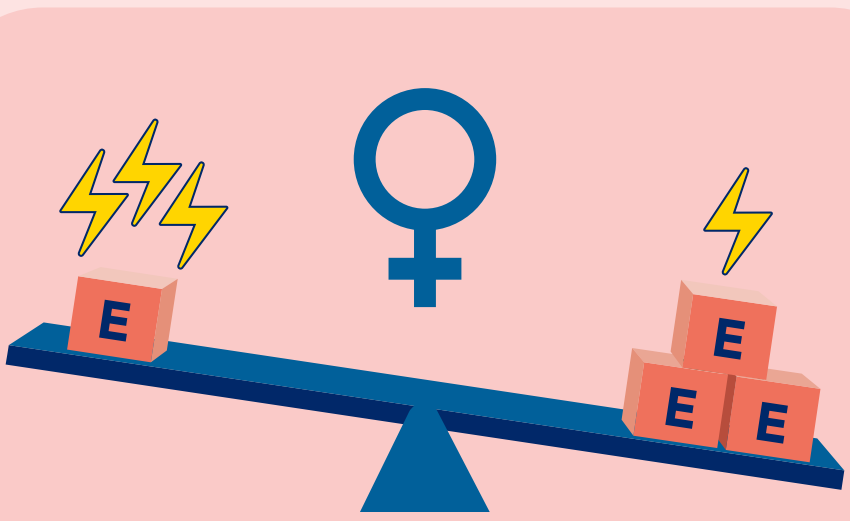
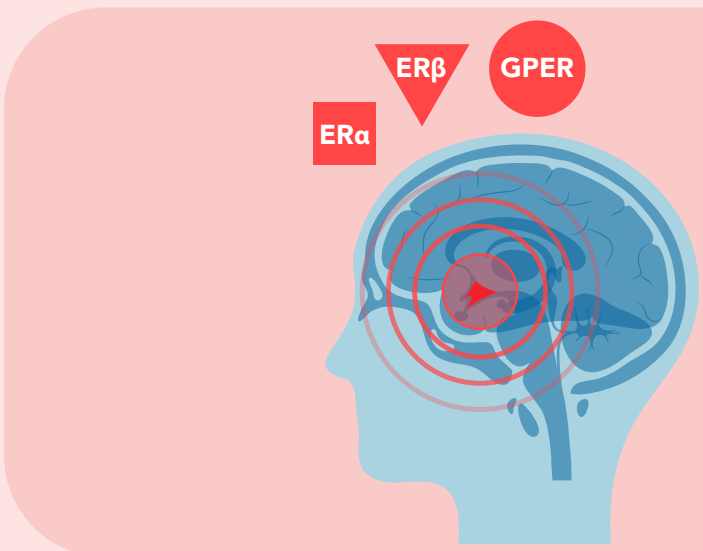
ESTROGEN AND THE PATIENT JOURNEY FOR WOMEN WITH MIGRAINE

Migraine is twice as common in women as in men (cumulative incidence **43% in women**, **18% in men**),[1] and the 1-year prevalence of migraine is three times higher in women[2]

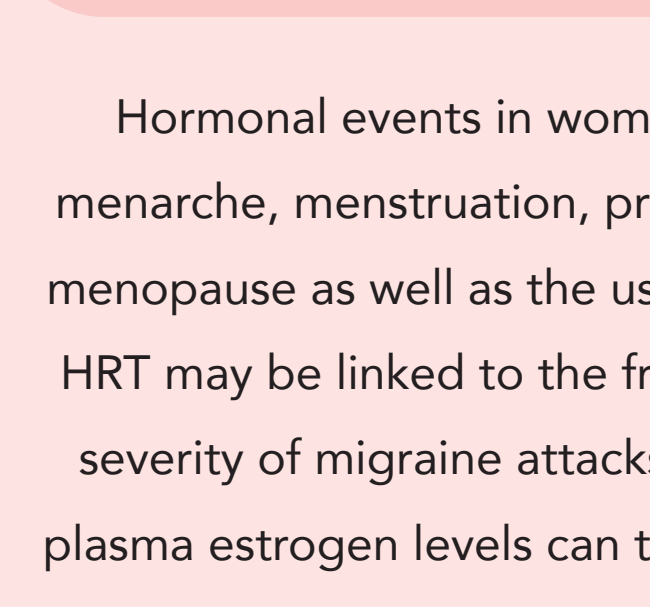
ESTROGEN AND MIGRAINE PATHOPHYSIOLOGY



Hormonal events in women such as menarche, menstruation, pregnancy, and menopause as well as the use of OCs and HRT may be linked to the frequency and severity of migraine attacks[3] — a fall in plasma estrogen levels can trigger attacks of migraine without aura, whereas higher estrogen levels seem to be protective[4]



