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The global burden of migraine

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Abstract Migraine is a highly prevalent headache disorder that has a substantial impact on the individual and on society. Over the past decade, substantial advances in research have increased understanding of the pathophysiology, diagnosis, epidemiology, and treatment of the disorder. This article reviews the burden of migraine, emphasizing population-based studies that used standardized diagnostic criteria. We highlight descriptive epidemiology, burden of disease, patterns of diagnosis and treatment, as well as approaches to improving health care delivery for migraine.

Key-words Migraine •
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Introduction

Headache disorders include a number of conditions characterized by recurrent episodes of head pain and associated symptoms. Though almost everyone gets occasional

headaches, particular headache disorders vary in incidence, prevalence and duration. Headache disorders are divided into the primary and secondary disorders. Secondary disorders have an identifiable underlying cause, such as an infection, a brain tumor or stroke. In primary headache disorders, there is no apparent underlying cause [1, 2].

Migraine is one of the most burdensome of the primary headache disorders. Epidemiologic data helps to describe the burden of migraine as well as its scope and distribution [3–5]. Understanding sociodemographic, genetic and environmental risk factors helps identify those groups at highest risk for migraine and may provide clues to preventive strategies or disease mechanisms. Epidemiological studies have identified a number of conditions that are comorbid with migraine; these conditions occur with migraine at a higher frequency than would be expected by chance. Comorbidities for other headache disorders are less well established. Comorbidity must be considered in formulating treatment plans and may provide insights into the mechanisms of disease [6].

Epidemiological studies assess individuals, whether or not they seek care for their headache disorders. This approach is important since less than half of individuals with active migraine sufferers actually see a doctor each year for migraine [7, 8]. From a research perspective, this means that substantial selection bias occurs in clinic-based studies, where factors that predispose individuals to consult may be mistaken for attributes of the disease.

In exploring the burden of migraine, we distinguish clinical and public health perspectives. Clinicians are concerned with the diagnosis of individual patients as a prelude to effective treatment. From a public health perspective, it is the distribution of diagnoses in a defined population that is of importance. While clinicians are interested in the burden of headache disorders imposed on each individual patient, from a societal perspective, the direct and indirect costs of illness are priorities.

In this article, we review the burden of migraine, emphasizing the population-based studies that used standardized diagnostic criteria. We highlight descriptive epidemiology, burden of disease, patterns of diagnosis and treatment, as well as approaches to improving health care delivery for migraine. We focus on migraine because this is probably the most important primary headache disorder from the perspective of societal burden. We also focus on studies based on the criteria of the International Headache Society (IHS) because they are more explicit and rigorous than earlier criteria [3, 4, 9–15].

Diagnosis

Diagnosis is an essential prelude to measuring the burden of disease. Precise case definitions are essential to facilitate reliable and valid diagnoses [3, 4]. While there is no true diagnostic gold standard for the primary headache disorders, the IHS criteria provide the operational definitions that have been widely used in epidemiologic research [9].

For primary headache, the most difficult boundary to identify is the one between migraine and tension-type headache [1, 2, 16, 17].

Epidemiological studies often focus on the incidence and prevalence of disease in defined populations. Incidence refers to the rate of onset of new cases of a disease in a given population over a defined period. Prevalence is defined as the proportion of a given population that has a disease over a defined period. Prevalence is determined by the product of average incidence and average duration of disease. For example, migraine prevalence may increase because either incidence or duration of disease is increasing. Prevalence may also be affected by demographic shifts in the population if the proportion of the population at high risk for a disease increases. For example, the aging of the population may increase the prevalence of the headache disorders most common in the elderly (e.g. headache secondary to intracranial disease, giant cell arteritis).

Primary and secondary headaches

The first population studies to apply the IHS criteria were conducted in Copenhagen; the population distribution of all headache disorders was examined using in-person clinical assessment in a large, representative community sample [4, 10]. The lifetime prevalences of various headache disorders from this population are summarized in Table 1.

Tension-type headache is a far more common primary headache than migraine [4, 10]. Cluster headache is relatively uncommon, with a prevalence of 0.1% of this population [4, 10]. Of the secondary headaches, fasting headache (a headache precipitated by missing meals) is the most common type, followed by the headache due to nose and sinus diseases and headache secondary to head trauma. Non-vascular intracranial diseases, which include infections and brain tumors, are rare. For the rest of this review, we focus on the burden of migraine.

