Migraine & Hormones

Women and migraine – why it is important
Endogenous hormones — how do they influence migraine
Exogenous hormones — which to use when and why

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Royal Devon & Exeter Hospital · Exeter Headache Care · National Migraine Centre · BASH

Four common stories you may have heard

We will meet these women again through the talk.

Aisha, 24

Migraine without aura

New relationship and would like contraception.
Diary evidence of headache and nausea when she gets her period in most cycles.
Occasionally has a migraine attack at other times, particularly when stressed.
BMI 24, non-smoker.

What could she start?

Kate, 36

Migraine with aura

Six years on a combined pill continuously. No problems and happy. Came about a knee injury.
No headaches.
History of migraine in teens and early 20s, often with period.
Last attack of aura was peripartum 8 years ago.
Fit and well: BMI 22, active, non-smoker

Stop, switch or continue?

Mona, 48

Migraine with aura

Attacks have worsened over the past 12 months and, for the first time, seem to be related to her menstrual cycle.
Also getting flushes, night sweats, and broken sleep.
Asking about HRT, as it has made a big difference for her friends, but she was told she could never have it.

Is this true?

Jen, 52

Daily headache

Headache is present most days of the month. She is using co-codamol most days, as it helps with sleep and headaches, and nothing else has worked.
Teenagers at home, a mother with dementia, a full-time job. Not sought help because ‘everyone gets headaches’.

Where do you start?

Fictional cases

How many women are affected by migraine?

Prevalence peaks between 25 and 55 — the reproductive and perimenopausal years, and the working and caring years.

1 in 5

18% of women have migraine in any year [1]

Migraine

1 in 3

have 3 or more migraine attacks a month [1]

Attack frequency

>50%

report severe impairment or the need for bed rest during attacks [1]

Attack severity

2.5%

of episodic migraine will progress to chronic migraine each year [2]

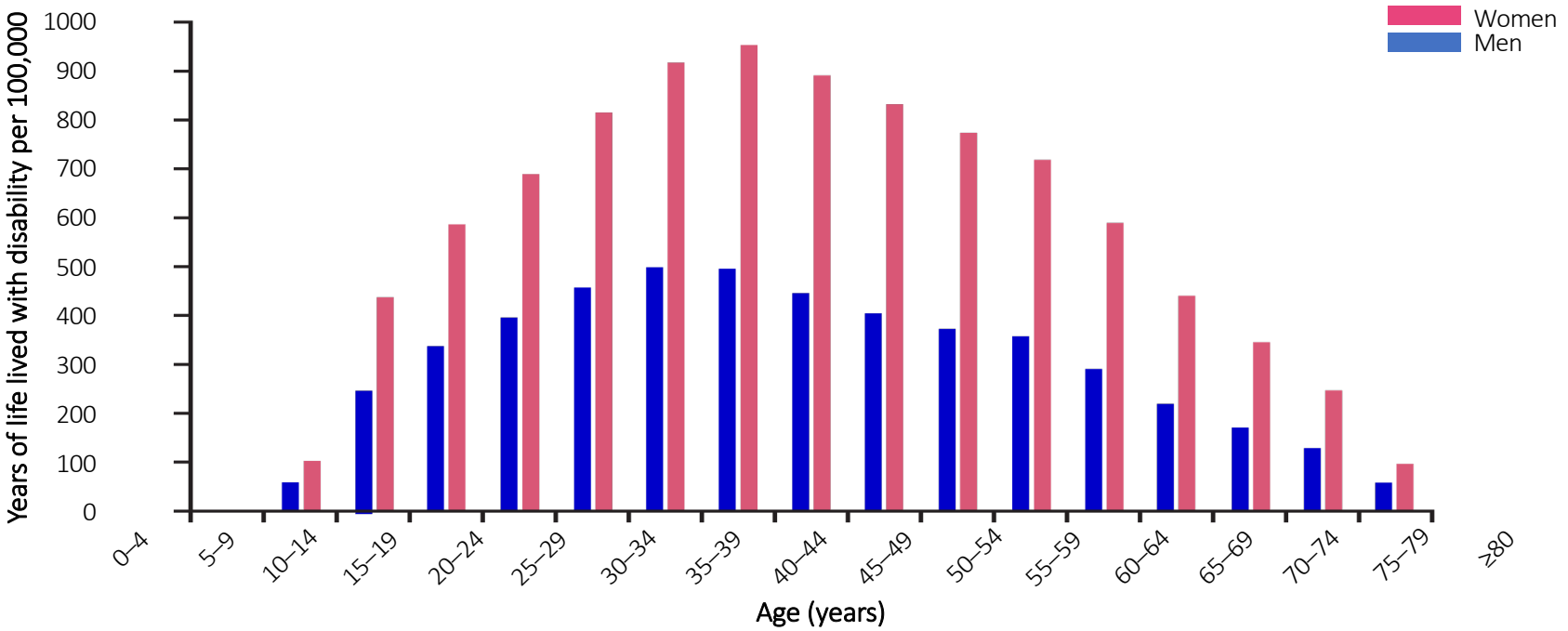
Chronic migraine

Migraine is two to three times more common in women than in men

1. Lipton RB, et al. Neurology 2. Katsarava Z et a.., Curr Pain Headache Rep. 2012

Migraine is the leading cause of disability among women of reproductive age (15–49 years) worldwide[1]

Global years lived with disability (YLD) from migraine in men and women[2]

