

# Population Variation in Migraine Prevalence – The Unsolved Problem

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## ABSTRACT

*Migraine is one of the most prevalent types of headache, which imposes a substantial burden on society as measured by direct and indirect costs. In the present work we review the obstacles to carrying out migraine epidemiological studies. Knowledge of the epidemiology of migraine has expanded because of the recent proliferation of large scale population-based studies using standardized case definitions. Previous surveys of the prevalence of migraine have given widely differing results. Even in population-based studies, there have been wide variations in estimates of migraine prevalence. The development of International Headache Society (IHS) criteria for migraine has facilitated international comparisons in epidemiologic studies by providing explicit and consistent diagnostic criteria. Recent studies using IHS diagnostic criteria have given relatively consistent estimates of migraine prevalence (about 15–18% of women and 6% of men). Studies of racial diversity in the prevalence of migraine and other headaches are still not conclusive. Further work is needed on epidemiology of migraine and collaboration between epidemiologists and clinicians seems the most likely way to advance understanding in this field.*

## Introduction

Headaches are traditionally classified into two major groups: primary and secondary disorders<sup>1–11</sup>. Primary headaches are mainly divided into migraine, tension-type headache, and cluster headache<sup>6,11</sup>.

Several factors have complicated the classification of headache, including the continuing debate as to whether tension-type headache and migraine are distinct

categories of disease or rather share a common pathophysiology, differing more in degree of severity than in kind<sup>5,10,12</sup>.

From a public health perspective, migraine and tension-type headache are the two most important primary headache disorders because of their high prevalence and the associated disability. Despite the fact that headache is one of the most frequently reported symptoms in the adult general population, little is

known about the epidemiology of the headache disorders. The major problem has been that of defining the disease entities, since no laboratory correlate or other objective defining marker exists.

Migraine is one of the most prevalent types of headache. In addition, it constitutes a pathology which due to its cyclic, recurring and highly incapacitating characteristics has enormous repercussions on the quality of life of those affected; it is responsible for the loss of an important number of working days and of production; responsible too for the vast consumption of medicaments and consequently represents a considerable economic cost.

An epidemiological study of migraine, however, poses countless difficulties owing to its characteristics and its association with risk factors. In this present paper we review the obstacles to carrying out migraine epidemiological studies and we also comment upon many such studies found in the literature.

#### *Importance of migraine epidemiology studies*

There are a number of reasons to study the epidemiology of migraine:

- First, epidemiologic methods can be used to assess the reliability and validity of various case definitions<sup>13,14</sup> and – also – to improve the case-definitions used in clinical practice and research;
- Studies of migraine prevalence provide one measure of the scope of the headache problem;
- Consequently, epidemiologic methods can be used to assess the impact of migraine on individuals and society;
- Epidemiologic methods can clarify the relationship of migraine to other primary headache disorders<sup>4,5,6</sup>;
- Examination of sociodemographic, genetic and environmental risk factors help us to identify groups at highest

risk for some kinds of migraine headaches, which may provide clues to preventive strategies or clues to disease mechanisms.

- Epidemiology methods are useful to determine the natural history of migraine including health consequences and co-morbid conditions.
- Last, but not the least, epidemiology may help us to assess current patterns of diagnosis and treatment of migraine as a prelude to public health interventions.

#### **Methodological Problems**

There are several methodological problems related to the study of the epidemiology of migraine. At the beginning, we have problems of defining disease entities. Perhaps most importantly, there is no biological test to ensure definitive diagnosis of the primary headache disorders, including migraine<sup>10</sup>.

Diagnosis of migraine is, therefore, based on clinical assessment, which is complicated by some factors:

- The episodic nature of migraine, which necessitates reliance on patients' recollections of symptoms.
- The poor demarcation among the primary headache disorders; we are often faced with the fact that patients often have more than one type of headache<sup>2</sup>.
- Problems connected with the composition and representativeness of the study population.

The development of International Headache Society (IHS) criteria for primary headaches has facilitated international comparisons in epidemiologic studies by providing – we believe – explicit and consistent diagnostic criteria<sup>11</sup>.

## Controversies in Epidemiology of Migraine

Now, let's try to answer the question: How common is migraine?

Most epidemiologic studies of migraine have emphasized disease prevalence. Prevalence is the proportion of a given population, which has migraine over a defined period of time. Lifetime prevalence of migraine refers to the proportion of individuals who have ever had the condition. Period prevalence refers to the proportion of individuals who have had at least one migraine attack within some defined interval, usually within 1 week, 4 weeks, 3 months, or one year of the time of ascertainment. Prevalence increases as the period selected for study increases.

Migraine epidemiology has been studied extensively in the United States, Great Britain, and Western Europe, while this type of study is very rare in developing countries. Using the IHS criteria, large population-based epidemiological studies in Denmark, the United States, France, Germany and elsewhere have shed light on the descriptive epidemiology of migraine. According to most famous names in the field of headache epidemiology – Rasmussen, Lipton and Stewart – the one-year prevalence of migraine in Western countries is approximately 6% among men and 15% to 17.6% among women<sup>3,7</sup>.