Table 1 Lifetime prevalence of primary and secondary headaches (modified from [10])

	Prevalence (%)
Primary headache	
Tension-type headache	78
Migraine	16
Secondary headache	
Fasting	19
Nose or sinus disease	15
Head trauma	4
Non-vascular intracranial disease (brain tumor and other disorders)	0.5

Migraine incidence

Though cross-sectional data can also be used to derive incidence estimates, the incidence of migraine is best evaluated in longitudinal studies. Stewart et al. [18] estimated migraine incidence using reported age at onset from a prevalence study. In males, the incidence of migraine with aura peaked around 5 years of age at 6.6 per 1000 person-years; the peak for migraine without aura was 10 per 1000 person-years between 10 and 11 years. New cases of migraine were uncommon in men in their twenties. In females, the incidence of migraine with aura peaked between ages 12 and 13 (14.1 per 1000 person-years); migraine without aura peaked between ages 14 and 17 (18.9 per 1000 person-years). Thus, migraine begins earlier in males than in females and migraine with aura begins earlier than does migraine without aura.

Stang et al. [19] used the linked medical records system in Olmstead County, Minnesota to identify migraine sufferers who sought medical care for headaches. Their incidence was lower (probably because many people with migraine do not consult doctors or receive a medical diagnosis) [5, 6, 20] and their peaks are later than those identified by Stewart et al. [18] (because medical diagnosis may occur long after the age at onset).

Migraine prevalence studies

The published estimates of migraine prevalence have varied widely (reviewed in [3, 4, 21]). In 1995, a meta-analysis of 24 studies that met inclusion criteria included only 5 that used IHS criteria [22]. This meta-analysis revealed that case definition, along with age and gender distribution of the study samples, explained 70% of the variation in migraine prevalence among studies. In a second meta-analysis confined to studies using the IHS criteria, in gender-specific models (women and men were modeled separately), age and geography accounted for much of the variation in prevalence as described below [3]. Because case definition so powerfully influences prevalence estimates, we focus on studies that used the IHS criteria for migraine.

In the greater Copenhagen study, for men, the lifetime prevalences were 93% for any kind of headache, 8% for migraine and 69% for tension-type headache [10]. For women, the lifetime prevalences were 99% for all headaches, 25% for migraine and 88% for tension-type headache. The 1-year prevalence of migraine was 6% in men and 16% in women; the 1-year prevalence of tension-type headache was 63% and 86%, respectively.

In the United States, the first American Migraine Study, based on data collected in 1989, used questionnaires mailed

to 15 000 households selected to be representative of the U.S. population [11]. Migraine diagnoses were based on the IHS criteria but headache duration and the lifetime number of previous migraine attacks were not considered. Migraine prevalence was 17.6% for women and 6% for men, in the same range as the estimates of Rasmussen et al. [10]. A follow-up study, the American Migraine Study II, used virtually identical methodology 10 years later and demonstrated very similar prevalence estimates [7, 15].

In France, Henry and co-workers reported that the prevalence of IHS migraine was 11.9% in women and 4.0% in men [12]. In this study, diagnoses were assigned based on lay interviews using a validated algorithm. For the group that included “borderline migraine”, prevalence estimates were 17.6% for females and 6.1% for males, remarkably close to the findings of Stewart et al. [11]. A number of other recent studies in Western Europe and North America have examined the prevalence of migraine [13, 14, 21, 23].

Age and sex influence migraine prevalence

Analyzing prevalence in various sociodemographic groups can help clarify the distribution of illness. Sociodemographic variables, including age, gender, education, income and geography, influence migraine prevalence. Before puberty, migraine prevalence is higher in boys than in girls; as adolescence approaches, incidence and prevalence increase more rapidly in girls than in boys [18, 24–30]. A meta-analytic summary of the prevalence studies show that prevalence increases throughout childhood and early adult life until approximately age 40, after which it declines (Fig. 1) [3, 4, 9, 13]. These dramatic age effects account for some of the variation in prevalence estimates from previous studies

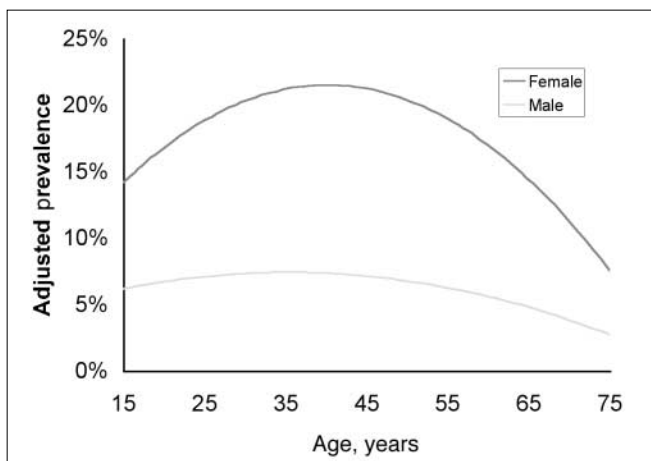


Fig. 1 Adjusted prevalence of migraine by age from a meta-analysis of studies using IHS criteria. (From [3] with permission)

[3]. The gap between peak incidence in adolescence and peak prevalence in middle life indicates that migraine is a condition of long duration.