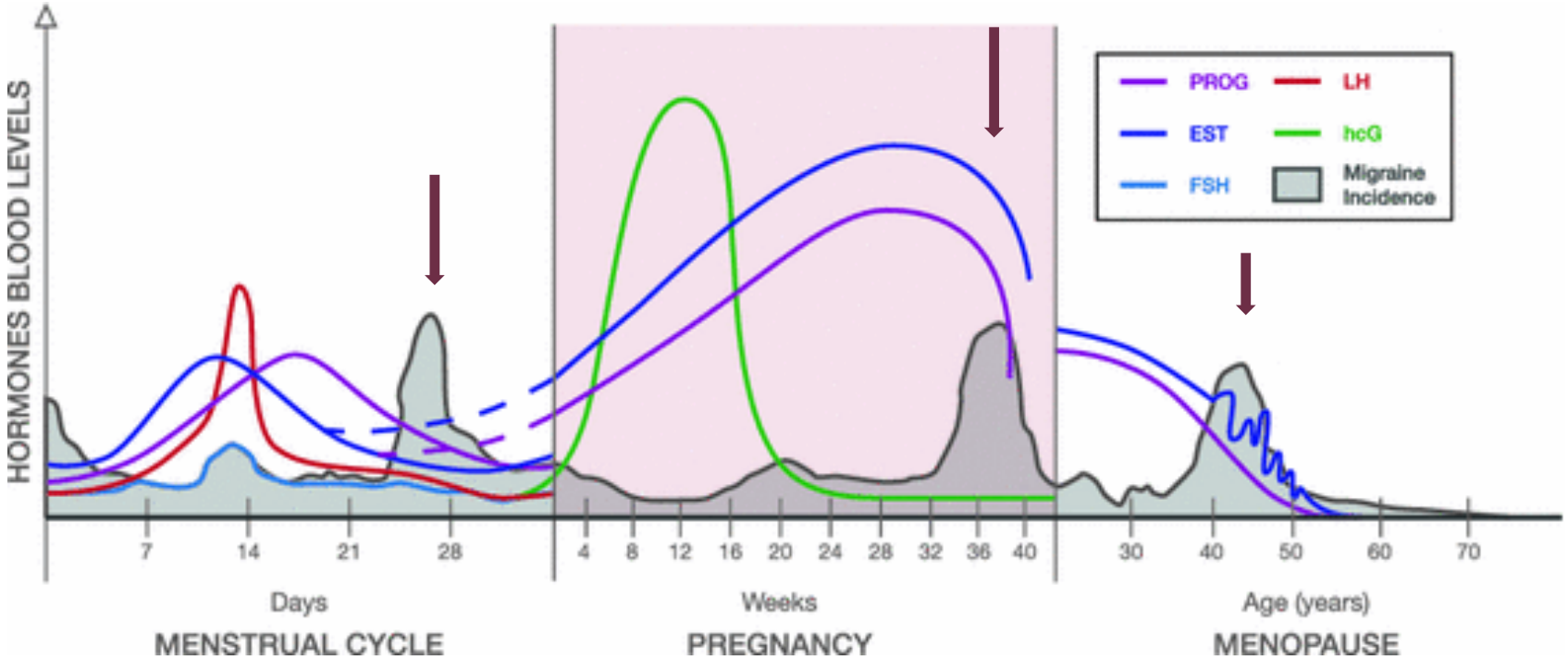


Adapted from Vetvik KG, *et al. Lancet Neurol* 2017.[2]

1. Steiner TJ, *et al. J Headache Pain* 2020;21(1):4–7 · 2. Vetvik KG, *et al. Lancet Neurol* 2017;16:76–87.

Migraine through the reproductive years

Hormone levels across the menstrual cycle, pregnancy and the menopause, with migraine incidence overlaid



1. Sacco S, et al. J Headache Pain. 2012;13(3):177-89.

Adapted from: Sacco et al. J Headache Pain. 2012

Women are care givers — at home and at work

Women care for people in their families and communities — and they dominate the public sector workforce that cares for everyone else.

79%
Scotland

England 76%

NHS / healthcare workforce

84%
Scotland

England 82%

Social care workforce

89% / 64%
Scotland primary / secondary

England 76% all teachers

School teachers

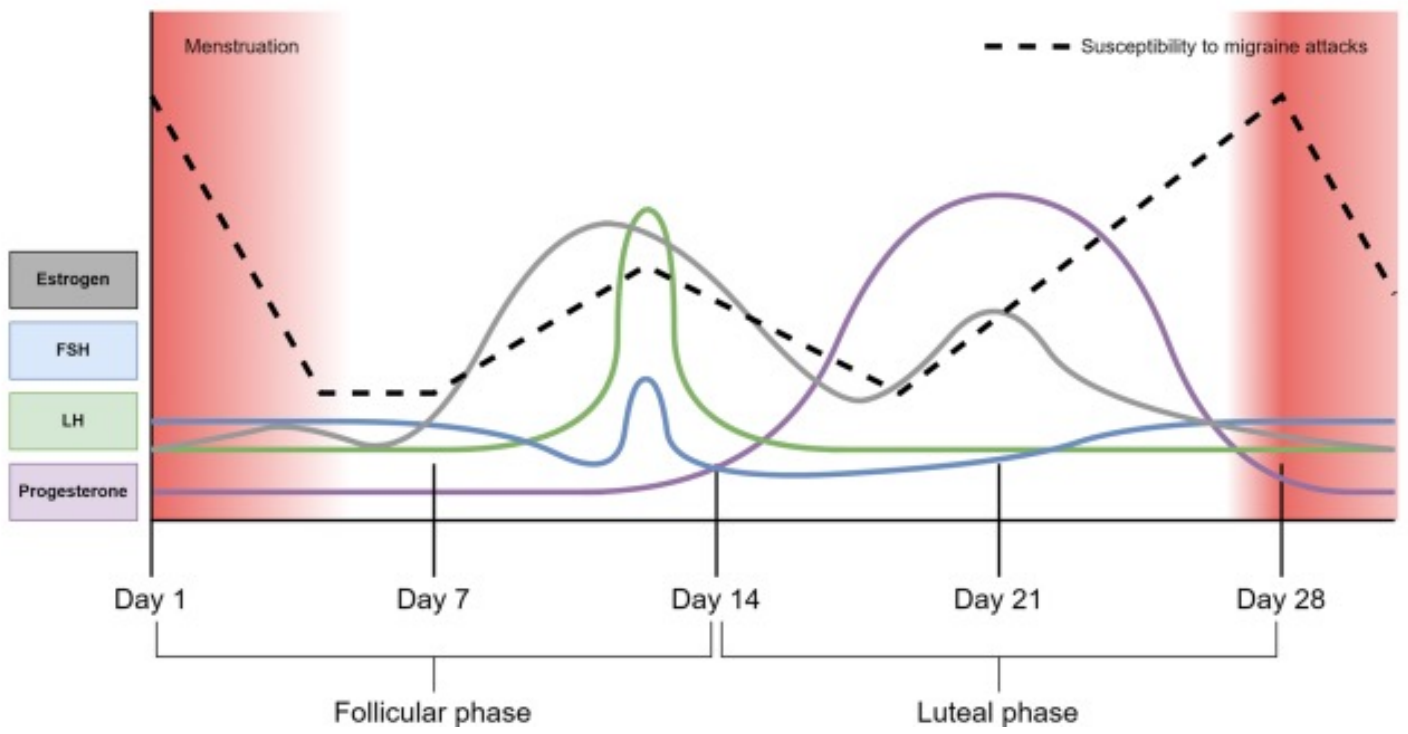
20% of the total NHS workforce are women of menopausal age [4]

‘Caring for and supporting women with migraine benefits everyone’

Dr Dawn Buse MD

Scotland: NHS Scotland workforce report, NES Turas (78.8% of staff female; 77.1% WTE) · SSSC Report on 2023 Workforce Data (16% of the social service workforce are men) · Scottish Government school staff census (89% of primary and 64% of secondary teachers are female). England: The King’s Fund, NHS workforce in a nutshell (76%) · The King’s Fund, health and care workforce (82% of social care) · Ethnicity facts and figures, school teacher workforce (75.6%, 2024/25).

Susceptibility to Migraine Attacks (1): Oestrogen withdrawal hypothesis [1,2]



