.

Extended: One-way and probabilistic sensitivity analyses were conducted to evaluate the robustness of the findings and to account for the effect of the uncertainty of key model inputs on the ICER.

Introduction

Preventive therapies are deemed appropriate for patients who suffer from higher frequencies of migraines, namely those classified as episodic migraineurs (EM), with 4–14 migraines per month, and chronic migraineurs (CM), with 15 or more migraines per month [182].

Topiramate, an antiepileptic drug that was found to be highly cost effective in preventing migraines by modulating the trigeminovascular signaling, is currently used as a first-line preventive therapy for CM in Greece [466–469].

Clinical trials indicated that, compared to the placebo, erenumab led to a significant reduction in the monthly frequency of migraines and to sustained improvements in psychosocial and disability-related outcomes in patients with CM [470, 471].

The objective of this study was to examine the cost effectiveness of erenumab 140 mg compared to the existing preventive treatment with ONBTA for patients with CM from the payer and the societal perspective in Greece.

Methods

Similar to previous studies, we further adjusted our model to account for costs of lost productivity for migraine attacks during workdays [350].

Since triptans are more effective in mitigating the symptoms of a migraine crisis compared to no acute care medication or to usual care, we assigned different outcomes for working hours lost, depending on the choice of acute treatment therapy.

The difference in migraine reduction between ONBTA and erenumab was obtained through the following formula:where $\Delta TE_{[O|P]}$ indicates the difference in treatment effects in the placebo-controlled trials for ONBTA, obtained through weighted pooling of the two studies' outcomes, $\Delta TE_{[E|P]}$ the difference in treatment effects in the placebo-controlled trials for erenumab, and $\Delta TE_{[E|O]}$ the analogous difference in treatment effects between the two drugs of interest.

Based on Greek experts' feedback, patients with CM use acute treatment medications to mitigate the symptoms of a migraine crisis at an approximate rate of 80% during ongoing attacks.

Results

The annual cost difference between erenumab and ONBTA was €216 higher from the payer's perspective (€3936), attributed mainly to the exclusion of indirect costs and out-of-pocket payments from payer costs.

The greater effectiveness of erenumab in migraine reduction had a stronger impact on the ICER from the societal perspective compared to the payer perspective.

Even when we adjusted our sensitivity analyses to account only for the ONBTA lower adherence identified in Greek patients' study, the ICER remained above €100,000, driven by the higher costs associated with the use of healthcare services, acute medications, and productivity costs (societal perspective) [472].

We also conducted a price and co-pay threshold analysis from the payer's perspective to explore the potential impact of a lower negotiated price for erenumab, coupled with shifting a higher share of the cost of purchasing erenumab from the national health-insurance payer to the patient by establishing various patient co-pay levels.

Discussion

This study offers critical insight into the decisions that have to be made in the imminent future regarding treatment guidelines for CM, price negotiations for erenumab, and cost-sharing policies towards value-based payment [473].

In the case of Greece, economic evaluations have not received the same attention compared to other countries; possible reasons for that could be related to a less developed Health Technology Assessment (HTA) and reimbursement environment in Greece, coupled with the absence of an officially established willingness-to-pay threshold to define which treatments are likely to be considered cost effective.

Our base-case finding of an incremental difference of 0.017 QALYs gained for the erenumab treatment aligns with previous research using different cost-effectiveness methodologies, which found incremental differences of 0.03 and 0.18 QALYs gained over a 2- or 10-year time horizon, respectively, indicating the consistency of our model [343, 350].

Conclusion
The additional benefit of erenumab treatment in terms of migraines averted and QALYs gained for patients with chronic migraines in Greece will exceed commonly accepted willingness-to-pay thresholds based on this analysis.

In the absence of an officially established threshold of willingness-to-pay for new healthcare technologies in Greece, coupled with the large proportion of patients who cannot tolerate topiramate (due to its adverse effects), erenumab could be included in the national drug formulary and in the local clinical guidelines for treatment of CM as a third-line treatment option, when initial treatment with antiepileptic agents fails, and subsequent treatment with ONBTA also fails.

Acknowledgement
A machine generated summary based on the work of Giannouchos, Theodoros V.; Mitsikostas, Dimos-Dimitrios; Ohsfeldt, Robert L.; Vozikis, Athanassios; Koufopoulou, Paraskevi. 2019 in Clinical Drug Investigation.

Costs of Acute Headache Medication Use and Productivity Losses Among Patients with Migraine: Insights from Three Randomized Controlled Trials

DOI: https://doi.org/10.1007/s41669-018-0105-0

Abstract-Summary
By reducing the number of monthly migraine days (MMD) experienced by patients, effective preventive treatments can reduce acute medication use and costs of lost productivity.

The number of days per month on which patients used acute medication was estimated as a function of MMD.

Zero-inflated Poisson regression models were used to predict acute medication use and productivity losses per MMD.

The results demonstrated that as MMD increased, use of acute medication also increased.

The relationship of MMD to both acute headache medication use and lost productivity was non-linear, with marginal outcomes increasing with frequency.

As MMD increased, acute medication use and productivity loss also increased, but the relationship was non-linear.

By reducing the MMD experienced by patients, effective preventive agents may reduce the requirement for acute medication and also reduce productivity loss, which may translate into potential economic savings.

Extended: The number of days on which patients used any headache AM was also recorded.

Zero-inflated Poisson regression models were fitted with the number of absenteeism and presenteeism days as response variables and regressed against MMD using the covariates set described previously.

Introduction

The condition is divided into episodic migraine (EM; 0–14 headache days per month [defined as 28 days]) and chronic migraine (CM; ≥ 15 headache days per month for at least 3 months, ≥ 8 of which meet the criteria for migraine and/or respond to migraine-specific treatments), and migraine classification may guide the treatment choices available to patients [320, 474, 475].

Migraine is associated with both high direct healthcare costs and indirect costs due to lost workplace productivity [10, 50, 142, 181–374].

Migraine prevention aims to reduce the frequency, severity, and duration of attacks, which are associated with high costs to patients, employers, and healthcare systems [476, 477].

Effective preventive agents reduce the number of monthly migraine days (MMD) and, consequently, reduce acute treatment costs and patient disability [478].

The erenumab clinical studies included endpoints which recorded the use of acute medication (AM) and the impact of migraine on patients' productivity.

Methods

The EM studies recruited patients with 4–14 MMD and headache days, and the CM study recruited patients with ≥15 headache days, of which ≥8 were migraine days.

To understand how MMD is associated with the use of AM across the cohort and duration of the studies, the reported number of days of AM use was regressed against MMD, employing a set of covariates, including age, sex, race, treatment group, prior failed preventive migraine medication status, and MMD at study baseline.

As the response variables are count data, and given the considerable proportion of patients who reported no AM use, zero-inflated Poisson regression models were determined as the most appropriate to assess two AM use outcomes independently: days on which patients reported using migraine-specific AM and days on which patients reported using non-migraine-specific AM.

Absenteeism is defined as the number of days on which a patient misses work or study altogether; presenteeism is the number of days on which productivity is reduced by at least 50% (but not qualifying as absenteeism days).

Results

A patient experiencing 8 MMD is predicted to use migraine-specific AM on 2.82 (95% confidence interval [CI] 2.80–2.85) days and non-migraine-specific AM on 2.75 (95% CI 2.74–2.77) days per month.

A patient with CM experiencing 18 MMD is predicted to use migraine-specific AM on 7.06 (95% CI 7.01–7.12) days and non-migraine-specific AM on 4.81 (95% CI 4.79–4.84) days per month.

The results indicate a greater use of AM per migraine day for patients with higher MMD.

A patient experiencing 8 MMD is predicted to have 0.95 (95% CI 0.94–0.96) absenteeism days and 2.34 (95% CI 2.32–2.35) presenteeism days per month.

A patient with CM with 18 MMD is predicted to have 1.86 (95% CI 1.85–1.87) absenteeism days and 5.18 (95% CI 5.15–5.21) presenteeism days per month.

Discussion

The zero-inflated regression models applied here account for the proportions of patients in the clinical studies who reported no AM use or productivity losses.

By lowering the MMD of patients, migraine preventives may reduce lost productive time and the requirement for AM.

As these relationships are non-linear, considering only mean MMD in economic evaluations may misrepresent outcomes of patient cohorts as the impact of each additional migraine day is not constant.

MIDAS data from the clinical studies only capture workplace productivity losses among employed patients, who can quantify the number of work days impacted by their migraines.

Productivity losses of patients with migraine could be underestimated in this study, especially for those with higher MMD.

To the MMD reduction, active treatment with erenumab may impact the severity and duration of migraines, which may also impact productivity losses and AM use compared with placebo.

Acknowledgement

A machine generated summary based on the work of Porter, Joshua K.; Di Tanna, Gian Luca; Lipton, Richard B.; Sapra, Sandhya; Villa, Guillermo. 2018 in PharmacoEconomics—Open.

1.4 Governance

Machine generated keywords: headache service, service, model, solution, primary care, neurologist, tertiary, clinic, tertiary care, brain, ltb, specialist, healthcare system, doctor, specialty.

Structured headache services as the solution to the ill-health burden of headache: 1. Rationale and Description

DOI: https://doi.org/10.1186/s10194-021-01265-z

Abstract-Summary
In countries where headache services exist at all, their focus is usually on specialist (tertiary) care.

This is clinically and economically inappropriate: most headache disorders can effectively and more efficiently (and at lower cost) be treated in educationally supported primary care.

High demand for headache care, estimated here in a needs-assessment exercise, is the biggest of the challenges to reform.

The structured headache services model presented here by experts from all world regions on behalf of the Global Campaign against Headache is the suggested health-care solution to headache.

It develops and refines previous proposals, responding to the challenge of high demand by basing headache services in primary care, with two supporting arguments.

Only primary care can deliver headache services equitably to the large numbers of people needing it.

The model calls for vertical integration between care levels (primary, secondary and tertiary), and protection of the more advanced levels for the minority of patients who need them.

Introduction
Governments, politicians and health-service managers concerned about the cost of headache care for very large numbers of people fail to recognize a fundamentally important aspect of the economics of headache disorders: untreated, they are a huge financial drain.

A wealth of evidence attests the efficacy of treatments for migraine and other primary headache disorders that can well be provided by non-specialists [479].

In a reasonable expectation, good health care delivering these treatments efficiently to those who will benefit from them will substantially reduce the ill-health burden of headache.

Regrettably, throughout the world, the opportunity is missed: health-care systems that ought to provide this care either do not exist or, where they do, fail to reach many who need it [36, 480].

Methods
Experts from all world regions, in headache, health service organization or health-technology assessment, were brought together to contribute to these proposals through email correspondence.

They took evidence from the published literature and, using this, built a headache-care model by developing and refining previous proposals for headache service

organisation [13, 50, 90, 118, 131, 142, 178–482] put forward by Lifting The Burden (LTB) [483] and the European Headache Federation (EHF) [484].

They extended the applicability of the model beyond Europe through their own expertise and local knowledge and by drawing from experience and understanding gained by the Global Campaign against Headache during its 16 years of activities worldwide [483].

The Problems

In a United Kingdom (UK) study based in primary care 20 years ago, 17% of registered patients aged 16–65 years had consulted a general practitioner (GP) because of headache [485].

Effective treatments exist [479, 486], but the proposal that everyone with headache has need for professional care is not arguable in a resource-limited world.

The first is that only those with disabling headache need professional care.

In every million people in the world, therefore, there are 80,000 adults (12% of the 660,000 aged 15–64 years) who need care because of migraine-attributed disability.

In the absence of better data, a conservative but reasonable working basis is that headache-care needs in these age groups, in terms of numbers, are, proportionately, half those of adults [178, 482]: another 17,000 (0.5*13.5% of the 250,000 aged 14 or under) in each million of the population.

The Health-Care Solution

Nationwide structured and educationally supported headache services embedded and integrated within a country's health-care system are the means of efficiently, effectively and equitably mitigating the personal and societal burdens of headache to the greatest extent possible with resources available, a proposition put forward by LTB and endorsed by WHO a decade ago [90].

Structured headache services pull elements together from primary, secondary and specialist (tertiary) care, and, importantly, from pharmacy services.

The model does not require every HCP in primary care to offer headache services if they can share caseload between themselves according to their skills and interests, an arrangement that may be administratively easy in group practices or health centres.

With these and the educational supports, this level should competently meet the needs of most people needing professional care for headache [178, 487]: most cases of migraine (and almost all of TTH, if needing care) can be diagnosed and managed here by HCPs who should be familiar with recommended acute and preventative drugs [484] and aware of the constraints in managing fertile women (important since these are a high proportion of people with migraine).

Concluding Remarks

Many problems beset the current compartmentalized division of headache services between primary, secondary and tertiary care.

The model is amenable to horizontal integration with other care services, and capable of adaptation to suit local cultures and health-care systems.

The need for better—and better resourced—headache services exists in all countries, differing only quantitatively.

At a time when momentum is again developing for health-service reform diverting resources from secondary to primary care [488, 489], there is opportunity for change.

Acknowledgement
A machine generated summary based on the work of Steiner, Timothy J.; Jensen, Rigmor; Katsarava, Zaza; Stovner, Lars Jacob; Uluduz, Derya; Adarmouch, Latifa; Al Jumah, Mohammed; Al Khathaami, Ali M.; Ashina, Messoud; Braschinsky, Mark; Broner, Susan; Eliasson, Jon H.; Gil-Gouveia, Raquel; Gómez-Galván, Juan B.; Gudmundsson, Larus S.; Herekar, Akbar A.; Kawatu, Nfwama; Kissani, Najib; Kulkarni, Girish Baburao; Lebedeva, Elena R.; Leonardi, Matilde; Linde, Mattias; Luvsannorov, Otgonbayar; Maiga, Youssoufa; Milanov, Ivan; Mitsikostas, Dimos D.; Musayev, Teymur; Olesen, Jes; Osipova, Vera; Paemeleire, Koen; Peres, Mario F. P.; Quispe, Guiovanna; Rao, Girish N.; Risal, Ajay; de la Torre, Elena Ruiz; Saylor, Deanna; Togha, Mansoureh; Yu, Sheng-Yuan; Zebenigus, Mehila; Zewde, Yared Zenebe; Zidverc-Trajković, Jasna; Tinelli, Michela, 2021 in The Journal of Headache and Pain.

Editorial. Valuing headache's solution

DOI: https://doi.org/10.1186/s10194-021-01246-2

[Section 1]
According to the 2019 Global Burden of Disease study (GBD2019), headache disorders are the world's third leading cause of disability, and top cause in young adults, responsible globally for 46.6 million years lived with disability (YLDs), 5.4% of all YLDs [368, 369].

GBD2019 drew attention to headache disorders, remarking that their prominence among the ranked causes of lost health had "received little attention in global health policy debates" [368, 369].

Everywhere, headache disorders are under-recognized in society and under-prioritized and under-resourced in health policy.

Health-care providers, without the requisite training or resources to manage headache effectively, achieve poor and disillusioning outcomes.

LTB has gathered evidence from around the world of the magnitude of public ill health attributable to headache and of the inadequate responses to it [90], supporting and building research capacity in many countries while doing so [490].

It applies this methodology to headache services in Europe, finding and reporting clear evidence of the model's cost-effectiveness to justify the up-front investment in its implementation [491].

Acknowledgement
A machine generated summary based on the work of Steiner, TJ; Tinelli, M. 2021 in The Journal of Headache and Pain.

Structured headache services as the solution to the ill-health burden of headache. 2. Modelling effectiveness and cost-effectiveness of implementation in Europe: methodology

DOI: https://doi.org/10.1186/s10194-021-01310-x

Abstract-Summary
Health economic evaluations support health-care decision-making by providing information on the costs and consequences of health interventions.

No universally accepted methodology exists for modelling effectiveness and cost-effectiveness of interventions designed to close treatment gaps for headache disorders in countries of Europe (or elsewhere).

Our aim here, within the European Brain Council's Value-of-Treatment project, was to develop headache-type-specific analytical models to be applied to implementation of structured headache services in Europe as the health-care solution to headache.

We developed three headache-type-specific decision-analytical models using the WHO-CHOICE framework and adapted these for three European Region country settings (Luxembourg, Russia and Spain), diverse in geographical location, population size, income level and health-care systems and for which we had population-based data.

Each model compared current (suboptimal) care vs target care (delivered in accordance with the structured headache services model).

Headache-related costs (including use of health-care resources and lost productivity) and health outcomes (HLYs) were mapped across populations.

This study presents the first headache-type-specific analytical models to evaluate effectiveness and cost-effectiveness of implementing structured headache services in countries in the European Region.

Extended: No universally accepted methodology exists for modelling effectiveness and cost-effectiveness of service-delivery interventions designed to close headache treatment gaps.

Our aim here, through decision-analytical modelling, is to generate the required evidence of value needed to influence policy.

We developed three separate headache-type-specific decision-analytical models from an earlier exercise using the WHO-CHOICE framework [492], and simulated outcomes for the populations of 18–65-year-olds with migraine, TTH or MOH.

This study presents the first headache-type-specific analytical models for comparing the effectiveness and cost-effectiveness of implemented structured headache services across European Region country settings.

Background

Each million of the population in Europe loses an estimated 400,000 days from work or school every year to migraine alone, while the estimated cost of headache disorders in Europe, due in the main to lost productivity, is well in excess of €100 billion per year [13].

No universally accepted methodology exists for modelling effectiveness and cost-effectiveness of service-delivery interventions designed to close headache treatment gaps.

We describe current care and the treatment management plan to achieve target care, the types of intervention, and the coverage and uptake estimates used in three headache-type-specific decision-analytical models.

We explain how we calculate economic and health outcomes, and report the key results of applying the three analytical models to population data from three paradigmatic countries in the European Region, including healthy life years (HLYs) gained and cost differences when changing from current to target care.

Methods

We ran a population model for the two alternatives (current vs target care) over one- and five-year time frames to estimate total HLYs lived by the populations in each country in each alternative.

The differences between these two simulations represented the population-level health gain (HLYs gained) from the intervention relative to current care.

For migraine and TTH, we calculated headache-attributed disability at individual level in YLDs as the product of proportion of time in ictal state (pTIS: itself estimated as a product of attack frequency (F) and mean duration), with and without intervention, and the DW for the disorder in question.

We modelled treatment effect as reduction in pTIS, adopting the universal outcome measure previously developed for this purpose [493] but, since this was a population-level analysis, expressing effect in terms of HLYs gained rather than hours lived with disability (HLDs) averted.

Results

We set out results for the three countries in terms of headache-related costs (including use of health-care resources and lost productivity) and health outcomes (HLYs) attached to each alternative (current vs target care) only to demonstrate how the models worked.

Analyses of the differences in costs and health outcomes between alternatives and the incremental cost-effectiveness ratios are presented elsewhere [494].

The same calculations are repeated for each alternative (current vs target care) and for the differences between these.

The same calculations are again repeated for each alternative (current vs target care) and for the differences between these.

Discussion
The models linked direct costs (resources sunk into health-care provision) and indirect costs (lost work productivity) with health outcomes (in terms of HLYs).

The countries included—Luxembourg, Russia and Spain—were diverse in terms of geographical location, population size, level of income and organisation of their health-care systems.

This allowed us to re-run the models from the broader societal perspective, covering both health-care provider costs and those due to lost productivity.

A major difficulty lay in the relationship between headache-attributed disability, estimated from DWs generated in GBD2015, and headache-attributed lost work productivity.

This was expected, because predicted savings in work productivity greatly exceeded the investments in health care estimated to be needed to achieve these savings.

In a conservative scenario, where we assumed that remedying disability would recover only 20% of the lost productivity attributed to it, the intervention remained cost-effective in all models and cost-saving in Luxembourg.

Conclusion
Despite these limitations, the study delivered robust models, with detailed results presented in the next paper in this series [494].

The models should greatly assist local health-policy makers, across Europe and very probably elsewhere, in allocating fixed health budgets between interventions to maximise health in society.

Health-care systems vary widely even within the European Region, and certainly outside it, but the analytical models should be applicable to any that adopt and fully implement the services model [495].

Acknowledgement
A machine generated summary based on the work of Tinelli, Michela; Leonardi, Matilde; Paemeleire, Koen; Mitsikostas, Dimos; de la Torre, Elena Ruiz; Steiner, Timothy J.; 2021 in The Journal of Headache and Pain.

Structured headache services as the solution to the ill-health burden of headache. 3. Modelling effectiveness and cost-effectiveness of implementation in Europe: findings and conclusions

DOI: https://doi.org/10.1186/s10194-021-01305-8

Abstract-Summary
There have been several calls for estimations of costs and consequences of headache interventions to inform European public-health policies.

In a previous paper, in the absence of universally accepted methodology, we developed headache-type-specific analytical models to be applied to implementation of structured headache services in Europe as the health-care solution to headache.

We considered three European Region case studies, from Luxembourg, Russia and Spain to include a range of health-care systems, comparing current (suboptimal) care versus target care (structured services implemented, with provider-training and consumer-education).

We made annual and 5-year cost estimates from health-care provider and societal perspectives (2020 figures, euros).

The models demonstrated increased effectiveness, and cost-effectiveness (migraine) or cost saving (TTH, MOH) from the provider perspective over one and 5 years and consistently across the health-care systems and settings.

From the societal perspective, we found structured headache services would be economically successful, not only delivering increased effectiveness but also cost saving across headache types and over time.

Lost productivity had a major impact on these estimates, but sensitivity analyses showed the intervention remained cost-effective across all models when we assumed that remedying disability would recover only 20% of lost productivity.

This is the first study to propose a health-care solution for headache, in the form of structured headache services, and evaluate it economically in multiple settings.