The female to male migraine prevalence ratio also varies with age [3, 11, 15]. The onset of hormonal changes associated with menses may contribute to this variation [31]. However, hormonal factors cannot be the sole cause; differences persist to age 70 years, well beyond the time that cyclical hormonal changes can be considered a factor [9, 13, 31].

Socioeconomic status may influence migraine prevalence

The relationship between migraine prevalence and socioeconomic status is uncertain. In physician- and clinic-based studies, migraine appears to be associated with high intelligence and social class. In his studies of children, Bille did not find association between migraine prevalence and intelligence [24, 25]. Similarly, in adults, epidemiologic studies do not support a relationship between occupation and migraine prevalence [32]. In the American Migraine Studies I and II, migraine prevalence was inversely related to household income [11, 15] (i.e. migraine prevalence fell as household income increased). This inverse relationship between migraine and socioeconomic status was confirmed in another U.S. study based on members of a managed care organization [33] and in the National Health Interview Study [34]. In the latter study, migraine prevalence was highest in low-income groups; prevalence was lowest for middle income groups and began to rise in the high-income group. Since this study relied on self-reported migraine, and migraine awareness rises with income, differential ascertainment by income may account for this relationship in higher income groups.

Population studies show that individuals from high-income groups were much more likely to report a medical diagnosis of migraine than were those with lower income [7, 20]. Perhaps migraine appears to be a disease of persons with high income in the doctor's office because high-income individuals seek care. As Waters suggested, people from higher income households are more likely to consult physicians and are therefore disproportionately included in clinic-based studies [32].

The higher prevalence in the lower socioeconomic groups may be a consequence of a circumstance associated with low income and migraine, such as poor diet, poor medical care or stress [3, 11, 15]. It may also reflect social selection, i.e. migraineurs may have lower incomes because migraine interferes with educational and occupational function, causing a loss of income or the ability to rise from a low-income group. The relationship of migraine and socioeconomic status requires further study. Since migraine prevalence appears unrelated to social class in a number of studies from Europe and elsewhere, it may be influenced by patterns of medical consulting behavior and access to medical care in different countries [4, 10, 13, 14, 35].

Race and geography influence migraine prevalence

Migraine prevalence also varies by race and geography. In the U.S., it is highest in Caucasians, intermediate in African Americans, and lowest in Asian Americans [3]. Similarly, a meta-analysis of prevalence studies suggested that migraine is most common in North and South America, similar in Europe, but lower in Africa, and often lowest in studies from Asia (Fig. 2) [3]. The influence of reporting bias on these findings cannot be excluded. Nonetheless, the data suggest that race-related differences in genetic risk may contribute.

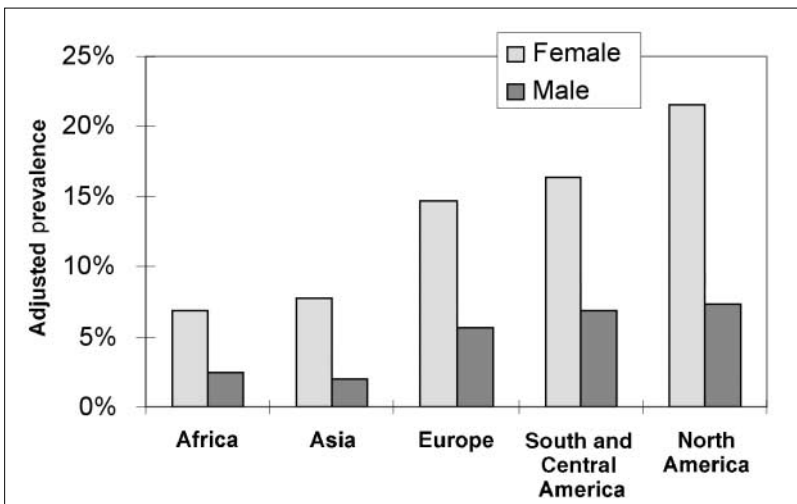


Fig. 2 Adjusted prevalence of migraine by geographic area and gender in a meta-analysis of studies using IHS criteria. (From [3] with permission)

Is migraine prevalence increasing?

The preponderance of evidence suggests that migraine prevalence has been stable over the last decade. According to the Centers for Disease Control, self-diagnosed migraine prevalence in the U.S. increased 60%, from 25.8 to 41 per 1000 persons, between 1981 and 1989 [36]. Medical records from Olmstead County also suggest prevalence is increasing [19]. The stability of prevalence in studies in the U.S. over the past decade does not support the view that prevalence is increasing [11, 15]. We have suggested instead that the demonstrable increases in medical consultation and diagnosis may have caused an apparent rather than a real increase [7, 20, 37].