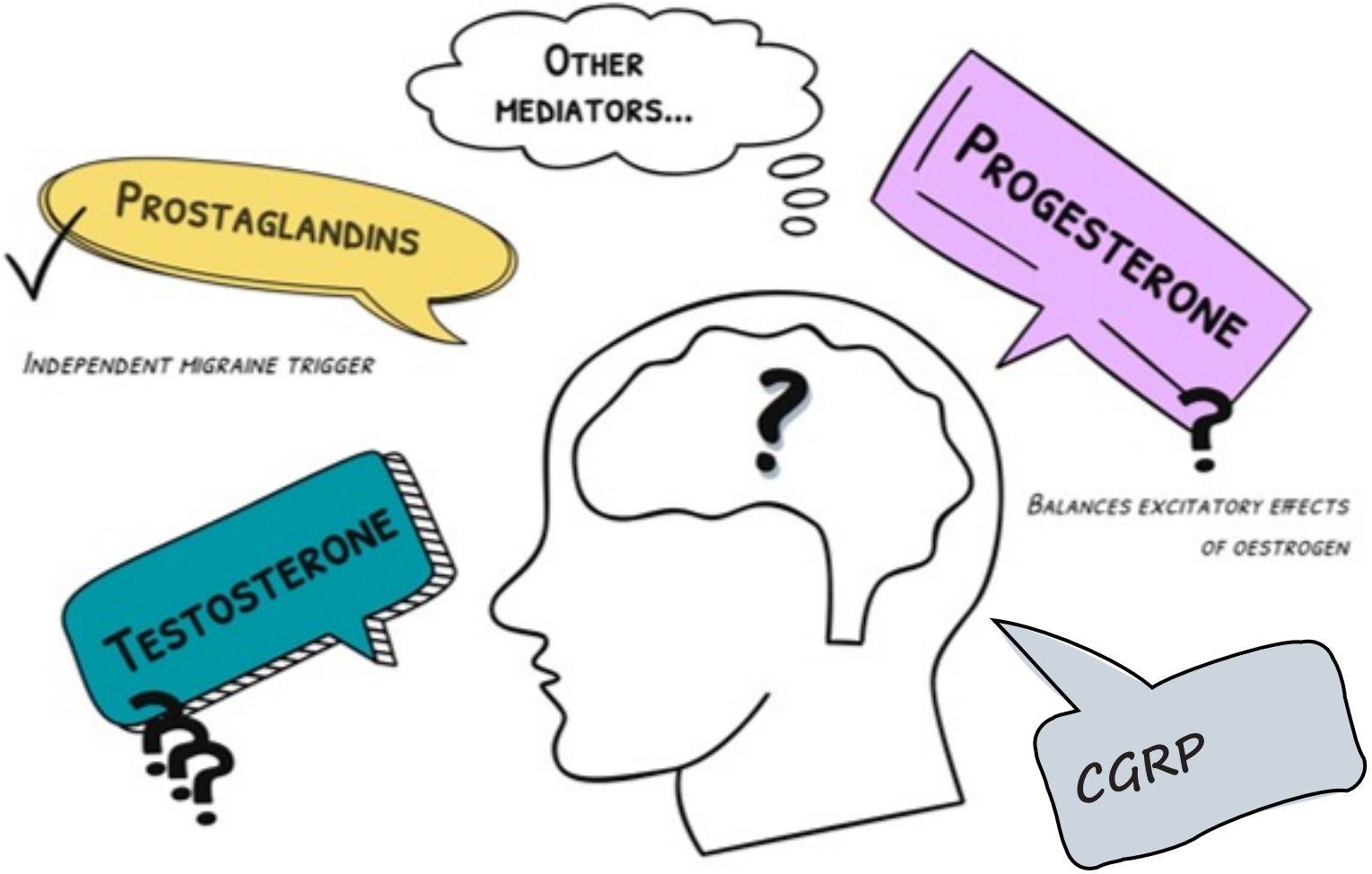
Hormonal changes and incidence of migraine during the menstrual cycle [1]

Excitatory effect of oestrogen [2]

Genetics [2]

Epigenetics [2]

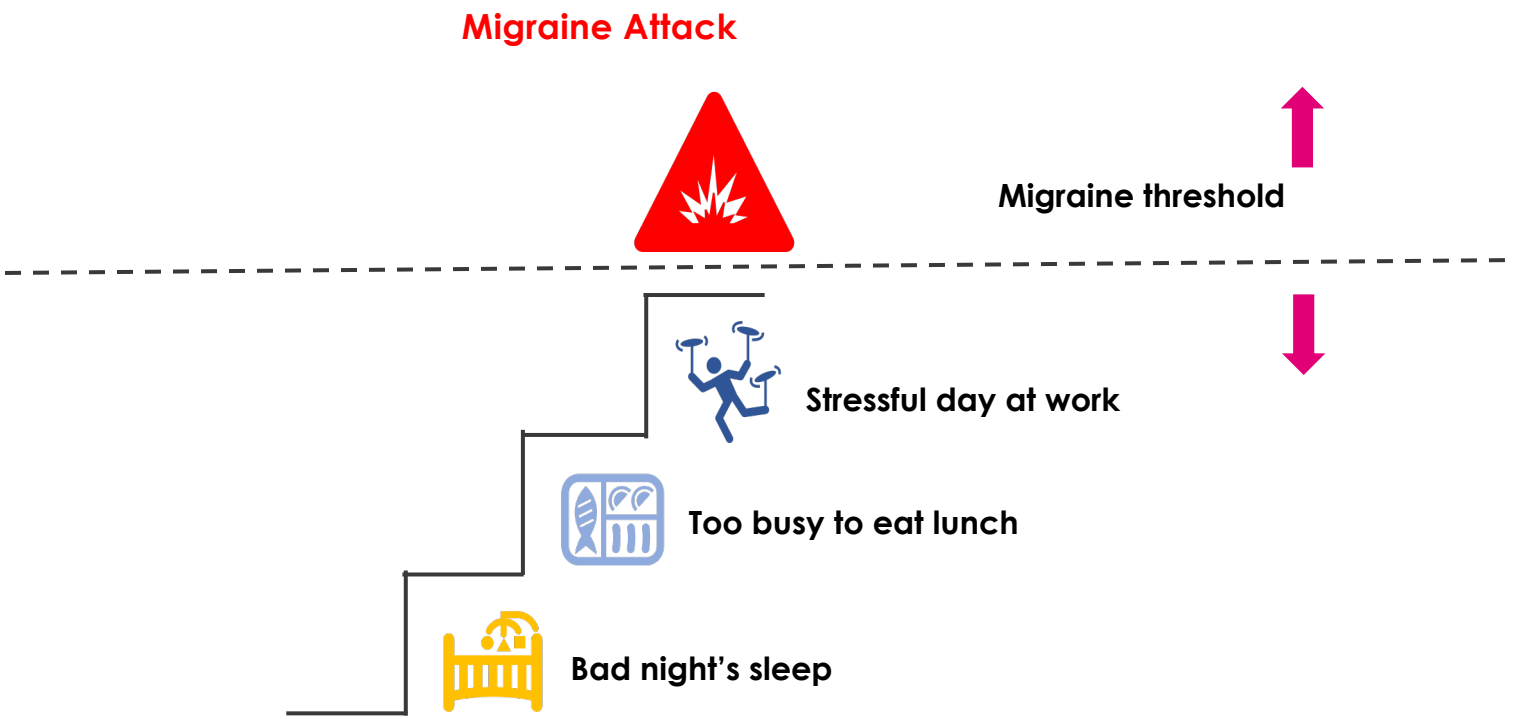
1. Raffaelli, B. *et al.* J Headache Pain. 2023. 2. Vetvik KG, MacGregor EA. Lancet Neurol. 2021



CGRP = Calcitonin Gene Related Peptide

Speaker's own image

Susceptibility to Migraine Attacks (2)
Migraine Threshold Theory [1]