Despite numerous challenges, we demonstrated that economic evaluation of headache services, in terms of outcomes and costs, is feasible as well as necessary.

Extended: There have been repeated calls for better modelling of costs and outcomes of headache interventions to inform public-health policies, given the very high prevalence of headache disorders [13, 44, 47–497].

Introduction

In a later paper, in the absence of universally accepted methodology, we developed headache-type-specific analytical models to be applied to economic evaluation of the model, implemented in three countries in the European Region [498].

Because headache disorders are disabling [13, 44, 50, 90, 95–499], lost productivity is an important consequence, at demonstrably high cost [13, 407, 500, 501].

Papers in this series assess the complex relationship between headache-attributed disability and lost productivity, and consider whether, and to what degree, alleviating the former will lead to recovery of the latter [502, 503].

Our evaluation here allows for the possibility that headache-attributed disability explains only part of lost productivity.

Methods

For the two alternatives of current (suboptimal) care and target care (structured services implemented, with provider-training and consumer-education), economic modelling incorporated patient outcomes and cost estimates over two separate timeframes: one and 5 years.

Methodological details are provided elsewhere on the decision-analytical models, on epidemiological data (including disability), estimations of intervention effectiveness, economic outcomes (including use of resources and lost productivity), treatment management plans and selection of interventions for migraine, TTH and MOH within the alternatives under comparison [498].

Economic and effectiveness outcomes were brought together to evaluate cost-effectiveness in terms of costs to be invested per HLY gained (incremental cost-effectiveness ratio [ICER]), with the three health-care systems of Russia, Luxemburg and Spain bringing different systems of health-care service delivery and financing into the model.

The principal analyses were conducted from the health-care provider perspective, with robustness tested in a series of sensitivity analyses inflating health-care costs and deflating HLYs gains while keeping to the same cost-effectiveness thresholds.

Results

From the health-care provider perspective, the hypothetical shift to target care would bring gains in HLYs (the longer the time frame the greater the gain).

For migraine, resources must be invested to secure these benefits (the longer the time frame, the lower, relatively, the investment).

For TTH and MOH, the benefits would be accompanied by cost savings (the longer the time frame the greater the economic gain).

Discussion

Effectiveness and cost-effectiveness of introducing structured headache services have been evaluated.

Our results show, across three diverse health-care systems in European Region, that structured headache services based in primary care and supported by consumer-education and provider-training [504] are an effective and economically viable solution to headache disorders and the disability they cause.

From the health-care provider perspective, TTH services are not only cost-effective, but also cost-saving (ICERs negative).

We relied on sensitivity analyses, in which the intervention remained cost-effective across all models even with the alternative conservative assumption that alleviating headache would recover only 20% of the lost productivity attributed to it.

There have been repeated calls for better modelling of costs and outcomes of headache interventions to inform public-health policies, given the very high prevalence of headache disorders [13, 44, 47–497].

Conclusions

Even with very conservative assumptions, highly inflating costings (or deflating expected gains), we could conclude that structured headache services would be cost-effective according to WHO thresholds [505]—and this held true for all headache types and across all settings.

Structured headache services offer an efficient, equitable, effective and cost-effective solution to headache, a cause of much population ill health [98, 500, 501] and heavy economic burden [47].

Structured headache services—offering care efficiently and equitably to the widest number of people [504] and, according to our findings here, an economically viable solution to headache as a cause of public ill health—are in accord with WHO's vision of universal health coverage (UHC) [506].

Care models like structured headache services that define a clear primary-care role [504] and allow economic evaluation promote the goal of UHC worldwide.

Acknowledgement
A machine generated summary based on the work of Tinelli, Michela; Leonardi, Matilde; Paemeleire, Koen; Raggi, Alberto; Mitsikostas, Dimos; de la Torre, Elena Ruiz; Steiner, Timothy J.; 2021 in The Journal of Headache and Pain.

Headache service quality evaluation: implementation of quality indicators in primary care in Europe

DOI: https://doi.org/10.1186/s10194-021-01236-4

Abstract-Summary
Lifting The Burden (LTB) and European Headache Federation (EHF) have developed a set of headache service quality indicators, successfully tested in specialist headache centres.

We assess their implementation in primary care.

We included 28 primary-care clinics in Germany (4), Turkey (4), Latvia (5) and Portugal (15).

Enquiries were in nine domains: diagnosis, individualized management, referral pathways, patient education and reassurance, convenience and comfort, patient satisfaction, equity and efficiency of headache care, outcome assessment and safety.

The principal finding was that Implementation proved feasible and practical in primary care.

Headache-related disability and quality of life were not part of routine clinical enquiry.

Most patients (>85%) expressed satisfaction with their care.

Almost all the participating clinics provided equitable and easy access to treatment, and follow-up for most headache patients, without unnecessary barriers.

The study demonstrated that headache service quality indicators can be used in primary care, proving both practical and fit for purpose.

These findings signal the need for additional training in headache diagnosis and management in primary care, where most headache patients are necessarily treated.

They underline the importance of headache service quality evaluation in primary care, not only to identify-quality failings but also to guide improvements.

This study also demonstrated that patients' satisfaction is not, on its own, a good indicator of service quality.

Background

In primary care management of headache, education does indeed improve practice [274].

There is need to take a much more expansive view: the concept of service quality must take centre-stage in headache care, wherever it is delivered [178].

In a series of evaluations, these indicators were first implemented in a pilot study in two highly specialized headache centres (at the University Hospital Essen, Germany, and the Hospital de Luz in Lisbon, Portugal) using the questionnaires developed for doctors, other health-care providers (HCPs), service managers, secretaries or administrators and patients [272].

Both studies found the quality indicators to be practical in specialist care and fit for purpose at this level: treatment deficits were identified and eliminated [507].

Its secondary purpose is to assess the quality of headache management currently in primary care in Europe, identifying deficits and providing guidance for improvement.

Methods

Approvals were obtained in each country in accordance with local regulations (some did not require ethics approval for studies with the primary purpose of service quality improvement).

During 2019, a total of 53 primary-care practices from four European countries were invited to participate (10 from Germany, five from Turkey, five from Latvia and 33 from Portugal), identified through personal contacts and selected to represent, as far as possible, the geographic distinctions of the four countries.

The data were collected prospectively under the supervision of the local principal investigator using the prescribed SQE questionnaires for each group of interviewees and for extraction of data from patients' records.

Data were entered locally and anonymously into spreadsheets provided, and in this form transferred to the data collection centre (Clinic for Neurology, Geriatric Medicine and Neurorehabilitation in the Evangelical Hospital Unna), where they were merged and analyzed descriptively.

Results

Diagnostic diaries were available in a minority (0% in Germany to 30% in Latvia), with many HCPs unaware of them and others believing they were too time-consuming.

One third of practices in Latvia, but fewer elsewhere, used an instrument for disability assessment at the time of diagnosis.

In Germany and Portugal, two thirds of practices had an access route to psychological therapies, but in Turkey and Latvia only one-third.

Almost all practices were able to offer their patients follow-up, when considered necessary, although few used standardized follow-up diaries or outcome assessment instruments to monitor progress.

Most practices (83%, but only 67% in Turkey) offered equal access to their (headache) service for all patients.

The most marked differences could be identified in domain A (Accurate diagnosis) and domain H (Outcome assessment), but there were notable deficits in primary care relative to specialist care in other individual quality indicators (for example in the availability of information leaflets [D1a]).

Discussion
Basic but structured education of GPs has been shown to improve their practice, significantly increasing proportions of patients given specific diagnoses and treatments, both indicators of headache care quality [274, 508].

Pertaining to this, an important particular finding was that a substantial proportion of patients of these primary-care practices received non-specific ICD codes such as R51 ("headache") rather than specific headache diagnoses.

While the study fulfilled its primary goal of demonstrating that the SQE methodology is applicable and practical in primary care, understandable to HCPs and patients without being unduly time consuming, we note a limitation and caveat in regard to this: only 53% of invited primary-care clinics agreed to participate.

Despite that it was not the study's primary purpose, it uncovered opportunities for improvement in the management of headache patients in primary care.

Conclusion
This study, the first evaluating headache service quality indicators in primary care in Europe, confirmed the indicators to be practical and fit for purpose, able to identify areas for improvement in pursuit of care quality.

While quality criteria must be deployed at all levels within health-care-systems (and this study has confirmed that they can be), primary care is the setting of greatest importance since it is where management of the majority of headache-patients can and should be based [178, 509, 510].

This study, in the context of the collaborative LTB/EHF SQE project of which it is part, is a step towards bringing headache service quality centre-stage.

Acknowledgement
A machine generated summary based on the work of Lenz, B.; Katsarava, Z.; Gil-Gouveia, R.; Karelis, G.; Kaynarkaya, B.; Meksa, L.; Oliveira, E.; Palavra, F.; Rosendo, I.; Sahin, M.; Silva, B.; Uludüz, D.; Ural, Y. Z.; Varsberga-Apsite, I.; Zengin, S. T.; Zvaune, L.; Steiner, T. J.; 2021 in The Journal of Headache and Pain.

Poor medical care for people with migraine in Europe—evidence from the Eurolight study

DOI: https://doi.org/10.1186/s10194-018-0839-1

Abstract-Summary
Migraine is prevalent everywhere, and disabling.

We analysed data from the Eurolight study on consultations and utilization of migraine-specific medications as indicators of adequacy of medical care in Europe.

We recorded migraine prevalence and frequency, and utilization of medical services and medications (acute and preventative).

Among 9247 participants (mean age 43.9 ± 13.9 years, M/F ratio 1:1.4), 3466 (37.6%) were diagnosed with migraine (definite or probable).

Of these, 1175 (33.8%) reported frequent migraine (>5 days/month) and might clearly expect benefit from, and therefore had need of, preventative medication.

In population-based samples, minorities of participants with migraine had seen a GP (9.5–18.0%) or specialist (3.1–15.0%), and smaller minorities received adequate treatment: triptans 3.4–11.0%, with Spain outlying at 22.4%; preventative medication (1.6–6.4% of those eligible, with Spain again outlying at 13.7%).

Proportions were greater in GP-based samples (13.6–24.5% using triptans, 4.4–9.1% on preventative medication) and among those from lay organisations (46.2–68.2% and 16.0–41.7%).

Participants with migraine who had consulted specialists (3.1–33.8%) were receiving the best care by these indicators; those treated by GPs (9.5–29.6%) fared less well, and those dependent on self-medication (48.0–84.2%) were, apparently, inadequately treated.

In wealthy European countries, too few people with migraine consult physicians, with proportionately too many of these seeing specialists, and migraine-specific medications are used inadequately even among those who do.

Extended: In population-based samples, 3.4–22.4% of participants with migraine used triptans and 1.6–13.7% of those eligible used preventative medication.

Background

From a public-health perspective, they are also among the most disabling at population level: according to the Global Burden of Disease (GBD) study, headache disorders collectively are the third highest cause in the world of years of healthy life lost to disability (YLDs), migraine alone being sixth (third in those aged under 50 years) [32, 91–94].

It might be expected that headache disorders would, everywhere, be considered important: as a personal medical problem by people directly affected by them, and as a public-health priority by health-care providers and health policy-makers.

Eurolight gathered data on headache disorders in a cross-sectional survey in 10 countries, which together represented >60% of the adult population (18–65 years) of the European Union (EU): Austria, France, Germany, Ireland, Italy, Lithuania, Luxembourg, Netherlands, Spain and United Kingdom (UK) [198].

Methods

Enquiry into health-care utilisation entailed questions on use for headache of acute and preventative medications, consultations for headache (yes or no) with nurse, GP, neurologist or headache specialist, investigations for headache (MRI, CT, X-rays of the neck, blood tests, ophthalmic examination), and admissions (number) to hospital because of headache.

This first identified, and separated, participants reporting headache on ≥15 days/month, of whom additional questions had enquired into frequency of acute medication use.

Probable medication-overuse headache (pMOH) was diagnosed when, in addition, simple analgesics were used on ≥15 days/month or medication including compound analgesics, opioids, triptans and/or ergots was taken on ≥10 days/month.

We selected the following as indicators of adequacy of care: (a) proportion receiving migraine-specific acute medications (triptans); (b) proportion of those clearly eligible receiving any preventative medication; (c) proportions receiving medical care through GP or specialist (neurologist or specialist in headache medicine).

Results

The ranges were, for triptans, 3.4–68.2% of all participants with migraine and, for preventative medications, 1.6–41.7% of those deemed clearly eligible for them.

In population-based samples, 3.4–22.4% of participants with migraine used triptans and 1.6–13.7% of those eligible used preventative medication.

Participants with migraine who had consulted specialists (2.1–33.8% across all studies) were receiving the best care by these indicators; those treated by GPs (9.5–29.6%) fared less well, and the larger numbers dependent on self-medication (48.0–84.2%) appeared to be inadequately treated.

In the studies with a general-population basis, a minority of participants (15.8–33.0%) had done so: 3.1–15.0% had consulted a specialist (averaged across countries: 6.8%), and 9.5–18.0% had seen a GP (average: 14.4%).

Discussion

Worse, while use of preventative medication by people with >5 migraine days/month ought by any objective standard to be close to 100%, the best we saw outside the self-selecting lay-organization members was 13.7%, and this was in an employee group with, probably, facilitated access to care.

In Germany, in three regions of the country, a population-based study of 10,000 people found only 8% of those with migraine used triptans and only 2.3% received preventative treatment, both positively associated with socio-economic status [511] and suggesting inequitable access to health care.

In order to relieve an otherwise insupportable load on specialists, health-care providers in general and GPs in particular need better knowledge of how to recognise, diagnose and treat migraine (along with the small number of other headache disorders that are of public-health importance) [178, 512].

Conclusion

These findings represent yet another call for action in Europe to improve care for people with headache.

Acknowledgement

A machine generated summary based on the work of Katsarava, Zaza; Mania, Maka; Lampl, Christian; Herberhold, Johanna; Steiner, Timothy J. 2018 in The Journal of Headache and Pain.

Characteristics of Patients Referred to a Specialized Headache Clinic

DOI: https://doi.org/10.1038/s41598-020-58234-w

Abstract-Summary
Recent studies raised the possibility of increasing rate of specialty referrals, inappropiate treatment and advanced imaging for simple headache.

The aim of our study was to analyze the characteritics of patients (including duration of symptoms, headache type, brain imaging, treatment) referred to our specialized headache clinic between 01/01/2014 and 01/01/2015 by their general practitioners and primary care neurologists due to chronic/treatment-resistant headache syndromes.

202 plain brain CT, 60 contrast-enhanced CT and 128 MRI were carried out by their general practitioners or other healthcare professioners including neurologists before referral to our headache centre.

Despite of extensive brain imaging appropiate treatment was started less than 1/3 of all patients and significant proportion received benzodiazepines or opioid therapy.

More than 10% of referred patients presented with secondary headache including one meningitis.

Vast majority of our patients should not be referred to our specialized headache clinic as they had uncomplicated headache or other underlying conditions than pain.

Extended: Vast majority of our patients fulfilled the criteria of chronic headache syndromes (those with migraine and tension-type headache) and were not properly managed in the primary care.

Vast majority of our primary headache patients fulfilled the criteria of chronic headache, but less than one-third of them received proper prohylactic or maintenance therapy in accordance with the current European and Hungarian recommendations.

Introduction
As headache disorders are amongst the leading cause of years lived with disability worldwide (migraine alone is ranked as third among people aged 15 to 49 years) to improve the management of patients with headache, the Hungarian Headache Society established 29 Specialized Headache Centers, which accept referrals from general practitioners (and other medical professioners) or from neurologists not specialized in headache [46, 513].

Our specialized headache center was established in 2014 in Szigetvar, accepting referrals from 3 primary hospitals, 4 general outpatient clinics and 25 general practitioners, overall covering more than 70,000 patients in South West Hungary [513].

As only several reports (and no studies from our country) are available with regard to primary care management of headache patients we overtook a retrospetive study to analyze the characteritics of patients (including duration of symptoms, headache type, brain imaging, treatment and cardiovascular risk factors) referred to

our headache clinic by their general practitioners and primary care neurologists due to chronic/treatment-resistant headache syndromes.

Patients and Methods

202 patients were referred to our outpatient service between 01/01/2014 and 01/01/2015 and data were retrospectively analyzed.

Duration of symptoms, brain imaging (including plain computer tomograph / CT/, contrast-enhanced CT and magnetic resonance imaging /MRI/), previous outpatient/hospital attendance due to headache and treatment strategies were extracted from hospital notes.

Cardiovascular risk profile factors and previous diseases of relevance to this study included, smoking habit, diabetes mellitus, hypertension, dyslipidaemia, ischaemic heart disease (IHD), history of stroke and peripheral artery disease.

Informed consent were not given to the patients due to the retrospective nature of the study.

Results

Migraine was diagnosed in 84 patients (mean age 46.1 ± 14.7 years) corresponding to the IHS criteria (66 females, mean age 47.12 ± 15.3 years and 18 males, mean age 42.22 ± 11.3 years).

Tension-type headache was diagnosed in 76 patients (mean age 59.66 ± 17.9 years) corresponding to the IHS criteria (22 females, mean age 61.8 ± 17.3 years and 54 males, mean age 54.18 ± 18.4 years, $p < 0.05$).

Trigeminal-autonomic cephalagia was diagnosed in 18 patients (mean age 45.33 ± 12.3 years) corresponding to the IHS criteria (8 females, mean age 57.7 ± 5.1 years and 10 males, mean age 35.4 ± 5.1 years, $p < 0.05$), including 15 cluster headaches, 1 short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) syndrome and 2 hemicrania continua headache [514].

Discussion

About 20% of headache patients were properly managed in primary care which resulted in unnecessary emergency admissions and enourmous number of brain imaging.

Despite all guidelines recommend against opioids as first-line treatment for acute migraine and other primary headaches, they were prescribed for about 20% of our patients (with the highest rate in secondary headaches).

Vast majority of our patients fulfilled the criteria of chronic headache syndromes (those with migraine and tension-type headache) and were not properly managed in the primary care.

This is in concodance with recent studies, the diagnosis and management of migraine (and other primary headache syndromes - especially chronic forms) are still a challenge for primary care physicians [515].

Due to inappropiate primary care management, our patients had several emergency admissions, which were the most common in patients with trigeminal-automic cephalagia, females with migraine and males with tension-type headache.

Acknowledgement
A machine generated summary based on the work of Fejes, Eva; Feher, Gergely; Gurdan, Zsuzsanna; Gombos, Katalin; Koltai, Katalin; Pusch, Gabriella; Tibold, Antal. 2020 in Scientific Reports.

Are doctors accurate when diagnosing themselves with migraine? A study on migraine prevalence among doctors in a tertiary care hospital

DOI: https://doi.org/10.1007/s13760-021-01727-w

Abstract-Summary
Different studies show a higher prevalence in neurologists.

There are few studies about its prevalence in doctors of other specialties, where it could also be superior than in general population.

Our aim was to define migraine lifetime prevalence among doctors according to three parameters (previous diagnosis, self-diagnosis and positivity of a screening test).

Participants who reported 5 or more headaches throughout their lives were considered "headache sufferers" and were divided in different groups according to their position (specialists or trainees) and their specialty (medical, medical-surgical and surgical or specialties with no direct contact with the patient).

77% were "headache sufferers" Among all participants, migraine lifetime prevalence according to diagnosis by another physician was 15.2%, self-diagnosis 38.2% and positivity of the MS-Q 20.3%; those categories were not mutually exclusive Greater but not statistically significant coexistence of self-diagnosis and positive MS-Q was seen in specialists compared to trainees and in medical specialties.

Migraine prevalence among doctors in a tertiary care hospital was higher than in general population, according to all three parameters analyzed.

Extended: These findings could be useful for future prevalence studies and might also help the development of more accurate screening tools for migraine diagnosis in both general population and subgroups with a former knowledge of the disease.

Introduction
Different studies have shown higher migraine prevalence in neurologists and headache specialists [516–518], which may be explained by a deeper knowledge on the disease that could help them reach a migraine self-diagnosis, without needing another doctor's confirmation [519].

Those fewer studies that have evaluated migraine prevalence in other specialties, most of them focused on primary care doctors, have shown a similar prevalence to that of the general population [520–523].

To the best of our knowledge, there are no studies that have compared migraine prevalence in doctors from different specialties.

Thanks to their medical training and their familiarity with migraine, a higher prevalence could be expected in doctors responsible for the diagnosis and/or treatment of this disease, as observed in neurologists.

The main objective of our study was to estimate migraine prevalence in doctors of a tertiary hospital according to three parameters: previously diagnosed by another doctor (PD), self-diagnosis (SM) and positivity of the Spanish validated screening test, the Migraine Screen Questionnaire (positive MS-Q).

Methods

The sample included doctors from different specialties working at that moment in the hospital.

We classified participants in groups according to their specialty and position (specialists and trainees) and we determined migraine prevalence in the general sample and in the different subgroups according to PD, SM and positive MS-Q. We also analyzed the coexistence of SM and positive MS-Q in the different subgroups.

A descriptive analysis of the characteristics of both groups was performed: for the nominal variables, the sample size (N) and the percentage (%) per group were shown, and a χ^2 test or the Fisher exact test was performed.

Model, variables that in the descriptive had shown a $p \leq 0.1$ were included.

Results

Of the 95 specialists participating in our study, 75 (78.9%) have had ≥5 headaches throughout their lives, as they are necessary to consider a migraine diagnosis according to ICHD-3 criteria [20].

When asked about the type of headache they thought they suffered, 83 participants answered migraine (prevalence according to SM 83/217 (38.2%)).

According to specialties, 26/119 (21.8%) of the participants in the group of "medical specialties" presented SM and positive MS-Q, while this proportion was 5/30 (16.7%) in the participants of the group "surgical and medical-surgical" and 6/18 (3.3%) in group of specialists with "no direct treat with patients".