Prevalence varies by age, increasing to about age 40 years and declining thereafter in both men and women. Migraine occurs across all age groups, but the most commonly affected are those in the so-called »earning« years (25 to 44 years of age), the time of maximum employment and productivity. The gender ratio also appears to vary by age, increasing from menarche to about age 42 years and declining thereafter. The majority of migraine sufferers do not regularly seek

medical help. Although only a small percentage of migraine sufferers actually seek care at any given time, about 85% of females and 77% of males sought medical attention at some point for migraine. 8% of migraineurs were hospitalized for the disorder<sup>3,7</sup>.

On the other hand, we must admit that other, numerous surveys of the prevalence of migraine headache have given widely differing, indeed often conflicting results.

For example, estimates of migraine prevalence in different countries of Europe vary from less than 5% to more than a quarter of the total population. (Table 1)<sup>8,15–22</sup>. There are a number of possible reasons for these differences.

Perhaps the most unlikely is that the published findings represent real differences in the prevalence of migraine in the populations studied. More likely, in our present state of knowledge, they represent methodological differences between the various surveys and differences in the diagnostic criteria. The meta-analysis of 24 population-based headache prevalence studies, made by Stewart, showed that 70% of the variation in estimated prevalence of migraine is accounted for by differences in the definitions of migraine, as well as the age and gender distribution of the study samples<sup>23</sup>. In particular, the studies which included »warning signs« of migraine as diagnostic criteria tended to give the highest prevalence estimates<sup>24</sup>.

Most migraine epidemiology studies have involved small numbers of subjects, specific age groups, limited geographical areas, or study samples chosen from speciality clinics, outpatient practices, or tertiary care centers<sup>2,3,25</sup>.

Not all of those suffering with migraine seek medical attention<sup>7,10,26</sup>. Therefore, some groups may be under represented in studies of patients consulting

**TABLE 1**  
ONE-YEAR PREVALENCE OF MIGRAINE IN SOME EUROPEAN COUNTRIES. DATA ARE PRESENTED FROM THE LOWEST TO THE HIGHEST VALUE OF PREVALENCE

State	Sample	Prevalence (total)	Prevalence (female)	Prevalence (male)
France (1993) <sup>15</sup>	1,563	4.27	6	1.7
Finland (1993) <sup>16</sup>	22,809	6.3	10.1	2.5
France (1992) <sup>8</sup>	4,204	8.1	11.9	4.0
Portugal (1995) <sup>17</sup>	2,008	8.8	–	–
Norway (1992) <sup>18</sup>	230	11.7	13.8	5.4
Denmark (1995) <sup>19</sup>	740	–	15	6
Denmark (1992) <sup>20</sup>	1,000	–	15.3	5.9
Netherlands (1999) <sup>21</sup>	6,491	–	25	7.5
Germany (1994) <sup>22</sup>	4,061	27.5	32	22

physicians for treatment of migraine. Persons with low income, individuals with headache that responds to over-the-counter analgesics, those who experience no disability, and those who perceive their headache to be of mild-to-moderate intensity or of short duration are most likely to be overlooked<sup>4</sup>.

The same pattern as in European countries – obviously differing data – we have in epidemiologic studies of primary headaches outside Europe. For example, we present data of migraine one-year prevalence from both Americas and Asia (Table 2)<sup>7,27–33</sup>. Except the first one (this study was included because of the huge representative sample), they were also conducted according to IHS criteria.

Which explanation we could offer here?

International variation in migraine prevalence could result from methodological differences among studies, cultural differences in symptom reporting, variation in environmental risk factors, or race-related differences in genetic susceptibility to migraine. The available evidence supports a possible role for both environmental and genetic risk factors<sup>21,34,35</sup>.

Comparative studies in different races, or different geographical areas, have

yielded important insights into risk factors for other diseases. For example, the role of cholesterol as a risk factor for myocardial infarction was discovered, in part, because of international differences in the prevalence of heart disease. Application of this strategy to migraine requires that we search for variation in migraine prevalence across various definable groups and then identify the genetic or environmental factors which account for the variation.

Epidemiologic studies show that tension-type headache is 2 to 6 times more likely than migraine, but there are also significant variations in estimated prevalence of these kind of headache<sup>36–38</sup>. The same problem we have in prevalence of cluster headache, too<sup>39,40</sup>.

Because the prevalence of migraine appears to be increasing, especially in those under 45 years of age, additional societal costs due to lost productivity and increased utilization of health care services can be expected. Because it is unclear what proportion of migraine sufferers seek medical attention for their headache, more rigorous detection is necessary to adequately study the full impact of this disease.