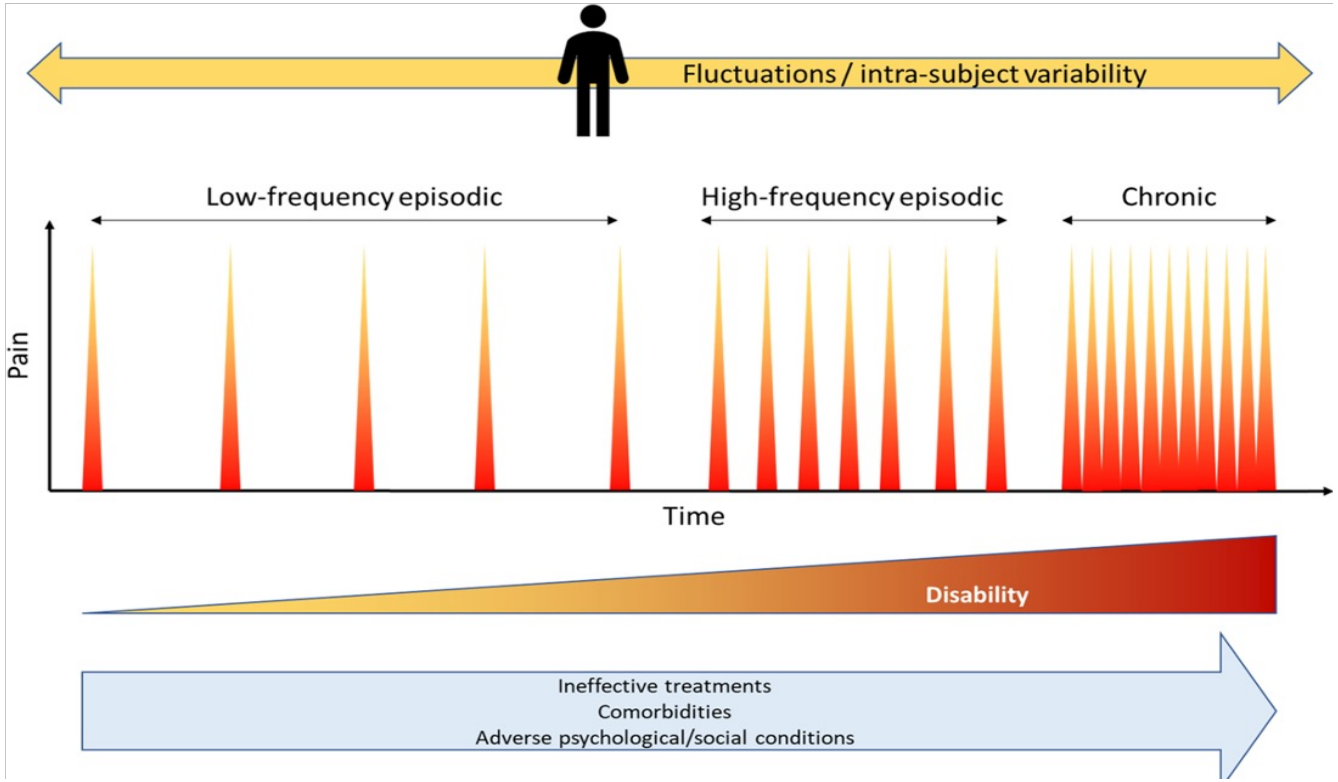


Speaker's own image: adapted from Peng et. al, Pain. 2019 Jul;160(7):1494-1501.

1. Peng KP, *Pain* 2019

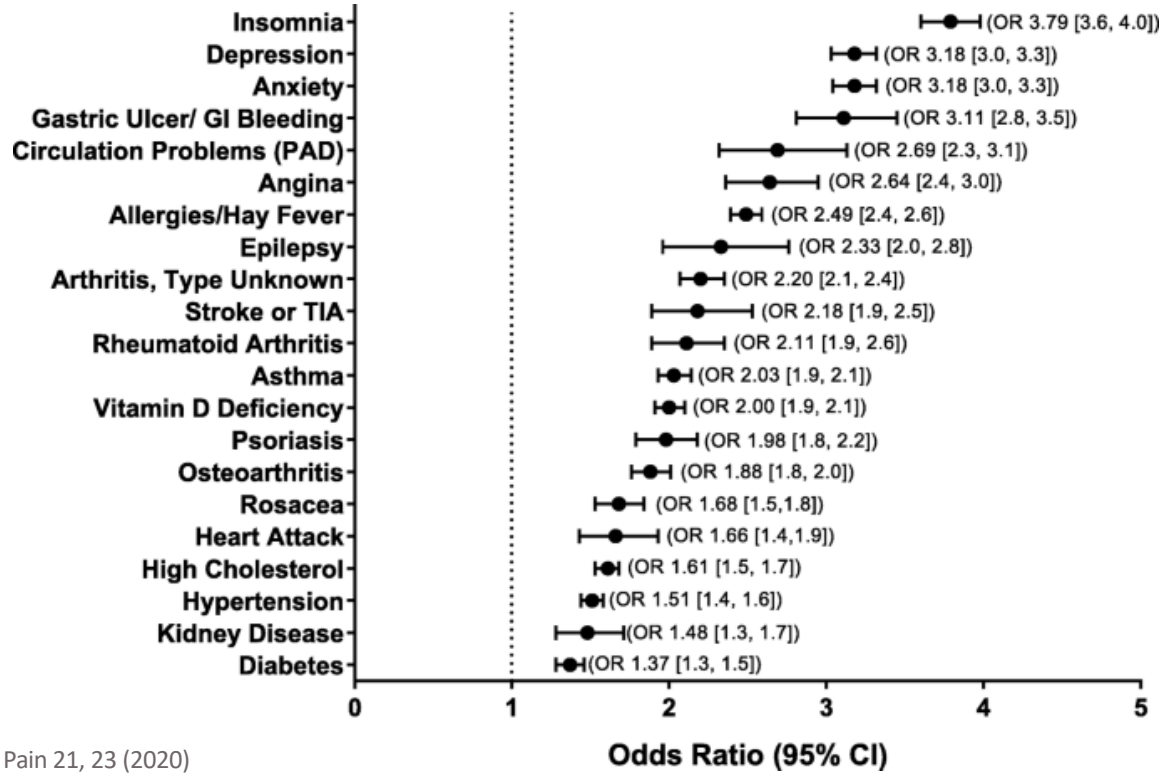
Migraine Transformation

Progression from low-frequency episodic, to high-frequency episodic, to chronic migraine



1. Rossignoli C, et al. Journal of Headache and Pain 2022;23:100.

Susceptibility to Migraine Transformation (1): Comorbidities



Adapted from Buse, D.C., et al., J Headache Pain 21, 23 (2020)

- Fibromyalgia [2]
- Restless legs [3]
- Hypermobility [4]
- IBS [5]
- Adverse Childhood Events [6]
- Endometriosis [7]
- Menopause Transition [8]

Key: IBS = Irritable bowel syndrome

1.Buse et al. Comorbid and co-occurring conditions in migraine and associated risk of increasing headache pain intensity and headache frequency: results of the migraine in America symptoms and treatment (MAST) study. *Headache. The Journal of Headache and Pain.* 2020; 21:23
2.Penn et al. Bidirectional association between migraine and fibromyalgia: retrospective cohort analyses of two populations. *Epidemiology Research.* 2019; 9: 4
3.Schürks et al. Migraine and restless legs syndrome: A systematic review. *Cephalalgia. 2014; 34 (10): 777-794*
4.Neilson et al. Joint Hypermobility and Headache: Understanding the Glue That Binds the Two Together – Part 1. *Headache. The Journal of Headache and Pain.* 2014; 54 (8): 1393-1402.
5.Lau et al. Association between migraine and irritable bowel syndrome: a population-based retrospective cohort study. *European Journal of Neurology.* 2014; 21 (9): 1198-1204.
6.Mansuri et al. Adverse Childhood Experiences (ACEs) and Headaches Among Children: A Cross-Sectional Analysis. *Headache. The Journal of Headache and Pain.* 2020; 60 (4): 735-744
7.Yang MH, Wang PH, Wang SJ, Sun WZ, Oyang YJ, Fuh JL. Women with endometriosis are more likely to suffer from migraines: a population-based study. PLoS One. 2012;7(3):e33941.