Regarding work position, 18/82 (21.9%) of the trainees and 29/75 (38.7%) of the specialists had both SM and positive MS-Q. However, these differences observed in SM and MS-Q coexistence between specialty groups and work position did not reach statistical significance ($p = 0.086$ and $p = 0.083$, respectively).

Discussion

According to our work, 58.3% of the neurologists reported a self-diagnosis of migraine while only 20.8% had a positive MS-Q. Both percentages are within the range of migraine prevalence in neurologists in different studies (27.6% and 71%) [517–519].

Our study also showed a higher prevalence of migraine in specialists than in trainees according to both SM and positive MS-Q. Not only age and time with the disease could have affected the difference in migraine prevalence, but also working experience could be reflected in these results.

Ours is the first study that has tried to estimate migraine prevalence in doctors of different specialties and working position, regarding three parameters (previous diagnosis of migraine, self-diagnosis or positivity of MS-Q).

Acknowledgement
A machine generated summary based on the work of Muro, Ines; Gago-Veiga, Ana Beatriz; Vivancos, Jose; Vega-Piris, Lorena; Ruiz, Miguel; Quintas, Sonia. 2021 in Acta Neurologica Belgica.

Shortcomings and missed potentials in the management of migraine patients—experiences from a specialized tertiary care center

DOI: https://doi.org/10.1186/s10194-019-1034-8

Abstract-Summary
Despite the availability of evidence-based national and international guidelines, the management of migraine patients often remains poor, which is often attributed to a low availability of headache specialists.

The aim of this study was to investigate the adherence to national guidelines and to assess the possible potential of optimized therapy regimens in migraine patients.

We collected data of migraine patients presenting to our out-patient clinic via standardized questionnaires regarding headache, diagnostics and experience with previous treatments.

1935 migraine patients were included between 2010 and 2018.

In the 12 months before consulting our headache clinic 89.5% of the patients had consulted a general practitioner and 74.9% had consulted a neurologist because of their migraine.

Out of 1031 patients who had not been prescribed a preventative treatment 627 (60.8%) had in average 3 or more migraine attacks per month and thus qualified for a preventative treatment.

Our data suggest, that many migraine patients to this day do not receive state-of-the-art therapy.

Adherence to national and international European guidelines could improve the outcome in migraine patients.

Extended: Despite the availability of evidence-based national [524] and international [183] guidelines, the management and care provided to migraine patients is far from ideal [261].

The aim of the current study is therefore to investigate the adherence to national migraine guidelines for diagnosis and medical treatment in a sample of nearly 2000 patients consulting a third referee center for headache.

Introduction

Migraine patients still experience significant time delays in the diagnosis of their headache disorder [525] and the majority of migraine patients seem to not receive adequate acute [261] and preventative treatment [526].

Since the headache syndromes of these patients are per definition recognized by the patient and by the medical community, the question arises whether these patients were treated correctly or not, i.e. whether these patients suffer from particularly severe headache disorders and therefore are medically intractable or whether they have not been treated properly despite recognition of the disease.

The aim of the current study is therefore to investigate the adherence to national migraine guidelines for diagnosis and medical treatment in a sample of nearly 2000 patients consulting a third referee center for headache.

Methods

The headache and facial pain outpatient clinic is a specialized tertiary care center within the University Medical Center Hamburg-Eppendorf with approximately 1000 to 1200 annual registered patient contacts.

These contacts reflect all combined consultations by migraine patients, patients with other primary or secondary headaches as well as patients suffering from primary and secondary facial pain syndromes.

Due to German data protection law, data from patients not willing to participate in this study was not saved and we are therefore not able to provide a complete overview over all patients who consulted us.

Since migraine comprises the largest group of patients, providing meaningful data, we focused on migraine according to ICHD-3 criteria [527] in the following.

For all our parameters that we report we focused on the first contact with the patients to get a clear picture what type of patients consult a university outpatient specialist clinic.

Results

Patients with no prior preventative treatment missed in the 3 months prior to their first consultation on average 5.1 ± 10.9 (SD) work or school days (MIDAS, Item 1), could not do household work on 8.2 ± 11.1 days (MIDAS, Item 3) and missed on an average of 7.3 ± 11.0 days family or leisure activities (MIDAS, Item 5) because of their migraine headaches.

Patients with no prior preventative treatment and more than 3 migraine attacks per month had consulted a genral practitioner in 87.9% (551/627) of the casesand a neurologist in 67.5% (423/627) of the cases.

Of 904 patients who used preventative medications prior to their consultation, 45.8% had one, 21.2% had two and 10.3% reported three unsuccessful treatment attempts.

These patients were highly affected by their migraine headaches and previous preventative treatment had been unsuccessful or never tried.

Discussion

Most patients improve clinically, when we treated pharmacologically according to guidelines, the low adherence to evidence-based treatment strategies has considerable, and more importantly, avoidable personal as well as socio-economic consequences.

This study is not powered or designed to reflect the amount of patients who are treated properly by primary or secondary care specialists, however as mentioned the experience of many headache specialists and literature suggests that many migraine patients are treated poorly [261].

Half of the patients, presenting to a specialized tertiary care headache clinic, had never been prescribed a preventative treatment.

The rates of the improved outcome in patients that had previously not been prescribed a preventative treatment should therefore be seen as an indication that adherence to guideline therapy possibly improves the outcome, as expected.

Acknowledgement

A machine generated summary based on the work of Ziegeler, Christian; Brauns, Greta; Jürgens, Tim P.; May, Arne. 2019 in The Journal of Headache and Pain.

Prevalence and burden of headache disorders in Lithuania and their public-health and policy implications: a population-based study within the Eurolight project

DOI: https://doi.org/10.1186/s10194-017-0759-5

Abstract-Summary

The Eurolight project assessed the impact of headache disorders in ten EU countries, using the same structured questionnaire but varying sampling methods.

In Lithuania, sample selection employed methods in line with consensus recommendations for population-based burden-of-headache studies.

Of 1137 people in the pre-identified sample, 573 (male 237 [41.4%], female 336 [58.6%]; mean age 40.9 ± 13.8 years) completed interviews (participation proportion: 50.4%).

Gender-adjusted 1-year prevalences were: any headache 74.7%; migraine 18.8%; tension-type headache (TTH) 42.2%; all headache on ≥15 days/month 8.6%; probable medication-overuse headache (pMOH) 3.2%.

Migraine (OR: 3.6) and pMOH (OR: 2.9) were associated with female gender.

All headache types except TTH were associated with significantly diminished quality of life.

Lost per-person times due to TTH were much less, but to pMOH and other headache on ≥15 days/month much higher.

Among the entire workforce, lost productivity to migraine was estimated at 0.7%, to TTH 0.3% and to pMOH or other headache on ≥15 days/month 0.5%.

The multiple burdens from headache in Lithuania indicate substantial ill-health and unmet need for health care.

Of particular concern is the high prevalence of headache on ≥15 days/month, seen also in Russia and Georgia.

Health policy in Lithuania must heed WHO's advice that effective treatment of headache, clearly desirable for its health benefits, is also expected to be cost-saving.

Extended: All headache types were associated with diminutions, which were significant for all but TTH.

Health policy in Lithuania must take note of these findings, and of WHO's advice that effective treatment of headache is desirable not only for its health benefits but also because it is likely to be cost-saving [528].

We present the Lithuania findings as national estimates.

Background

Disorders, migraine and tension-type headache (TTH) are often lifelong illnesses which, as well as causing pain and disability, also diminish productivity, hinder family and social relationships and impoverish quality of life (QoL).

Medication-overuse headache (MOH), usually a sequela of migraine or TTH caused by mistreatment of one or the other, occurs by definition on most days and is especially damaging to QoL. Epidemiologically, many published studies demonstrate that headache disorders are ubiquitous and common [89].

In Europe, meanwhile, despite many studies reporting migraine prevalence, there were still major knowledge gaps regarding TTH and MOH, and for all headache types there were few published data on headache-attributed burden [443, 529].

Multiple scientific and lay organisations collaborated with headache experts in these countries, and not all were able to draw population-based samples.

These procedures came close to matching the recommended methodology for population-based burden-of-headache studies [51].

Methods

In order to obviate recall error [50, 51], we assessed burden on the preceding day: in respect of HY, we enquired into duration and intensity of the headache, and lost productivity as a consequence of it.

According to the algorithm used to convert questionnaire responses to diagnoses [50], headache occurring on ≥15 days/month was first set aside from episodic headaches (frequency < 15 days/month), and diagnosed according to reported acute medication consumption either as probable MOH (pMOH) or other headache on ≥15 days/month.

When a participant reporting HY described one type of headache only, we assumed HY was of this type.

We recorded headache frequency in days/month, duration in hours (for HY only, this was categorized as <1, 1–4, 5–12 and > 12 h), and intensity in terms meaning "mild", "moderate" or "severe", which we converted to a numerical rating scale of 1–3 (0 being no pain) and treated as continuous data.

Results

TTH (OR: 1.1 [0.8–1.6]) and other headache on ≥15 days/month (OR: 1.3 [0.6–2.6] were reported more commonly, but insignificantly so, by males.

The gender-adjusted 1-year prevalences were 18.8% for migraine, 42.2% for TTH, 3.2% for pMOH and 5.4% for other headache on ≥15 days/month.

Of the 70 reports of HY, one third were in participants with pMOH (n = 10) or other headache on ≥15 days/month (n = 13).

Participants with migraine scored 27.1 ± 6.0 (Student's t-test, 2-sided: p = 0.0025 versus no headache), those with TTH 28.4 ± 6.0 (p = 0.126), those with pMOH 25.8 ± 4.8 (p = 0.0048) and those with other headache on ≥15 days/month 24.9 ± 4.8 (p < 0.0001).

Discussion

At population level, lost paid worktime for those with TTH can likewise be estimated at 0.3% (0.7*42.2%) overall, and those for pMOH or other headache on ≥15 days/month (very approximately from small numbers) at 0.5%.

The gender-adjusted 1-year prevalences were 20.8% for migraine (compared with 18.8% for Lithuania), 30.8% for TTH (42.2% for Lithuania) and 10.4% for all headache on ≥15 days/month (8.6% for Lithuania) [98].

The countries differ is in pMOH: among the 10.4% in Russia with headache on ≥15 days/month, 68.1% were overusing acute medication [98], giving rise to an estimated prevalence of pMOH of 7.1% against Lithuania's 3.2%.

Georgia had a larger participating sample of 1145, of whom 15.6% were diagnosed with migraine, 37.3% with TTH and 7.6% with any headache on ≥15 days/month (including, perhaps, 0.9% with pMOH) [97].

Conclusions

The symptom, disability, lost-productivity and impaired-QoL burdens signal substantial ill-health, and therefore unmet need for health care [91].

This is a message that has been repeated to policy-makers in countries all over the world [530], but here, from this study, is empirical evidence to underpin it in Lithuania.

As in other countries, the high impact on individuals is matched by high economic burden; both are unmitigated by failures in health care.

Health policy in Lithuania must take note of these findings, and of WHO's advice that effective treatment of headache is desirable not only for its health benefits but also because it is likely to be cost-saving [528].

Acknowledgement

A machine generated summary based on the work of Rastenytė, Daiva; Mickevičienė, Dalia; Stovner, Lars Jacob; Thomas, Hallie; Andrée, Colette; Steiner, Timothy J. 2017 in The Journal of Headache and Pain.

Lifting the burden of headache in China: managing migraine in a SMART way

DOI: https://doi.org/10.1186/s10194-017-0790-6

Abstract-Summary
This project, which was within the Global Campaign against Headache, showed that headache disorders have a major adverse impact on public health in China.

As essential support for implementing headache services around the country, an enactment of stage 3 (intervention) of the Global Campaign against Headache – the continuing medical education (CME) program Headache Schools – was established. '.

As we promote SMART in CME, we can use the database of our computerized clinical decision support systems to evaluate the impact on treatment outcomes.

Correspondence/Findings
A finding of the survey was that there is a large gap between the medical needs of the Chinese population with migraine and the diagnostic and treatment skills of, among others, neurologists who manage headache in China [531].

As part of the educational activities and clinical practice training, a systematic and operational disease management model known as 'SMART' (Screen, Migraine, Aura, Red flag and Treatment) was introduced to standardize clinical diagnosis and treatment approaches to migraine.

This disease management model has provided opportunities for practitioners to enhance their knowledge of primary headaches, especially migraine, and use this knowledge to improve their daily practice and clinical outcomes.

The Screen element of the model emphasizes the use of validated scales to recognize possible migraine among patients with headache—the first step in successful management.

In headache clinics, healthcare providers have adopted CDSSs in combination with SMART to optimize their management of headache disorders, especially migraine.

Acknowledgement
A machine generated summary based on the work of Yu, Shengyuan; Steiner, Timothy J. 2017 in The Journal of Headache and Pain.

References

1. Hung PH, Fuh JL, Wang SJ. Validity, reliability and application of the Taiwan version of the migraine disability assessment questionnaire. J Formos Med Assoc. 2006;105(7):563–8.
2. Wang SJ, Wang PJ, Fuh JL, Peng KP, Ng K. Comparisons of disability, quality of life, and resource use between chronic and episodic migraineurs: a clinic-based study in Taiwan. Cephalalgia. 2013;33(3):171–81.

3. Iigaya M, Sakai F, Kolodner KB, Lipton RB, Stewart WF. Reliability and validity of the Japanese Migraine Disability Assessment (MIDAS) Questionnaire. Headache. 2003;43(4):343–52.
4. Yu S, Liu R, Zhao G, Yang X, Qiao X, Feng J, et al. The prevalence and burden of primary headaches in China: a population-based door-to-door survey. Headache. 2012;52(4):582–91.
5. Fuh JL, Wang SJ, Lu SR. Impact of migraine on the employed labor force in Taiwan. J Chin Med Assoc. 2008;71(2):74–8.
6. Tang CH, Chen YC, Ng K, Wang SJ. A retrospective matched case-control study on medical costs of refractory migraine in Taiwan. Headache. 2013;53(3):526–39.
7. Roh JK, Kim JS, Ahn YO. Epidemiologic and clinical characteristics of migraine and tension-type headache in Korea. Headache. 1998;38(5):356–65.
8. GBD 2016 Headache Collaborators. Global, regional, and national burden of migraine and tension-type headache, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2018;17(11):954–976.
9. Peng KP, Wang SJ. Epidemiology of headache disorders in the Asia-Pacific region. Headache. 2014;54(4):610–8.
10. Blumenfeld AM, Varon SF, Wilcox TK, Buse DC, Kawata AK, Manack A, et al. Disability, HRQoL and resource use among chronic and episodic migraineurs: results from the International Burden of Migraine Study (IBMS). Cephalalgia. 2011;31(3):301–15.
11. Vo P, Fang J, Bilitou A, Laflamme AK, Gupta S. Patients' perspective on the burden of migraine in Europe: a cross-sectional analysis of survey data in France, Germany, Italy, Spain, and the United Kingdom. J Headache Pain. 2018;19(1):82.
12. GBD 2019 Demographics Collaborators. Global age-sex-specific fertility, mortality, healthy life expectancy (HALE), and population estimates in 204 countries and territories, 1950–2019: a comprehensive demographic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1160–203. https://doi.org/10.1016/S0140-6736(20)30977-6.
13. Linde M, Gustavsson A, Stovner LJ, et al. The cost of headache disorders in Europe: the Eurolight project. Eur J Neurol. 2012;19(5):703–11. https://doi.org/10.1111/j.1468-1331.2011.03612.x.
14. Irimia P, Garrido-Cumbrera M, Santos-Lasaosa S, et al. Estimating the savings associated with a migraine-free life: results from the Spanish Atlas. Eur J Neurol. 2020;27(12):2616–24. https://doi.org/10.1111/ene.14431.
15. Messali A, Sanderson JC, Blumenfeld AM, Goadsby PJ, Buse DC, Varon SF, et al. Direct and indirect costs of chronic and episodic migraine in the United States: a web-based survey. Headache. 2016;56(2):306–22.
16. Vicente-Herrero T, Burke TA, Laínez MJA. The impact of a worksite migraine intervention program on work productivity, productivity costs, and non-workplace impairment among Spanish postal service employees from an employer perspective. Curr Med Res Opin. 2004;20(11):1805–14. https://doi.org/10.1185/030079904X10151.
17. Schaetz L, Rimner T, Pathak P, et al. Employee and employer benefits from a migraine management program: disease outcomes and cost analysis. Headache. 2020;60(9):1947–60. https://doi.org/10.1111/head.13933.
18. Haw NJ, Cabaluna IT, Kaw GE, Cortez JF, Chua MP, Guce K. A cross-sectional study on the burden and impact of migraine on work productivity and quality of life in selected workplaces in the Philippines. J Headache Pain. 2020;21(1):125. https://doi.org/10.1186/s10194-020-01191-6.
19. Wong LP, Alias H, Bhoo-Pathy N, et al. Impact of migraine on workplace productivity and monetary loss: a study of employees in banking sector in Malaysia. J Headache Pain. 2020;21(1):68. https://doi.org/10.1186/s10194-020-01144-z.
20. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38(1):1–211. https://doi.org/10.1177/0333102417738202.
21. Yang M, Rendas-Baum R, Varon SF, Kosinski M. Validation of the headache impact test (HIT-6TM) across episodic and chronic migraine. Cephalalgia. 2011;31(3):357–67. https://doi.org/10.1177/0333102410379890.

22. Prasad M, Wahlqvist P, Shikiar R, Shih YCT. A review of self-report instruments measuring health-related work productivity: a patient-reported outcomes perspective. PharmacoEconomics. 2004;22(4):225–44. https://doi.org/10.2165/00019053-200422040-00002.
23. Grupo de Trabajo Multidisciplinar del Atlas de la Migraña en España (2018) Impacto y Situación de La Migraña En España: Atlas 2018. Editorial Universidad de Sevilla 1–183. ISBN:978-84-472-2832-4.
24. Marcus SC, Shewale AR, Silberstein SD, et al. Comparison of healthcare resource utilization and costs among patients with migraine with potentially adequate and insufficient triptan response. Cephalalgia. 2020;40(7):639–49. https://doi.org/10.1177/0333102420915167.
25. World Health Organization. Workers' health: global plan of action. https://www.who.int/occupational_health/publications/global_plan/en/. Accessed 13 Dec 2020.
26. Chandana SR, Movva S, Arora M, et al. Primary brain tumors in adults. Am Fam Physician. 2008;77:1423–30.
27. Goffaux P, Fortin D. Brain tumor headaches: from bedside to bench. Neurosurgery. 2010;67:459–66.
28. Purdy RA, Kirby S. Headaches and brain tumors. Neurol Clin. 2004;22:39–53.
29. Pfund Z, Szapary L, Jaszberenyi O, et al. Headache in intracranial tumors. Cephalalgia. 1999;19:787–90.
30. Index Mundi. Ethiopia age structure 2019. https://www.indexmundi.com/ethiopia/age_structure.html (accessed 4 April 2020).
31. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V, Abraham J, Ackerman I, Aggarwal R, Ahn SY, Ali MK, Alvarado M, Anderson HR, Anderson LM, Andrews KG, Atkinson C, Baddour LM, Bahalim AN, Barker-Collo S, Barrero LH, Bartels DH, Basáñez MG, Baxter A, Bell ML, Benjamin EJ, Bennett D, Bernabé E, Bhalla K, Bhandari B, Bikbov B, Bin Abdulhak A, et al. Years lived with disability (YLD) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the global burden of disease study 2010. Lancet. 2012;380:2163–96.
32. Vos T, Barber RM, Bell B, Bertozzi-Villa A, Biryukov S, Bolliger I, Charlson F, Davis A, Degenhardt L, Dicker D, Duan L, Erskine H, Feigin VL, Ferrari AJ, Fitzmaurice C, Fleming T, Graetz N, Guinovart C, Haagsma J, Hansen GM, Hanson SW, Heuton KR, Higashi H, Kassebaum N, Kyu H, Laurie E, Liang X, Lofgren K, Lozano R, MacIntyre MF, Moradi-Lakeh M, Naghavi M, Nguyen G, Odell S, Ortblad K, Roberts DA, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the global burden of disease study 2013. Lancet. 2015;386:743–800.
33. GBD (2015) Disease and injury incidence and prevalence collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the global burden of disease study 2015. Lancet. 2016;388:1545–602.
34. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1211–59.
35. GBD (2017) Disease and injury incidence and prevalence collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the global burden of disease study 2017. Lancet. 2017;392:1789–858.
36. Steiner TJ. Lifting the burden: the global campaign against headache. Lancet Neurol. 2004;3:204–5.
37. Steiner TJ. Lifting The Burden: the global campaign to reduce the burden of headache worldwide. J Headache Pain. 2005;6:373–7.
38. Steiner TJ, Birbeck GL, Jensen R, Katsarava Z, Martelletti P, Stovner LJ. The global campaign, World Health Organization and Lifting The Burden: collaboration in action. J Headache Pain. 2011;12:273–4.