**TABLE 2**  
ONE-YEAR PREVALENCE OF MIGRAINE IN SOME AMERICAN AND ASIAN COUNTRIES

State	Sample	Prevalence (total)	Prevalence (female)	Prevalence (male)
China (1988) <sup>27</sup>	246,812	0.69	1.13	0.24
USA (1989) <sup>28</sup>	20,000	4.1	5.77	2.32
USA (1992) <sup>7</sup>	20,468	–	17.6	5.7
Japan (1993) <sup>29</sup>	5,477	3.5	5.2	1.8
Japan (1997) <sup>30</sup>	4,029	6	13	3.6
Malaysia (1996) <sup>31</sup>	595	9	11.3	6.7
Chile (1997) <sup>32</sup>	1,540	7.3	11.9	2.0
China (1997) <sup>33</sup>	1,533	3	–	–

To obtain accurate estimates of migraine headache prevalence, population-based studies are required. Clinic-based studies include a highly selected group of migraine sufferers. Population based studies examine sufferers whether or not they consult doctors by actively identifying migraine symptoms in representative samples. For example, most migraine studies are clinic based, yet less than 15% of migraine sufferers ever consult neurologists, and less than 2% consult headache specialists. This can result in substantial selection bias<sup>19,41,42</sup>.

As it was shown earlier, even in population-based studies there have been wide variations in estimates of migraine prevalence. Although the use of the IHS criteria has resulted in a more coherent picture across population-based studies, efforts must be made to assess the reliability and validity of these criteria in population-based samples.

In theory, aggregation of data from multiple trials should enhance the precision and accuracy of any pooled result. But combining data requires a leap of faith: it presumes that the differences among studies are primarily due to chance. In fact, differences in the direction or size of treatment effects may be caused by other factors, including subtle differences in treatments, populations,

outcome measures, study design, and study quality. Thus meta-analyses may generate misleading results by ignoring meaningful heterogeneity among studies, entrenching the biases in individual studies, and introducing further biases through the process of finding studies and selecting results to be pooled<sup>43</sup>.

In sum, meta-analysis has made and continues to make major contributions to medical research, clinical decision making, and standards of research reportage. However, it is no panacea. Readers need to examine any meta-analyses critically to see whether researchers have overlooked important sources of clinical heterogeneity among the included trials. They should demand evidence that the authors undertook a comprehensive search, avoiding covert duplicate data and unearthing unpublished trials and data. Lastly, readers and researchers alike need to appreciate that not every systematic review should lead to an actual meta-analysis of data with aggregate effect size estimates. If the process of pooling data inadvertently drowns clinically important evidence from individual studies, then a meta-analysis can do more harms than good.

At last, something about using the questionnaires in migraine epidemiology studies. Many of the epidemiological

studies on the prevalence of headaches in the general population of children have used more or less standardized questionnaires<sup>1–7</sup>. Given the variety of instruments and classifications, it is not surprising that these investigations mention a variety of prevalences for migraine headaches. A difficulty in investigating all kinds of primary headaches with questionnaires is that many individuals suffer from both typical migraine and non-migrainous headaches. A possible source of bias is the different responses that result from the use of a questionnaire in different situations. Obviously, the actual wording of the questions is also important. Further, the diagnosis is very often made by incompetent person<sup>44</sup>.

Studies of observer variation in medicine often show wide discrepancies but few such studies have been concerned

with migraine. Such studies are needed and should be carefully designed and conducted.

## Conclusions

More documentation of the age at onset, symptoms, frequency of attacks, and other characteristics related to migraine would be very useful to compare properly results between studies. We need additional descriptive epidemiologic studies of migraine, which would include reliable estimates of age-specific incidence, prevalence, remission rates, and natural history of the various migraine subtypes. Further work is needed on epidemiology of primary headaches and collaboration between epidemiologists and clinicians seems the most likely way to advance understanding in this field.

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## POPULACIJSKE VARIJACIJE U PREVALENCIJI MIGRENE: NERIJEŠENI PROBLEM

### S A Ž E T A K

Migrena predstavlja jedan od najučestalijih tipova glavobolje, te kroz neposredne i posredne troškove koje izaziva predstavlja značajno opterećenje za širu društvenu zajednicu. U izloženom su osvrtno predočene zapreke na koje nailazimo u provođenju epidemioloških istraživanja migrene. Posljednjih su godina spoznaje o epidemiologiji migrene proširene brojnim populacijskim istraživanjima, pri čemu su korištene standardizirane definicije podtipova sindroma glavobolje. Ranija su istraživanja prevalencije migrene rezultirala, uglavnom, vrlo neujednačenim rezultatima. Čak su i u populacijskim istraživanjima postojale izrazite razlike u procjeni prevalencije migrene. Uspostavljanje tzv. IHS (*International Headache Society*) kriterija za dijagnozu migrene omogućilo je usporedbu rezultata epidemioloških istraživanja u raznim dijelovima svijeta, jer su njihovim prihvaćanjem dijagnostički kriteriji bili usuglašeni i općenito razumljiviji. Novija epidemiološka istraživanja temeljena na spomenutim IHS kriterijima rezultirala su uglavnom sličnim procjenama prevalencije migrene (oko 15-18% žena i 6% muškaraca). Međutim, istraživanja populacijskih razlika u prevalenciji migrene i drugih tipova glavobolje još uvijek daju vrlo neujednačene rezultate. Stoga se nameće potreba za daljnjim naporima na unaprjeđivanju metodologija u istraživanju epidemiologije migrene. Suradnja epidemiologa i kliničara je vjerojatno je najispravniji put prema unaprjeđivanju spoznaja na tom području.