Susceptibility to Migraine Transformation (2): the Mother Load

Concepts from sociology and stress physiology

Mental load

Invisible work of anticipating, planning and tracking household and family needs

Second shift

Unpaid domestic and childcare work after paid work; paired with emotional labour

Sandwich generation

Caring for children and ageing parents simultaneously

Allostatic load

Cumulative biological wear from chronic stress

Medication-overuse headache (MOH)

Regular use of rescue medication for > 10 days per month for more than 3 months [1]
(excl. Gepants [2])

Medication Overuse Headache

- **Three times** more common in women [3, 4]
- Most common in **middle age:** 35–54 yrs [5]
- Most frequently associated with **underlying migraine** [4]
- More common with **comorbid** depression, anxiety, and other chronic pain conditions [6]
- MOH-related YLDs are more than twice as high in women [4]

What she says when you ask

'I don't have a choice, nothing else works'

'It's the only way I can get through the day'

'I don't like taking medication all the time'

'I have been worried about how much medication I am taking, but I didn't know it could make my headaches worse'

MOH is a common, disabling and PREVENTABLE complication of uncontrolled migraine that disproportionately affects women in middle age

1. StatPearls: www.ncbi.nlm.nih.gov/books/NBK538150 · 2. Croop R, et al. Cephalalgia 2024 · 3. Diener HC, Lancet Neurol 2019 · 4. GBD 2023 Headache Collaborators. Global, regional, and national burden of headache disorders, 1990–2023. *Lancet Neurol* 2025 · 5. Constantinidis TS, et al. Cephalalgia 2023 · 6. Schwedt TJ, et al. Headache 2021

Why is the bigger picture important?

Speaker's own views

AI generated image

Menstrual Migraine

Menstrual migraine (MM): common, disabling, under-diagnosed

Perimenstrual window = day 1 of menstruation ± 2 days, in at least 2 of 3 cycles (ICHD-3)

22–70% of women presenting to headache clinics [1]

32% have a confirmed diagnosis — a further 14% report menstruation as a trigger but were never labelled [2]

35% longer attack duration perimenstrually (20.0 vs 16.1 hours) [3]

1 The attacks behave differently [3]

- Longer, and they recur after triptan use
- Higher intensity, more sensory sensitivity
- Less likely to be associated with aura
- Medication-overuse risk

Note: *These attacks are often not recognised as migraine. They are associated with* ***a high interictal burden: FUNCTIONAL, EMOTIONAL, BEHAVIOURAL disability***

2 Traditional strategies

- **Intermittent prevention:** Frovatriptan with naproxen started 1–2 days before menses
- Older guides suggest perimenstrual oestrogen – outdated [4]

Note: *Semi-prophylactic regimens are hard to implement reliably,* ***often associated with recurrence and risk MOH***

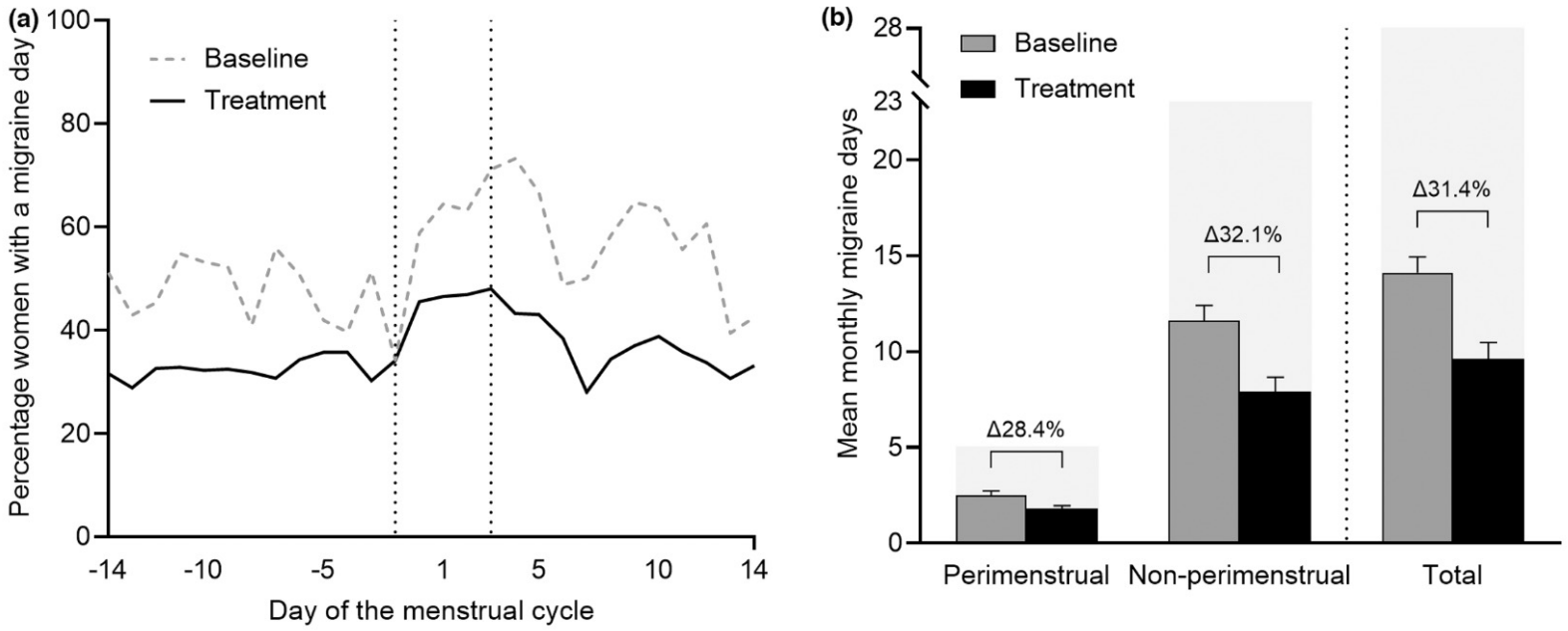
3 What the newer treatments do

- **Anti-CGRP mAbs reduce migraine days consistently across the whole cycle [5]**
- But perimenstrual days improve less than non-perimenstrual ones in real-world data — a residual unmet need [6]

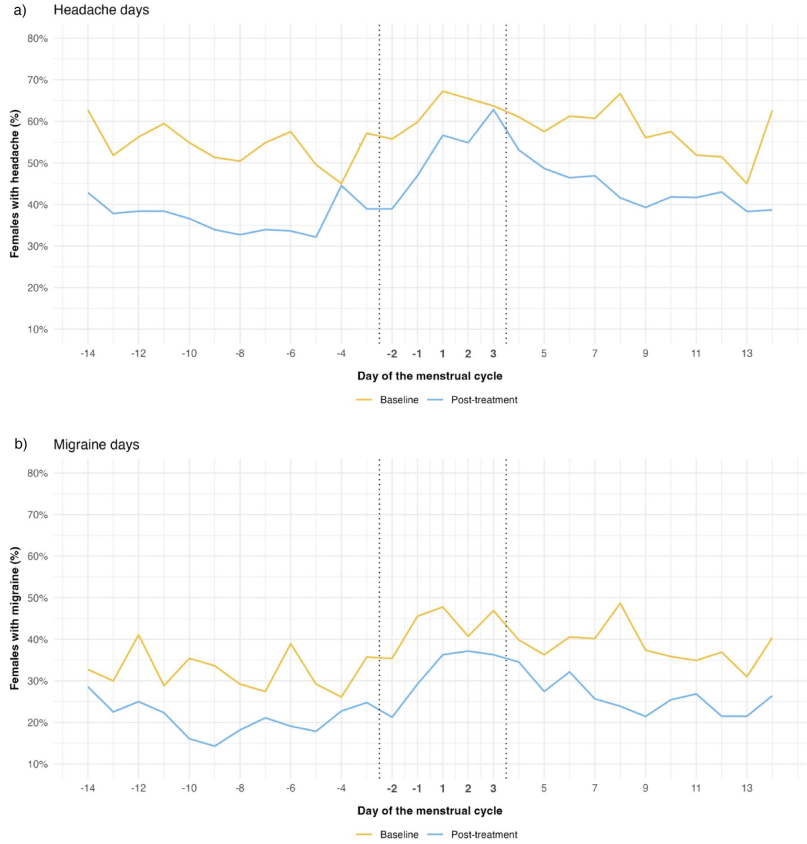
Note: *The influence of hormones on migraine activity* ***does not always disappear*** *once established on otherwise effective CGRP-blocking therapy*

