



Migraine in the EU: Bringing women out of the shadows

EMHA European
Migraine &
Headache
Alliance

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European Migraine & Headache Alliance

The European Migraine & Headache Alliance (EMHA) is a non-profit umbrella organization, with over 30 patient associations for migraine, cluster headache, trigeminal neuralgia and other headache diseases, across Europe.

The Alliance was launched in 2006 and advocates for the rights and needs of the 138 million people living with headache disorders in Europe. Its goal is to represent European migraine and headache associations, help them advocate for headache disorders and be recognised as key partners in the healthcare system. It also helps patients to be well informed and have equal access to appropriate diagnosis and treatment.

EMHA is an active member of the European Federation of Neurological Associations (EFNA), the International Association of Patient Organizations (IAPO) and the European Patients Forum (EPF). It also works closely with organisations such as the European Headache Federation (EHF) and the European Brain Council (EBC).



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Executive Summary

Migraine is more than a bad headache. It is a common, yet invisible, neurological disease that affects 41 million people in Europe. It is the second leading cause of disability in the world and the first among young women. The disease is most troublesome during people's most productive years (late teens to 50s) and costs the European economies as much as € 50 billion a year. The indirect costs associated with reduced productivity represent a substantial proportion of the migraine costs. Regrettably, the COVID pandemic has inflicted an additional toll on people with migraine.

Migraine is under-diagnosed and under-treated due to lack of awareness and stigma, clinical and social barriers, poor access to treatment. The lack of knowledge about headaches among healthcare providers is the principal clinical barrier. The substantial burden of migraine on society is not recognised by governments that seek to constrain healthcare costs. All this generates a number of hurdles to overcome.

Migraine is a public health challenge that overwhelmingly affects women: it is three times more common in women. Its manifestations differ between men and women and are influenced by sex-specific factors. A better understanding of both biological and gender aspects related to migraine development and management is thus highly needed to provide personalised medical and social approaches. Involving patients in research design and research projects, and looking at sex and gender in basic science and research hold the keys for personalised medicine.

This Policy Paper looks at 5 important aspects of women and migraine that can instruct future policy makers' decisions: disease prevalence, sex-specific factors, the impact of migraine on women's work-life and personal life, and gendered stigma. The paper ends with policy recommendations seeking to increase the visibility of migraine and raise awareness to improve the quality of life of people with migraine, secure funding streams to counteract the disease (education, brain and gender research), gather intelligence to inform policy making and develop migraine policies. Gender mainstreaming in all policies is more than relevant when it comes to women and neurological diseases.

Migraine is a societal and public health challenge that significantly compromises the quality of life of the individuals and their family. Therefore, policy makers have the power to:

- recognise migraine as a disabling neurological disease and a legitimate condition and break the stigma associated with the disease
- fund training for professionals to fill the medical education gap and improve diagnosis
- remove the barriers to treatment and delivery of services to improve diagnosis and the quality of life of people with migraine
- recognise the gender bias and disproportionate impact of migraine on women
- implement a unified strategy to leave nobody behind during public health emergencies.

Time to act is now!

Migraine: A public health challenge that overwhelmingly affects women

Migraine is a major public health challenge. It remains largely ignored at EU and national level, despite the associated disability and financial burden on individuals and society as well as the poor quality of life of patients and their families. In 2020, the European Migraine and Headache Alliance (EMHA) issued a 'Call To Action' to make migraine a European and national health priority (Appendix).

Migraine is a common, yet invisible, neurological disease that impacts 1 in 7 people across the globe. There are 41 million people in Europe living with migraine and it is three times more common in women.¹ It is the second leading cause of disability in the world and the first among young women.² Despite its widespread and debilitating nature, migraine is still misunderstood, ignored, and stigmatised.

Migraine is most troublesome during people's productive years (late teens to 50s). It impacts career opportunities and work life. Its personal, financial and societal impact cannot be dismissed. Migraine costs the European economies as much as €50 billion a year. In 2011, the mean per-person annual costs were estimated to be €1,222 for migraine (93% being attributed to indirect costs).³ Indirect costs associated with reduced productivity represent a substantial proportion of the total cost of migraine. The cost per patient/year from an observational, cross-sectional analysis of data from migraine patients in Spain in 2020 were €16,578.2 for chronic migraine and €6,227.8 for episodic migraine. A reduction of one migraine-day per month decreased average total costs by €744.14 per patient/year for episodic migraine and €663.20 per patient/year for chronic migraine. A reduction in the number of migraine-days by 50% would result in economic savings of €2,232.44 per patient/year for episodic migraine and €6,631.99 per patient/year for chronic migraine.⁴

People with migraine suffer in terms of career advancement and earnings. The Eurolight data collected in 2014⁵ show that 7.4% of people with migraine believed their careers were negatively influenced by the disease, while 5.9% felt having migraine reduced their lifetime earnings. In the 'My Migraine Voice'

Survey in 2019⁶, 13% of the participants changed their profession/career path because of migraine, 12% changed jobs, 11% lost their job and 7% were not hired. In the 'Beyond Migraine' Study⁷ performed in 2020, 50% of participants stated they have lost out in their careers (ranging from 49% for those suffering from episodic migraine and 56% for those affected by chronic migraine). Furthermore 63% of the responded declared they had hidden migraine from employees. Four in 5 young women stated that migraines had posed a challenge in their career.

Timely diagnosis and proper management of the disease can improve the quality of life of people affected by migraine and empower the healthcare systems to respond effectively. Targeted migraine resources and funding should allow for awareness campaigns, implementation of healthcare structures that offer timely and equal access to diagnosis and treatment, adaptation of the education system and workplace to create migraine-friendly environments and increase in research funding to better understand the causes of the disease and find specific treatments.

Regrettably, the current COVID pandemic has inflicted an additional toll on people with migraine.