Comorbidity of migraine

The term “comorbidity”, coined by Feinstein, is now widely used to refer to the greater than coincidental association of two conditions in the same individual [6, 38]. The burden of migraine is attributable in part to the neurologic and psychiatric disorders associated with it. These include stroke, epilepsy, depression and anxiety disorders. Understanding the comorbidity of migraine is potentially important from a number of different perspectives [4]. First, comorbidity has implications for diagnosis. Migraine overlaps in symptom profile with several of the conditions comorbid with it. For example, both migraine and epilepsy can cause transient alterations of consciousness as well as headache. This problem of differential diagnosis is well known. Less well-known is the problem of concomitant diagnosis. When two conditions are comorbid, the presence of migraine should increase, not reduce, the index of suspicion for disorders such as epilepsy, depression and anxiety disorders. Comorbid conditions may impose therapeutic limitations, but may also create therapeutic opportunities. When migraine and depression occur together, an antidepressant may successfully treat both conditions. When migraine and epilepsy occur together, the anti-migraine anti-epileptic agent, divalproex sodium, may prevent attacks of both migraine and epilepsy. Third, the study of comorbidity may provide epidemiological clues to the fundamental mechanisms of migraine. Finally, the presence of comorbidity may lead to overestimates of the burden of disease. Migraine sufferers may utilize healthcare resources not just because of migraine, but because of comorbid depression.

Individual burden of migraine

Migraine is a public health problem of enormous scope that has an impact on both the individual sufferer and on society

[4, 7, 11, 15]. The American Migraine Study II estimated that 28 million U.S. residents have severe migraine headaches [15]. Nearly one in four U.S. households has someone with migraine [15]. Twenty-five percent of women in the U.S. who have migraine experience four or more severe attacks per month; 35% experience 1–4 severe attacks per month; 38% experience one, or less than one, severe attack per month [15]. Similar frequency patterns were observed for men [15].

In the American Migraine Study II, 92% of women and 89% of men with severe migraine had some headache-related disability [15]. About half were severely disabled or needed bed rest [19]. In addition to the attack-related disability, many migraineurs live in fear, knowing that at any time an attack can disrupt their ability to work, care for their families or meet social obligations. Abundant evidence indicates that migraine reduces health-related quality of life (HRQoL).

Societal impact of migraine

Migraine has an enormous impact on society. Recent U.S. studies have evaluated both the indirect costs of migraine as well as the direct costs [39–41]. Indirect costs include the aggregate effects of migraine on productivity at work (paid employment), for household work and in other roles. The largest component of indirect costs are the productivity losses that take the form of absenteeism and reduced productivity while at work. Hu et al. [39] estimated that productivity losses due to migraine cost American employers 13 billion dollars per year. These issues have been recently reviewed in more detail elsewhere [39–42].

Migraine’s impact on healthcare utilization is marked as well. The National Ambulatory Medical Care Survey, conducted from 1976 to 1977, found that 4% of all visits to physicians’ offices (over 10 million visits per year) were for headache [43]. Migraine also results in major utilization of emergency rooms and urgent care centers [5, 44]. Vast amounts of prescription and over-the-counter (OTC) medications are taken for headache disorders. OTC sales of pain medication (for all conditions) were estimated to be 3.2 billion dollars in 1999 (U.S.) and headache accounts for about one-third of OTC analgesic use (Consumer Healthcare Products Association, OTC Sales Statistics, 1995–1999. ACNielsen, April 2000). Gross sales for the triptans are about one billion dollars per year in the United States.

Migraine is a lifelong disorder. Bille followed a cohort of children with severe migraine for up to 37 years [24, 25]. As young adults, 62% were migraine-free for more than 2 years, but only 40% continued to be migraine-free after 30 years, suggesting that migraine is often a lifelong disorder.

For 15 years, Fry collected information on migraine patients in his general practice in Kent [44]. His data showed a tendency for the severity and frequency of attacks to decrease as the patients got older. After 15 years, 32% of the men and 42% of the women no longer had migraine attacks. Waters noted a similar decrease in migraine prevalence [17, 32].

Measuring migraine disability

Recent efforts to assess the burden of migraine have focused on disability, also referred to as activity limitations. Disability measures assess impairment in role functioning (i.e. reduced ability to function in defined roles). Some studies focus on the proportion of migraine sufferers who experience activity limitations of a particular time. For example, a Canadian population survey of migraine found that half of migraine sufferers discontinued normal activities during their attacks and almost one-third required bed-rest [45]. In more than 70% of the headache sufferers in this survey, interpersonal relationships were impaired. Other studies measured disability by estimating lost time due to migraine capturing the inability to do things (i.e. work absenteeism) as well as reduced effectiveness [46–49]. Disability is the major determinant of the cost of illness [50]. Measures of lost time are more readily translated into economic terms because absenteeism and reduced productivity at work are the principal determinants of this cost [50].