1. Vetvik & MacGregor, Lancet Neurol 2021, 2. Terwindt et al, Headache 2025;65:1413–27 3. van Casteren et al, Neurology 2021;97:e1661–71 4. Speaker's own opinion. 5. Verhagen et al, Eur J Neurol 2023 6. Mas-de-les-Valls et al, Cephalalgia 2025

CGRP blockers and Menstrual Migraine



From: Verhagen IE, et al. Eur J Neurol. 2023



From: Mas-de-les-Valls R, et al. E *Cephalalgia*. 2025;45(4)

Perimenstrual and non-perimenstrual migraine days respond to CGRP antibodies [1], but CGRP may not be the dominant influence in these attacks [2]

1. Verhagen IE, et al. Eur J Neurol. 2023; 30: 2117-2121. 2. Mas-de-les-Valls R, et al. E *Cephalalgia*. 2025;45(4). CGRP = Calcitonin gene-related peptide

Cyclical syndromes: MM, endometriosis and PMDD

Another argument for taking a menstrual history in a headache consultation and encouraging cycle tracking:

Endometriosis

Endometrial-like tissue outside the uterus — cyclical pelvic pain, dysmenorrhoea and subfertility

- Commonly comorbid: OR 2.25 for migraine in endometriosis [1]
- 1 in 3 women with endometriosis have migraine (30–45%) [2]
- 1 in 5 women with migraine have endometriosis: 22% vs 10% of controls [6]
- Association is with migraine WITHOUT aura and dysmenorrhoea
- Possible shared biology: CGRP-releasing nerve fibres innervate endometrial deposits
- UK time to diagnosis is 9 years 4 months, and around 11 years for women from ethnically diverse communities [4]

*47% had seen their GP **ten or more** times before endometriosis was raised* [5]

PMDD

Severe luteal-phase mood and physical symptoms that remit with menses — a DSM-5 diagnosis, not simply PMS

- 68.7% of women with PMDD also have migraine [8]
- PMDD in 5.6% with menstrual migraine vs 1.9% without — population rate 1.6% [9]
- Impairment is comparable to major depression [10]
- Around 4 days lost every month, across three decades of cycles [11]

Raised risk of suicidal ideation and attempts; may meet the Equality Act 2010 definition of disability [12]

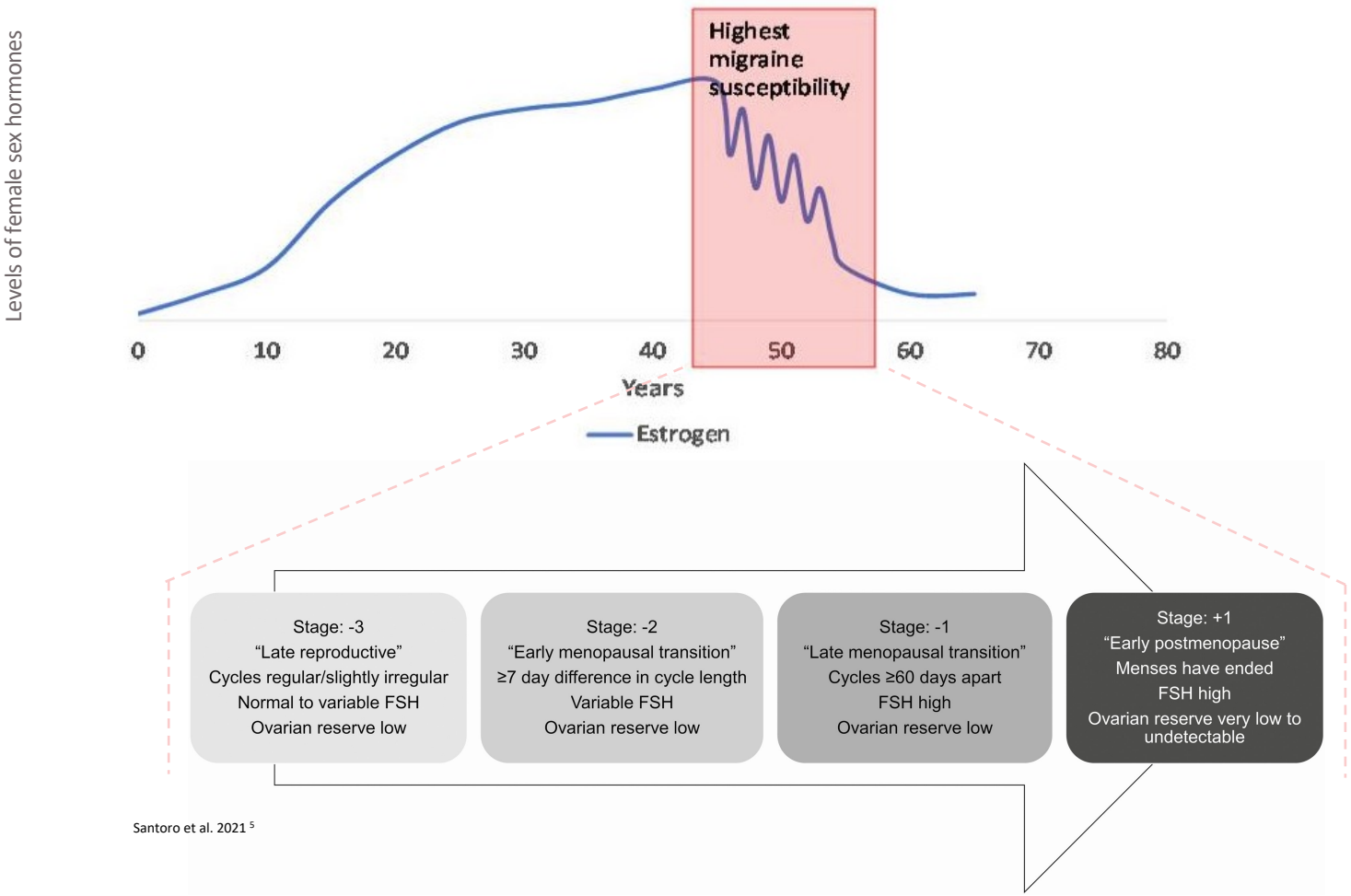
If you discover one cyclical condition, consider asking about others, as they commonly coexist and share treatment strategies

1. Colombo GE, et al., *J Headache Pain* 2025. 2. Gómez-Dabó et al, *Cephalalgia* 2025. 3. Tokushige et al, *Hum Reprod* 2006. 4. Endometriosis UK 2026. 5. Merki-Feld et al 2025. 6. Tietjen GE, *Headache* 2007. 8. Yamada K, *Cephalalgia* 2016 (PMDD survey). 9. Premenstrual syndrome, PMDD and coping strategies in menstrual migraine, *Front Neurol* 2026. 10. Halbreich U, et al. Psychoneuroendocrinology 2003. 12. Disability associated with premenstrual dysphoric disorder, Archives of Mental Health. 13. Frontiers in Psychiatry 2024 narrative review; IAPMD written evidence to UK Parliament (FWD0082).