This Policy Paper provides a clear insight into the challenges people with migraine, their families, the healthcare systems and economy at large have to overcome, with a focus on women. The paper calls on national and EU policy makers to embrace the challenges migraine inflict on individuals and society. It offers targeted recommendations for national and European policy makers to improve the quality of life of people with migraine and women in particular.

Migraine affects many Europeans' lives, but it is treatable and controllable if we just pay adequate attention. Migraine has to be taken seriously and more resources need to be dedicated to it. Apart from being a social and economic issue, migraine is very much an equality affair as well: migraine prevalence is three times more common in women and often occurs during women's most productive years. This is why EMHA's Policy Paper on Women and Migraine is important: we need to acknowledge conditions that affect women disproportionately and in the best case limit their impact in our societies.

**Sirpa Pietikäinen, MEP, Finland,
Member of the European Parliament
Alliance**

Migraine adversely affects 1 in 7 people across the world, with more than 41 million people in Europe living with this neurological condition. I welcome this policy paper focusing on Women and Migraine. Migraine is three times more common in women affecting them during their most productive years. It is vital we make Migraine a European health priority to improve awareness and education surrounding this debilitating condition.

**Deirdre Clune, MEP, Ireland
Member of the European
Parliament Migraine Alliance**

What is migraine?

Migraine is more than a bad headache

Migraine is a distinct, life-span and complex neurological disease. Migraine typical manifestation is a severe throbbing recurring pain, usually on one side of the head, but in about 1/3 of attacks, both sides are affected. Pain is associated to other disabling symptoms: nausea, vomiting, increased sensitivity to light and noise and, although less frequently, visual or sensory-motor disturbances.

Attacks usually last between 4 and 72 hours and more than 4 million adults experience chronic daily migraine – with at least 15 migraine days per month. Despite being a common disease, migraine is an invisible disease and still widely misunderstood.⁸

The WHO recently updated International Classification of Disease describes migraine as a 'primary headache disorder, in most cases episodic. Migraine attacks have a range of manifestations: they start with premonitory (prodromal) symptoms with cognitive

manifestations, yawning, food craving, passing urine..., moving on to canonical symptoms (pain, nausea, vomiting...) and ending-up in postdrome symptoms (tiredness, concentration problems...). Migraine's manifestations are repeated attacks: migraine can be episodic (< 15 days per month) or chronic (≥ 15 days/month), it has a family history and responds to a number of biological factors (sleep, food, hormones, sensory triggers (light, smells...), alcohol, stress...)⁹.

Women suffer longer attack duration than men and a higher recurrence rate. The difference in attack frequency between age groups is significant for women but not for men migraineurs. Migraine attack duration is also age-related: it is longer in women aged 30 and over. In general, the symptoms accompanying migraine (nausea, vomiting, phonophobia, photophobia) are more frequent among women.¹⁰

Migraine attacks triggers

Triggers are different from one person to another. A combination of environmental and genetic factors is likely to trigger migraine attacks. Identifying risk factors of migraine and maintaining a healthy lifestyle are key for managing migraine, starting from adolescence but it is usually not enough to control the disease.

Environmental triggers

- Situations causing anxiety, excitement, any form of tension and shock influenced by the environment (such as work, family life, bright sunlight, flickering lights)
- Air quality and odours
- Environmental aspects of indoor space and workplaces

Weather, high temperature and air pollution

- Possible association between higher relative humidity and onset of migraine headache, especially in warm season.
- Higher levels of ambient O₃ may be associated with higher risk of having migraine, particularly in the cold season.

Migraine and screens

- Use of a computer as a primary function of a job
- Time spent looking at a computer screen (especially if light is a trigger and/or if photophobia are prominent symptoms)

Air-conditioning

- Causes dehydration, muscles contraction
- Produces excessive noise.

Genetic factors

The complexity of migraine disorders is mirrored by their genetic complexity. Twin and family studies provide natural experiments investigating the genetic and environmental vulnerability to complex traits such as migraine.

Specific clinical features of common migraine seem to be determined by genetic factors. Recent studies have showed that the genetic load is higher in familial migraine cases than in nonfamilial cases, and higher for migraine with aura. A stronger family history of migraine is associated with lower age-at-onset, higher frequency and number of medication days and the migraine with aura subtype.¹¹ A child with

one parent with migraine has a 50% chance of inheriting it. If both parents have migraine, the chances rise to 75%. More than half of migraineurs have a close relative with the disease.¹²

Integration of genetic, phenotypic and epigenetic data will help to identify the biological mechanisms by which genetic factors contribute to migraine pathogenesis. It will show the impact of genetics on clinical features and comorbidities in migraine and may guide clinicians to an adequate genetic advice for patients.

I have had migraine since my earliest childhood, inherited from my mother AND father.
Maria, 46 years old, Vienna, Austria

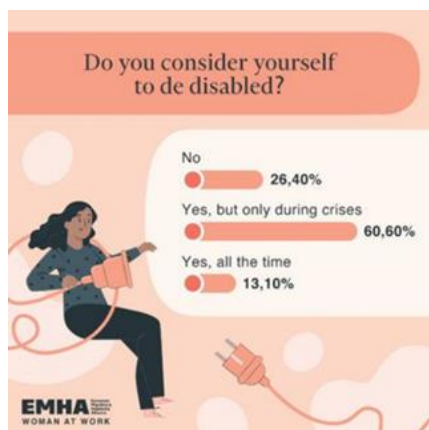
Migraine consequences

Disability, temporary incapacity

Migraine is a temporary disabling disease that generates temporary incapacity or activity limitation during the attacks. Activity limitation is recognised as a risk of poverty or social exclusion. In 2018, 28.7 % of the EU-28 population aged 16 or more and having an activity limitation was at risk of poverty compared with 19.2 % of those with no limitation.¹³

The Global Burden of Diseases Study 2019 shows that migraine on its own is the cause of 4.85% of all years of life lost to disability (YLDs): women are disproportionately affected (8.92%, 8.01% and 3.98%) for groups 10-14, 15-49 and 50-69, respectively.¹⁴

Given that young people and people of working age are disproportionately affected, this has significant implications on their education, work life and family life.