39. Lifting The Burden. http://www.l-t-b.org (Accessed 4 Apr 2020).
40. Wöber C, Wöber-Bingöl C, Uluduz D, Aslan TS, Uygunoglu U, Tüfekçi A, Alp SI, Duman T, Sürgün F, Emir GK, Demir CF, Balgetir F, Özdemir YB, Auer T, Siva A, Steiner TJ. Undifferentiated headache: broadening the approach to headache in children and adolescents, with supporting evidence from a nationwide school-based cross-sectional survey in Turkey. J Headache Pain. 2018;19:18.
41. Philipp J, Zeiler M, Wöber C, Wagner G, Karwautz AFK, Steiner TJ, Wöber-Bingöl C. Prevalence and burden of headache in children and adolescents in Austria—a nationwide study in a representative sample of pupils aged 10-18 years. J Headache Pain. 2019;20:101.
42. Zebenigus M, Tekle-Haimanot R, Worku DK, Thomas H, Steiner TJ. The prevalence of primary headache disorders in Ethiopia. J Headache Pain. 2016;17:110.
43. Wöber-Bingöl C, Wöber C, Uluduz D, Uygunoğlu U, Aslan T, Kernmayer M, Zesch H-E, Gerges NTA, Wagner G, Siva A, Steiner TJ. The global burden of headache in children and adolescents—developing a questionnaire and methodology for a global study. J Headache Pain. 2014;15:86.
44. Genc D, Vaičienė-Magistris N, Zaborskis A, Şaşmaz T, Tunç AY, Uluduz D, Steiner TJ. The prevalence of headache disorders in children and adolescents in Lithuania: a schools-based study. J Headache Pain. 2020;21:73.
45. Zewde YZ, Zebenigus M, Demissie H, Tekle-Haimanot R, Uluduz D, Şaşmaz T, Bozdag F, Steiner TJ. The prevalence of headache disorders in children and adolescents in Ethiopia: a schools-based study. J Headache Pain. 2020;21(1):108.
46. Saylor D, Steiner TJ. The global burden of headache. Semin Neurol. 2018;38:182–90.
47. Steiner TJ, Stovner LJ, Vos T, Jensen R, Katsarava Z. Migraine is first cause of disability in under 50s: will health politicians now take notice? J Headache Pain. 2018;19:17.
48. Lifting The Burden. http://www.l-t-b.org (Accessed 19 June 2019).
49. Steiner TJ, Birbeck GL, Jensen R, Katsarava Z, Martelletti P, Stovner LJ. Lifting The Burden: the first 7 years. J Headache Pain. 2010;11:451–5.
50. Steiner TJ, Gururaj G, Andrée C, Katsarava Z, Ayzenberg I, Yu S-Y, Al Jumah M, Tekle-Haimanot R, Birbeck GL, Herekar A, Linde M, Mbewe E, Manandhar K, Risal A, Jensen R, Queiroz L-P, Scher AI, Wang S-J, Stovner TJ. Diagnosis, prevalence estimation and burden measurement in population surveys of headache: presenting the HARDSHIP questionnaire. J Headache Pain. 2014;15:3.
51. Stovner LJ, Al Jumah M, Birbeck GL, Gururaj G, Jensen R, Katsarava Z, Queiroz L-P, Scher AI, Tekle-Haimanot R, Wang S-J, Steiner TJ. The methodology of population surveys of headache prevalence, burden and cost: principles and recommendations. A product of the Global Campaign against Headache. J Headache Pain. 2014;15:5.
52. Manandhar K, Risal A, Steiner TJ, Holen A, Linde M. The prevalence of primary headache disorders in Nepal: a nationwide population-based study. J Headache Pain. 2015;16:95.
53. Linde M, Edvinsson L, Manandhar K, Risal A, Steiner TJ. Migraine associated with altitude: results from a population-based study in Nepal. Eur J Neurol. 2017;24:1055–61.
54. Wang Y, Xie J, Yang F, et al. The prevalence of primary headache disorders and their associated factors among nursing staff in North China. J Headache Pain. 2015;16:4.
55. Yu SY, Cao XT, Zhao G, et al. The burden of headache in China: validation of diagnostic questionnaire for a population-based survey. J Headache Pain. 2011;12(2):141–6.
56. Minen MT, De Dhaem OB, Van Diest AK, Powers S, Schwedt TJ, Lipton R, et al. Migraine and its psychiatric comorbidities. J Neurol Neurosurg Psychiatry. 2016;87(7):741–9.
57. Teixeira AL, Costa EAC, da Silva AA, dos Santos IAM, Gómez RS, Kummer A, et al. Psychiatric comorbidities of chronic migraine in community and tertiary care clinic samples. J Headache Pain. 2012;13(7):551.
58. Subramaniam M, Vaingankar JA, Abdin E, Chong SA. Psychiatric morbidity in pain conditions: results from the Singapore Mental Health Study. Pain Res Manag. 2013;18(4):185–90.
59. Singapore Department of Statistics. Population trends 2014 2014. Retrieved from https://www.singstat.gov.sg/modules/infographics/population

60. McWilliams LA, Goodwin RD, Cox BJ. Depression and anxiety associated with three pain conditions: results from a nationally representative sample. Pain. 2004;111(1–2):77–83.
61. Risal A, Manandhar K, Holen A, Steiner TJ, Linde M. Comorbidities of psychiatric and headache disorders in Nepal: implications from a nationwide population-based study. J Headache Pain. 2016;17(1):45.
62. Buse DC, Loder EW, Gorman JA, Stewart WF, Reed ML, Fanning KM, et al. Sex differences in the prevalence, symptoms, and associated features of migraine, probable migraine and other severe headache: results of the American Migraine Prevalence and Prevention (AMPP) study. Headache. 2013;53(8):1278–99.
63. Tai M-LS, Yap JF, Goh CB. Dietary trigger factors of migraine and tension-type headache in a south east Asian country. J Pain Res. 2018;11:1255.
64. Zhang Y, Shi Z, Hock D, Yue W, Liu S, Zhang Y, et al. Prevalence of primary headache disorders in a population aged 60 years and older in a rural area of Northern China. J Headache Pain. 2016;17(1):83.
65. Camarda R, Monastero R. Prevalence of primary headaches in Italian elderly: preliminary data from the Zabut Aging Project. Neurol Sci. 2003;24(2):s122–4.
66. Victor T, Hu X, Campbell J, Buse D, Lipton R. Migraine prevalence by age and sex in the United States: a life-span study. Cephalalgia. 2010;30(9):1065–72.
67. Takeshima T, Ishizaki K, Fukuhara Y, Ijiri T, Kusumi M, Wakutani Y, et al. Population-based door-to-door survey of migraine in Japan: the Daisen study. Headache. 2004;44(1):8–19.
68. Bruti G, Magnotti M, Iannetti G. Migraine and depression: bidirectional co-morbidities? Neurol Sci. 2012;33(1):107–9.
69. Sivaji M, Manickavasagam J, Sundaramurthi I, Gopinathan S. A study on prevalence and co-morbidity of bipolar and anxiety disorders in chronic headache patients. Int J Res Med Sci. 2017;5(7):3038–43.
70. Jette N, Patten S, Williams J, Becker W, Wiebe S. Comorbidity of migraine and psychiatric disorders—a national population-based study. Headache. 2008;48(4):501–16.
71. Harnod T, Lin C-L, Kao C-H. Survival outcome and mortality rate in patients with migraine: a population-based cohort study. J Headache. 2018;19(1):57.
72. Sheffield RE. Migraine prevalence: a literature review. Headache. 1998;38:595–601.
73. Saed MG, Aly SM, Karim A Masood, editors. Red Sea Governorate achievement index. 2012. [Arabic].
74. Headache Classification Committee. The international classification of headache disorders (2nd edition). Cephalalgia. 2004;24:1–160.
75. Fernandes PT, Salgado PC, Naronha AL, de Boer HM, Prilipko L, Sander JW, Li LM. Epilepsy stigma perception in an urban area of a limited-resource country. Epilepsy Behav. 2007;11:25–32.
76. Nachit-Ouinekh F, Chrysostome V, Henry P, Sourgen C, Dartiques JE, El hasanoui A. Variability of reported headache symptoms and diagnosis of migraine at 12 months. Cephalalgia. 2005;25:117–23.
77. World Health Organization, Headache disorders. Fact sheet N_277, 2004.
78. Lipton R, Bigal M. Migraine: epidemiology, impact, and risk factors for progression. Headache J Head Face Pain. 2005;45:s1.
79. Tepper SJ, Dahlof C, Dowson A, Newman L, Mansbach H, Jones M, Pham B, Webster C, Salonen R. Prevalence and diagnosis of migraine in patients consulting their primary care physician with a complaint of headache: data from the landmark study. Headache. 2004;44:856–64.
80. Headache Classification Committee of the International Headache S. The international classification of headache disorders, 3rd edition (beta version). Cephalalgia. 2013;33:629–808.
81. Diamond M, Freitag F, Lipton R, Michael L, Reed L. Migraine prevention patterns in a community sample: results from the American Migraine Prevalence and Prevention (AMPP) study. Headache The Journal of Head and Face Pain. 2005;45. Confrence: 47th Annual Scientific Meeting of the theAmerican Headache Society.

82. Kandil M, Hamed S, Fadel K, Khalifa H, Ghanem M, Mohamed K. Migraine in Assiut governorate, Egypt: epidemiology, risk factors, comorbid conditions and predictors of change from episodic to chronic migraine. Neurol Res. 2016;38(3):232–41.
83. Ghorbani A, Abtahi S, Fereidan-Esfahani M, Abtahi S, Shemshaki H, Akbari M, et al. Prevalence and clinical characteristics of headache among medical students, Isfahan. Iran J Res Med Sci. 2013;18(Suppl 1):S24–7.
84. Davies PTG, Peatfield RC, Steiner TJ, Bond RA, Rose FC. Some clinical comparisons between common and classical migraine: a questionnaire-based study. Cephalalgia. 1991;11:223–7.
85. Ranson R, Igarashi H, MacGregor EA, Wilkinson M. The similarities and differences of migraine with aura and migraine without aura: a preliminary study. Cephalalgia. 1991;11:189–92.
86. Zielger DK, Hassanein RS. Specific headache phenomena: their frequency and coincidence. Headache. 1990;30:152–6.
87. Ibrahim N, Alotaibi A, Alhazmi A, Alshehri R, Saimaldaher R, Murad M. Prevalence, predictors and triggers of migraine headache among medical students and interns in king Abdulaziz University, Jeddah, Saudi Arabia. Pak J Med Sci. 2017;33(2):270–5.
88. Noor T, Sajjad A, Asma A. Frequency, character and predisposing factor of headache among students of medical college of Karachi. J Pak Med Assoc. 2016;66(2):159–64.
89. Stovner LJ, Hagen K, Jensen R, Katsarava Z, Lipton RB, Scher AI, Steiner TJ, Zwart J-A. The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia. 2007;27:193–210.
90. World Health Organization and Lifting The Burden. Atlas of headache disorders and resources in the world 2011. Geneva: WHO Press; 2011.
91. Steiner TJ, Birbeck GL, Jensen RH, Katsarava Z, Stovner LJ, Martelletti P. Headache disorders are third cause of disability worldwide. J Headache Pain. 2015;16:58.
92. United Nations Department of Economic and Social Affairs, Population Division. World population prospects: the 2015 revision. Key findings and advance tables (Working Paper No ESA/P/WP241). United Nations, New York 2015.
93. Kulkarni GB, Rao GN, Gururaj G, Stovner LJ, Steiner TJ. Headache disorders and public ill-health in India: prevalence estimates in Karnataka state. J Headache Pain. 2015;16:67.
94. Vos T, Allen C, Arora M, Barber RM, Bhutta ZA, Brown A, Carter A, Casey DC, Charlson FJ, Chen AZ, Coggeshall M, Cornaby L, Dandona L, Dicker DJ, Dilegge T, Erskine HE, Ferrari AJ, Fitzmaurice C, Fleming T, Forouzanfar MH, Fullman N, Gething PW, Goldberg EM, Graetz N, Haagsma JA, Hay SI, Johnson CO, Kassebaum NJ, Kawashima T, Kemmer L, Khalil IA, Kinfu Y, Kyu HH, Leung J, Liang X, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the global burden of disease study 2015. Lancet. 2016;388:1545–602.
95. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392:1789–858.
96. Lifting The Burden. http://www.l-t-b.org (Last accessed 29 Oct 2019).
97. Katsarava Z, Dzagnidze A, Kukava M, Mirvelashvili E, Djibuti M, Janelidze M, Jensen R, Stovner LJ, Steiner TJ. Primary headache disorders in the republic of Georgia: prevalence and risk factors. Neurology. 2009;73:1796–803.
98. Ayzenberg I, Katsarava Z, Sborowski A, Chernysh M, Osipova V, Tabeeva G, Yakhno N, Steiner TJ. The prevalence of primary headache disorders in Russia: a countrywide survey. Cephalalgia. 2012;32:373–81.
99. Mbewe E, Zairemthiama P, Yeh H-H, Paul R, Birbeck GL, Steiner TJ. The epidemiology of primary headache disorders in Zambia: a population-based door-to-door survey. J Headache Pain. 2015;16:30.
100. Herekar AA, Ahmad A, Uqaili UL, Ahmed B, Effendi J, Alvi SZ, Shahab MA, Javed U, Herekar AD, Khanani R, Steiner TJ. Primary headache disorders in the adult general

population of Pakistan—a cross sectional nationwide prevalence survey. J Headache Pain. 2017;18:28.
101. Kingdom of Saudi Arabia General Authority for Statistics. The general population and housing census 2010. https://www.stats.gov.sa/en/13 (Last accessed 29 Oct 2019).
102. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. Cephalalgia. 2004;24(suppl 1):9–160.
103. Streel S, Donneau AF, Hoge A, Albert A, Schoenen J, Guillaume M. One-year prevalence of migraine using a validated extended French version of the ID migraine™: a Belgian population-based study. Rev Neurol (Paris). 2015;171:707–14.
104. Stovner LJ, Zwart JA, Hagen K, Terwindt GM, Pascual J. Epidemiology of headache in Europe. Eur J Neurol. 2006;13:333–45.
105. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: data from the American migraine study II. Headache. 2001;41:646–57.
106. Leonardi M. Burden of migraine: what should we say more? Neurol Sci. 2015;36(Suppl 1):1–3.
107. Granella F, Cavallini A, Sandrini G, Manzoni GC, Nappi G. Long-term outcome of migraine. Cephalalgia. 1998;18:30–3.
108. Colombo B, Dalla Libera D, Dalla Costa G, Comi G. Refractory migraine: the role of the physician in assessment and treatment of a problematic disease. Neurol Sci. 2013;34(Suppl 1):109–12.
109. Vicente-Herrero MT, Iñiguez R, de la Torre MV, Capdevila García LM, López-González ÁA, Terradillos García MJ. Migraña crónica y trabajo. Riesgos laborales y aspectos preventivos. SEMERGEN - Med Familia. 2013;39(6):316–24. https://doi.org/10.1016/j.semerg.2012.10.006.
110. Mäki K, Vahtera J, Virtanen M, Elovainio M, Keltikangas-Järvinen L, Kivimäki M. Work Stress and New-Onset Migraine in a Female Employee Population. Cephalalgia. 2008;28(1):18–25. https://doi.org/10.1111/j.1468-2982.2007.01462.x.
111. Le H, Tfelt-Hansen P, Skytthe A, Kyvik KO, Olesen J. Association between migraine, lifestyle and socioeconomic factors: a population-based cross-sectional study. J Headache Pain. 2011;12(2):157–72. https://doi.org/10.1007/s10194-011-0321-9.
112. Etminan M, Brophy JM, Collins G, Nazemipour M, Mansournia MA. To adjust or not to adjust: the role of different covariates in cardiovascular observational studies. Am Heart J. 2021;237:62–7. https://doi.org/10.1016/j.ahj.2021.03.008.
113. Sjösten N, et al. Influence of retirement and work stress on headache prevalence: A longitudinal modelling study from the GAZEL Cohort Study. Cephalalgia. 2011;31(6):696–705. https://doi.org/10.1177/0333102410394677.
114. GBD (2019) Diseases and injuries collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of disease study 2019. Lancet. 2020;396:1204–22.
115. Colas R, Munoz P, Temprano R, Gomez C, Pascual J. Chronic daily headache with analgesic over-use: epidemiology and impact on quality of life. Neurology. 2004;62:1338–42.
116. Katsarava Z, Muessig M, Dzagnidze A, Fritsche G, Diener HC, Limmroth V. Medication overuse headache: rates and predictors for relapse in a 4-year prospective study. Cephalalgia. 2005;25:12–5.
117. Jonsson P, Hedenrud T, Linde M. Epidemiology of medication overuse headache in the general Swedish population. Cephalalgia. 2011;31:1015–22.
118. Lampl C, Thomas H, Stovner LJ, Tassorelli C, Katsarava Z, Laínez JMA, Lantéri-Minet M, Rastenyte D, Ruiz de la Torre E, Andrée C, Steiner TJ. Interictal burden attributable to episodic headache: findings from the Eurolight project. J Headache Pain. 2016;17:9.
119. Straube A, et al. Headache in school children: prevalence and risk factors. Dtsch Arztebl Int. 2013;110(48):811–8.
120. Xavier MK, et al. Prevalence of headache in adolescents and association with use of computer and videogames. Cien Saude Colet. 2015;20(11):3477–86.

121. Li C, et al. Prevalence of primary headache disorders among information technology staff in China: the negative effects of computer use and other correlative factors. BMC Public Health. 2020;20(1):443.
122. Wang J, et al. Mobile phone use and the risk of headache: a systematic review and meta-analysis of cross-sectional studies. Sci Rep. 2017;7(1):12595.
123. Altamura C, et al. Locking down the CGRP pathway during the COVID-19 pandemic lock-down: the PandeMig study. Neurol Sci. 2020;41(12):3385–9.
124. Porta-Etessam J, et al. Spectrum of headaches associated with SARS-CoV-2 infection: study of healthcare professionals. Headache. 2020;60:1697–704.
125. Al-Hashel JY, et al. Impact of coronavirus disease 2019 (COVID-19) pandemic on patients with migraine: a web-based survey study. J Headache Pain. 2020;21(1):115.
126. Smith AP. Acute tension-type headaches are associated with impaired cognitive function and more negative mood. Front Neurol. 2016;7:42.
127. Moore DJ, et al. Headache impairs attentional performance. Pain. 2013;154(9):1840–5.
128. Monzani L, et al. Anxiety and the severity of tension-type headache mediate the relation between headache presenteeism and workers' productivity. PLoS One. 2018;13(7):e0201189.
129. Andrée C, et al. Headache yesterday in Europe. J Headache Pain. 2014;15(1):33.
130. Suzuki N, Ishikawa Y, Gomi S, Ito N, Watanabe S, Yokoyama M, et al. Prevalence and characteristics of headaches in a socially active population working in the Tokyo metropolitan area -surveillance by an industrial health consortium. Intern Med. 2014;53(7):683–9.
131. Steiner TJ, Stovner LJ, Katsarava Z, Lainez JM, Lampl C, Lantéri-Minet M, Rastenyte D, Ruiz de la Torre E, Tassorelli C, Barré J, Andrée C. The impact of headache in Europe: principal results of the Eurolight project. J Headache Pain. 2014;15:31.
132. Lampl C, et al. Headache, depression and anxiety: associations in the Eurolight project. J Headache Pain. 2016;17:59.
133. Haag G, et al. Self-medication of migraine and tension-type headache: summary of the evidence-based recommendations of the deutsche Migräne und Kopfschmerzgesellschaft (DMKG), the deutsche Gesellschaft für Neurologie (DGN), the Österreichische Kopfschmerzgesellschaft (ÖKSG) and the Schweizerische Kopfwehgesellschaft (SKG). J Headache Pain. 2011;12(2):201–17.
134. Fernando Prieto Peres M, et al. Non-pharmacological treatment for primary headaches prevention and lifestyle changes in a low-income Community of Brazil: a randomized clinical trial. Headache. 2019;59:86–96.
135. Eysenbach G. Infodemiology and infoveillance: framework for an emerging set of public health informatics methods to analyze search, communication and publication behavior on the internet. J Med Internet Res. 2009;1:e11.
136. Vo P, et al. Burden of migraine in Europe using self-reported digital diary data from the migraine buddy© application. Neurol Ther. 2018;7(2):321–32.
137. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology. 2007;68:343–9.
138. Adams AM, Serrano D, Buse DC, et al. The impact of chronic migraine: the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study methods and baseline results. Cephalalgia. 2015;35(7):563–78.
139. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013;33(9):629–808.
140. Murray C, Vos T, Lozano R, Naghavi M, Flaxman A, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study 2010. Lancet. 2010;380:2197–223.
141. 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(suppl 1):S20–8.
142. Kosinski M, Bayliss MS, Bjorner JB, Ware JE, Garber WH, Batenhorst A, et al. A six-item short-form survey for measuring headache impact: the HIT-6. Qual Life Res. 2003;12:963–74.