Menopause transition: an unsettled environment

Average duration 7.4 years [1] · Menopause = final menstrual period · Postmenopausal 12 months amenorrhoea · Median age 51.4

Ornello R, et al. 2021.[2]



Santoro et al. 2021 [5]

Wide, rapid fluctuations in oestrogen levels [3]

Early perimenopause:

- Shorter, frequent cycles in early perimenopause [3]
- Shorter interictal phase [3]

Later perimenopause:

- Anovulatory cycles in later perimenopause: 'oestrogen dominance' [4]

Additional factors:

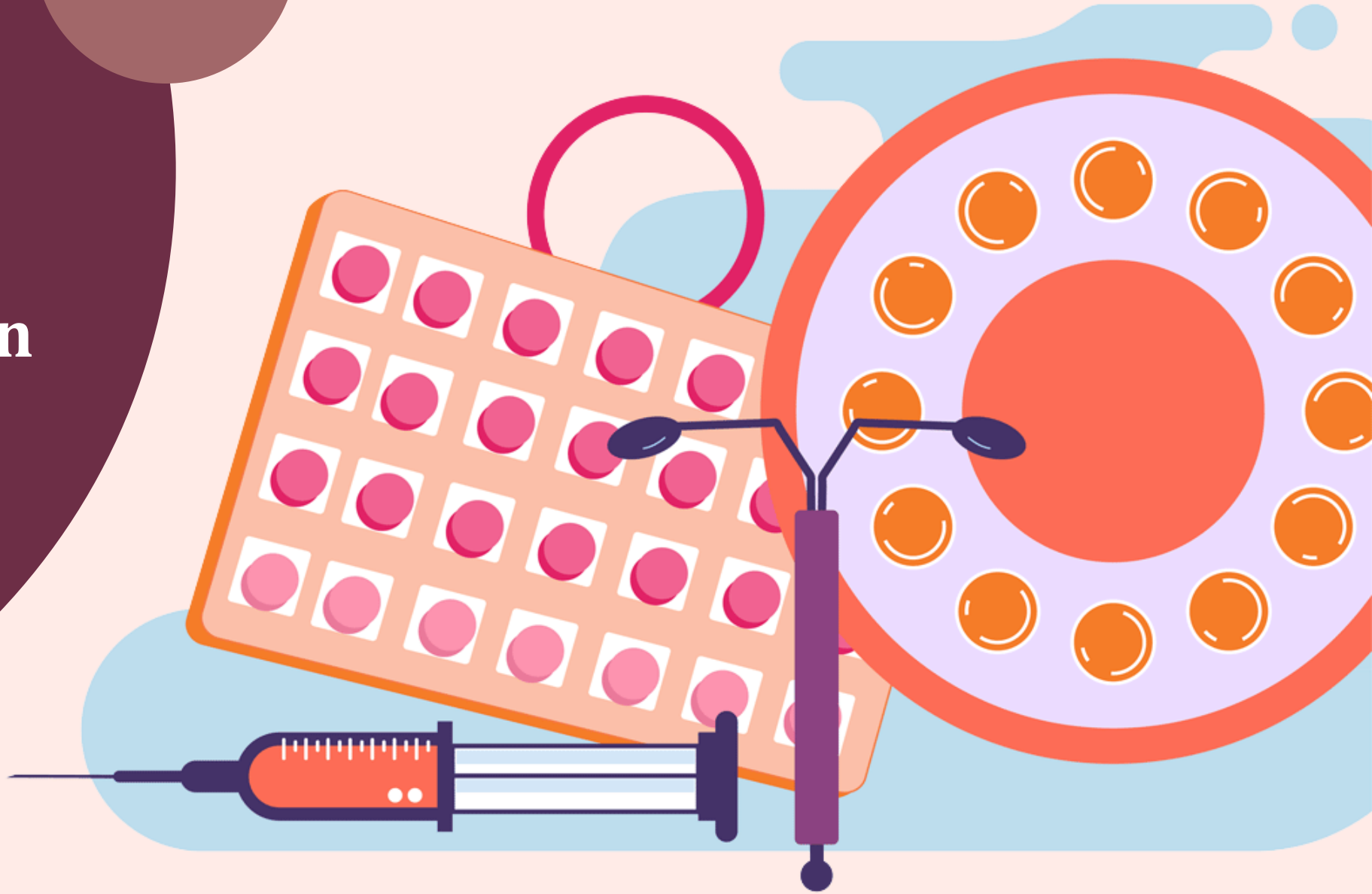
- Menopausal symptoms [3]
  - Vasomotor symptoms themselves last a median of 7.4 years, and 29% of women have them for 10 years or more
  - Vasomotor symptoms are worse in migraine [6]
- Hysterectomy with or without oophorectomy [3]

1. Harlow SD et al, STRAW+10, Menopause 2012 2. Ornello R, et al. Journal of Clinical Medicine. 2021;10(11):2263 3. MacGregor Maturitas 2020. 4. Vetvik KG, MacGregor EA. Lancet Neurol. 2021 Apr;20(4):304-315 5. Santoro N, et al., J Clin Endocrinol Metab. 2021 6. Faubion S et al, Mayo Clin Proc 2023

Addressing unmet need

- *Hormone therapies as an adjunct in migraine care*
  *- a practical approach: aiming for **STABILITY***

Contraception



Ischaemic stroke, aura and ethinylestradiol in combined contraception

Odds ratios vs no migraine and no combined hormonal contraception (Champaloux et al, n = 25,887 strokes)

No migraine : No CHC

1.0 reference

No migraine : On CHC

~1.6

Migraine without aura : No CHC

2.2 1.9 – 2.7

Migraine without aura : On CHC

1.8 1.1 – 2.9

Migraine with aura : No CHC

2.7 1.9 – 3.7

Migraine with aura : On CHC

6.1 3.1 – 12.1

Learning point

- CHC essentially adds no risk on top of migraine ***without*** aura in healthy women (2.2 → 1.8).
- CHC **doubles the risk** on top of migraine ***with*** aura (2.7 → 6.1).

Absolute risk stays small: 11 first strokes per 100,000 women aged 15–49 in that cohort.