Source: EMHA's Survey 'Migraine at Work'¹⁵

Marginalised groups and migraine

The migraine burden tends to be the highest among people from economically marginalised communities and remains particularly underdiagnosed and undertreated in women in this population group.^{16,17}

Migraine and school

In a European study of women with migraine, nearly three quarters (74%) were prevented from functioning fully at work or school and nearly half of them (46%) lost working or school days in the past 6 months.¹⁸ Children who have migraine are absent from school twice as often as those who do not. Children's and teenagers' symptoms may be different from adults' symptoms but they can be equally disabling.

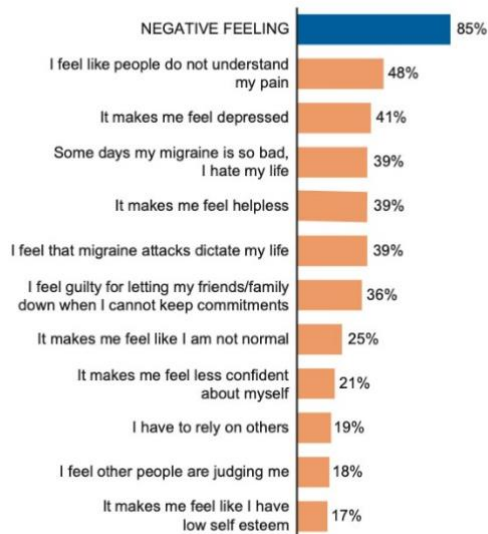
They may develop anticipatory anxiety and worry that an attack could disrupt their life at any time. Migraine keeps children and teenagers away from school and prevents them from participating in after-school and weekend activities.

The impact of migraine on mental health and well-being

The under-diagnosis and under-treatment of migraine generate a number of hurdles migraineurs have to overcome throughout their life. Migraine impacts the individual's quality of life and potential to be fully included in society. The extent to which migraine affects patients psychologically may not be fully appreciated either and needs to be further researched.

In the 'My Migraine Voice' Survey⁶, in which 75% of participants were women, overall 85% of the respondents reported at least one negative aspect of living with migraine, 48% mentioned the feeling of being misunderstood by people, 41% felt depressed, 39% had feelings related to hating their own life, 39% felt helpless and 39% felt migraine controlled and dictated their lives. In addition, 74% of respondents reported spending long periods of time in darkness and isolation, with an average of 19 hours per month. The impact of migraine on professional, private, or social domains was reported by 87% of respondents (70% professional life, 64%, 78% social activities).

Negative feeling associated with migraine



Living with migraine: a report from the My Migraine Voice survey⁶

Migraine and COVID-19

The COVID-19 pandemic has confronted migraineurs and healthcare systems with a huge challenge in managing chronic diseases.

The impact of the COVID-19 pandemic on patients

In a web-based survey carried in July 2019 among 1,018 patients (84% were females and 72% were in the 20-40 age bracket), close to 60% of the respondents reported an increase in migraine frequency and 10% transformation to chronic migraine. Severity increased in 64% of the respondents.¹⁹

Patients with migraine have been particularly vulnerable to inadequate medical care during the pandemic. In the same survey, the majority of respondents (61%) did not communicate with their neurologists, only close to 47% reported compliance to treatment and 59% reported overuse of analgesics. The cancellation of Onabotulinumtoxin A (Botox) injections had a negative impact on 66% of the respondents. Forty-one (4%) respondents were infected with COVID-19; 63% reported

worsening of their headaches during infection period.¹⁹

Aggravating factors

A number of factors that worsened the migraineurs' situation included sleep disturbance, symptoms of anxiety and/or depression, dietary habits, lack of communication with treating neurologist, non-compliance to treatment and working during the pandemic.¹⁹

The stress factor was illustrated with the Kaiser Family Foundation Coronavirus Poll conducted in March 2020. The poll found gender differences in how men and women were experiencing the pandemic. Women were more likely to worry about both the health and economic effects of the pandemic on their families.²⁰

WHO looked at the disruption of 25 essential health services during the pandemic. All services were affected, including essential services for non-communicable diseases,

mental health, child and adolescent health. Non-communicable disease diagnosis and treatment were among the most frequently disrupted services (in 69% of the countries).²¹

As the pandemic has led people to self-isolate and work from home, increased use of computers or phone screens cause eye strain and long exposure to screens can lead to migraine attacks.²²

Benefits of lockdown

Nevertheless, a study carried out in the Netherlands in 2020 showed that intelligent lockdown measures can positively impact migraine specific outcome measures and general well-being. A decrease in number of migraine days, acute medication days and an increase in general well-being during lockdown was reported. This can be due to a combined result of working from home, scaling down of demanding social lives and freedom to choose how to organise one's time. This can also be attributed to the possibility to bed rest during a migraine attack, possibly decreasing the risk of recurrence.²³

Migraine is under-diagnosed and under-treated due to lack of awareness and stigma

Despite being a common disease, migraine is an invisible disease and is still widely misunderstood, under-diagnosed and under-treated. Worldwide, about 50% of people with headache disorders are primarily self-treating, without guidance by health professionals. Only 10% are professionally diagnosed. This has major adverse health and economic consequences.²⁴

Thus, migraine patients frequently face a long and frustrating wait for an accurate diagnosis and/or effective treatment. Not only are the consequences emotional, they are also financial for individuals, healthcare systems and societies.

Women with migraine are more likely to take prescription medicine (acute treatment and preventive drugs) or a combination of prescription and over-the-counter medications to treat their attacks. They are also more likely

to use complementary and alternative medicine (acupuncture, homeopathy, massage, yoga).²⁵

Symptoms can vary at each stage of a person's life, especially in women where hormonal changes can influence attacks. Understanding the differences for each subtype of migraine and their associated comorbidities will help clinicians improve diagnosis and treatment: practitioners treating women with migraine need to have a clear understanding of these special considerations. This calls for awareness-raising about different brain disorders in women compared to men, a personalised approach to diagnosis and treatment, and increased brain research for women. Appropriate funding for high-quality migraine care and services must be allocated to fully complement the management of migraine.