All three ER subtypes — ERα, ERβ and GPER — are extensively expressed throughout migraine-related regions, in particular the hypothalamus (a putative migraine initiator) and the trigeminal ganglia and spinal trigeminal complex (involved in nociception)[4]



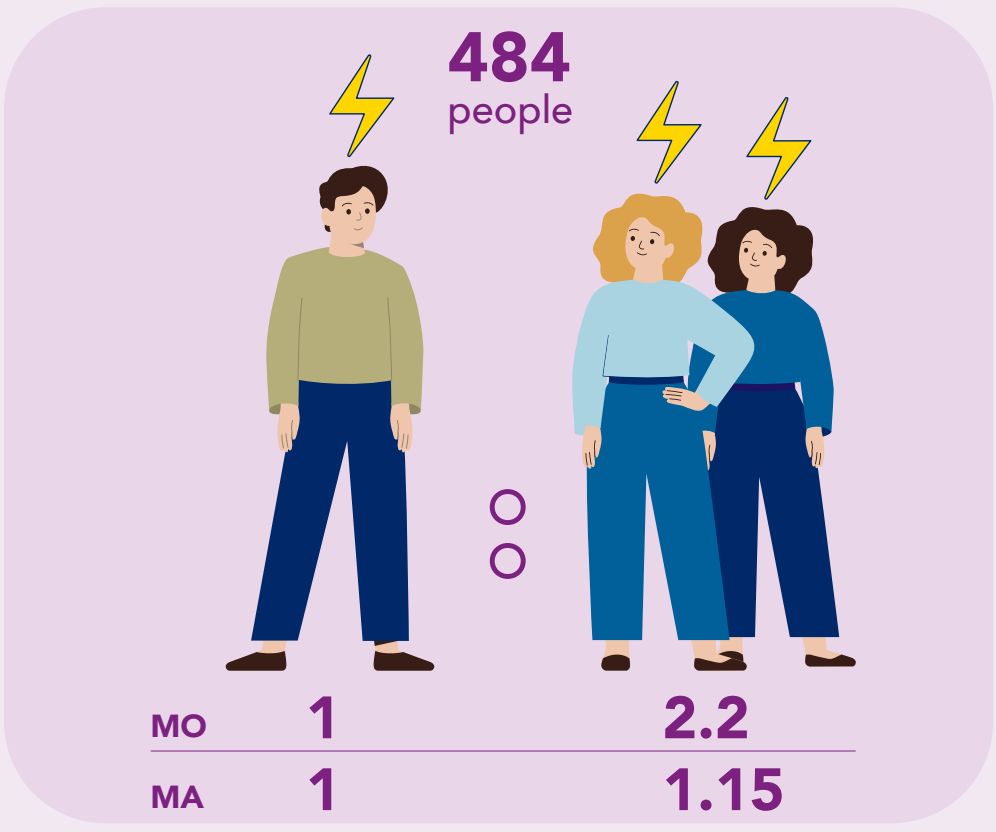
The actions mediated by ERα, ERβ and GPER are not clear, but these receptors are frequently colocalized with CGRP and CGRP receptors, and oxytocin and oxytocin receptors, suggesting the likely involvement of CGRP and oxytocin[4]

CGRP, calcitonin gene-related peptide; ER, estrogen receptor; GPER, G protein-coupled estrogen receptor; HRT, hormone replacement treatment; MO, migraine without aura; OCs, oral contraceptives; OXT, oxytocin