The most frequently used disability instrument in migraine research is the migraine disability assessment (MIDAS) questionnaire [51]. MIDAS consists of five questions that focus on lost time in three domains: school work or work for pay; household work or chores; and family, social and leisure activities [51]. All questions are asked about either days of missed activity or days in which productivity is reduced by at least at half. If productivity is decreased to 50% or below, the day is considered missed. The MIDAS score is derived as the sum of missed days due to a headache from paid work, household work, and non-work activities, and days at paid work and in household work where productivity was reduced by at least half (sum of responses to questions 1 through 5). Two additional questions on the MIDAS questionnaire not included in the score assess frequency and intensity of pain. MIDAS scores are used to assign patients to 1 of 4 MIDAS grades: Grade 1 (score range, 0 to 5), little or no disability; Grade 2 (score range, 6 to 10), mild disability; Grade 3 (score range, 11 to 20), moderate disability; Grade 4 (scores, 21 or greater), severe disability. These scores reflect the number of days missed due to headache over a 3-month period.

The reliability and validity of MIDAS have been extensively studied. MIDAS can serve several roles:

1. The Perceptions study showed that MIDAS can facilitate communication between doctors and patients, and help physicians to identify patients who need better medical care [52].
2. Stratifying as a prelude to selecting treatment: the US Headache Consortium Guidelines recommends stratified care based on the level of disability to help physicians target patients who require careful assessment and treatment [53], a concept also supported by the Disability in Strategies of Care (DISC) study [54]. There is substantial evidence to support the role of disability as a treatment strategy.
3. Use as an outcome measure in clinical trials, providing evidence that a treatment can reduce the burden of migraine.

Chronic migraine

The burden of migraine is particularly great in patients with frequent headaches. A subgroup of migraine sufferers is afflicted with a syndrome characterized by attacks which increase in frequency over a number of years until a pattern of daily or near-daily headache is established [32, 55–58]. In subspecialty clinics, about 80% of patients with this disorder are overusing acute headache medication. Medication overuse is believed to contribute to the accelerating pattern of pain through a mechanism that has been termed “rebound headache”. When the cycle of medication overuse is broken, the headaches often improve [58]. However, in subspecialty clinics, this process of acceleration occurs without medication overuse in about 20% of patients, suggesting that there is a subgroup of migraine sufferers with a progressive condition. The classification of these patients remains controversial. Within the IHS system, they would usually meet criteria for migraine, for chronic tension-type headache and, perhaps, medication-induced headaches. The term chronic or transformed migraine is sometimes applied to these patients [55–58].

Managing the burden of migraine

Measuring the burden of migraine should be a prelude to effective treatment designed to reduce the burden of migraine. A number of long-term studies have examined the impact of migraine and benefits of treatment on workplace and non-workplace productivity [59]. Sumatriptan was demonstrated to reduce migraine-associated productivity loss during a minimum 8-hour work shift by approximately 50% compared with placebo, alleviating headache in more

than three-fourths of subjects in the work-place [60]. A prospective sequential multinational (5-country) study evaluated the effects of subcutaneous sumatriptan on HRQoL [61]. Scores on all questionnaire domains were significantly improved after 12 weeks (in all countries) and 24 weeks (in 4 of 5 countries) of sumatriptan therapy compared with 12 weeks of customary therapy. Rizatriptan was also more efficacious than placebo in improve the functional disability [62]. Similar studies performed with other triptans also highlighted that acute treatment improves HRQoL, though benefits develop over months.

Figure 3 provides a schematic view of how the MIDAS questionnaire may be used to provide appropriate treatment, based on the patient's level of headache-related disability, in accordance to the US Headache Consortium Guidelines [53]. Simple analgesics are appropriate for first-line acute treatments for these patients for low MIDAS scores (MIDAS grades I or II). If simple analgesics are unsuccessful, various combination treatments (e.g. aspirin plus metoclopramide) may be needed. If these treatments fail, further escalation may be necessary. A MIDAS score of 11 or over (MIDAS grades III or IV) indicates high medical need. Specific acute therapies, such as the 5-HT_{1B/1D} receptor agonists, may be needed

by these patients, together with prophylaxis when necessary. Of course, any specific sequence of treatment recommendations requires empirical testing.

Conclusions

Using the IHS criteria, large population-based epidemiological studies from most regions of the world have shed light on the descriptive epidemiology and burden of headache. While migraine is a remarkably common cause of temporary disability, many migraineurs, even those with disabling headache, have never consulted a physician for the problem. Prevalence is highest in women, in persons between the ages of 25 and 55 years, and, at least in the United States, in individuals from low-income households. Nonetheless, prevalence is high in groups other than these high-risk groups. Migraine prevalence may be increasing in the United States, but this has not been proven. Longitudinal studies are required to better determine the incidence and natural history of migraine as well as the life course of comorbid conditions.