Three major barriers to diagnosis can be identified: clinical barriers, access to treatment and social barriers.

Clinical barriers

The lack of knowledge about headaches among healthcare providers is the principal clinical barrier. The reason can be attributed to the medical curriculum that dedicates only 4 hours to headache disorders in formal undergraduate medical training and 10 hours in specialist training.²⁶ Globally, health professionals diagnose migraine and tension-type headache in only about 40% of people with these disorders, and medication-overuse headache in 10% of cases.²⁴ Primary-care practitioners do not have sufficient time and preparation to manage adequately migraineurs and specialised centres have long waiting lists.

Adapted healthcare systems could greatly reduce the persisting burden of migraine. Their approach to migraine treatment and care is unsuited to the needs. This is mainly due to a lack of understanding about the condition and an education failure, at every level, as well as in limited accessibility to appropriate care. Greater familiarity with migraine of all healthcare professionals may help to make appropriate care accessible to all people with migraine and a stronger collaboration with specialists, especially for the more difficult migraine cases.

Access to treatment

The substantial burden of headache on society is not recognised by many governments that seek to constrain health-care costs. They may not recognize that the direct costs of treating headache are small in comparison with the huge indirect-cost savings that might be made (e.g. by reducing lost working days) if resources were allocated to treat headache disorders appropriately.²⁴

As evidenced in a study²⁷ carried out in 2015/2016 in 12 headache centres in 7 countries (Brazil, Italy, Moldova, Mexico, Argentina, Chile and Uruguay, and where

78.6% of participants were females), poor patient awareness about migraine leads to underdiagnosis and undertreatment: 28% of participants were aware that they suffered from migraine and 64% called their migraine 'headache'. Only 8% of general practitioners and 35% of specialists (of whom 51% were neurologists and/or headache specialists) gave the correct diagnosis.

The low consultation rates in developed countries may also indicate that many people with headache disorders are unaware that effective treatments exist.²⁴ They also testify to the stigma and society's attitudes toward migraine: stigma toward migraine and its impact on medical care and internalized stigma among those with migraine and its detrimental effect on quality of life and patient-physician relationships.²⁸

Reimbursement of a medical treatment is key for many people to have access to and benefit from medical treatments. Lack of access to approved drugs is a barrier to best management of migraine in countries of all income categories. Diagnosis can be delayed when the appropriate treatment cannot be offered to the patients. If effective drugs are available and affordable, then diagnosis is likely to improve.²⁴

EMHA will present the results of an on-going European survey on 'Patients' Access to Care' that will give a picture of the barriers that prevents the migraineurs from receiving adapted treatment.

Treatment for migraine in women may need a different approach as hormonal influences are implicated, leading to more prolonged and severe attacks during menstruation, but also because women may respond differently to both acute and preventive treatment, as was recently shown in a meta-analysis for triptans. This meta-analysis showed sex differences in adverse event frequency (higher in women), which may be partly because of drug exposure differences (higher drug exposure in women). This higher drug exposure in women is not reflected in different response rates. Despite higher

exposure, women have higher headache recurrence rates possibly because of longer attack duration related to sex hormonal changes.²⁹

Social barriers

Poor patient awareness about headaches also extends to the general public. Headache disorders are not perceived as serious since they are mostly episodic, do not cause death and are not contagious. Stigma and misconceptions of migraine are important social barriers that affect people's coping and help-seeking behaviour.

The association of neurological disorders and stigma is a hurdle to overcome for those affected. The development of stigma may be related to the invisible nature of pain and the false perception of migraine as an indicator of female weakness. It is a disease where pain is not observable and can be hard for others to understand.

Migraine treatment goals and treatment

The one common denominator that people with migraine can attest to is the pain and associated symptoms that accompany an attack and their pursuit of migraine attack freedom.^{31,32} Migraineurs want migraine treatments to act fast to relieve the symptoms, reduce disability or incapacity and avoid headache recurrence. This makes it important to match the treatment to the level of disability to gain the best possible relief and prompt return to function.

- **Treatment goals for acute migraine:** clinicians, patients, and regulators all strive for complete freedom from pain in the acute treatment of migraine attacks. People with migraine want rapid, sustained and complete alleviation of their migraine pain. Achieving these patient goals predicts favourable quality of life and facilitates patients' return to normal functioning following a migraine attack.³³

Stigma can also be more prevalent in patients with certain socio-demographic characteristics: unemployed, divorced, and those suffering from migraine with aura also present higher levels of stigma.³⁰

People with a disease cannot be discriminated from others who are disease-free, be it in their private, social or professional life. This is a basic human right recognised by various organisations (Universal Declaration of Human Rights, UN Convention on the Rights of Persons with Disabilities, Charter of Fundamental Rights of the European Union), or local legislations like The Equality Act 2010 in the UK, which promotes equality and prevents unlawful discrimination against specific groups (one of which is those who are disabled) in England, Scotland and Wales, as an example.

- **Treatment goals for preventive treatments:** people who experience several migraine days within any given month also want to reduce the frequency of the attacks. Preventive treatment goals should provide patients with a chance of total migraine headache freedom each month, while decreasing patients' migraine burden and improving their overall quality of life.³⁴

The goals of migraine prevention³⁵ are to:

- reduce attack frequency, severity, duration, and disability
- improve responsiveness to and avoid escalation in use of acute treatment
- improve function and reduce disability
- reduce reliance on poorly tolerated, ineffective, or unwanted acute treatments
- reduce overall cost associated with migraine treatment
- enable patients to manage their own disease to enhance a sense of personal control improve health-related quality of life
- reduce headache-related distress and psychological symptoms.