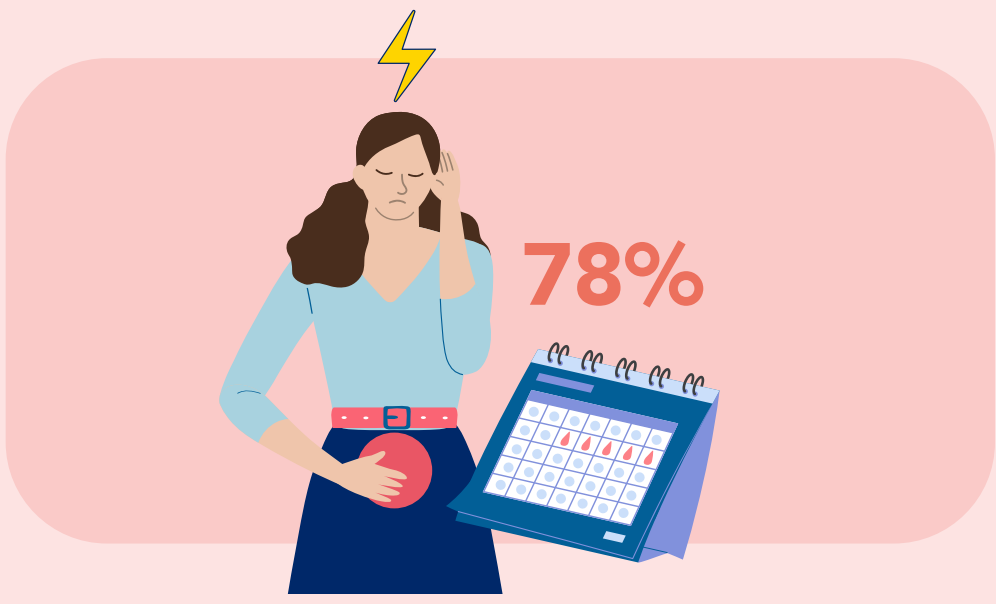
MENARCHE

Among **484 people** with migraine there was a significant lifetime female preponderance for both **MO** and **MA (male:female ratio 1:2.2** and **1:1.15**, respectively), but the female preponderance for MO only becomes apparent after menarche[5]

MA, migraine with aura; MO, migraine without aura

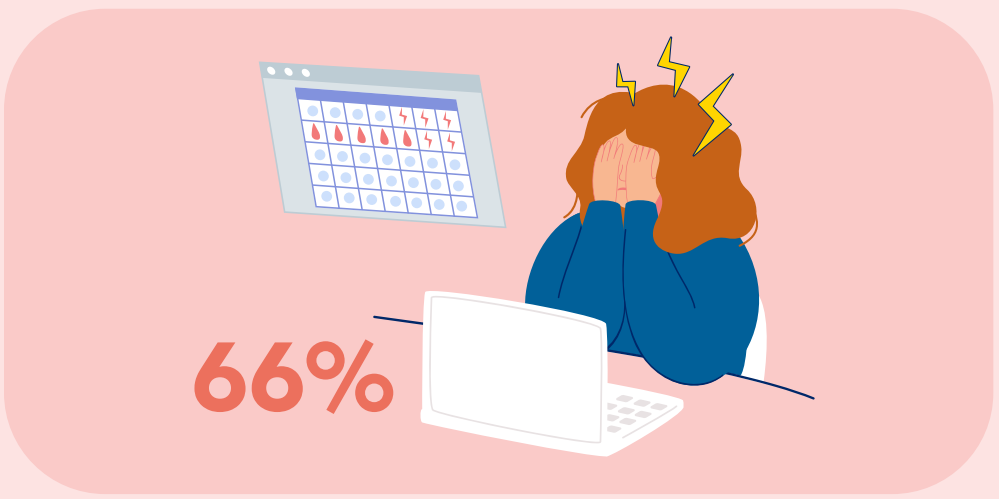


MENSTRUATION



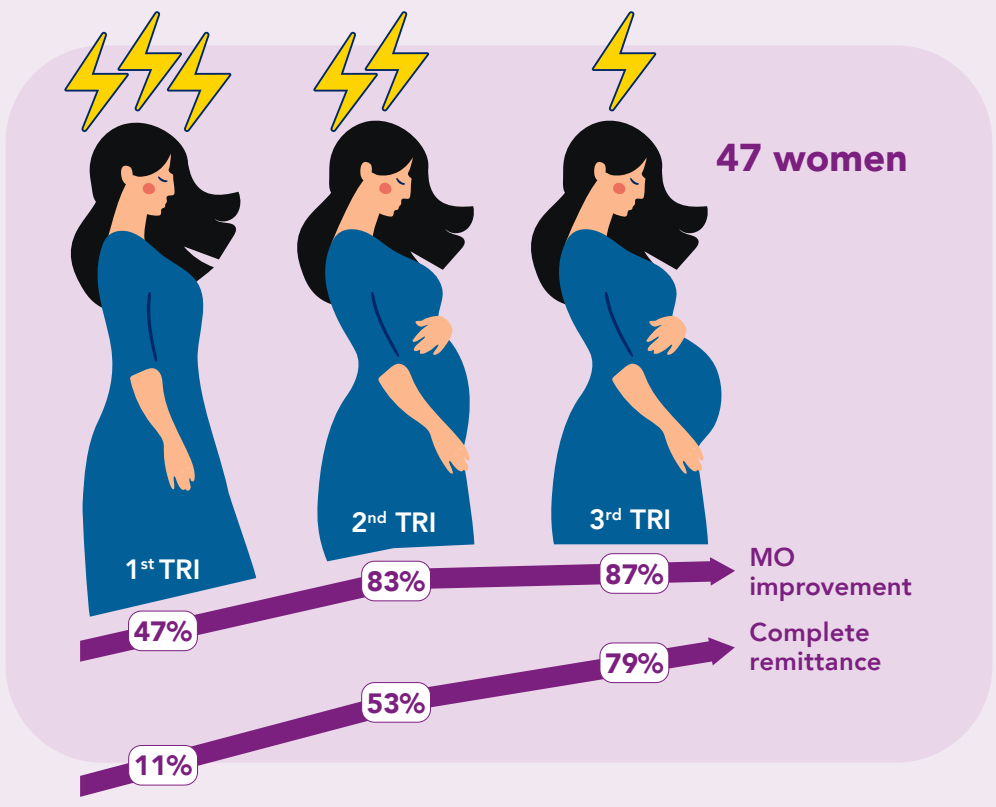
Among **5725 women** with migraine, menstruation was the most common migraine trigger factor and was reported by **78%**[6]

