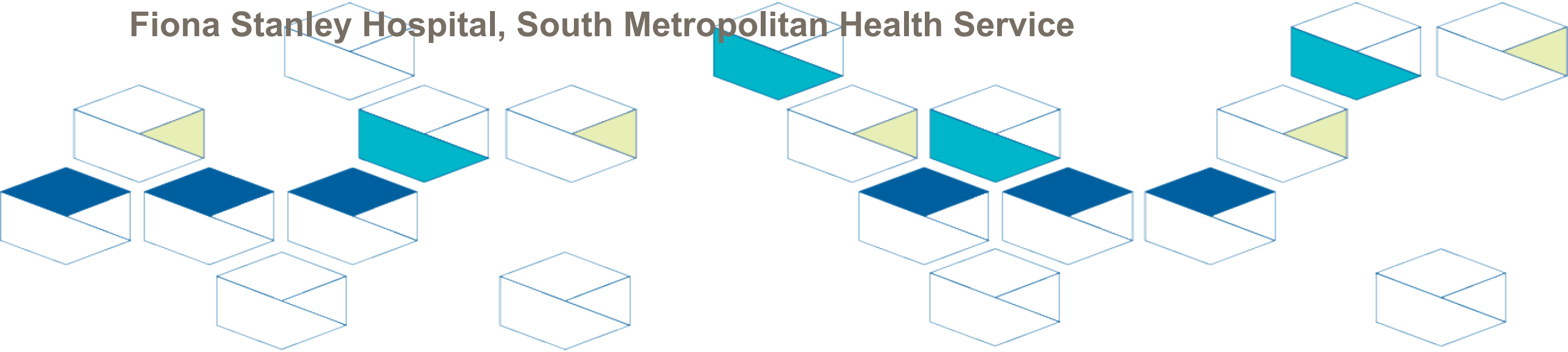
Government of Western Australia
South Metropolitan Health Service
Fiona Stanley Fremantle Hospitals Group

Hormones and more – Women's Mental Health
A Lifespan Approach

Dr Kiri von Klier
Specialist in Women's Mental Health
Child and Adolescent Psychiatrist

Cockburn Health: Women's Mental Health Clinic
Fiona Stanley Hospital, South Metropolitan Health Service



Developmental Stages and Neuroendocrine Transitions

- Childhood
- Adolescence
- Reproductive Years
- Pregnancy
- Post-Partum
- Perimenopause
- Menopause

What We Know

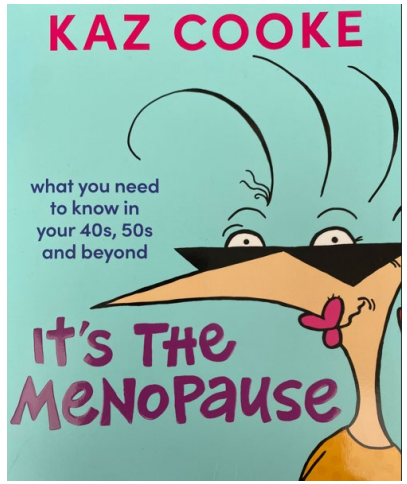
Estradiol, Progesterone and Testosterone are potent Neurosteroids

Facilitate or inhibit transmission via glutaminergic, serotonergic, dopaminergic & GABAergic pathways.

Impact on mood, behaviour and cognitions

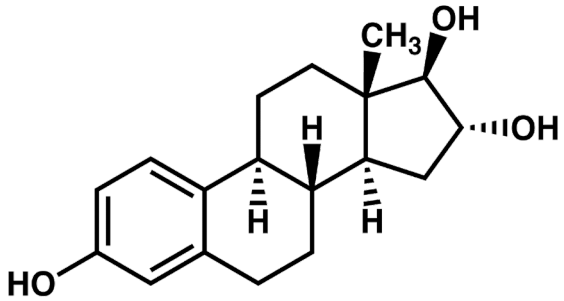
- Trauma changes the brain
- Correlation between trauma, childhood adversity and reproductive health issues e.g. polycystic ovarian syndrome (PCOS) and premenstrual dysphoric disorder (PMDD)
- Hypothalamic-pituitary-adrenal (HPA) axis is interwoven with the hypothalamic-pituitary-gonadal (HPG) axis.