143. Jacobson GP, Ramadan NM, Aggarwal SK, Newman CW. The Henry ford hospital headache disability inventory (HDI). Neurology. 1994;44:837.
144. El Hasnaoui A, Vray M, Richard A, Nachit-Ouinekh F, Boureau F, MIGSEV Group. Assessing the severity of migraine: development of the MIGSEV scale. Headache. 2003;43:628–35.
145. Wacogne C, Lacoste JP, Guillibert E, Hugues FC, Le Jeunne C. Stress, anxiety, depression and migraine. Cephalalgia. 2003;23(6):451–5.
146. Eskin M, Akyol A, Celik EY, Gultekin BK. Social problem-solving, perceived stress, depression and life-satisfaction in patients suffering from tension type and migraine headaches. Scand J Psychol. 2013;54(4):337–43.
147. Kelman L. The triggers or precipitants of the acute migraine attack. Cephalalgia. 2007;27(5):394–402.
148. Park JW, Chu MK, Kim JM, Park SG, Cho SJ. Analysis of trigger factors in episodic migraineurs using a smartphone headache diary applications. PLoS One. 2016;11(2):e0149577.
149. Lipton RB, Bigal ME, Ashina S, Burstein R, Silberstein S, Reed ML, Serrano D, Stewart WF. Cutaneous allodynia in the migraine population. Ann Neurol. 2008;63(2):148–58.
150. Lee J, Shin C, Ko YH, Lim J, Joe SH, Kim S, Jung IK, Han C. The reliability and validity studies of the Korean version of the Perceived Stress Scale. Korean J Psychosom Med. 2012;20(2):127–34.
151. Lee HS, Chung CS, Song HJ, Park HS. The reliability and validity of the MIDAS (Migraine Disability Assessment) Questionnaire for Korean migraine sufferers. J Korean Neurol Assoc. 2000;18(3):287–91.
152. Seo JG, Park SP. Validation of the Patient Health Questionnaire-9 (PHQ-9) and PHQ-2 in patients with migraine. J Headache Pain. 2015;16(1):65.
153. Seo JG, Park SP. Validation of the Generalized Anxiety Disorder-7 (GAD-7) and GAD-2 in patients with migraine. J Headache Pain. 2015;16(1):97.
154. Cho YW, Lee JH, Son HK, Lee SH, Shin C, Johns MW. The reliability and validity of the Korean version of the Epworth sleepiness scale. Sleep Breath. 2011;15(3):377–84.
155. Cho YW, Song ML, Morin CM. Validation of a Korean version of the insomnia severity index. J Clin Neurol. 2014;10(3):210–5.
156. Martin BC, Pathak DS, Sharfman MI, Adelman JU, Taylor F, Kwong WJ, Jhingran P. Validity and Reliability of the Migraine-Specific Quality of Life Questionnaire (MSQ Version 2.1). Headache. 2000;40(3):204–16.
157. Zenebe Zewde Y, Zebenigus M, Demissie H, Tekle-Haimanot R, Uluduz D, Şaşmaz T, Bozdag F, Steiner TJ. The prevalence of headache disorders in children and adolescents in Ethiopia: a schools-based study. J Headache Pain. 2020;21(1):108. https://doi.org/10.1186/s10194-020-01179-2.
158. Luvsannorov O, Anisbayar T, Davaasuren M, Baatar O, Batmagnai K, Tumurbaatar K, Enkhbaatar S, Uluduz D, Şaşmaz T, Solmaz ET, Steiner TJ. The prevalence of headache disorders in children and adolescents in Mongolia: a nationwide schools-based study. J Headache Pain. 2020;21(1):107. https://doi.org/10.1186/s10194-020-01175-6.
159. Lifting The Burden. http://www.l-t-b.org . Accessed 17 Dec 2020.
160. Steiner TJ, Lipton RB, on behalf of Lifting The Burden: The Global Campaign against Headache. The headache-attributed lost time (HALT) indices: measures of burden for clinical management and population-based research. J Headache Pain. 2018;19(1):12. https://doi.org/10.1186/s10194-018-0837-3.
161. Ravens-Sieberer U, Bullinger M. Assessing health-related quality of life in chronically ill children with the German KINDL: first psychometric and content analytical results. Qual Life Res. 1998;7(5):399–407. https://doi.org/10.1023/A:1008853819715.
162. Hunfeld JA, Perquin CW, Duivenvoorden HJ, Hazebroek-Kampschreur AA, Passchier J, van Suijlekom-Smit LW, van der Wouden JC. Chronic pain and its impact on quality of life in adolescents and their families. J Pediatr Psychol. 2001;26(3):145–53.
163. Wöber C, Wöber-Bingöl C. Clinical management of young patients presenting with headache. Funct Neurol. 2000;15:89–105.

164. Leonardi M, Raggi A. A narrative review on the burden of migraine: when the burden is the impact on people's life. J Headache Pain. 2019;20(1):41.
165. Al-Hashel JY, Ahmed SF, Alroughani R. Prevalence and burden of primary headache disorders in Kuwaiti children and adolescents: a community based study. Front Neurol. 2019;10:793.
166. Cavestro C, Montrucchio F, Benci P, Pompilio D, Mandrino S, Cencio PG, Frigeri MC, Di Pietrantonj C. Headache prevalence and related symptoms, family history, and treatment habits in a representative population of children in Alba, Italy. Pediatr Neurol. 2014;51(3):348–53.
167. van den Maagdenberg AM. Migraine genetics: New opportunities, new challenges. Cephalalgia. 2016;36(7):601–3.
168. Hershey AD, Powers SW, Vockell AL, LeCates SL, Segers A, Kabbouche MA. Development of a patient-based grading scale for PedMIDAS. Cephalalgia. 2004;24(10):844–9.
169. Virtanen R, Aromaa M, Koskenvuo M, Sillanpää M, Pulkkinen L, Metsähonkala L, Suominen S, Rose RJ, Helenius H, Kaprio J. Externalizing problem behaviors and headache: a follow-up study of adolescent Finnish twins. Pediatrics. 2004;114(4):981–7.
170. GBD 2015 DALYs and HALE Collaborators, NJ AM, Barber RM, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388:1603–58. https://doi.org/10.1016/S0140-6736(16)31460-X.
171. Edmeads J, Mackell JA. The economic impact of migraine: an analysis of direct and indirect costs. Headache. 2002;42:501–9.
172. Bloudek LM, Stokes M, Buse DC, Wilcox TK, Lipton RB, Goadsby PJ, et al. Cost of healthcare for patients with migraine in five European countries: results from the international burden of migraine study (IBMS). J Headache Pain. 2012;13(5):361–78.
173. De Matteis E, Guglielmetti M, Ornello R, Spuntarelli V, Martelletti P, Sacco S. Targeting CGRP for migraine treatment: mechanisms, antibodies, small molecules, perspectives. Expert Rev Neurother. 2020;20(6):627–41. https://doi.org/10.1080/14737175.2020.1772758.
174. Negro A, Sciattella P, Rossi D, Guglielmetti M, Martelletti P, Mennini FS. Cost of chronic and episodic migraine patients in continuous treatment for two years in a tertiary level headache Centre. J Headache Pain. 2019;20(1):120. https://doi.org/10.1186/s10194-019-1068-y.
175. Mecklenburg J, Raffaelli B, Neeb L, Sanchez Del Rio M, Reuter U. The potential of lasmiditan in migraine. Ther Adv Neurol Disord. 2020;13:1756286420967847. https://doi.org/10.1177/1756286420967847.
176. Raffaelli B, Neeb L, Reuter U. Monoclonal antibodies for the prevention of migraine. Expert Opin Biol Ther. 2019;19(12):1307–17. https://doi.org/10.1080/14712598.2019.1671350.
177. Tiseo C, Ornello R, Pistoia F, Sacco S. How to integrate monoclonal antibodies targeting the calcitonin gene-related peptide or its receptor in daily clinical practice. J Headache Pain. 2019;20(1):49. https://doi.org/10.1186/s10194-019-1000-5.
178. Steiner TJ, Antonaci F, Jensen R, Lainez MJ, Lanteri-Minet M, Valade D. Recommendations for headache service organisation and delivery in Europe. J Headache Pain. 2011;12(4):419–26. https://doi.org/10.1007/s10194-011-0320-x.
179. Agosti R. Migraine burden of disease: from the patient's experience to a socio-economic view. Headache. 2018;58:17–32.
180. Sakai F, Igarashi H. Prevalence of migraine in Japan: a nationwide survey. Cephalalgia. 1997;17(1):15–22.
181. Bonafede M, Sapra S, Shah N, Tepper S, Cappell K, Desai P. Direct and indirect healthcare resource utilization and costs among migraine patients in the United States. Headache. 2018;58(5):700–14.
182. Silberstein S, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2012;78:1337–45.
183. Evers S, Afra J, Frese A, et al. EFNS guideline on the drug treatment of migraine—revised report of an EFNS task force. Eur J Neurol. 2009;16(9):968–81.

184. Sanderson JC, Devine EB, Lipton RB, et al. Headache-related health resource utilisation in chronic and episodic migraine across six countries. J Neurol Neurosurg Psychiatry. 2013;84(12):1309–17.
185. Public Policy Committee. International Society of Pharmacoepidemiology. Guidelines for good pharmacoepidemiology practice (GPP). Pharmacoepidemiol Drug Saf. 2016;25:2–10.
186. Scher AI, Stewart WF, Lipton RB. Migraine and headache: a meta-analytic approach. In: Crombie IK, editor. Epidemiology of pain. WA: IASP press; 1999. p. 159–70.
187. Al-Hashel J, Ahmed SF, Alroughani R. Prevalence of primary headache disorders in Kuwait. Neuroepidemiology. 2017;48:138–46.
188. Steiner TJ, Gururaj G, Andrée C, Katsarava Z, Ayzenberg ISYY, Al Jumah M, Tekle-Haimanot R, Birbeck GL, Herekar A, Linde M, Mbewe E, Manandhar K, Risal A, Jensen R, Queiroz LP, Scher AI, Wang SJ, Stovner LJ. Diagnosis, prevalence estimation and burden measurement in population surveys of headache: presenting the HARDSHIP questionnaire. J Headache Pain. 2014;15:30.
189. Bener A. Frequency of headache and migraine in Qatar. Neuroepidemiology. 2006;27:61–6.
190. Deleu D, Khan MA, Al Shehab TA. Prevalence and clinical characteristics of headache in a rural community in Oman. Headache. 2002;42:963–73.
191. Ertas M, Baykan B, Orhan EK, Zarifoglu M, Karli N, Saip S, Onal A, Siva A. One-year prevalence and the impact of migraine and tension-type headache in Turkey: a nationwide home-based study in adults. J Headache Pain. 2012;13:147–57.
192. Rueda-Snchez M, daz-Martnez LA. Prevalence and associated factors for episodic and chronic daily headache in the Colombian population. Cephalalgia. 2008;28(3):216–25.
193. Allena M, Steiner TJ, Sances G, et al. Impact of headache disorders in Italy and the public-health and policy implications: a population-based study within the Eurolight project. J Headache Pain. 2015;16:100. https://doi.org/10.1186/s10194-015-0584-7.
194. Sillanpää M, Andlin-Sobocki P, Lönnqvist J. Costs of brain disorders in Finland. Acta Neurol Scand. 2008;117:167–72.
195. Martelletti P, Schwedt TJ, Lanteri-Minet M, et al. My Migraine Voice survey: a global study of disease burden among individuals with migraine for whom preventive treatments have failed. J Headache Pain. 2018;19(1):115.
196. Buse DC, Manack AN, Fanning KM, Serrano D, Reed ML, Turkel CC, et al. Chronic migraine prevalence, disability, and sociodemographic factors: results from the American Migraine Prevalence and Prevention study. Headache. 2012;52(10):1456–70.
197. Payne KA, Varon SF, Kawata AK, et al. The international burden of migraine study (IBMS): study design, methodology, and baseline cohort characteristics. Cephalalgia. 2011;31(10):1116–30.
198. Andrée C, Stovner LJ, Steiner TJ, Barré J, Katsarava Z, Lainez JM, Lair M-L, Lanteri-Minet M, Mick G, Rastenyte D, Ruiz de la Torre E, Tassorelli C, Vriezen P, Lampl C. The Eurolight project: the impact of primary headache disorders in Europe. Description of methods. J Headache Pain. 2011;12:541–9.
199. Silberstein SD, Lee L, Gandhi K, Fitzgerald T, Bell J, Cohen JM. Health care resource utilization and migraine disability along the migraine continuum among patients treated for migraine. Headache. 2018;58:1579–92.
200. Ford JH, Schroeder K, Nyhuis AW, Foster SA, Aurora SK. Cycling through migraine preventive treatments: implications for all-cause Total direct costs and disease-specific costs. J Manag Care Spec Pharm. 2018;25:1–12. https://doi.org/10.18553/jmcp.2018.18058.
201. Honkasalo ML, Kaprio J, Heikkilä K, Sillanpää M, Koskenvuo M. A population-based survey of headache and migraine in 22,809 adults. Headache. 1993;33:403–12.
202. Raggi A, Leonardi M. Burden and cost of neurological diseases: a European north–south comparison. Acta Neurol Scand. 2015;132:16–22.
203. Munakata J, Hazard E, Serrano D, et al. Economic burden of transformed migraine: results from the American migraine prevalence and prevention (AMPP) study. Headache. 2009;49:498–508.

204. Mbewe E, Zairemthiama P, Paul R, Birbeck GL, Steiner TJ. The burden of primary headache disorders in Zambia: national estimates from a population-based door-to-door survey. J Headache Pain. 2015;16:36.
205. World Health Organization, Burden LT. Atlas of headache disorders and resources in the world 2011. Geneva: WHO; 2011.
206. Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, Cassini A, Devleesschauwer B, Kretzschmar M, Speybroeck N, Murray CJ, Vos T. Disability weights for the Global Burden of Disease 2013 study. Lancet Glob Health. 2015;3:e712–23. https://doi.org/10.1016/S2214-109X(15)00069-8.
207. Wateraid UK. Where we work 2017. http://www.Wateraid.Org/Uk/Where-we-work/page/ethiopia (last accessed 3.2.17).
208. Shahbeigi S, Fereshtehnejad S-M, Mohammadi N, et al. Epidemiology of headaches in Tehran urban area: a population-based cross-sectional study in district 8, year 2010. Neurol Sci. 2013;34(7):1157–66. https://doi.org/10.1007/s10072-012-1200-0.
209. Ayatollahi SMT, Moradi F, Ayatollahi SAR. Prevalences of migraine and tension-type headache in adolescent girls of shiraz (southern Iran). Headache. 2002;42(4):287–90. http://www.ncbi.nlm.nih.gov/pubmed/12010386. Accessed November 16, 2018
210. Fallahzadeh H, Alihaydari M. Prevalence of migraine and tension-type headache among school children in Yazd, Iran. J Pediatr Neurosci. 2011;6(2):106–9. https://doi.org/10.4103/1817-1745.92818.
211. Romdhane NA, Ben Hamida M, Mrabet A, et al. Prevalence study of neurologic disorders in Kelibia (Tunisia). Neuroepidemiology. 1993;12(5):285–99. https://doi.org/10.1159/000110330.
212. Bener A, Swadi H, Qassimi EM, Uduman S. Prevalence of headache and migraine in schoolchildren in the United Arab Emirates. Ann Saudi Med. 18(6):522–4. http://www.ncbi.nlm.nih.gov/pubmed/17344729. Accessed 16 Nov 2018
213. Bahrami P, Zebardast H, Zibaei M, Mohammadzadeh M, Zabandan N. Prevalence and characteristics of headache in Khoramabad, Iran. Pain Physician. 15(4):327–32. http://www.ncbi.nlm.nih.gov/pubmed/22828686. Accessed 16 Nov 2018
214. Bessisso MS, Bener A, Elsaid MF, Al-Khalaf FA, Huzaima KA. Pattern of headache in school children in the State of Qatar. Saudi Med J. 2005;26(4):566–70. http://www.ncbi.nlm.nih.gov/pubmed/15900361. Accessed 16 Nov 2018
215. Free 2018 ICD-10-CM Codes. https://www.icd10data.com/ICD10CM/Codes. Accessed 4 June 2018.
216. Abu-Arafeh I, Razak S, Sivaraman B, Graham C. Prevalence of headache and migraine in children and adolescents: a systematic review of population-based studies. Dev Med Child Neurol. 2010;52(12):1088–97.
217. Wöber-Bingöl C. Epidemiology of migraine and headache in children and adolescents. Curr Pain Headache Rep. 2013;17(6):341.
218. Heinrich M, Morris L, Kröner-Herwig B. Self-report of headache in children and adolescents in Germany: possibilities and confines of questionnaire data for headache classification. Cephalalgia. 2009;29(8):864–72.
219. Anttila P, Metsähonkala L, Aromaa M, Sourander A, Salminen J, Helenius H, et al. Determinants of tension-type headache in children. Cephalalgia. 2002;22(5):401–8.
220. Pothmann R, Frankenberg SV, Muller B, Sartory G, Hellmeier W. Epidemiology of headache in children and adolescents: evidence of high prevalence of migraine. Int J Behav Med. 1994;1(1):76–89.
221. Antonaci F, Voiticovschi-Iosob C, Di Stefano AL, Galli F, Ozge A, Balottin U. The evolution of headache from childhood to adulthood: a review of the literature. J Headache Pain. 2014;15:15.
222. Karwautz A, Wöber C, Lang T, Böck A, Wagner-Ennsgraber C, Vesely C, et al. Psychosocial factors in children and adolescents with migraine and tension-type headache: a controlled study and review of the literature. Cephalalgia. 1999;19(1):32–43.

223. Juang K-D, Wang S-J, Fuh J-L, Lu S-R, Chen Y-S. Association between adolescent chronic daily headache and childhood adversity: a community-based study. Cephalalgia. 2004;24(1):54–9.
224. Kröner-Herwig B, Heinrich M, Morris L. Headache in German children and adolescents: a population-based epidemiological study. Cephalalgia. 2007;27(6):519–27.
225. Bugdayci R, Ozge A, Sasmaz T, Kurt AO, Kaleagasi H, Karakelle A, et al. Prevalence and factors affecting headache in Turkish schoolchildren. Pediatr Int. 2005;47(3):316–22.
226. GBD 2015 Neurological Disorders Collaborator Group. Global, regional, and national burden of neurological disorders during 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Neurol. 2017;16(11):877–97.
227. Rice ASC, Smith BH, Blyth FM. Pain and the global burden of disease. Pain. 2016;157:791–6.
228. Malta DC, Bernal RTI, Lima MG, Araújo SSC, MMAD S, MIDF F, et al. Noncommunicable diseases and the use of health services: analysis of the National Health Survey in Brazil. Rev Saude Publica. 2017;51(suppl 1):4s.
229. Lampe F. Validity of a self-reported history of doctor-diagnosed angina. J Clin Epidemiol. 1999;52:73–81.
230. Ramos RQ, Bastos JL, Peres MA. Diagnostic validity of self-reported oral health outcomes in population surveys: literature review. Rev Bras Epidemiol. 2013;16:716–28.
231. Chrestani MAD, Santos Ida S, Matijasevich AM. Self-reported hypertension: validation in a representative cross-sectional survey. Cad Saude Publica. 2009;25:2395–406.
232. Moreira NF, Luz VG, Moreira CC, Pereira RA, Sichieri R, Ferreira MG, et al. Self-reported weight and height are valid measures to determine weight status: results from the Brazilian National Health Survey (PNS 2013). Cad Saude Publica. 2018;34:(S)1-13.
233. Queiroz LP, Peres MFP, Piovesan EJ, Kowacs F, Ciciarelli MC, Souza JA, et al. A nationwide population-based study of migraine in Brazil. Cephalalgia. 2009;29:642–9.
234. Queiroz LP, Peres MFP, Piovesan EJ, Kowacs F, Ciciarelli MC, Souza JA, et al. A nationwide population-based study of tension-type headache in Brazil. Headache. 2009;49:71–8.
235. Queiroz LP, Peres MFP, Kowacs F, Piovesan EJ, Ciciarelli MC, Souza JA, et al. Chronic daily headache in Brazil: a nationwide population-based study. Cephalalgia. 2008;28:1264–9.
236. International Headache Society Classification Subcommittee. The international classification of headache disorders. Cephalalgia. 2014;24(suppl 1):1–160. 2nd edition
237. Stewart W, Lipton R, Kolodner K, Sawyer J, Lee C, Liberman J. Validity of the migraine disability assessment (MIDAS) score in comparison to a diary-based measure in a population sample of migraine sufferers. Pain. 2000;88(1):41–52.
238. Lucchetti G, Peres MFP. The prevalence of migraine and probable migraine in a Brazilian favela: results of a community survey. Headache. 2011;51:971–9.
239. Goulart AC, Santos IS, Brunoni AR, Nunes MA, Passos VM, Griep RH, et al. Migraine headaches and mood/anxiety disorders in the ELSA Brazil. Headache. 2014;54:1310–9.
240. Queiroz LP, Silva Junior AA. The prevalence and impact of headache in Brazil. Headache. 2015;55:32–8.
241. Krogh AB, Larsson B, Linde M. Prevalence and disability of headache among Norwegian adolescents: a cross-sectional school-based study. Cephalalgia. 2015;35:1181–91.
242. Chong SC, Chan YH, Ong HT, Low PS, Tay SK. Headache diagnosis, disability and comorbidities in a multi-ethnic, heterogeneous paediatric Asian population. Cephalalgia. 2010;30:953–61.
243. Kong CK, Cheng WW, Wong LY. Epidemiology of headache in Hong Kong primary-level schoolchildren: questionnaire study. Hong Kong Med J. 2001;7:29–33.
244. Rho YI, Chung HJ, Lee KH, Eun BL, Eun SH, Nam SO, et al. Prevalence and clinical characteristics of primary headaches among school children in South Korea: a nationwide survey. Headache. 2012;52(4):592–9.
245. Hublin C, Kaprio J, Partinen M, Koskenvuo M. Insufficient sleep--a population-based study in adults. Sleep. 2001;24(4):392–400.
246. Holt JB, Zhang X, Sizov N, Croft JB. Airport noise and self-reported sleep insufficiency, United States, 2008 and 2009. Prev Chronic Dis. 2015;12:E49.