There are different sorts of medical treatments to treat migraine:

- Medical acute treatments (analgesics and anti-emetics, triptans and non-steroidal anti-inflammatory drugs (NSAIDs))
- Preventive medicines (angiotensin receptor blockers/ACE inhibitors, beta-blockers, calcium channel blockers, CGRP monoclonal antibodies, neuromodulation, tricyclic antidepressants)
- Botox as a treatment option for adults with chronic migraine
- Non-medical treatment that can help relieve migraine attacks (sleep, acupuncture, relaxation and access to quiet and dark rooms...).

Why focus on women and migraine?

A large share of women are still in the front line for childcare and household chores. Due to the higher prevalence of migraine in women, addressing the issues that impact women will undoubtedly benefit a great part of the migraine population. A better understanding of both biological (sex) as well as socio-cultural (gender) aspects related to migraine development and management is highly needed to provide tailored approaches that can benefit women.

Important aspects of women and migraine can instruct future decisions by policy makers:

1. Disease prevalence
2. Sex-specific factors
3. Impact on work-life
4. Impact on personal life
5. Gendered stigma

Disease prevalence: migraine is more prevalent and severe in women

Migraine and it is three times more common in women.¹ The Global Burden of Diseases Study 2019¹⁴ shows that migraine is highly prevalent worldwide: 12.73%, 20.37% and 15.67% for both sexes in age groups 10-14, 15-49 and 50-69, respectively. Women are disproportionately affected (15.54%, 25.55% and 18.98%) for the same age groups.

Women report a longer attack duration, increased risk of headache recurrence, greater disability, and require a longer period of time to recover.³⁶

Before puberty, more boys than girls suffer from migraine. The mean age of onset is 11 for girls and 23% of young girls will have experienced a migraine by the time they turn 17³⁷. With puberty, the incidence increases more rapidly in girls than in boys. By the time they turn 17, as many as 8% of boys and 23% of girls have experienced a migraine.³⁸ After puberty, migraine in women

increases until age 40 or so, when it starts to decrease. This suggests a clear involvement of sexual hormones in the development of the disease in women.

The prognosis for children with migraine is variable. However, 60% migraineurs who had adolescent-onset migraine report on-going

migraines after age 30. The prognosis for boys tends to be better than for girls.³⁹

Women have an overall tougher migraine journey: they report longer attack duration, increased risk of headache recurrence, greater disability and longer period of time to recover. Headache disorders ranked 5 as a cause for DALYs.¹⁴

Area	Age	Prevalence		DALYs	
		Women	Men	Women	Men
Western Europe	10-14	19.80	18.03	9.29	6.29
	15-49	36.93	22.44	8.38	4.38
	50-69	24.02	14.89	2.95	1.17
Eastern Europe	10-14	14.27	8.67	7.21	3.95
	15-49	26.47	13.94	5.25	1.48
	50-69	21.23	11.95	2.12	0.64
Central Europe	10-14	14.83	7.97	9.02	4.60
	15-49	26.43	6.50	13.77	2.72
	50-69	20.27	2.02	10.92	0.70

Migraine: prevalence and DALYs by sex in Western, Eastern and Central Europe

The Global Burden of Diseases Study (2019)¹⁴

(Western Europe includes Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Malta, the Netherlands, Portugal, Spain, Sweden, United Kingdom and Central Europe includes Bulgaria, Croatia, Czech Republic, Hungary, Poland, Romania, Slovakia, Slovenia; Eastern Europe includes Estonia, Latvia and Lithuania)

Since my first attack when I was 12, I have lost 104 days/year due to the recurrence of my migraine attacks. This amounts to 4,888 days during my 47 years of life with migraine. I am now 59 and I have lost 13.4 years of my life (an eternity to me) due to migraine. In fact, I have actually lived 45.6 years.

Elena Ruiz de la Torre, EMHA Executive Director

Sex-specific risk factors: the impact of female sex hormones on migraine

The higher prevalence and incidence of migraine among women, and the increased risk during specific periods of a woman's reproductive life characterised by hormonal changes, clearly indicate the existence of specific, hormone-related risk factors for women to migraine.

A lot of data exists on the role of female sex hormones as a major factor in determining migraine risk and characteristics. Migraine in women fluctuates with both monthly and life-stage dependent natural hormonal changes^{40-41,42} The onset of migraine increases at menarche, peaks in prevalence in the late 30s, and rapidly declines after menopause.

Fewer than 10% of women develop a specific type of migraine during their cycle, called

menstrual migraine. It most likely occurs in the two days leading up to a period and the first three days of a period. The two most accepted theories on the cause for menstrual migraine at the moment are the withdrawal of oestrogen as part of the normal menstrual cycle and the normal release of prostaglandin during the first 48 hours of menstruation.⁴³

While migraine develops in women in their teens or twenties, 8–13% of women report the new onset of migraine during perimenopause.⁴⁴ Migraine is significantly affected by fluctuating sex hormone levels in women during menses and across the menopause transitions. While migraine generally tends to improve post-menopause, perimenopause can be associated with significant worsening in frequency and symptoms presumably due to fluctuating estrogen levels.⁴⁵ Many women's migraine attacks improve in pregnancy, especially after the first three months.

One of the most recurrent attacks trigger for me are the hormones before and during the menstruation. At younger age, this was not as remarkable as recently – in my early 30s.

**Tereza, 31 years old, employed,
Czech Republic.**

Hormonal fluctuations associated with the menstrual cycle represent a potential trigger factor for migraine and continuous use of

Impact on work-life: women's work limitations due to migraine –a root of gender gap

67% of women are currently in employment in the EU.⁴⁹ A number of studies show that there is a causal link between poor quality work and stress, and that work-related stress can trigger migraine attacks. Managing work stress is potentially one way of improving the quality of life of people with migraine.