So, the stress regulation axis and the reproductive functions axis **interact and impact each other.**



Kaz Cooke It's the the Menopause book, Cartoon – theaustralian.com.au

What We Know



Estrogen (E2 Estradiol)

- Has a facilitative effect on dopaminergic transmission through a variety of mechanisms, as well as serotonin and noradrenaline
- Neuroprotective and anti-inflammatory
- **Low estrogen levels are linked to reduced emotional regulation** through its effects on the dorsolateral prefrontal cortex and dorsal anterior cingulate cortex, which result in a negative mood state and an increased risk of depression. (Newhouse & Albert, 2015)

- Estrogens have a role impacting the vulnerability to stress.
- Estrogens have been used with benefit in treatment of menopausal depression, PMDD, schizophrenia.
- Also, elevated estradiol levels predicted **heightened anxiety symptoms** in women with a menstrually-related mood disorder, **especially those with a history of sexual abuse**. (Hantsoo & Payne, 2023)

What We Know: Progesterone

- GABA-A receptor modulator, anxiolytic effect, ”natures’ benzo” sleep inducing

- Levels of progesterone (PROG) and its metabolite, allopregnanolone (ALLO), increase during the luteal phase and rapidly reduce during menses, then remain low during the follicular phase.

- Allopregnanolone (ALLO), a neuroactive steroid, modulates GABAergic neurotransmission primarily through GABA-A receptors.

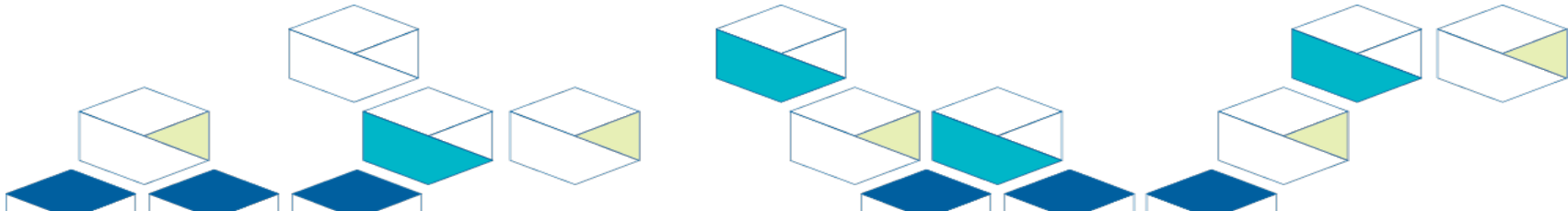
Low progesterone and altered serotonin sensitivity during parts of the menstrual cycle mean an un-steady brain state.

Brains like stability.

What We Know: Testosterone

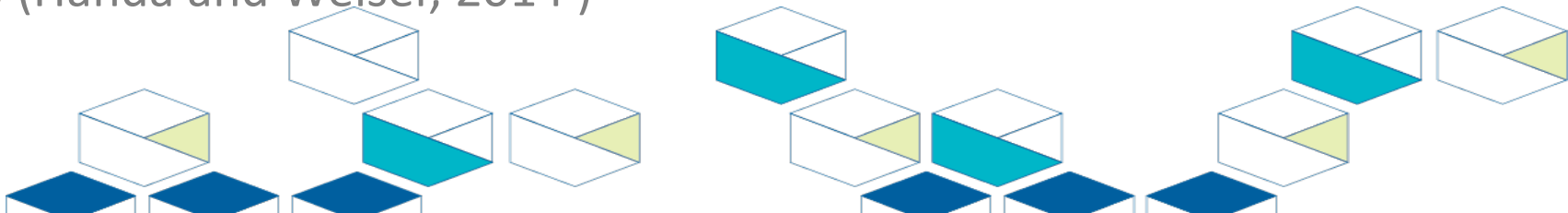
- Important in neurocognitive function, memory, visuospatial ability
- Has been shown to improve mood, motivation, libido and brain fog (Newson et al 2023)
- Sleep quality improvement
- Pivotal role in pathophysiology of major depressive disorder (MDD). Low levels associated with depression.
- Increases libido

