



# INFORMATION FOR HEALTH CARE PROFESSIONALS



## Is Migraine a Progressive Disorder?

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### **The Prognosis of Migraine**

From epidemiologic studies, we know that migraine is most prevalent in mid-life, with lower prevalence in later life and childhood. While migraine is more prevalent in women than men in adulthood – including in later life – the prevalence in boys and girls is roughly similar. The reasons for these well-known demographic patterns are not fully understood. These studies provide a snapshot of migraine at a population level at a particular point in time, which is not the same as studying the course of migraine at an individual level. For example, at a population level, migraine could be less prevalent in older adults because migraine tends to improve with age (the more likely explanation) or because people with migraine have substantially higher mortality rates compared to others (the less likely explanation).

Understanding the natural course of migraine, including which individuals tend to improve and which tend to worsen, is an area of active research. Longitudinal studies in which individuals are followed over time provide better evidence than cross-sectional studies. The natural history of headache attack frequency by itself is incompletely understood and appears to be highly variable over time within individuals – at least for those in the general population. Understanding how to conceptualize and model migraine attack frequency within individuals is critical information that will lead to better observational and interventional studies. In the meantime, the accepted definition of “chronic” vs “episodic” headache - based in part on the arbitrary cut-point of 15 headache days per month - we now know is an oversimplification and that a more nuanced and empirically derived conceptualization of chronic or episodic headache is needed.

### **Defining Migraine Progression or Transformation**

Conceptually, four non-exclusive patterns for the long-term prognosis of migraine have been suggested based on population and clinical studies. Some migraine sufferers become symptom-free for prolonged periods of time (Clinical Remission). Others continue to have headaches with fewer or less typical migraine features, resembling tension-type headaches, rather than full-blown migraine (Partial Clinical Remission). Migraine attacks may continue over many years without major changes in frequency, severity or symptom profile (Persistence). Finally, in some, migraine attack frequency and disability may increase over time (Migraine Progression).

Progression or transformation should be understood as the potential for evolution to a different form. Migraine does not inexorably progress like the neurodegenerative diseases. Furthermore, chronic migraine (CM) may also remit to an episodic form.

Progression or transformation of migraine is subdivided in three potentially overlapping forms. Typically, transformation refers to increases in attack frequency over time leading to CM; this process, termed clinical transformation, occurs in about 3% of episodic migraine sufferers in the population over the course of a year based on the 15 headache day per month cut-point.

A less discussed issue is the physiological transformation of migraine, manifested through alterations in nociceptive thresholds (allodynia) and alterations in pain pathways (e.g., central sensitization). Allodynia refers to normally non-painful stimuli being perceived as painful. This state often develops after having migraine attacks for many years. Patients with allodynia during a migraine attack complain about not being able to comb their hair or to have a ponytail, shave or take a warm shower, etc. Allodynia, per se, seems to be a risk factor for clinical transformation.

Finally, in some individuals, definitive brain lesions including stroke and deep white matter lesions emerge; this process of anatomic transformation, particularly stroke, is sometimes considered a complication of migraine and is rare.

### **Risk Factors for Migraine Frequency Progression**

With the above caveats about chronic migraine / episodic migraine case definitions, a number of observational studies have identified risk factors that are associated with headache frequency progression to CM as presently defined. Some observed risk factors are non-modifiable (e.g. age, female sex, white race, low educational level, socioeconomic status and genetic factors) and some are potentially modifiable. Addressing modifiable factors may, at least theoretically, decrease the rate of migraine progression and increase the rate of remission. The potentially modifiable risk factors below are divided into incidence risk factors (e.g. associated with increased risk of chronic migraine or headache in those with episodic migraine or headache) and prognostic risk factors (e.g. associated with increased or decreased likelihood of remission in those with chronic headache or migraine. See the recent reviews by Schwedt 2014 and Probyn 2017 for more details of the evidence behind these observed risk factors.

Incidence risk factors include:

- Obesity
- Snoring / sleep disorders
- Psychiatric disease
- High baseline headache frequency
- Overuse of migraine abortive drugs, high caffeine intake
- Major life changes
- Head or neck injury
- Cutaneous allodynia
- Comorbid pain disorders

Prognostic factors include:

- Depression (negative)
- Anxiety (negative)
- Poor sleep and stress (negative)
- Overuse of migraine abortive drugs (negative)
- Comorbid pain disorders (negative)
- Poor-self-efficacy for managing headaches (negative)
- Ineffective acute treatment (negative)
- Lower baseline headache frequency (positive)

- Absence of cutaneous allodynia (positive)
- Withdrawal of overused abortive drugs (positive)
- Physical exercise (positive)
- Adherence to migraine prophylactic drugs (positive)

### **Medication overuse**

The role of excessive use of acute pain medication as a risk factor for headache frequency progression (e.g. medication overuse headache) is a controversial topic that has implications for prevention and treatment of chronic migraine. The International Classification of Headache Disorders (ICHD), as well as observational studies, have identified medication overuse as an important or primary risk factor for the development of chronic migraine. A common recommendation is to limit use of acute pain medications to below a specific limit (e.g. 15 days per month for simple analgesics including NSAIDs and 10 days per month for combination analgesics, triptans, opioids, ergotamine) in order to prevent headache frequency progression.

It is important to note however that this recommendation is based on expert consensus rather than formal evidence and there is no published evidence at this time that these treatment limitations are effective in terms of preventing chronic migraine. Further, medication withdrawal studies have largely been uncontrolled and many have high dropout rates.

### **Conclusion and recommendations**

While we await clinical trials regarding the benefits of intervention in the prevention of CM, several are justifiable based on their other established benefits including efforts to decrease headache frequency, monitoring body mass index, and encouraging maintenance of normal body weight. Avoiding excessive use of acute treatments for migraine is desirable apart from its theoretical benefit in preventing progression, although the harm associated with pain under-treatment should also be considered. Sleep problems should be investigated and treated. Psychiatric comorbidities should be identified and addressed. For these interventions, the possibility of preventing progression may motivate clinicians to offer good care and patients to engage in the treatment plan.

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