247. Cho SJ, Chung YK, Kim JM, Chu MK. Migraine and restless legs syndrome are associated in adults under age fifty but not in adults over fifty: a population-based study. J Headache Pain. 2015;16:554.
248. Song TJ, Cho SJ, Kim WJ, Yang KI, Yun CH, Chu MK. Anxiety and depression in probable migraine: A population-based study. Cephalalgia. 2017;37(9):845–54.
249. Oh K, Cho SJ, Chung YK, Kim JM, Chu MK. Combination of anxiety and depression is associated with an increased headache frequency in migraineurs: a population-based study. BMC Neurol. 2014;14:238.
250. Wijeratne T, Grisold W, Dodick D, Carroll W. World brain day 2019: migraine, the painful truth. Lancet Neurol. 2019;18(10):914. https://doi.org/10.1016/S1474-4422(19)30281-9.
251. Lipton RB, Manack Adams A, Buse DC, Fanning KM, Reed ML. A comparison of the chronic migraine epidemiology and outcomes (CaMEO) study and American Migraine Prevalence and Prevention (AMPP) study: demographics and headache-related disability. Headache. 2016;56(8):1280–9. https://doi.org/10.1111/head.12878.
252. Buse DC, Fanning KM, Reed ML, Murray S, Dumas PK, Adams AM, Lipton RB. Life with migraine: effects on relationships, career, and finances from the chronic migraine epidemiology and outcomes (CaMEO) study. Headache. 2019;59(8):1286–99. https://doi.org/10.1111/head.13613.
253. Song TJ, Cho SJ, Kim WJ, Yang KI, Yun CH, Chu MK. Sex differences in prevalence, symptoms, impact, and psychiatric comorbidities in migraine and probable migraine: a population-based study. Headache. 2019;59(2):215–23. https://doi.org/10.1111/head.13470.
254. Takeshima T, Wan Q, Zhang Y, Komori M, Stretton S, Rajan N, et al. Prevalence, burden, and clinical management of migraine in China, Japan, and South Korea: a comprehensive review of the literature. J Headache Pain. 2019;20:111.
255. Wang SJ, Chung CS, Chankrachang S, Ravishankar K, Merican JS, Salazar G, Siow C, Cheung RT, Phanthumchinda K, Sakai F. Migraine disability awareness campaign in Asia: migraine assessment for prophylaxis. Headache. 2008;48:1356–65.
256. Ueda K, Ye W, Lombard L, Kuga A, Kim Y, Cotton S, et al. Real-world treatment patterns and patient-reported outcomes in episodic and chronic migraine in Japan: analysis of data from the Adelphi migraine disease specific programme. J Headache Pain. 2019;20(1):68.
257. Liu R, Yu S, He M, Zhao G, Yang X, Qiao X, et al. Health-care utilization for primary headache disorders in China: a population-based door-to-door survey. J Headache Pain. 2013;14:47.
258. Bagley CL, Rendas-Baum R, Maglinte GA, Yang M, Varon SF, Lee J, et al. Validating migraine-specific quality of life questionnaire v2.1 in episodic and chronic migraine. Headache. 2012;52(3):409–21.
259. Jo NJ, Kim BK. Clinical characteristics of migraine with Aura in Korean: a clinic based study. J Korean Neurol Assoc. 2015;33(4):278–81. https://doi.org/10.17340/jkna.2015.4.6.
260. Dodick DW, Loder EW, Manack Adams A, Buse DC, Fanning KM, Reed ML, Lipton RB. Assessing barriers to chronic migraine consultation, diagnosis, and treatment: results from the chronic migraine epidemiology and outcomes (CaMEO) study. Headache. 2016;56(5):821–34. https://doi.org/10.1111/head.12774.
261. Katsarava Z, Mania M, Lampl C, Herberhold J, Steiner TJ. Poor medical care for people with migraine in Europe—evidence from the Eurolight study. J Headache Pain. 2018;19:10.
262. Lipton RB, Buse DC, Serrano D, Holland S, Reed ML. Examination of unmet treatment needs among persons with episodic migraine: results of the American Migraine Prevalence and Prevention (AMPP) study. Headache. 2013;53(8):1300–11. https://doi.org/10.1111/head.12154.
263. Rao GN, Kulkarni GB, Gururaj G, Stovner LJ, Steiner TJ. The burden attributable to headache disorders in India: estimates from a community-based study in Karnataka state. J Headache Pain. 2015;16:94.
264. Manandhar K, Risal A, Linde M, Steiner TJ. The burden of headache disorders in Nepal: estimates from a population-based survey. J Headache Pain. 2016;17:3.
265. Herekar AD, Herekar AA, Ahmad A, Uqaili UL, Ahmed B, Effendi J, Alvi SZ, Steiner TJ. The burden of headache disorders in Pakistan: methodology of a population-based nationwide study, and questionnaire validation. J Headache Pain. 2013;14:73.

266. Zebenigus M, Tekle-Haimanot R, Worku DK, Thomas H, Steiner TJ. The burden of headache disorders in Ethiopia: national estimates from a population-based door-to-door survey. J Headache Pain. 2017;18:58.
267. Ayzenberg I, Katsarava Z, Sborowski A, Chernysh M, Osipova V, Tabeeva G, Steiner TJ. Headache-attributed burden and its impact on productivity and quality of life in Russia: structured healthcare for headache is urgently needed. Eur J Neurol. 2014;21:758–65.
268. Rastenytė D, Mickevičienė D, Stovner LJ, Thomas H, Andrée C, Steiner TJ. Prevalence and burden of headache disorders in Lithuania and their public-health and policy implications: a population-based study within the Eurolight project. J Headache Pain. 2017;18:53.
269. Allena M, Steiner TJ, Sances G, Carugno B, Balsamo F, Nappi G, Andrée C, Tassorelli C. Impact of headache disorders in Italy and the public-health and policy implications: a population-based study within the Eurolight project. J Headache Pain. 2015;16:100.
270. Selekler MH, Gökmen G, Steiner TJ. Productivity impact of headache on a heavy-manufacturing workforce in Turkey. J Headache Pain. 2013;14:88.
271. Selekler HM, Gökmen G, Alvur TM, Steiner TJ. Productivity losses attributable to headache, and their attempted recovery, in a heavy-manufacturing workforce in Turkey: implications for employers and politicians. J Headache. 2015;16:96.
272. Katsarava Z, Gil Gouveia R, Jensen R, Gaul C, Schramm S, Schoppe A, Steiner TJ. Evaluation of headache service quality indicators: pilot implementation in two specialist-care centres. J Headache Pain. 2015;16:53.
273. Schramm S, Uluduz D, Gil Gouveia R, Jensen R, Siva A, Uygunoglu U, Gvantsa G, Mania M, Braschinsky M, Filatova E, Latysheva N, Osipova V, Skorobogatykh K, Azimova J, Straube A, Emre Eren O, Martelletti P, De Angelis V, Negro A, Linde M, Hagen K, Radojicic A, Zidverc-Trajkovic J, Podgorac A, Paemeleire K, De Pue A, Lampl C, Steiner TJ, Katsarava Z. Headache service quality: evaluation of quality indicators in 14 specialist-care centres. J Headache Pain. 2016;17:111.
274. Braschinsky M, Haldre S, Kals M, Iofik A, Kivisild A, Korjas J, Koljal S, Katsarava Z, Steiner TJ. Structured education can improve primary-care management of headache: the first empirical evidence, from a controlled interventional study. J Headache Pain. 2016;17:24.
275. Braschinsky M, Haldre S, Kals M, Arge M, Saar B, Niibek M, Katsarava Z, Steiner TJ. Structured education to improve primary-care management of headache: how long do the benefits last? A follow-up observational study. Eur J Neurol. 2018;25(3):497–502.
276. Steiner TJ. The HALT and HART indices. J Headache Pain. 2007;8(suppl 1):S22–5.
277. Stovner LJ, Al Jumah M, Birbeck GL, Gururaj G, Jensen R, Katsarava Z, Queiroz LP, Scher AI, Tekle-Haimanot R, Wang SJ, Steiner TJ. The methodology of population surveys of headache prevalence, burden and cost: principles and recommendations from the global campaign against headache. J Headache Pain. 2014;15:5.
278. Eiser C, Morse R. Quality-of-life measures in chronic diseases of childhood. Health Technol Assess. 2001;5(4):1–157.
279. Raggi A, Covelli V, Schiavolin S, Giovannetti AM, Cerniauskaite M, Quintas R, Leonardi M, Sabariego C, Grazzi L, D'Amico D. Psychosocial difficulties in patients with episodic migraine: a cross-sectional study. Neurol Sci. 2016;37(12):1979–86.
280. Juang KD, Wang SJ, Fuh JL, Lu SR, Su TP. Comorbidity of depressive and anxiety disorders in chronic daily headache and its subtypes. Headache. 2000;40:818–23.
281. Lipton R, Liberman J, Kolodner K, et al. Migraine headache disability and health-related quality-of-life: a population-based case-control study from England. Cephalalgia. 2003;23:441–50. https://doi.org/10.1046/j.1468-2982.2003.00546.x.
282. Bigal ME, Rapoport AM, Lipton RB, et al. Assessment of migraine disability using the migraine disability assessment (MIDAS) questionnaire: a comparison of chronic migraine with episodic migraine. Headache. 2003;43:336–42.
283. Gelfand A. Pathophysiology, clincal features, and diagnosis of migraine in children [internet]. UpToDate, Wolters Kluwer. 2017. p. 1–13. https://www.uptodate.com/contents/pathophysiology-clinical-features-and-diagnosis-of-migraine-in-children

284. Wöber-Bingöl C, Wöber C, Wagner-Ennsgraber C, Zebenholzer K, Vesely C, Geldner J, et al. IHS criteria and gender: a study on migraine and tension-type headache in children and adolescents. Cephalalgia. 1996;16(2):107–12.
285. Dooley JM, Gordon KE, Wood EP. Self-reported headache frequency in Canadian adolescents: validation and follow-up. Headache. 2005;45(2):127–31.
286. Özge A, Şaşmaz T, Buğdayci R, Çakmak SE, Kurt AÖ, Kaleağasi SH, et al. The prevalence of chronic and episodic migraine in children and adolescents. Eur J Neurol. 2013;20(1):95–101.
287. Casucci G, Terlizzi R, Cevoli S. Headache in school age. Neurol Sci. 2014;35(SUPPL. 1):31–5.
288. Millichap GJ, Yee MM. The diet factor in pediatric and adolescent migraine. Pediatr Neurol. 2003;28:9–15.
289. Robberstad L, Dyb G, Hagen K, Stovner LJ, Holmen TL, Zwart JA. An unfavorable lifestyle and recurrent headaches among adolescents: the HUNT study. Neurology. 2010;75(8):712–7.
290. Hershey AD, Powers SW, Nelson TD, Kabbouche MA, Winner P, Yonker M, et al. Obesity in the pediatric headache population: a multicenter study. Headache. 2009;49(2):170–7.
291. Isik U, Ersu RH, Ay P, Save D, Arman AR, Karakoc F, et al. Prevalence of headache and its association with sleep disorders in children. Pediatr Neurol. 2007;36(3):146–51.
292. Casez O, Dananchet Y, Besson G. Migraine and somnambulism. Neurology. 2005;65(8):1334–5.
293. Milde-Busch A, Blaschek A, Borggräfe I, Heinen F, Straube A, Von Kries R. Associations of diet and lifestyle with headache in high-school students: results from a cross-sectional study. Headache. 2010;50(7):1104–14.
294. Moschiano F, Messina P, D'Amico D, Grazzi L, Frediani F, Casucci G, et al. Headache, eating and sleeping behaviors and lifestyle factors in preadolescents and adolescents: preliminary results from an Italian population study. Neurol Sci. 2012;33(SUPPL. 1):S87–90.
295. Chakravarty A, Mukherjee A, Roy D. Trigger factors in childhood migraine: a clinic-based study from eastern India. J Headache Pain. 2009;10(5):375–80.
296. Connelly M, Miller T, Gerry G, Bickel J. Research submission electronic momentary assessment of weather changes as a trigger of headaches in children. Headache. 2010;50: 779–89.
297. Russo A, Bruno A, Trojsi F, Tessitore A, Tedeschi G. Lifestyle factors and migraine in childhood. Curr Pain Headache Rep. 2016;20(2):9.
298. Varni J, Burwinkle T, Seid M, Skarr D. The PedsQL™ 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr. 2003;3(6):329–41.
299. Neut D, Fily A, Cuvellier JC, Vallée L. The prevalence of triggers in paediatric migraine: a questionnaire study in 102 children and adolescents. J Headache Pain. 2012;13(1):61–5.
300. Solotareff L, Cuvellier JC, Duhamel A, Vallée L, Tich SNT. Trigger factors in childhood migraine: a prospective clinic-based study from north of France. J Child Neurol. 2017;32(8):754–8.
301. Todd C, Lagman-Bartolome AM, Lay C. Women and migraine: the role of hormones. Curr Neurol Neurosci Rep. 2018;18(7):42.
302. Martin VT, Behbehani M. Ovarian hormones and migraine headache: understanding mechanisms and pathogenesis--part 2. Headache. 2006;46(3):365–86.
303. Martin VT, Pavlovic J, Fanning KM, Buse DC, Reed ML, Lipton RB. Perimenopause and menopause are associated with high frequency headache in women with migraine: results of the American Migraine Prevalence and Prevention study. Headache. 2016;56(2):292–305.
304. Pavlovic JM, Allshouse AA, Santoro NF, Crawford SL, Thurston RC, Neal-Perry GS, et al. Sex hormones in women with and without migraine: evidence of migraine-specific hormone profiles. Neurology. 2016;87(1):49–56.
305. Murialdo G, Martignoni E, De Maria A, Bonura ML, Sances G, Bono G, et al. Changes in the dopaminergic control of prolactin secretion and in ovarian steroids in migraine. Cephalalgia. 1986;6(1):43–9.
306. Epstein MT, Hockaday JM, Hockaday TD. Migraine and reproductive hormones throughout the menstrual cycle. Lancet. 1975;1(7906):543–8.

307. van Oosterhout WPJ, Schoonman GG, van Zwet EW, Dekkers OM, Terwindt GM, MaassenVanDenBrink A, et al. Female sex hormones in men with migraine. Neurology. 2018;91(4):e374–ee81.
308. Cobey KD, Buunk AP, Roberts SC, Klipping C, Appels N, Zimmerman Y, Bennink HJTC, Pollet TV. Reported jealousy differs as a function of menstrual cycle stage and contraceptive pill use: a within-subjects investigation. Evol Hum Behav. 2012;33(4):395–401.
309. Cobey KD, Roberts SC, Buunk AP. Hormonal contraceptive congruency: implications for relationship jealousy. Pers Individ Differ. 2013;55:569–73.
310. Lantagne A, Furman W. Romantic relationship development: the interplay between age and relationship length. Dev Psychol. 2017;53(9):1738–49.
311. Murtaza M, Kisat M, Daniel H, Sonawalla AB. Classification and clinical features of headache disorders in Pakistan: a retrospective review of clinical data. PLoS One. 2009;4(6):e5827.
312. D'Amico D, Grazzi L, Curone M, Di Fiore P, Proietti Cecchini A, Leonardi M, et al. Difficulties in work activities and the pervasive effect over disability in patients with episodic and chronic migraine. Neurol Sci. 2015;36(Suppl 1):9–11.
313. Park JW, Shin HE, Kim JS, Lee KS. Assessing migraine disability by diary-based measurement: relationship to the characteristics of individual headache attacks. Eur J Neurol. 2008;15(8):817–21.
314. Nagpal M, Jangid R, Sathyanarayan RT. A comparative study of the sexual functioning of women with primary headache in India. Indian J Psychiatry. 2018;60(2):224–8. https://doi.org/10.4103/psychiatry.IndianJPsychiatry_290_17.
315. Blumenfeld A, Bloudek LM, Becker WJ, et al. Patterns of use and reasons for discontinuation of prophylactic medications for episodic migraine and chronic migraine: results from the second international burden of migraine study (IBMS-II). Headache. 2013;53:644–55.
316. Stark RJ, Ravishankar K, Siow HC, Lee KS, Pepperle R, Wang SJ. Chronic migraine and chronic daily headache in the Asia-Pacific region: a systematic review. Cephalalgia. 2013;33(4):266–83.
317. Freitag FG. The cycle of migraine: patients' quality of life during and between migraine attacks. Clin Ther. 2007;29(5):939–49.
318. Deb P, Norton EC. Modeling health care expenditures and use. Annu Rev Public Health. 2018;39(1):489–505.
319. ICF International, Philippine Statistics Authority. National Demographic and Health Survey 2017. Manila, Philippines and Rockville, Maryland, USA: PSA and ICF International; 2018.
320. Katsarava Z, Buse DC, Manack AN, Lipton RB. Defining the differences between episodic migraine and chronic migraine. Curr Pain Headache Rep. 2012;16(1):86–92.
321. Bigal ME, Rapoport AM, Lipton RB, Tepper SJ, Sheftell FD. Assessment of migraine disability using the migraine disability assessment (MIDAS) questionnaire: A comparison of chronic migraine with episodic migraine. Headache. 2003;43(4):336–42.
322. Bigal ME, Bordini CA, Sheftell FD, Speciali JG, Bigal JO. Migraine with aura versus migraine without aura: Pain intensity and associated symptom intensities after placebo. Headache. 2002;42(9):872–7.
323. Buse D, Manack A, Serrano D, Reed M, Varon S, Turkel C, et al. Headache impact of chronic and episodic migraine: Results from the American migraine prevalence and prevention study. Headache. 2012;52(1):3–17.
324. American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. Headache. 2019;59(1):1–18.
325. Kawata AK, Coeytaux RR, Devellis RF, Finkel AG, Mann JD, Kahn K. Psychometric properties of the HIT-6 among patients in a headache-specialty practice. Headache. 2005;45(6):638–43.
326. Yang M, Rendas-Baum R, Varon SF, Kosinski M. Validation of the headache impact test (HIT-6) across episodic and chronic migraine. Cephalalgia. 2011;31(3):357–67.
327. Lipton RB, Kolodner K, Bigal ME, Valade D, Lainez MJ, Pascual J, et al. Validity and reliability of the migraine-treatment optimization questionnaire. Cephalalgia. 2009;29(7):751–9.

328. Smelt AF, Assendelft WJ, Terwee CB, Ferrari MD, Blom JW. What is a clinically relevant change on the HIT-6 questionnaire? An estimation in a primary-care population of migraine patients. Cephalalgia. 2014;34(1):29–36.
329. Rendas-Baum R, Yang M, Varon SF, Bloudek LM, DeGryse RE, Kosinski M. Validation of the headache impact test (HIT-6) in patients with chronic migraine. Health Quality Life Outcomes. 2014;12:117.
330. Bayliss MS, Batenhorst AS. The HIT-6™: A user's guide. Lincoln, RI: QualityMetric Incorporated; 2002.
331. Lipton RB, Goadsby PJ, Smith J, Schaeffler BA, Biondi DM, Hirman J, et al. Efficacy and safety of eptinezumab in patients with chronic migraine. PROMISE-2. Neurology. 2020;94(13):e1365–77.
332. Ayer DW, Skljarevski V, Ford JH, Nyhuis AW, Lipton RB, Aurora SK. Measures of functioning in patients with episodic migraine: Findings from a double-blind, randomized, placebo-controlled phase 2b trial with galcanezumab. Headache. 2018;58(8):1225–35.
333. Bagley CL, Rendas-Baum R, Maglinte GA, Yang M, Varon SF, Lee J, et al. Validating migraine-specific quality of life questionnaire v2.1 in episodic and chronic migraine. Headache. 2011;52(3):409–21.
334. Cole JC, Lin P, Rupnow MF. Validation of the migraine-specific quality of life questionnaire version 2.1 (MSQ v. 2.1) for patients undergoing prophylactic migraine treatment. Qual Life Res. 2007;16(7):1231–7.
335. Kawata AK, Hsieh R, Bender R, Shaffer S, Revicki DA, Bayliss M, et al. Psychometric evaluation of a novel instrument assessing the impact of migraine on physical functioning: The migraine physical function impact diary. Headache. 2017;57(9):1385–98.
336. Sauro KM, Rose MS, Becker WJ, Christie SN, Giammarco R, Mackie GF, et al. HIT-6 and MIDAS as measures of headache disability in a headache referral population. Headache. 2010;50(3):383–95.
337. Sculpher MJ, Pang FS, Manca A, Drummond MF, Golder S, Urdahl H, et al. Generalisability in economic evaluation studies in healthcare: a review and case studies. Health Technol Assess. 2004;8(49):iii–iv. 1–192
338. Augustovski F, Iglesias C, Manca A, Drummond M, Rubinstein A, Martí SG. Barriers to generalizability of health economic evaluations in Latin America and the Caribbean region. PharmacoEconomics. 2009;27(11):919–29.
339. Drummond M, Manca A, Sculpher M. Increasing the generalizability of economic evaluations: recommendations for the design, analysis, and reporting of studies. Int J Technol Assess Health Care. 2005;21(2):165–71.
340. Ruggeri M, Manca A, Coretti S, Codella P, Iacopino V, Romano F, et al. Investigating the generalizability of economic evaluations conducted in Italy: a critical review. Value Health. 2015;18(5):709–20.
341. Yu J, Smith KJ, Brixner DI. Cost effectiveness of pharmacotherapy for the prevention of migraine. CNS Drugs. 2010;24(8):695–712.
342. Batty AJ, Hansen RB, Varon LF, Sepideh JH, Pennington EW, Lipton BR, et al. The cost-effectiveness of onabotulinumtoxinA for the prophylaxis of headache in adults with chronic migraine in the UK. J Med Econ. 2013;16(7):877–87.
343. Sussman M, Benner J, Neumann P, Menzin J. Cost-effectiveness analysis of erenumab for the preventive treatment of episodic and chronic migraine: results from the US societal and payer perspectives. Cephalalgia. 2018;38(10):1644–57.
344. Lofland JH, Nash DB. Oral serotonin receptor agonists: a review of their cost effectiveness in migraine. PharmacoEconomics. 2005;23:259–74.
345. McCormack PL, Foster RH. Rizatriptan: a pharmacoeconomic review of its use in the acute treatment of migraine. PharmacoEconomics. 2005;23:1283–98.
346. Yu J, Goodman JM, Gary O. Economic evaluation of pharmacotherapy of migraine pain: a review of the literature. J Pain Palliat Care Pharmacother. 2009;23:396–408.