In the 'My Migraine Voice' survey⁵⁰ in which 75% of the participants were women, 52% of the respondents stated that they could not

hormonal contraceptives is considered as an option to reduce migraine frequency.⁴⁶ However, the use of contraceptives in an individual with migraine is controversial. It must however be noted that several studies show that ischaemic stroke in people with migraine is strongly associated with MA, young age, female sex, use of oral contraceptives and smoking habit.⁴⁷ Hence, a better management of migraine in women in relation to hormone fluctuations is highly needed.

Reproductive hormones are a key influence underlying sex differences and fluctuating susceptibility to attacks in women. Understanding where and how relevant hormones such as estrogen act on migraine targets will provide a foundation for improved management and therapy for hormone-related migraine.⁴⁸

For many years I only had migraines around my periods. These attacks were particularly severe, with intense pain, nausea and vomiting. During the two pregnancies, on the other hand, I had almost no problem with migraines at all. I tried numerous contraceptive methods in the hope that they might also improve the migraines, but unfortunately to no avail. The migraines got really bad around the menopause. Thanks to the new antibody therapy, I am now feeling better.

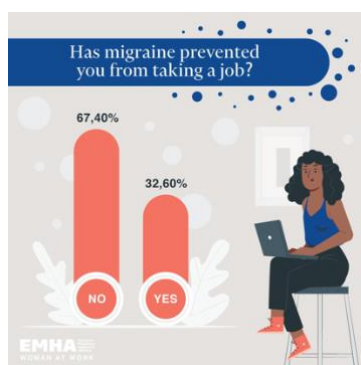
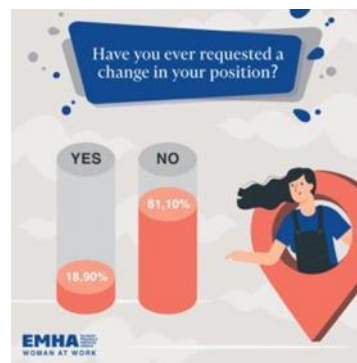
**Veronika Bäcker, 61 years, retired,
Germany**

concentrate due to their migraine, making it difficult to perform job tasks effectively. 70% indicated that migraine affected their professional life. The top 3 impacts of migraine on work reported were inability to concentrate on work (52%), missing too many days of work (32%), and lack of understanding among colleagues about their condition or not taking it seriously (27%). An average of 4.6 working days being missed a month was reported. Migraine led to a reduction of 13% in the respondents' working time (absenteeism) and 48% in productivity while working (presenteeism); 52% reported impairment in

both overall work productivity (absenteeism and presenteeism combined) and daily activities due to migraine.

light on how women have to juggle between migraine attacks and work

In 2018 EMHA organised a survey⁵¹ among migraine patients working in 7 EU countries (Ireland, Italy, France, Germany, Portugal, Spain and United Kingdom). The survey shed



In the EU, women are less present in the labour market than men. There is a clear gender employment gap with 67.3 % of women across the EU being employed compared to 79% of men. Women spend fewer hours in paid work than men on average but more hours in unpaid work (such as caring). The gender pay gap stands at 14.1% (meaning that women earn 14.1%

on average less per hour than men).⁵² Women also suffer pension gaps inter alia due to fewer years of work in their career and fewer work hours per year. Women are also more limited in their usual activities due to health problems.⁵³ Addressing the burden of migraine has the potential to unlock female resources and improve women’s quality of life overall.

Impact on personal life: family role and pregnancy

Beyond impact on career, migraine can significantly affect a woman’s family life. In all EU Member States, a large share of women are still in the front line for childcare, household chores. In 2016, 93 % of women aged 25 to 49

(with children under 18) took care of their children on a daily basis.⁵⁴

Migraine can condition women’s family choices. A recent study showed that almost 20% of women with migraine chose to avoid pregnancy because of their disease. The most commonly cited concerns for choosing to avoid having a child centred around worries that

migraine might worsen during or after pregnancy (72.5%), complicate pregnancy (68.3%), or make parenting difficult (82.6%). Furthermore, 76% of women were concerned that their inability to discontinue migraine medications could harm their baby's development, and 72.3% were apprehensive about passing on migraine to their child. This adds evidence to the correlation between migraine disease severity and the bearing it has on significant life decisions.⁵⁵

Women with migraine becoming pregnant fare differently. The majority of women suffering from migraine without aura report improvement of their migraine attacks during pregnancy. Migraine with aura attacks can also improve during pregnancy, but more often remain the same or worsen. An ovulation caused by lactation is generally associated with a decrease in migraine attacks in breastfeeding women.⁵⁶ There is also data that show that breastfeeding may be protective against developing more frequent and severe migraine attacks in the postpartum period.⁵⁷

In 2011, the results of a study on headache and migraine during pregnancy and puerperium confirmed previous studies findings: many women with earlier headache became headache free during pregnancy (in this study, this favourable course was even more than twice as common as developing new-onset headache); they experienced a gradual decrease of headaches in general during pregnancy and self-considered migraine towards birth; they suffered an increase in headache activity around birth and during the following 3 weeks. In the study, the number of doses of acute medication was lower in pregnancy, which is also consistent with other findings.⁵⁸

There is little information available about the use of medicines during pregnancy. Women and their physicians need comprehensive safety information to make informed decisions about medication use during pregnancy. The IMI-funded ConcePTION project aims to solve this problem by building a system where information from children, mothers and their

doctors will help develop reliable information about how safe a medicine is for women who are pregnant or breastfeed. This will be achieved by generating, cataloguing, linking, collecting and analysing data from pharmacovigilance, modelling, routine healthcare, breastmilk samples through a large network.⁵⁹

Migraine can have a ripple effect on children of parents with migraine and affect parent-child relationship. The 'Beyond Migraine' Study⁷ revealed that 61% of women felt the disease had had an impact on their children. A study that assessed how living with a parent who has migraine affects children showed that the perceived burden was greater for adolescents of parents with chronic migraine vs episodic migraine. This entailed loss of parental support and reverse caregiving, emotional experience, interference with school and missed activities and events. Rates of moderate-to-severe anxiety symptoms were higher among adolescents of parents with chronic migraine.⁶⁰

Gendered stigma

The development of stigma may be related to the false perception of migraine as a disease of women. It remains plagued by gendered images, metaphors, and stereotypes. Despite better understanding of migraine as a disease, it is still associated with personality characteristics often seen as 'feminine'. Doctors and society at large often associate migraine with 'feminine' characteristics like neuroticism and hysteria, which leads to migraines often being trivialised.