Among **607 menstruating women** with migraine >18 years of age, use of a prospective headache e-diary revealed that **two-thirds** of the women had menstrual migraine but pure menstrual migraine was rare (<1%)[7]



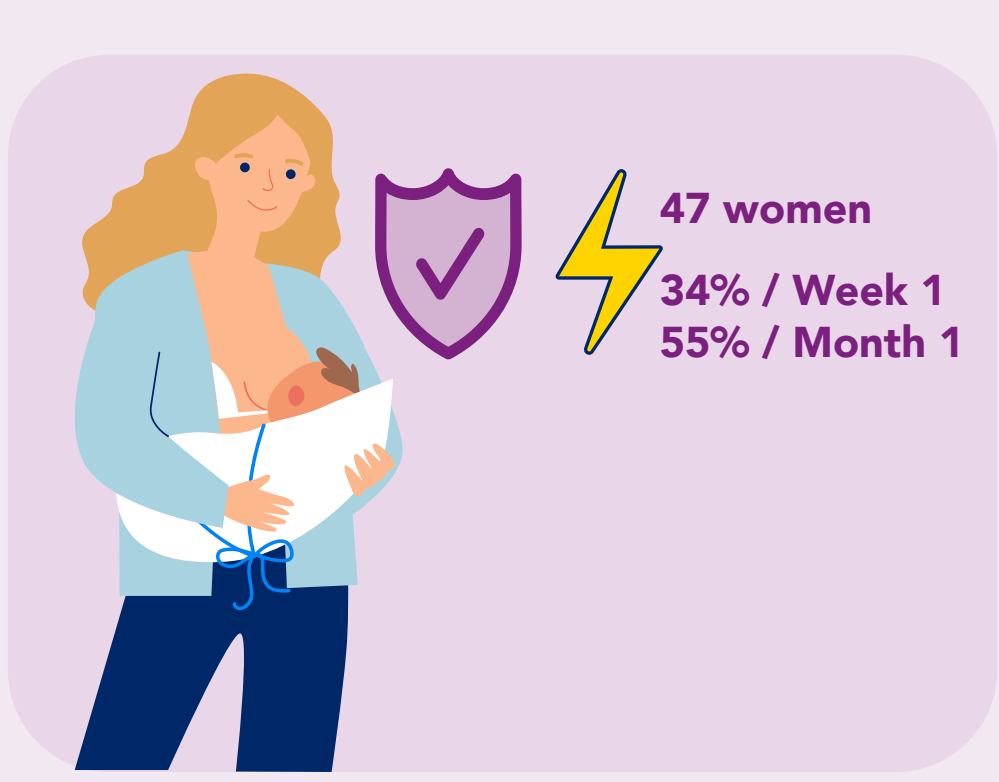
Perimenstrual migraines are longer duration and associated with higher triptan intake than migraines in women without menstrual migraine; women with menstrual migraine may therefore be at increased risk for medication overuse headache and conversion to chronic migraine[7]