347. Ambrósio EM, Bloor K, Macpherson H. Costs and consequences of acupuncture as a treatment for chronic pain: a systematic review of economic evaluations conducted alongside randomised controlled trials. Complement Ther Med. 2012;20:364–74.
348. Hens M, Villaverde-Hueso A, Alonso V, Abaitua I, Posada de la Paz M. Comparative cost-effectiveness analysis of oral triptan therapy for migraine in four European countries. Eur J Health Econ. 2014;15(4):433–7.
349. Ruggeri M. The cost effectiveness of Botox in Italian patients with chronic migraine. Neurol Sci. 2014;35(Suppl. 1):45–7.
350. Lipton RB, Brennan A, Palmer S, Hatswell AJ, Porter JK, Sapra S, et al. Estimating the clinical effectiveness and value-based price range of erenumab for the prevention of migraine in patients with prior treatment failures: a US societal perspective. J Med Econ. 2018;21(7):666–75.
351. Mwamburi M, Tenaglia AT, Leibler EJ, Staats PS. Cost-effectiveness of noninvasive vagus nerve stimulation for acute treatment of episodic migraine and role in treatment sequence strategies. Am J Manag Care. 2018;24(24 Suppl):S527–33.
352. Slof J. Cost effectiveness analysis of early versus non-early intervention in acute migraine based on evidence from the "Act when mild" study. Appl Health Econ Health Policy. 2012;10(3):201–15.
353. Hollier-Hann G, Curry A, Onishchenko K, Akehurst R, Ahmed F, Davies B, et al. Updated cost-effectiveness analysis of onabotulinumtoxinA for the prevention of headache in adults with chronic migraine who have previously received three or more preventive treatments in the UK. J Med Econ. 2019;4:1–11.
354. Giannouchos TV, Mitsikostas DD, Ohsfeldt RL, Vozikis A, Koufopoulou P. Cost-effectiveness analysis of erenumab versus onabotulinumtoxinA for patients with chronic migraine attacks in Greece. Clin Drug Investig. 2019;39(10):979–90.
355. Shauly O, Gould DJ, Patel KM. Cost-utility analysis of surgical decompression relative to injection therapy for chronic migraine headaches. Aesthet Surg J. 2019;39(12):NP462–70.
356. Asseburg C, Peura P, Oksanen T, Turunen J, Purmonen T, Martikainen J. Cost-effectiveness of oral triptans for acute migraine: mixed treatment comparison. Int J Technol Assess Health Care. 2012;28(4):382–9.
357. World Bank List of Economies. http://www.databank.worldbank.org/data/download/site--content/CLASS.xls . June 2017.
358. Woldeamanuel YW, Cowan RP. Migraine affects 1 in 10 people worldwide featuring recent rise: a systematic review and meta-analysis of community-based studies involving 6 million participants. J Neurol Sci. 2017;372:307–15.
359. Masterson Creber RM, Smeeth L, Gilman RH, Miranda JJ. Physical activity and cardiovascular risk factors among rural and urban groups and rural-to-urban migrants in Peru: a cross-sectional study. Rev Panam Salud Publica. 2010;28(1):1–8.
360. Hallal PC, Andersen LB, Bull FC, Guthold R, Haskell W, Ekelund U, et al. Global physical activity levels: surveillance progress, pitfalls, and prospects. Lancet. 2012;380(9838):247–57.
361. Muthuri SK, Wachira LJ, Leblanc AG, Francis CE, Sampson M, Onywera VO, et al. Temporal trends and correlates of physical activity, sedentary behaviour, and physical fitness among school-aged children in Sub-Saharan Africa: a systematic review. Int J Environ Res Public Health. 2014;11(3):3327–59. This systematic review addresses the trends and correlates of physical inactivity in Africa. It describes the increasing health problem related to sedentary behavior in low-resource setting
362. Peltzer K. Health behavior and protective factors among school children in four African countries. Int J Behav Med. 2009;16(2):172–80.
363. Guthold R, Cowan MJ, Autenrieth CS, Kann L, Riley LM. Physical activity and sedentary behavior among schoolchildren: a 34-country comparison. J Pediatr. 2010;157(1):43–9.e1.
364. Al-Hashel JY, Ahmed SF, Alroughani R, Goadsby PJ. Migraine misdiagnosis as a sinusitis, a delay that can last for many years. J Headache Pain. 2013;14:97. This article describes that headache misdiagnosis are delayed by many years in low-resource settings

365. World Health Organization. Traditional medicine strategy 2002–2005. Rome: WHO; 2002.
366. NCD and the Sustainable Development Goals. WHO Global Coordination Mechanism on the Prevention and Control of NCDs. http://www.who.int/global-coordination-mechanism/ncd-themes/sustainable-development-goals/en/ .
367. Temu F, Leonhardt M, Carter J, Thiam S. Integration of non-communicable diseases in health care: tackling the double burden of disease in African settings. Pan Afr Med J. 2014;18:202.
368. GBD. Diseases and Injuries Collaborators (2020) Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2019;396(10258):1204–22. https://doi.org/10.1016/S0140-6736(20)30925-9.
369. Steiner TJ, Stovner LJ, Jensen R, Uluduz D, Katsarava Z, on behalf of Lifting The Burden: the Global Campaign against Headache. Migraine remains second among the world's causes of disability, and first among young women: findings from GBD2019. J Headache Pain. 2020;21(1):137. https://doi.org/10.1186/s10194-020-01208-0.
370. Kothari SF, Jensen RH, Steiner TJ. The relationship between headache-attributed disability and lost productivity. 1. A review of the literature. J Headache Pain. 2021;22:73.
371. World Health Organization. WHO methods and data sources for global burden of disease estimates 2000–2015 (2017) Global Health Estimates Technical Paper WHO/HIS/IER/GHE/2017.1. https://www.who.int/healthinfo/global_burden_disease/GlobalDALYmethods_2000_2015.pdf (last accessed 22.10.21).
372. Radtke A, Neuhauser H. Prevalence and burden of headache and migraine in Germany. Headache. 2009;49:79–89. https://doi.org/10.1111/j.1526-4610.2008.01263.x.
373. Mennini FS, Gitto L, Martelletti P. Improving care through health economics analyses: cost of illness and headache. J Headache Pain. 2008;9:199–206.
374. Stokes M, Becker WJ, Lipton RB, et al. Cost of health care among patients with chronic and episodic migraine in Canada and the USA: results from the international burden of migraine study (IBMS). Headache. 2011;51:1058–77. https://doi.org/10.1111/j.1526-4610.2011.01945.x.
375. Gustavsson A, Svensson M, Jacobi F, Allgulander C, Alonso J, Beghi E, CDBE2010Study group, et al. Cost of disorders of the brain in Europe 2010. Eur Neuropsychopharmacol. 2011;21(10):718–79.
376. Deloitte. Migraine in Australia whitepaper. Prepared for Novartis Australia by Deloitte access economics 2018. https://www2.deloitte.com/au/en/pages/economics/articles/migraine-australia-whitepaper.html . Accessed 8 Jan 2019.
377. Stewart WF, Wood GC, Manack A, Varon SF, Buse DC, Lipton RB. Employment and work impact of chronic migraine and episodic migraine. J Occup Environ Med. 2010;52(1):8–14. https://doi.org/10.1097/JOM.0b013e3181c1dc56.
378. Centrālās Statistikas Pārvaldes Datubāses. IKG10_010. Total gross domestic product, per capita and per person employed. https://data1.csb.gov.lv/pxweb/en/ekfin/ekfin__ikp__IKP__ikgad/IKG10_010.px . Accessed 8 Feb 2019.
379. GDP, at current prices. Oficialiosios Statistikos Portalas, Statistics Lithuania. https://osp.stat.gov.lt/statistiniu-rodikliu-analize?indicator=S7R183#/ . Accessed 8 Feb 2019.
380. Linde M, Dahlöf C. Attitudes and burden of disease among self-considered migraineurs—a nation-wide population-based survey in Sweden. Cephalalgia. 2004;24(6):455–65. https://doi.org/10.1111/j.1468-2982.2004.00703.x.
381. Brown JS, Neumann PJ, Papadopoulos G, et al. Migraine frequency and health utilities: findings from a multisite survey. Value Health. 2008;11:315–21.
382. Stafford MR, Hareendran A, Ng-Mak DS, Insinga RP, Xu R, Stull DE. EQ-5D-derived utility values for different levels of migraine severity from a UK sample of migraineurs. Health Qual Life Outcomes. 2012;10:65.
383. Stewart WF, Lipton RB, Kolodner K, Liberman J, Sawyer J. Reliability of the migraine disability assessment score in a population-based sample of headache sufferers. Cephalalgia. 1999;19(2):107–14. discussion 74

384. Xu R, Insinga RP, Golden W, Hu XH. EuroQol (EQ-5D) health utility scores for patients with migraine. Qual Life Res. 2011;20(4):601–8.
385. EuroQol. https://euroqol.org/. Accessed 1 Mar 2018.
386. Headache Impact Test (HIT-6). https://www.optum.com/solutions/life-sciences/answer-research/patient-insights/condition-specific-surveys.html. Accessed 3 May 2018.
387. Steiner TJ, Jensen R, Katsarava Z, Stovner LJ, Uluduz D, Adarmouch L, Al Jumah M, Al Khathaami AM, Ashina M, Braschinsky M, Broner S, Eliasson JH, Gil-Gouveia R, Gómez-Galván JB, Gudmundsson LS, Herekar AA, Kawatu N, Kissani N, Kulkarni GB, Lebedeva ER, Leonardi M, Linde M, Luvsannorov O, Maiga Y, Milanov I, Mitsikostas DD, Musayev T, Olesen J, Osipova V, Paemeleire K, Peres MFP, Quispe G, Rao GN, Risal A, de la Torre ER, Saylor D, Togha M, Yu SY, Zebenigus M, Zewde YZ, Zidverc-Trajković J, Tinelli M; Lifting The Burden: the Global Campaign against Headache. Structured headache services as the solution to the ill-health burden of headache: 1. Rationale and description. J Headache Pain. 2021;22(1):78.
388. Biddle AK, Shih Y-CT, Kwong WJ. Cost-benefit analysis of sumatriptan tablets versus usual therapy for treatment of migraine. Pharmacotherapy. 2000;20:1356–64.
389. Ramsberg J, Henriksson M. The cost-effectiveness of oral triptan therapy in Sweden. Cephalalgia. 2007;27:54–62.
390. Slof J, Badia X, Magaz S, Láinez MJA, Galván J, Heras J. Cost-efficacy of oral triptans in the treatment of acute migraine. J Med Econ. 2005;8:27–43.
391. Witt CM, Reinhold T, Jena S, Brinkhaus B, Willich SN. Cost-effectiveness of acupuncture treatment in patients with headache. Cephalalgia. 2008;28:334–45.
392. National Institute for Health and Care Excellence (2012, updated 2015) Headaches in over 12s: diagnosis and management. Clinical guideline [CG150]. NICE, at: https://www.nice.org.uk/Guidance/CG150. (Surveillance report 2016, https://www.nice.org.uk/guidance/cg150/resources/surveillance-report-2016-headaches-in-over-12s-diagnosis-and-management-2012-nice-guideline-cg150-2721165808/chapter/Surveillance-decision?tab=evidence; Appendix A: Summary of new evidence from surveillance, https://www.nice.org.uk/guidance/cg150/evidence/appendix-a-summary-of-new-evidence-pdf-2721165806).
393. Ruggeri M, Drago C, Rosiello F, Orlando V, Santori C. Economic evaluation of treatments for migraine: an assessment of the generalizability following a systematic review. PharmacoEconomics. 2020;38:473–84.
394. International Headache Society Clinical Trials Subcommittee, Tfelt-Hansen P, Pascual J, Ramadan N, Dahlöf C, D'Amico D, Diener H-C, Møller Hansen J, Lanteri-Minet M, Loder E, McCrory D, Plancade S, Schwedt T. Guidelines for controlled trials of drugs in migraine: Third edition. A guide for investigators. Cephalalgia. 2012;32:6–38.
395. Derry S, Wiffen PJ, Moore RA. Aspirin for acute treatment of episodic tension-type headache in adults. Cochrane Database Syst Rev. 2017;1:CD011888. https://doi.org/10.1002/14651858.CD011888.pub2.
396. Derry CJ, Derry S, Moore RA. Sumatriptan (oral route of administration) for acute migraine attacks in adults. Cochrane Database Syst Rev. 2012;2:CD008615. https://doi.org/10.1002/14651858.CD008615.pub2.
397. Ferrari MD, Goadsby PJ, Roon KI, Lipton RB. Triptans (serotonin, 5-HT1B/1D agonists) in migraine: detailed results and methods of a meta-analysis of 53 trials. Cephalalgia. 2002;22:633–58.
398. Steiner TJ. What efficacy measures are clinically relevant and should be used in Cochrane reviews of acute migraine trials? An alternative viewpoint. Cephalalgia. 2015;35:460–2.
399. Tfelt-Hansen PC. What efficacy measures are clinically relevant and should be used in Cochrane Reviews of acute migraine trials? A comment. Cephalalgia. 2015;35:457–9.
400. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38:1–211.
401. Landy SH, Runken MC, Bell CF, Higbie RL, Haskins LS. Assessing the impact of migraine onset on work productivity. J Occup Environ Med. 2011;53:74–81.

402. Raggi A, Grazzi L, Grignani E, Leonardi M, Sansone E, Scaratti C, D'Amico D. The use of MIDAS in patients with chronic migraine and medication-overuse headache: should we trust it? Neurol Sci. 2018;39:S125–7.
403. D'Amico D, Grazzi L, Curone M, Leonardi M, Raggi A. Cost of medication overuse headache in Italian patients at the time-point of withdrawal: a retrospective study based on real data. Neurol Sci. 2017;38(Suppl 1):3–6.
404. Raggi A, Leonardi M, Scaratti C, Sansone E, Grazzi L, D'Amico D. Gender and education inequalities in the cost of medication-overuse headache. Neurol Sci. 2018;39:S117–9.
405. Yu S, He M, Liu R, Feng J, Qiao X, Yang X, Cao X, Zhao G, Fang Y, Steiner TJ. Headache yesterday in China: a new approach to estimating the burden of headache, applied in a general-population survey in China. Cephalalgia. 2013;33(15):1211–7. https://doi.org/10.1177/0333102413490347.
406. Steiner TJ, Rao GN, Kulkarni GB, Gururaj G, Stovner LJ. Headache yesterday in Karnataka state, India: prevalence, impact and cost. J Headache Pain. 2016;17(1):74. https://doi.org/10.1186/s10194-016-0669-y.
407. Ayzenberg I, Katsarava Z, Sborowski A, Obermann M, Chernysh M, Osipova V, Tabeeva G, Steiner TJ. Headache yesterday in Russia: its prevalence and impact, and their application in estimating the national burden attributable to headache disorders. J Headache Pain. 2015;16(1):7. https://doi.org/10.1186/1129-2377-16-7.
408. Tinelli M, Leonardi M, Paemeleire K, Mitsikostas D, de la Torre ER, Steiner TJ; European Brain Council Value of Treatment Headache Working Group, the European Headache Federation, the European Federation of Neurological Associations, and Lifting The Burden: the Global Campaign against Headache. Structured headache services as the solution to the ill-health burden of headache. 2. Modelling effectiveness and cost-effectiveness of implementation in Europe: methodology. J Headache Pain. 2021;22(1):99.
409. Linde M, Gustavsson A, Stovner LJ, Steiner TJ, Barré J, Katsarava Z, Lainez JM, Lampl C, Lantéri-Minet M, Rastenyte D, Ruiz de la Torre E, Tassorelli C, Andrée C. The cost of headache disorders in Europe: the Eurolight project. Eur J Neurol. 2012;19:703–11.
410. Dent W, Stelzhammer B, Meindl M, Matuja WB, Schmutzhard E, Winkler AS. Migraine attack frequency, duration, and pain intensity: disease burden derived from a community-based survey in northern Tanzania. Headache. 2011;51:1483–92.
411. Cristofolini A, Dalla Serra P, Scherillo G, Orrico D, Micciolo R. The prevalence of headache in a population of health care workers and the effects on productivity costs. Med Lav. 2008;99:8–15.
412. Vinding GR, Zeeberg P, Lyngberg A, Nielsen RT, Jensen R. The burden of headache in a patient population from a specialized headache centre. Cephalalgia. 2007;27:263–70.
413. Unalp A, Dirik E, Kurul S. Prevalence and characteristics of recurrent headaches in Turkish adolescents. Pediatr Neurol. 2006;34:110–5.
414. Moens G, Johannik K, Verbeek C, Bulterys S. The prevalence and characteristics of migraine among the Belgian working population. Acta Neurol Belg. 2007;107:84–90.
415. D'Amico D, Genco S, Perini F. Workplace disability in migraine: an Italian experience. Neurol Sci. 2004;25:s251–2.
416. Schwartz BS, Stewart WF, Lipton RB. Lost workdays and decreased work effectiveness associated with headache in the workplace. J Occup Environ Med. 1997;39:320–7.
417. Kryst S, Scherl E. A population-based survey of the social and personal impact of headache. Headache. 1994;34:344–50.
418. Selekler HM, Gökmen G, Alvur TM, Steiner TJ. Productivity losses attributable to headache, and their attempted recovery, in a heavy-manufacturing workforce in Turkey: implications for employers and politicians. J Headache Pain. 2015;16(1):96. https://doi.org/10.1186/s10194-015-0579-4.
419. Steiner TJ, Jensen R, Katsarava Z, Stovner LJ, Uluduz D, Adarmouch L, Al Jumah M, Al Khathaami AM, Ashina M, Braschinsky M, Broner S, Eliasson JH, Gil-Gouveia R, Gómez-Galván JB, Gudmundsson LS, Herekar AA, Kawatu N, Kissani N, Kulkarni GB, Lebedeva

ER, Leonardi M, Linde M, Luvsannorov O, Maiga Y, Milanov I, Mitsikostas DD, Musayev T, Olesen J, Osipova V, Paemeleire K, Peres MFP, Quispe G, Rao GN, Risal A, de la Torre ER, Saylor D, Togha M, Yu SY, Zebenigus M, Zewde YZ, Zidverc-Trajković J, Tinelli M; Lifting The Burden: the Global Campaign against Headache. Structured headache services as the solution to the ill-health burden of headache: 1. Rationale and description. J Headache Pain. 2021;22(1):78.
420. Wagner B, Riggs P, Mikulich-Gilbertson S. The importance of distribution-choice in modeling substance use data: a comparison of negative binomial, beta binomial, and zero-inflated distributions. Am J Drug Alcohol Abuse. 2015;41(6):489–97.
421. JBA P, Palmer S, Sapra S, Shah N, Desai P, Villa G, Lipton RB. Modeling migraine day frequency using the beta-binomial distribution: A case study of erenumab as migraine prophylaxis. Presented at ISPOR 22nd Annual International Meeting, Boston, United States; 2017.
422. Porter JK, Brennan A, Palmer S, Sapra S, Cristino J. Parametric simulation of headache day frequency using a negative binomial distribution: a case study of Erenumab in episodic migraine. Value Health. 2016;19(7):A361.
423. Lee JH, Han G, Fulp WJ, Giuliano AR. Analysis of overdispersed count data: application to the human papillomavirus infection in men (HIM) study. Epidemiol Infect. 2012;140(6):1087–94.
424. Quan HM, Mao X, Wang L. A case study of modeling and exposure-response prediction for count data. J Biopharm Stat. 24(5):1073–90.
425. Houle TT, Turner DP, Houle TA, et al. Rounding behavior in the reporting of headache frequency complicates headache chronification research. Headache. 2013;53(6):908–19.
426. Silberstein SD, Hulihan J, Karim MR, Wu SC, Jordan D, Karvois D, et al. Efficacy and tolerability of topiramate 200 mg/d in the prevention of migraine with/without aura in adults: a randomized, placebo-controlled, double-blind, 12-week pilot study. Clin Ther. 2006;28(7):1002–11.
427. Altman DG, Royston P. The cost of dichotomising continuous variables. BMJ. 2006;332(7549):1080.
428. Ministry of Health, Labour and Welfare. Basic Survey on Wage. Structure. 2017; https://www.mhlw.go.jp/english/database/db-l/ordinary.html. Accessed 1 Oct 2020
429. World Health Organization. Headache disorders 2016. https://www.who.int/news-room/fact-sheets/detail/headache-disorders. Accessed 1 Oct 2020.
430. Kotani K, Shimomura T, Ikawa S, Sakane N, Ishimaru Y, Adachi S. Japanese with headache: suffering in silence. Headache. 2004;44(1):108–9.
431. Chinese Medical Association Group. Guide to the prevention and treatment of migraine in China [Chinese]. Chin J Pain Med. 2016;22:721–7.
432. Marmura MJ, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: the American Headache Society evidence assessment of migraine pharmacotherapies. Headache. 2015;55(1):3–20. https://doi.org/10.1111/head.12499.
433. Meyers JL, Davis KL, Lenz RA, Sakai F, Xue F. Treatment patterns and characteristics of patients with migraine in Japan: a retrospective analysis of health insurance claims data. Cephalalgia. 2019;39(12):1518–34.
434. Lanteri-Minet M. Economic burden and costs of chronic migraine. Curr Pain Headache Rep. 2014;18(1):385.
435. Insinga RP, Ng-Mak DS, Hanson ME. Costs associated with outpatient, emergency room and inpatient care for migraine in the USA. Cephalalgia. 2011;31:1570–5. 2011/10/21. https://doi.org/10.1177/0333102411425960.
436. Jacob L, Kostev K. Prescription patterns and the cost of migraine treatments in German general and neurological practices. Pain Pract. 2017;17:747–52. 2016/09/14. https://doi.org/10.1111/papr.12520.
437. Albers L, Kries RV, Straube A, et al. Age- and sex-specific first health care use for migraine in 2016 in children and adolescents from prospectively collected health insurance data in Germany. Cephalalgia. 2019;39:1156–63. 2019/04/13. https://doi.org/10.1177/0333102419844543.