These gendered associations are also reinforced by a feminised concept of the disease by pharmaceutical advertising and marketing practices. The pharmaceutical industry directs its marketing of migraine medication to women, pharmaceutical advertisements portray women as the prototypical migraine sufferer. This creates the impression that migraine is a 'women's disorder', which, in turn, exacerbates gender bias in help seeking and diagnosis of migraine.⁶¹ These pharmaceutical marketing practices have a paradoxical effect: even as

they educate and raise awareness about migraine, they also create barriers to seeking help and diagnosis.

Migraine patients are portrayed as middle-class white women unfit to fulfil their task as mothers due to their pain, but the situation is quickly relieved by a pill.⁶² The stereotype of women using headache as an 'excuse' and being the topic of various jokes leads to women suffering from migraine not being taken seriously and thus being dismissed. When experiencing the invalidation and/or dismissal of the pain experienced, the person affected will internalise the stigma, thus impacting their

mental health, self-esteem and health-related behaviours (e.g. feeling ashamed to talk about their symptoms and seek help).

Increased awareness of gendered norms and potential gender bias is a prerequisite to counter gender bias in healthcare. To counteract gender bias in healthcare and to support healthcare professionals in providing more equitable care that meets women's needs, awareness about gendered norms is important, both in research and clinical practice.⁶³ Reframing of migraine to alleviate societal stigma is paramount. This involves use of unified language, education, and advocacy.

Why sex and gender matter in migraine

In health, it is important to make a distinction between sex (biological) and gender (behavioural and social) variables. Migraine affects women differently than men, both physiologically and socially. The biological differences between women and men, as well as socio-cultural norms, are key variables in the etiology, diagnosis, and management of migraine.

Both men and women can be suffering from migraine. Yet, as in many other disorders, their experiences are different. Understanding these differences can help improving research, care and treatment.

There are four aspects that make the study of sex and gender differences a key priority in the field of migraine, and neurology at large:

1. **Basic science and research:** sex differences, in particular the role of hormones, hold the key for novel and tailored treatments. Understanding why and how hormones interact with the brain to modulate the experience of pain and promote migraine might give new cues on the mechanism of the disease and help identifying new treatments. Yet, most basic research is performed in male mice.
2. **Precision medicine:** emerging science of migraine demonstrates that the disease is highly heterogeneous, and treatment requires a personalised approach. Each migraine attack may be different, and each individual responds differently; this is particularly true for men vs women. Nowadays patients are treated with a one size fits all approach which does not take into consideration specific needs of patients, for instance pregnant women.
3. **Reducing stigma:** feminisation of migraine leads to under-treatment. Addressing the specific needs of women with the disease, based on scientific facts, will help reducing such gendered stigma and increase awareness and access to care.
4. **Addressing the gender gap:** supporting and treating migraineurs must be a top priority in the EU due to the enormous costs of loss productivity. In this regard, as women are the vast majority of people living with migraine, supporting girls with migraine at school and women with migraine in the workplace will promote a positive change in their career choices and chances, thus helping to reduce the gender gap.

Another aspect of gender differences relates to pain and its gender stereotypes and gendered norms.⁶² At a psychosocial level, both stigma and gender are embedded in culture and include norms and expectations that affect our perceptions and behaviour. Through socialisation, girls and boys learn how to react to pain. Boys and men are taught to be tough, tolerate pain, and sustain painful experience.

This can be linked to consequences such as underdiagnosis. On the other hand, girls and

women are socialised to be sensitive, careful, and to verbalise discomfort. Women are also more likely to be viewed as being hysterical and fabricating pain. This can have consequences both for women's private family as well as for employment. Moreover, women face the stigma of complaining about 'just a headache' in case of migraine linked with the idea of using headaches as an excuse thus dismissing the seriousness of this pain.

Tackling migraine at EU level: policy recommendation

Migraine is a disease that comes with huge personal and societal challenges, with a particular burden on women. It contributes substantially to public ill-health. Given its high costs to the individual and society, greater awareness, education and investment in health directed at migraine are required to counteract the disease burden. A long-term and strategic portfolio of specific measures focussing on migraine and brain health is urgently needed overcome the disease burden on individuals and society. The gender aspect of the disease needs to be fully included in all initiatives.

Increase the visibility of migraine and raise awareness to improve the quality of life of people with migraine

- Fund awareness-raising campaigns on migraine targeted at the public, professionals and policy-makers to break stigma associated with the disease, empower patients and trigger policy action
- Raise awareness about the migraine gender bias and attitude regarding the disproportionate impact of migraine on women
- Adapt the workplace to avoid absenteeism and presentism by implementing migraine-friendly work environments
- Adapt the education system to give children with migraine an equal chance to education by implementing migraine-friendly schools

Secure funding streams to counteract the disease

- Fund innovative EU education and training projects and programmes to fill the medical education gaps
- Increase brain research funding to better understand the brain and brain diseases, develop new treatments and prevention measures
- Involve patients as experts in research design and participants in research projects
- Ensure migraine research addresses both sex (biological) and gender (societal) factors and supports personalised medicine

Gather intelligence to inform policy making

- Increase social research to better assess the impact of migraine on individuals and society
- Promote joint actions to share best practices and develop migraine policies

Develop migraine policies

- Recognize migraine as a disabling neurological disease and a legitimate condition
- Implement a unified strategy for migraine especially during public health emergencies
- Develop national migraine strategies that encompass diagnosis, prevention, access to treatment and care, research
- Remove all barriers to access to diagnosis, treatment (reimbursement) and improve the organisation and delivery of healthcare through long-term care pathways
- Promote the gender aspect of migraine to support gender mainstreaming in all EU and national policies

Looking ahead and implementing the policy recommendations

At EU level

EU4Health, the new EU health framework program, has given a clear signal by adding neurology to the list of EU non-communicable diseases (NCDs). This gives an impetus for increased visibility and priority to neurology and migraine in particular at EU level. The programme must contribute to raising awareness about migraine, its burden and challenges, promote early diagnosis, access to treatment, equal access to health services and combat stigma.