UKMEC SUMMARY TABLE HORMONAL AND INTRAUTERINE CONTRACEPTION

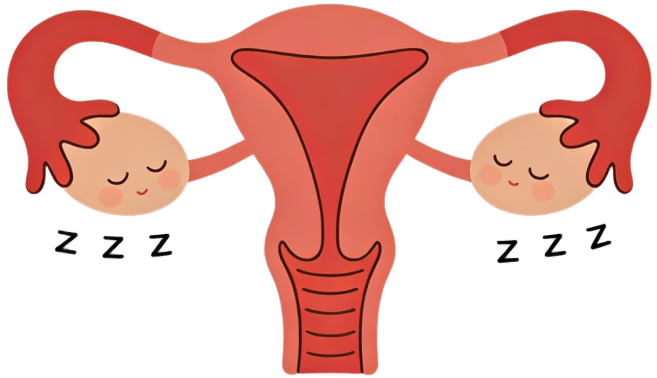
CONDITION	Cu-IUD	LNG-IUS	IMP	DMPA	POP	CHC
	I = Initiation, C = Continuation					
Headaches						
a) Non-migrainous (mild or severe)	1	1	1	1	1	I 1 / C 2
b) Migraine without aura, at any age	1	2	2	2	I 1 / C 2	I 2 / C 3
c) Migraine with aura, at any age	1	2	2	2	2	4
d) History (≥5 years ago) of migraine with aura, any age	1	2	2	2	2	3

Champaloux SW et al, Am J Obstet Gynecol 2017;216:489.e1–7 · UKMEC 2025 summary tables, CoSRH · CHC = Combined Hormonal Contraception

Contraceptive options with potential therapeutic benefit for MRM

Trigger 1 · Oestrogen withdrawal

Addressed by any strategy that 'quietens the ovaries'



Trigger 2 · Prostaglandin release

Endometrial prostaglandin can be addressed by suppressing bleeding

Progesterone Only Contraceptives

- **Desogestrel 75 mcg OD**
- **Drospirenone 4 mg (Slynd)** *24/4*

- No excess VTE or stroke risk
- Use in **Migraine with and without aura**
- Slynd can be taken continuously

LARC

- **LNG-IUS (e.g. Mirena)**
  - Long-acting, 5 yrs
  - 60–70% amenorrhoeic
  - Ovulation is suppressed in 1 in 5
  - No increase in VTE risk
- **Depo-Provera Injection**
  - 3-monthly injections
  - Risk of loss of bone density use > 5 years

Combined Hormonal Contraception

- **Gedarel 20/150** (low oestrogen)
- **Rigevidon 30/150**

- **Migraine without aura only**
- In an otherwise healthy woman*
- **Omit** the hormone-free interval to remove the withdrawal trigger

CYCLE SUPPRESSION

- These strategies may help women manage menstrual migraine, endometriosis, support menopause care and provide contraception

https://www.cosrh.org/Public/Public/Standards-and-Guidance/uk-medical-eligibility-criteria-for-contraceptive-use-ukmec.aspx

Key: LARC = long-acting reversible contraception, LNG-IUS = Levonorgestrel releasing intrauterine system

**BMI 18 – 25, non-smoker, active, no VTE history

What is the evidence?

Summary findings from the EHF & ESCRH Consensus Statement

Desogestrel 75 mcg daily

- May benefit MO and MA
- Considered low cardiovascular risk
- May cause headache

Extended CHC (pill or patch)

- May benefit women with oestrogen withdrawal migraine or headache
- Particularly women already experiencing headache in the PFI
- Not MA, or MO in women with additional risk factors

Interpret with care: limited evidence of low quality — considerations, not guidelines or recommendations. Hormone therapies are not licensed treatment options for migraine.

EHF = European Headache Federation · ESCRH = European Society of Contraception and Reproductive Health · MO = migraine without aura · MA = migraine with aura · CHC = combined hormonal contraception · PFI = pill-free interval

Sacco S et al, J Headache Pain 2018

The newer 'natural oestrogen' pills — and Scotland

Marketed as a gentler oestrogen. Unfortunately, not available on NHS Scotland formularies but may be in future.

Qlaira

Estradiol valerate + dienogest

26/2 quadraphasic

Not recommended by SMC

Licensed for heavy menstrual bleeding

Zoely

Estradiol hemihydrate + nomegestrol acetate

24/4 monophasic

Not recommended

Drovelis

Estetrol + drospirenone

24/4 monophasic

Not recommended

Estetrol is a fetal oestrogen, not estradiol

What 'gentler' means: a weaker effect on clotting factors, not proven fewer events. Reported VTE rates are lower with the natural oestrogens — lowest for estetrol–drospirenone — but no outcome study confirms it, and there is no arterial or stroke outcome data. **A gentler oestrogen does not lift UKMEC 4 in migraine with aura as yet**. They remain an option for otherwise healthy women without aura who struggle with tolerability of the others, and can be considered as a form of HRT, (see next slide).

SMC advice: Zoely, Drovelis SMC2564 (Jan 2023), Qlaira · West of Scotland CHC Guideline · NHS Tayside Hormonal Contraception Guide · Natural vs synthetic oestrogen and VTE: systematic review and meta-analysis, Front Endocrinol 2024;15:1428597 · EudraVigilance disproportionality analysis, Contraception 2024

HRT


Lenzetto
Oestrogel
Pump-pack
Oestrogel
Pump-pack
Evorel Conti
POM
Theramex

Migraine in early perimenopause

Foundations for every woman and why suppressing the cycle is key

Foundations — for every woman, at every stage of menopause

- Healthy weight; regular aerobic and weight-bearing exercise
- Mediterranean-style diet, good hydration, regular sleep routine
- A simple diary identifies whether attacks track the menstrual cycle
- Non-hormonal options: Escitalopram 10–20 mg/day or Venlafaxine 37.5–150 mg/day

Why suppress the cycle in early perimenopause

Cycle-suppressing hormonal therapies do many jobs:

- Suppress fluctuating oestradiol levels – lows and highs that trigger:
  - Menstrual migraine, PMS/PMDD
- Prevent release of endometrial Prostaglandins that trigger:
  - Menstrual migraine, dysmenorrhoea
- Provide effective contraception
- Provide endometrial protection part of HRT

Scenario:

Migraine with aura and other contraindications to oral oestrogen

- Progestogen-only pill (e.g. Desogestrel 150 mcg or Drosperinone 4 mg, off licence) with transdermal estradiol (patch, spray, gel)
- By 55, ovarian oestradiol activity has declined enough in most women to

Scenario: up to age 50 — migraine without aura

- Healthy women with migraine without aura can use CHC taken continuously, omitting the pill-free interval
- CHC containing estradiol (Zoely) or estetrol (Drovelis) has a safer thrombotic profile — not yet reflected in the SmPCs

Why it matters: in early perimenopause the problem is **instability**. Suppressing the erratic cycle does more for migraine than adding oestrogen on top of it.

Late perimenopause and post menopause

Hormone replacement for vasomotor symptoms — with the migraine caveats

Late perimenopause and early postmenopause

- Continuous combined hormone replacement
- Transdermal estradiol — patch, spray or gel — is preferred: more stable levels than oral estradiol
- Use the lowest oestrogen dose that controls vasomotor symptoms — higher doses can be associated with increased headache and migraine
- Migraine aura does not contraindicate HRT

The natural cycle may still be running

- Unsuppressed ovarian activity causes irregular bleeding on continuous combined regimens
- LOOP and anovulatory cycles may occur throughout menopause transition
- Cycle suppression may therefore be the more appropriate route until ovarian activity has settled, e.g., desogestrel 150 mcg or Drosperinone 4 mg (both off-label)

Counselling point

- Migraine tends to decline gradually over the years that follow a natural menopause
- Women who continue HRT may not benefit from that decline — include this in the conversation

Why it matters: aura is not a barrier to HRT, and regimens that offer stability of delivery and cycle suppression tend to suit migraine best.

Summary

How do you feel when a woman with migraine with aura asks you about HRT?

What you now have

Aura does not contraindicate HRT.

Aura rules out any combined contraceptive.

The right progestogen or CHC, if appropriate, can do many jobs through cycle suppression

The headache and menstrual diary are still the most useful things you can do.

What might you do differently on Monday?

Thank you

Questions and discussion