438. Law EF, Palermo TM, Zhou C, et al. Economic Impact of Headache and Psychiatric Comorbidities on Healthcare Expenditures Among Children in the United States: A Retrospective Cross-Sectional Study. Headache. 2019;59:1504–15. 2019/09/15. https://doi.org/10.1111/head.13639.
439. Hjalte F, Olofsson S, Persson U, Linde M. Burden and costs of migraine in a Swedish defined patient population–a questionnaire-based study. J Headache Pain. 2019;20(1):65.
440. European Medicines Agency (EMA). Summary of Product Characteristics. BOTOX® 50 Allergan Units, Powder for Solution for Injection. European Medicines Agency (EMA). 2019.
441. Chalmer MA, Hansen TF, Lebedeva ER, Dodick DW, Lipton RB, Olesen J. Proposed new diagnostic criteria for chronic migraine. Cephalalgia. 2019:1–8.
442. Manack AN, Buse DC, Lipton RB. Chronic migraine: epidemiology and disease burden. Curr Pain Headache Rep. 2011;15(1):70–8.
443. Stovner LJ, Andrée C, Committee ES. Impact of headache in Europe: a review for the Eurolight project. J Headache Pain. 2008;9:139–46. https://doi.org/10.1007/s10194-008-0038-6.
444. Buse DC, Manack AN, Serrano D, Varon SF, Turkel LRB. Headache impact of chronic and episodic migraine: predictors of impact from the American migraine prevalence and prevention (AMPP) study. Headache. 2012;52(1):3–17.
445. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. PharmacoEconomics. 1993;4:353–65.
446. Natoli JL, Manack A, Dean B, Butler Q, Turkel CC, Stovner L, Lipton RB. Global prevalence of chronic migraine: a systematic review. Cephalalgia. 2010;30(5):599–609.
447. Sumelahti M-L, Mattila K, Sumanen M. Painful musculosceletal disorders and depression among working aged migraineurs. Acta Neurol Scand. 2018;138:93–8.
448. Giorgi G, Arcangeli G, Perminiene M, Lorini C, Ariza-Montes A, Fiz-Perez J, Di Fabio A, Mucci N. Work-related stress in the banking sector: a review of incidence, correlated factors, and major consequences. Front Psychol. 2017;8:2166.
449. Burton WN, Conti DJ, Chen CY, Schultz AB, Edington DW. The economic burden of lost productivity due to migraine headache: a specific worksite analysis. J Occup Environ Med. 2002;44:523–9.
450. Nagata T, Mori K, Ohtani M, Nagata M, Kajiki S, Fujino Y, Matsuda S, Loeppke R. Total health-related costs due to absenteeism, presenteeism, and medical and pharmaceutical expenses in Japanese employers. J Occup Environ Med. 2018;60:e273.
451. Hepp Z, Dodick DW, Varon SF, et al. Persistence and switching patterns of oral migraine prophylactic medications among patients with chronic migraine: a retrospective claims analysis. Cephalalgia. 2017;37:470–85. https://doi.org/10.1177/0333102416678382.
452. Buse DC, Yugrakh MS, Lee LK, et al. Burden of illness among people with migraine and >/= 4 monthly headache days while using acute and/or preventive prescription medications for migraine. J Manag Care Spec Pharm. 2020;26:1334–43. https://doi.org/10.18553/jmcp.2020.20100.
453. Hines D, Shah S, Multani J, et al. Changes in acute migraine-specific medications after initiating erenumab: results from a real-world retrospective cohort study in the United States (1685). Neurology. 2020;94:1685.
454. Tepper S, Fang J, Vo P, et al. Impact of erenumab on acute medication usage and healthcare resource utilization among migraine patients: a US claims database study. Cephalalgia. 2020;40:97–9.
455. Faust E, Pivneva I, Yang K, et al. Reductions in migraine frequency and duration in patients with chronic migraine treated with erenumab: interim results from a real-world multicenter chart-review study of US headache centers MTV20-DP-001. Cephalalgia. 2020;40:18–110.
456. Freitag FG, Lyss H, Nissan GR. Migraine disability, healthcare utilization, and expenditures following treatment in a tertiary headache center. Bayl Univ Med Cent Proc. 2013;26(4):363–7.
457. Bonafede M, Cai Q, Cappell K, et al. Factors associated with direct health care costs among patients with migraine. J Manag Care Spec Pharm. 2017;23(11):1169–76.

458. Miller S. The acute and preventative treatment of episodic migraine. Ann Indian Acad Neurol. 2012;15(Suppl 1):S33–9.
459. Weatherall MW. The diagnosis and treatment of chronic migraine. Ther Adv Chronic Dis. 2015;6(3):115–23.
460. Wu J, Hughes MD, Hudson MF, Wagner PJ. Antimigraine medication use and associated health care costs in employed patients. J Headache Pain. 2012;13(2):121–7.
461. Messali A, Owens G, Bloudek L, Kori S, Cole A, Chia J. Health care resource utilization following initiation of a triptan: a retrospective claims analysis. J Manag Care Spec Pharm. 2014;20(4):368–75.
462. Etemad LRea. Costs and utilization of triptan users who receive drug prophylaxis for migraine versus triptan users who do not receive drug prophylaxis. J Manag Care Pharm. 2005;11(2):137–44.
463. Swedish Headache Society. Treatment guidelines migraine. 2017. http://www.huvudvarkssallskapet.se/diagnostik_behandling.php?category_id=3. Accessed Sept 2019.
464. Goadsby PJ, Paemeleire K, Broessner G, et al. Efficacy and safety of erenumab (A MG334) in episodic migraine patients with prior preventive treatment failure: a subgroup analysis of a randomized, double-blind, placebo-controlled study. Cephalalgia. 2019;39:817–29.
465. Ashina M, Tepper S, Brandes JL, Reuter U, et al. Efficacy and safety of erenumab (A MG334) in chronic migraine patients with prior preventive treatment failure: a subgroup analysis of a randomized, double-blind, placebo-controlled study. Cephalalgia. 2018;38(10):1611–21.
466. Brown JS, Papadopoulos G, Neumann PJ, Price M, Friedman M, Menzin J. Cost-effectiveness of migraine prevention: the case of topiramate in the UK. Cephalalgia. 2006;26(12):1473–82.
467. Silberstein SD, Lipton RB, Dodick D, et al. Efficacy and safety of topiramate for the treatment of chronic migraine: a randomized, double-blind, placebo-controlled trial. Headache. 2007;47(2):170–80.
468. Brandes JL, Saper JR, Diamond M, et al. Topiramate for Migraine prevention. JAMA. 2004;291(8):965–73.
469. Láinez MJ. The effect of migraine prophylaxis on migraine-related resource use and productivity. CNS Drugs. 2009;23(9):727–38.
470. Tepper S, Ashina M, Reuter U, Brandes JL, Dolezil D, Silberstein S, et al. Safety and efficacy of erenumab for preventive treatment of chronic migraine: a randomised, double-blind, placebo-controlled phase 2 trial. Lancet Neurol. 2017;16(6):425–34.
471. Lipton RB, Tepper SJ, Reuter U, Silberstein S, Stewart WF, Nilsen J, Leonardi DK, Desai P, Cheng S, Mikol DD, Lenz R. Erenumab in chronic migraine: Patient-reported outcomes in a randomized double-blind study. Neurology. 2019;92(19):e2250–60.
472. Vikelis M, Argyriou AA, Dermitzakis EV, Spingos KC, Mitsikostas DD. Onabotulinumtoxin-A treatment in Greek patients with chronic migraine. J Headache Pain. 2016;17(1):84.
473. Fendrick AM, Smith DG, Chernew ME, Shah SN. A benefit-based copay for prescription drugs: patient contribution based on total benefits, not drug acquisition cost. Am J Manag Care. 2001;7(9):861–74.
474. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38:1–211.
475. Lipton RB, Silberstein SD. Episodic and chronic migraine headache: breaking down barriers to optimal treatment and prevention. Headache. 2015;55(Suppl 2):103–22. (quiz 23–6)
476. Lafata JE, Moon C, Leotta C, Kolodner K, Poisson L, et al. The medical care utilization and costs associated with migraine headache. J Gen Intern Med. 2004;19:1005–7.
477. Antonaci F, Dumitrache C, De Cillis I, Allena M. A review of current European treatment guidelines for migraine. J Headache Pain. 2010;11:13–9.
478. Goldberg LD. The cost of migraine and its treatment. Am J Manag Care. 2005;11:S62–7.
479. Steiner TJ, Jensen R, Katsarava Z, Linde M, MacGregor EA, Osipova V, Paemeleire K, Olesen J, Peters M, Martelletti P, on behalf of the European Headache Federation and Lifting The Burden: the Global Campaign against Headache. Aids to management of headache disorders in primary care (2nd edition). J Headache Pain. 2019;20:57.

480. Katsarava Z, Steiner TJ. Neglected headache: ignorance, arrogance or insouciance? Cephalalgia. 2012;32:1019–20.
481. Antonaci F, Valade D, Lanteri-Minet M, Láinez JM, Jensen J, Steiner TJ. Proposals for the organisation of headache services in Europe. Intern Emerg Med. 2008;3:S25–8.
482. Steiner TJ, Jensen R, Katsarava Z, Uluduz D, Tinelli M, Thomas H, Stovner LJ. The healthcare solution to headache. Ch 15. In: Steiner TJ, Stovner LJ, editors. Societal impact of headache. Burden, costs and response. Cham: Springer Nature; 2019. p. 203–24.
483. Lifting The Burden. The global campaign against headache. http://www.l-t-b.org. Accessed 6 June 2021.
484. European Headache Federation. https://ehf-org.org. Accessed 6 June 2021.
485. Laughey WF, Holmes WF, Mac Gregor AE, Sawyer JPC. Headache consultation and referral patterns in one UK general practice. Cephalalgia. 1999;19:328–9.
486. Tfelt-Hansen P. Review. Pharmacological strategies to treat attacks of episodic migraine in adults. Expert Opin Pharmacother. 2020;22(3):305–16. https://doi.org/10.1080/14656566.2020.1828347.
487. World Health Organization. Headache disorders and public health. Education and management implications. Geneva: WHO (WHO/MSD/MBD/00.9); 2000.
488. World Health Assembly. Synergies in addressing the burden of epilepsy and other neurological disorders. WHA73_5_en WHO 2020; 2020.
489. World Health Organization and United Nations Children's Fund (UNICEF) Global Conference on Primary Health Care (2018) Declaration of Astana. From Alma-Ata towards universal health coverage and the sustainable development goals. WHO/UNICEF, Astana.
490. Lifting The Burden. http://www.l-t-b.org.
491. Tinelli M, Leonardi M, Paemeleire K, Raggi A, Mitsikostas D, de la Torre ER, Steiner TJ; European Brain Council Value of Treatment Headache Working Group, the European Headache Federation, the European Migraine and Headache Alliance and Lifting The Burden: the Global Campaign against Headache. Structured headache services as the solution to the ill-health burden of headache. 3. Modelling effectiveness and cost-effectiveness of implementation in Europe: findings and conclusions. J Headache Pain. 2021;22(1):90.
492. Linde M, Steiner TJ, Chisholm D. Cost-effectiveness analysis of interventions for migraine in four low- and middle-income countries. J Headache Pain. 2015;16:15.
493. Steiner TJ, Linde M, Schnell-Inderst P. A universal outcome measure for headache treatments, care-delivery systems and economic analysis. J Headache Pain. 2021;22:63.
494. Tinelli M, Leonardi M, Paemeleire K, et al. Structured headache services as the solution to the ill-health burden of headache. 3. Modelling effectiveness and cost-effectiveness of implementation in Europe: findings and conclusions. J Headache Pain. 2021;22:90. https://doi.org/10.1186/s10194-021-01305-8.
495. Steiner TJ, Jensen R, Katsarava Z, Stovner LJ, Uluduz D, Adarmouch L, Al Jumah M, Al Khathaami AM, Ashina M, Braschinsky M, Broner S, Eliasson JH, Gil-Gouveia R, Gómez-Galván JB, Guðmundsson LS, Herekar AA, Kawatu N, Kissani N, Kulkarni GB, Lebedeva ER, Leonardi M, Linde M, Luvsannorov O, Maiga Y, Milanov I, Mitsikostas DD, Musayev T, Olesen J, Osipova V, Paemeleire K, Peres MFP, Quispe G, Rao GN, Risal A, Ruiz de la Torre E, Saylor D, Togha M, Yu SY, Zebenigus M, Zenebe Zewde Y, Zidverc-Trajković J, Tinelli M, on behalf of Lifting The Burden: the Global Campaign against Headache. Structured headache services as the solution to the ill-health burden of headache. 1. Rationale and description. J Headache Pain. 2021;22:78.
496. GBD 2016 Neurology Collaborators. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18(5):459–80. https://doi.org/10.1016/S1474-4422(18)30499-X.
497. Viana M, Khaliq F, Zecca C, Figuerola MDL, Sances G, Di Piero V, Petolicchio B, Alessiani M, Geppetti P, Lupi C, Benemei S, Iannacchero R, Maggioni F, Jurno ME, Odobescu S, Chiriac E, Marfil A, Brighina F, Barrientos Uribe N, Pérez Lago C, Bordini C, Lucchese F, Maffey V, Nappi G, Sandrini G, Tassorelli C. Poor patient awareness and frequent misdiagnosis of

migraine: findings from a large transcontinental cohort. Eur J Neurol. 2020;27(3):536–41. https://doi.org/10.1111/ene.14098.
498. Tinelli M, Leonardi M, Paemeleire K, Mitsikostas D, de la Torre ER, Steiner TJ, on behalf of the European Brain Council Value of Treatment Headache Working Group, the European Headache Federation, the European Federation of Neurological Associations, and Lifting The Burden: the Global Campaign against Headache. Structured headache services as the solution to the ill-health burden of headache. 2: modelling effectiveness and cost-effectiveness of implementation in Europe: methodology. J Headache Pain. 2021;22:99.
499. GBD. Viewpoint collaborators (2020) Five insights from the global burden of disease study 2019. Lancet. 2019;396:1135–59.
500. Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. JAMA. 2003;290(18):2443–54. https://doi.org/10.1001/jama.290.18.2443.
501. Simić S, Rabi-Žikić T, Villar JR, Calvo-Rolle JL, Simić D, Simić SD. Impact of individual headache types on the work and work efficiency of headache sufferers. Int J Environ Res Public Health. 2020;17(18):6918. https://doi.org/10.3390/ijerph17186918.
502. Kothari SF, Jensen RH, Steiner TJ. The relationship between headache-attributed disability and lost productivity: 1. A review of the literature. J Headache Pain. 2021;22(1):73.
503. Thomas H, Kothari SF, Husøy A, Jensen RH, Katsarava Z, Tinelli M, Steiner TJ. The relationship between headache-attributed disability and lost productivity: 2. Empirical evidence from population-based studies in nine disparate countries. J Headache Pain. 2021;22(1):153.
504. Steiner TJ, Jensen R, Katsarava Z, Stovner LJ, Uluduz D, Adarmouch L, Al Jumah M, Al Khathaami AM, Ashina M, Braschinsky M, Broner S, Eliasson JH, Gil-Gouveia R, Gómez-Galván JB, Guðmundsson LS, Kawatu N, Kissani N, Kulkarni GB, Lebedeva ER, Leonardi M, Linde M, Luvsannorov O, Maiga Y, Milanov I, Mitsikostas DD, Musayev T, Olesen J, Osipova V, Paemeleire K, Peres MFP, Quispe G, Rao GN, Risal A, Ruiz de la Torre E, Saylor D, Togha M, Yu SY, Zebenigus M, Zenebe Zewde Y, Zidverc-Trajković J, Tinelli M, on behalf of Lifting The Burden: the Global Campaign against Headache. Structured headache services as the solution to the ill-health burden of headache. 1: rationale and description. J Headache Pain. 2021;22:78.
505. World Health Organization. Choosing Interventions that are Cost–Effective (WHO-CHOICE). Project WHO | WHO-CHOICE. WHO https://www.who.int/news-room/feature-stories/detail/new-cost-effectiveness-updates-from-who-choice (Accessed 27 July 2021) 2014.
506. World Health Organization. Universal health coverage 2020. https://www.who.int/health-topics/universal-health-coverage#tab=tab_1 (Accessed 13 Dec 2020).
507. Schramm S, Uluduz D, Gouveia RG, et al. Headache service quality: evaluation of quality indicators in 14 specialist-care centres. J Headache Pain. 2016;17(1):111.
508. Braschinsky M, Haldre S, Kals M, Arge M, Saar B, Niibek M, Katsarava Z, Steiner TJ. Structured education to improve primary-care management of headache: how long do the benefits last? A follow-up observational study. Eur J Neurol. 2018;25(3):497–502. https://doi.org/10.1111/ene.13524.
509. World Health Organization and Lifting The Burden. Atlas of headache disorders and resources in the world 2011. Geneva: World Health Organization; 2011.
510. Steiner TJ, Jensen R, Katsarava Z, et al. Aids to management of headache disorders in primary care (2nd edition): on behalf of the European Headache Federation and Lifting The Burden: the Global Campaign against Headache. J Headache Pain. 2019;20(1):57.
511. Yoon MS, Katsarava Z, Obermann M, Fritsche G, Oezyurt M, Kaesewinkel K, Katsarova A, Santowski I, Diener H, Moebus S. Prevalence of primary headaches in Germany: results of the German headache consortium study. J Headache Pain. 2012;13:215–23.
512. Steiner TJ, Paemeleire K, Jensen R, Valade D, Savi L, Lainez MJA, Diener H-C, Martelletti P, Couturier EGM. European principles of management of common headache disorders in primary care. J Headache Pain. 2007;8(suppl 1):S3–S21.

513. Hungarian Headache Society. List of headache centers in Hungary http://fejfajas-tarsasag.hu/info.aspx?sp=17.
514. May A, et al. EFNS guidelines on the treatment of cluster headache and other trigeminal-autonomic cephalalgias. Eur J Neurol. 2006;13:1066–77.
515. Cevoli S, D'Amico D, Martelletti P, Valguarnera F, Del Bene E, De Simone R, Sarchielli P, Narbone M, Testa L, Genco S, Bussone G, Cortelli P. Underdiagnosis and undertreatment of migraine in Italy: a survey of patients attending for the first time 10 headache centres. Cephalalgia. 2009;29(12):1285–93. https://doi.org/10.1111/j.1468-2982.2009.01874.x.
516. Brockmann N, Evers S. Migraine in neurologists and headache specialists. Headache. 2010;50(1):138–40.
517. Alstadhaug KB, Hernandez A, Næss H, et al. Migraine among Norwegian neurologists. Headache. 2012;52(9):1369–76.
518. Lu SR, Wang SJ, Fuh JL. The practice pattern of migraine management among neurologists in Taiwan. Cephalalgia. 2006;26(3):310–3.
519. Yeh WZ, Blizzard L, Taylor BV. What is the actual prevalence of migraine. Brain Behav. 2018;8(6):e00950.
520. Hettiarachchi J, Lipton RB, Dodick D, et al. A self administered screener for migraine in primary care. Neurology. 2012;61(3):375–82.
521. Evans RW, Evans RE, Kell HJ. A survey of family doctors on the likeability of migraine and other common diseases and their prevalence of migraine. Cephalalgia. 2010;30(5):620–3.
522. Waters WE. Migraine in general practitioners. Br J Prev Soc Med. 1975;29:48–52.
523. Dalsgaard-Nielsen T, Ulrich J. Prevalence and heredity of migraine and migrainoid headaches among 461 Danish doctors. Headache. 1973;12(4):168–72.
524. Diener H-C, Holle-Lee D, Nägel S, Dresler T, Gaul C, Göbel H, Heinze-Kuhn K, Jürgens T, Kropp P, Meyer B, May A, Schulte L, Solbach K, Straube A, Kamm K, Förderreuther S, Gantenbein A, Petersen J, Sandor P, Lampl C. Treatment of migraine attacks and prevention of migraine: Guidelines by the German Migraine and Headache Society and the German Society of Neurology. Clin Translational Neurosci. 2019;3:1–40.
525. Viticchi G, Silvestrini M, Falsetti L, Lanciotti C, Cerqua R, Luzzi S, Provinciali L, Bartolini M. Time delay from onset to diagnosis of migraine. Headache. 2011;51(2):232–6. https://doi.org/10.1111/j.1526-4610.2010.01778.x.
526. Goadsby PJ, Sprenger T. Current practice and future directions in the prevention and acute management of migraine. Lancet Neurol. 2010;9:285–98.
527. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition. Cephalalgia Int J Headache. 2018;38(1):1–1211.
528. World Health Organization. Atlas of headache disorders and resources in the world 2011. Geneva: WHO; 2011.
529. Stovner LJ, Andree C. Prevalence of headache in Europe: a review for the Eurolight project. J Headache Pain. 2010;11:289–99.
530. World Bank. http://www.worldbank.org/en/results . Accessed 6 Feb 2017.
531. Yu S, Zhang M, Zhou J, Liu R, Wan Q, Li Y. Headache care in China. Headache. 2014;54(4):601–9. https://doi.org/10.1111/head.12330.