PREGNANCY



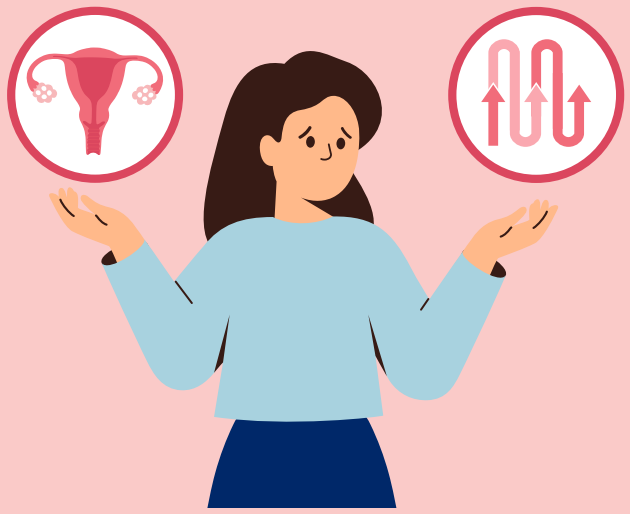
Most women with migraine, especially those with menstrual migraine, experience less severe migraine as they progress during pregnancy[3] — among **47 pregnant women**, **MO improved** during the first, second, and third trimesters in **47%, 83%,** and **87%**, and **completely remitted** in **11%, 53%,** and **79%** of the women, respectively[8]

Among **47 pregnant women** with MO, migraine recurred during the **first week after childbirth in 34%** and during the **first month in 55%**; breastfeeding seemed to protect from migraine recurrence postpartum[8]

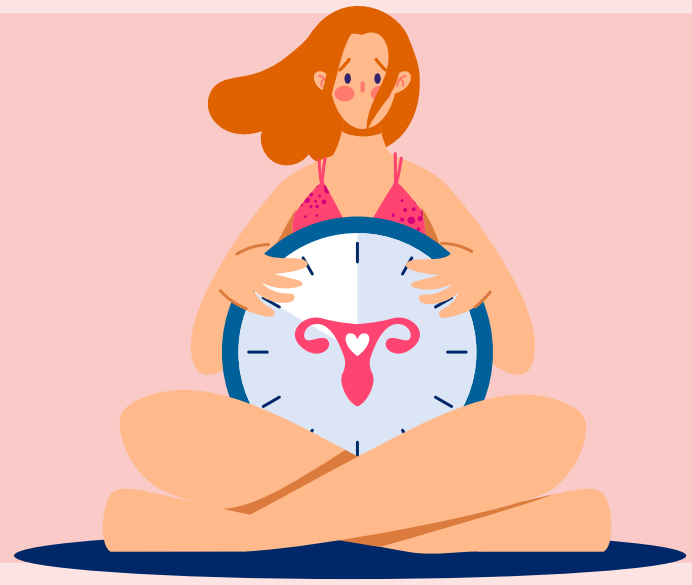


MO, migraine without aura

MENOPAUSE



During perimenopause the fluctuating circulating sex hormone levels are often associated with worsening or a change in migraine patterns[3]



Headache significantly decreases in the transition to[9] and after menopause[3]

References

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2. Lipton RB, Bigal ME, Diamond M, Freitag F, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology 2007;68:343–9. **3.** Sacco S, Ricci S, Degan D, Carolei A. Migraine in women: the role of hormones and their impact on vascular diseases. J Headache Pain. 2012;13(3):177–89. **4.** Krause DN, Warfvinge K, Haanes KA, Edvinsson L. Hormonal influences in migraine – interactions of oestrogen, oxytocin and CGRP. Nat Rev Neurol. 2021;17(10):621–33. **5.** Russell MB, Rasmussen BK, Fenger K, Olesen J. Migraine without aura and migraine with aura are distinct clinical entities: a study of four hundred and eighty-four male and female migraineurs from the general population. Cephalalgia. 1996;16(4):239–45. **6.** van Casteren DS, Verhagen IE, Onderwater GL, et al. Sex differences in prevalence of migraine trigger factors: A cross-sectional study. Cephalalgia. 2021;41(6):643–8. **7.** Verhagen IE, Spaink HA, van der Arend BW, et al. Validation of diagnostic ICHD-3 criteria for menstrual migraine. Cephalalgia. 2022:3331024221099031. **8.** Sances G, Granella F, Nappi RE, et al. Course of migraine during pregnancy and postpartum: a prospective study. Cephalalgia. 2003;23(3):197–205. **9.** Freeman EW, Sammel MD, Lin H, Gracia CR, Kapoor S. Symptoms in the menopausal transition: hormone and behavioral correlates. Obstet Gynecol. 2008;111(1):127–36.