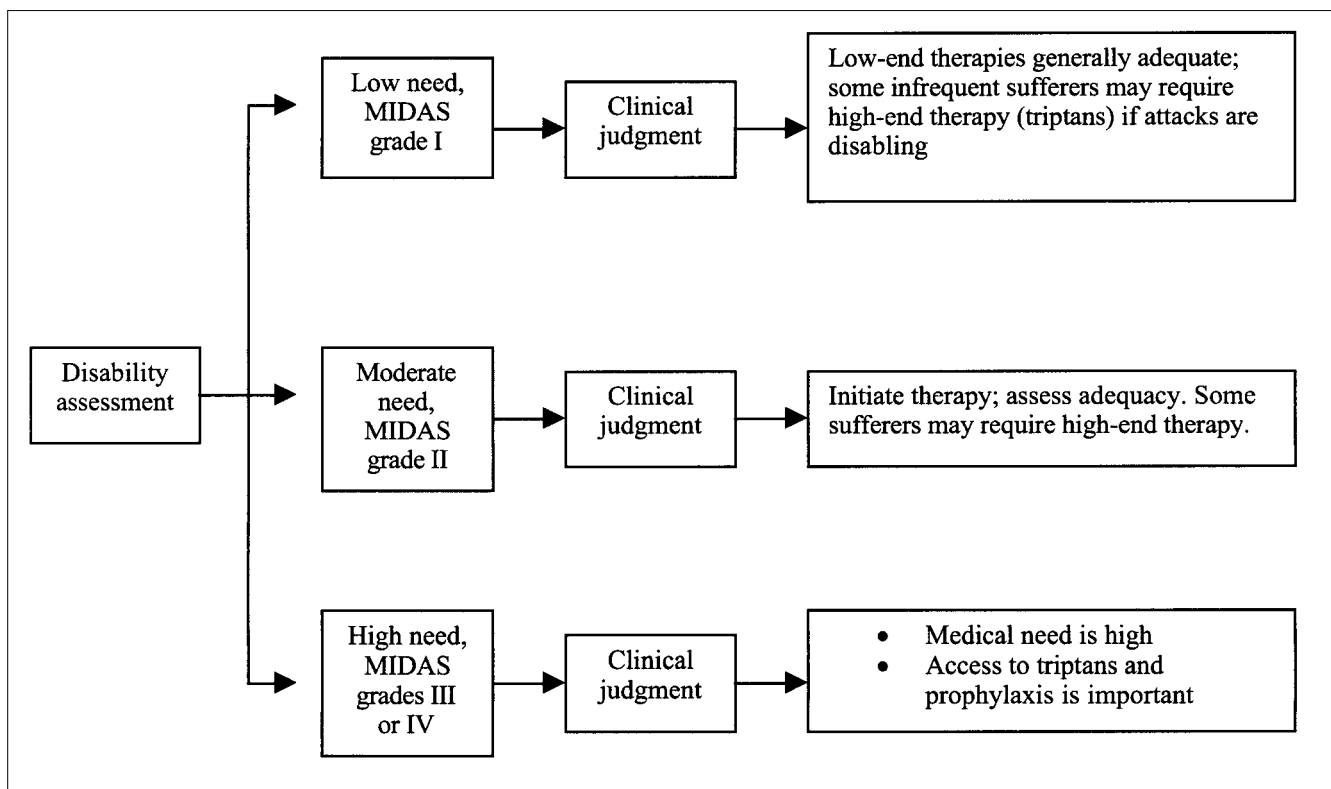


Fig. 3 The disability-based approach to the management of migraine (according to [53])