The Steering Group on Health Promotion and Disease Prevention is a relevant platform to gather policies and best practices between Member States that can trigger policy interventions in the prevention and management of neurological diseases, including migraine.

Setting-up a thematic network on migraine under the EU Health Policy Platform gives the opportunity to reach out to a wide range of like-minded stakeholders and drive the policy agenda.

The EU Disability strategy 2021-2030 and the EU Gender Equality Strategy can provide incentives to remove the many hurdles migraineurs have to overcome. Emphasis must be put on the education system (by developing an inclusive and high quality mainstream education system where pupils and students at risk of failure due to migraine are able to receive a continuous high-quality education)

and on the workplace (by implementing inclusive migraine-friendly environments). Gender mainstreaming in all policies is more than relevant when it comes to women and neurological diseases.

The EU Digital Education Action Plan 2021-2027 can support the development of high quality and inclusive education and training. For instance, online medical training can be developed to bridge the medical education gap in migraine and deliver continuous medical training for professionals to be kept abreast of medical developments.

One of the priorities under Health Cluster of Pillar 2 of Horizon Europe, the EU research programme, is to give priority to and reduce disease burden. Emphasis is being put on better understanding diseases, their drivers and consequences, better methodologies and diagnostics that allow timely and accurate diagnosis, identification of personalised treatment options. This is particularly relevant with migraine. A gender component must be added too. Patient engagement in EU and national funded research must be improved with active collaboration from patients in the governance, priority setting, conducting and knowledge translation of research.

The EU pharmaceutical strategy to incentivise investment in areas of unmet needs and cooperation on HTA to enable access to new treatments must support research in brain diseases such as migraine and develop new drugs that must quickly reach the patients.

The COVID pandemic has had a heavy toll on migraineurs too. In case of pandemics, individuals with migraine must be part of the public response to avoid long-term neurological and mental health consequences.

The implementation of the European Pillar of Social Rights and the European Semester offer other opportunities to raise awareness about migraine, respond to its challenges and its gender bias by implementing adapted and resilient care pathways, promoting migraine-friendly environments.

In the current economic and social context, the EU Recovery Plan can contribute to facilitating the full inclusion of migraineurs in society and give people with neurological diseases and women the opportunities to become more visible and participate fully in society.

At global level

At global level, the global momentum to deliver a more coordinated response to the challenges

and burden generated by neurological disorders has increased. ‘Mental health and neurological disorders’ were added to WHO’s list of priority NCDs in 2020. The same year, a ‘Global Actions on epilepsy and other neurological disorders’ Resolution was adopted and a 10-year Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders will be developed. The Plan will inter alia address gaps and need for research in prevention, early detection, care and treatment options to cure neurological disorders. The Plan will also address the social, economic, educational and inclusion needs of persons and families living with neurological disorders.

The UN Sustainable Development Goals, a blueprint to achieve a better and more sustainable future for all, resonate with the migraine community as they pave the way for a better quality of life.



Appendix

EMHA's Call To Action presented in September 2020 embeds policy recommendations to make migraine a EU and national health priority. This Call will guide EMHA and its members' policy advocacy work over the coming years.

Call to Action for a comprehensive EU action on migraine

EUROPEAN COMMISSION

- Make migraine a EU health, social and research priority.
- Ensure neurological disorders like migraine receive due attention in the Commission's current and future work (gender equality, demographic change, pharmaceutical strategy, disability, education, social affairs)
- Include a 'Brain Mission' In Horizon Europe that also looks at migraine
- Dedicate a significant and long-term funding in neurological disorders medical and social research (Horizon Europe, IMI) to fill the migraine knowledge gap
- Ensure all Artificial Intelligence developments at EU level respond to the needs of people with migraine
- Ensure the implementation of the Work-Life Balance Directive positively affects the migraine community
- Ensure migraine is included in the delivery of the European Pillar of Social Rights and the European Semester

EUROPEAN PARLIAMENT

- Support the setting-up of a Migraine Alliance in the EP to raise awareness, influence policies and develop migraine initiatives
- Ensure migraine is enshrined in the EP work on disability, gender equality, demographic change, the pharmaceutical strategy
- Include migraine in the EP work on health (depression, pain, women's health)
- Steer initiatives to better understand migraine, its development, how it affects society as a whole and how to improve the situation
- Help join forces to fight stigma associated with migraine
- Invite MEPs to be migraine ambassadors at EU and national level

NATIONAL GOVERNMENT

- Support migraine awareness campaigns to educate the public about the differences between migraine and headache
- Develop national migraine strategies with the involvement of migraine patient associations
- Ensure access to timely and quality diagnosis and access to available treatments
- Develop and support care pathways that fully address patients' needs
- Improve the medical curriculum to dedicate sufficient time to headache disorders and migraine in particular
- Engage healthcare professionals to better diagnose migraine, discourage self-medication and drug overuse and direct patients to headache services
- Help break the stigma associated with migraine to empower people with migraine and society to be fully inclusive of people with migraine
- Adapt school and work-place legislation to give people with migraine equal opportunities to contribute to society
- Increase migraine research funding to better understand how the disease develops and affects patients and develop treatments
- Support migraine associations as key partners in awareness-raising, professional education, social support and drug development

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