References

- Raskin NH (1998) *Headache*, 2nd edn. Churchill-Livingstone, New York
- Waters WE (1986) *Headache*. PSG, Littleton (Series in clinical epidemiology)
- Scher AI, Stewart WF, Lipton RB (1999) Migraine and headache: a meta-analytic approach. In: Crombie IK (ed) *Epidemiology of pain*. IASP, Seattle, pp 159–170
- Rasmussen BK (1995) Epidemiology of headache. *Cephalalgia* 15:45–68
- Lipton RB, Amati JC, Ferrari MD et al (1994) Migraine: identifying and removing barriers to care. *Neurology* 44[Suppl 6]:56–62
- Lipton RB, Silberstein SD (1994) Why study the comorbidity of migraine. *Neurology* 44(7):4–5
- Lipton RB, Diamond S, Reed M, Diamond ML, Stewart WF (2001) Migraine diagnosis and treatment: results from the American Migraine Study II. *Headache* 41:638–645
- Stang PE, Osterhaus JT, Celentano DD (1994) Migraine: patterns of health care use. *Neurology* 44[Suppl 4]:47–55
- (1988) Classification and diagnostic criteria for headache disorders, cranial neuralgias, and facial pain. *Headache Classification Committee of the International Headache Society*. *Cephalalgia* 8[Suppl 7]:1–96
- Rasmussen BK, Jensen R, Schroll M, Olesen J (1991) Epidemiology of headache in a general population - a prevalence study. *J Clin Epidemiol* 44:1147–1157
- Stewart WF, Lipton RB, Celentano DD, Reed ML (1992) Prevalence of migraine headache in the United States. *JAMA* 267:64–69
- Henry P, Michel P, Brochet B et al (1992) A nationwide survey of migraine in France: prevalence and clinical features in adults. *Cephalalgia* 12:229–237
- Gobels H, Petersen-Braun M, Soyka D (1994) The epidemiology of headache in Germany: a nationwide survey of a representative sample on the basis of the headache classification of the International Headache Society. *Cephalalgia* 14:97–106
- Launer LJ, Terwindt GM, Ferrari MD (1999) The prevalence and characteristics of migraine in a population-based cohort: the GEM Study. *Neurology* 53:537–542
- Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M (2001) Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache* 41:646–657
- Featherstone HJ (1985) Migraine and muscle contraction headaches: a continuum. *Headache* 24:194–198
- Waters WE (1972) Headache and migraine in general practitioners, the Migraine Headache and Dixarit. Proceedings of a symposium held at Churchill College. Boehringer Ingelheim Brachnell, Cambridge
- Stewart WF, Linet MS, Celentano DD, Van Natta M, Ziegler D (1993) Age and sex-specific incidence rates of migraine with and without visual aura. *Am J Epidemiol* 138:1111–1120
- Stang PE, Yanagihara T, Swanson JW et al (1992) Incidence of migraine headaches: a population-based study in Olmstead County, Minnesota. *Neurology* 42:1657–1662
- Lipton RB, Stewart WF, Celentano DD, Reed ML (1992) Undiagnosed migraine: a comparison of symptom-based and self-reported physician diagnosis. *Arch Int Med* 152:1273–1278
- Lipton RB, Hamelsky SW, Stewart WF (2001) Epidemiology and impact of headache. In: Silberstein SD, Lipton RB, Dalessio DJ (eds) *Wolff's headache and other head pain*, 7th edn. Oxford University, New York, pp 85–107
- Stewart WF, Simon D, Shechter A, Lipton RB (1995) Population variation in migraine prevalence: a meta-analysis. *J Clin Epidemiol* 48:269–280
- Rasmussen BK (2001) Epidemiology of headache. *Cephalalgia* 21(7):774–777
- Bille B (1962) Migraine in school children. *Acta Paediatr Scand* 51[Suppl 136]:1–151
- Bille B (1989) Migraine in children: prevalence, clinical features, and a 30-year follow-up. In: Ferrari MD, Lataste X (eds) *Migraine and other headaches*. Parthenon, New Jersey
- Sillanpaa M (1976) Prevalence of migraine and other headache in Finnish children starting school. *Headache* 15:288–290
- Sillanpaa M (1983) Prevalence of headache in prepuberty. *Headache* 23:10–14
- Sillanpaa M (1983) Changes in the prevalence of migraine and other headaches during the first seven school years. *Headache* 23:15–19
- Sillanpaa M, Piekkala P, Kero P (1991) Prevalence of headache at preschool age in an unselected child population. *Cephalalgia* 11:239–242
- Sillanpaa M (1994) Headache in children. In: Olesen J (ed) *Headache classification and epidemiology*. Raven, New York, pp 273–281
- Silberstein SD, Merriam GR (1997) Sex hormones and headache. In: Goadsby P, Silberstein SD (eds) *Blue books of practical neurology: headache*. Butterworth Heinemann, Boston, pp 143–176
- Waters WE (1971) Migraine: intelligence, social class, and familial prevalence. *Br Med J* 2:77–81
- Stang PE, Sternfeld B, Sidney S (1996) Migraine headache in a pre-paid health plan: ascertainment, demographics, physiological and behavioral factors. *Headache* 36:69–76
- Stang PE, Osterhaus JT (1993) Impact of migraine in the United States: Data from the National Health Interview Survey. *Headache* 33:29–35
- D'Alessandro R, Benassi G, Lenzi PL et al (1988) Epidemiology of headache in the Republic of San Marino. *J Neurol Neurosurg Psychiatry* 51:21–27
- (1991) Prevalence of chronic migraine headaches: United States, 1980–89. *MMWR* 40:331–338
- Lipton RB, Stewart WF, Simon D (1998) Medical consultation for migraine: results from the American Migraine Study. *Headache* 38:87–96
- Feinstein AR (1970) The pretherapeutic classification of comorbidity in chronic disease. *J Chronic Dis* 23:455–468
- Hu XH, Markson LE, Lipton RB, Stewart WF, Berger ML (1999) Burden of migraine in the United States: disability and economic costs. *Arch Intern Med* 159:813–818

40. Osterhaus JT, Gutterman DL, Plachetka JR (1992) Health care resources and lost labor costs of migraine headaches in the United States. *Pharmacoeconomics* 2:67–76
41. Holmes WF, MacGregor A, Dodick D (2001) Migraine-related disability: impact and implications for sufferers' lives and clinical issues. *Neurology* 56[Suppl 1]:S13–S19
42. – (1979) Vital and health statistics of the United States. Advance data. National Center for Health Statistics, Hyattsville (DHEW, PHS publication no. 53)
43. Celentano DD, Stewart WF, Lipton RB, Reed ML (1992) Medication use and disability among migraineurs: a national probability sample. *Headache* 32:223–228
44. Fry J (1996) Profiles of disease. Livingstone, Edinburgh
45. Edmeads J, Findlay H, Tugwell P et al (1993) Impact of migraine and tension-type headache on life-style, consulting behavior, and medication use: a Canadian population survey. *Can J Neurol Sci* 20:131–137
46. Stewart WF, Lipton RB, Simon D (1996) Work-related disability: results from the American Migraine study. *Cephalalgia* 16:231–238
47. Michel P, Dartigues JF, Lindousli A, Henry P (1997) Loss of productivity and quality of life in migraine sufferers among French workers: results from the GAZEL cohort. *Headache* 37:71–78
48. Von-Korff M, Stewart WF, Simon DJ, Lipton RB (1998) Migraine and reduced work performance: a population-based diary study. *Neurology* 50:1741–1745
49. Hu XH, Markson LE, Lipton RB et al (1999) Burden of migraine in the United States: disability and economic costs. *Arch Intern Med* 159:813–818
50. Stewart WF, Lipton RB, Kolodner K, Liberman J, Sawyer J (1999) Reliability of the migraine disability assessment score in a population-based sample of headache sufferers. *Cephalalgia* 19:107–113
51. Stewart WF, Lipton RB, Kolodner K, Sawyer J, Lee C, Liberman JN (2000) Validity of the Migraine Disability Assessment (MIDAS) score in comparison to a diary-based measure in a population sample of migraine sufferers. *Pain* 88:41–52
52. Stewart WF, Lipton RB (2002) Need for care and perceptions of MIDAS among headache sufferers study. *CNS Drugs* 16[Suppl 1]:5–11
53. Matchar DB, Young WB, Rosenerg J et al (2000) Multispecialty consensus on diagnosis and treatment of headache: pharmacological management of acute attacks. www.aan.com/public/practiceguidelines/03.pdf
54. Lipton RB, Stewart WF, Stone AM et al (2000) Stratified care vs step care strategies for migraine: results of the Disability in Strategies of Care (DISC) Study. *JAMA* 284:2599–605
55. Mathew NT, Stubits E, Nigam MP (1982) Transformation of episodic migraine into daily headache: analysis of factors. *Headache* 22:66–68
56. Mathew NT, Reuveni U, Perez F (1987) Transformed or evolutive migraine. *Headache* 27:102–106
57. Silberstein SD, Lipton RB, Solomon S, Mathew NT (1994) Classification of daily and near daily headaches. Proposed revisions to the IHS criteria. *Headache* 34:1–7
58. Silberstein SD, Silberstein JR (1992) Chronic daily headache: long-term prognosis following inpatient treatment with repetitive IV DHE. *Headache* 32:439–445
59. Lipton RB, Stewart WF, von Korff M (1997) Burden of migraine: societal costs and therapeutic opportunities. *Neurology* 48[Suppl 3]:4–9
60. Cady RC, Ryan R, Jhingran P, O'Quinn S, Pait DG (1998) Sumatriptan injection reduces productivity loss during a migraine attack: results of a double-blind, placebo-controlled trial. *Arch Intern Med* 158:1013–1018
61. Dahlof C, Bouchard J, Cortelli P, Heywood J, Jansen JP, Pham S, Hirsch J, Adams J, Miller DW (1997) A multinational investigation of the impact of subcutaneous sumatriptan. II: Health-related quality of life. *Pharmacoeconomics* 11[Suppl 1]:24–34
62. Santanello NC, Polis AB, Hartmaier SL, Kramer MS, Block GA, Silberstein SD (1997) Improvement in migraine-specific quality of life in a clinical trial of rizatriptan. *Cephalalgia* 17:867–872