Contraindications around Hyperandrogenemia e.g. with PCOS



Influence of Sex Hormones during Childhood and Adolescence

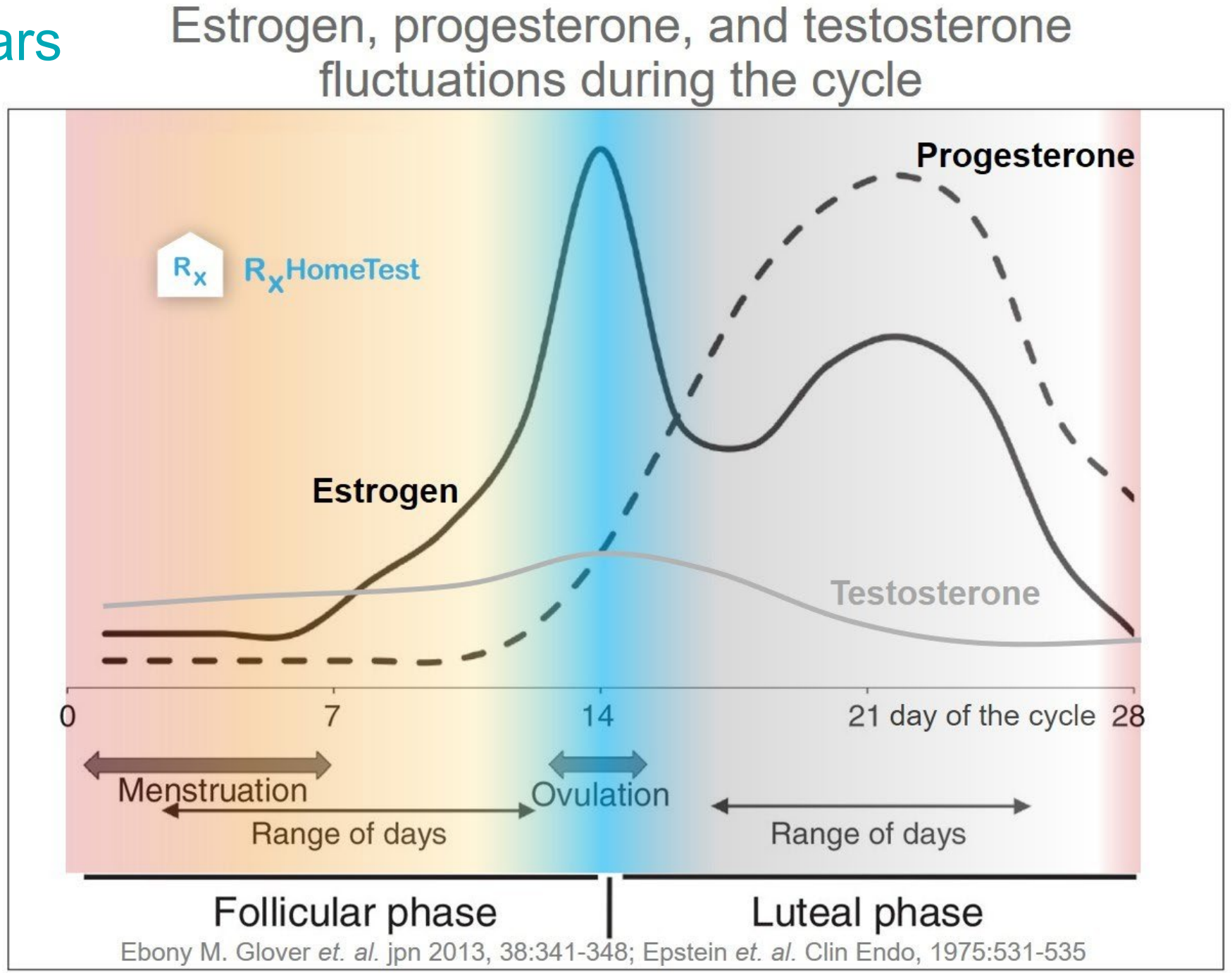
- In puberty, low baseline levels of Dopamine. Neural Pruning.
- Childhood adversity and trauma affects neural pruning and sensitivity to hormonal influences during development.
- Sex hormones during puberty have been related to increased risk of depression.
- Childhood adversities (eg CSA) predict early maturation in females.
- There is a sex dependent reaction to childhood abuse, with amplification of trauma on symptoms, possibly mediated by estrogens effects on the HPA axis. (Kulkarni, 2023) (Handa and Weiser, 2014)



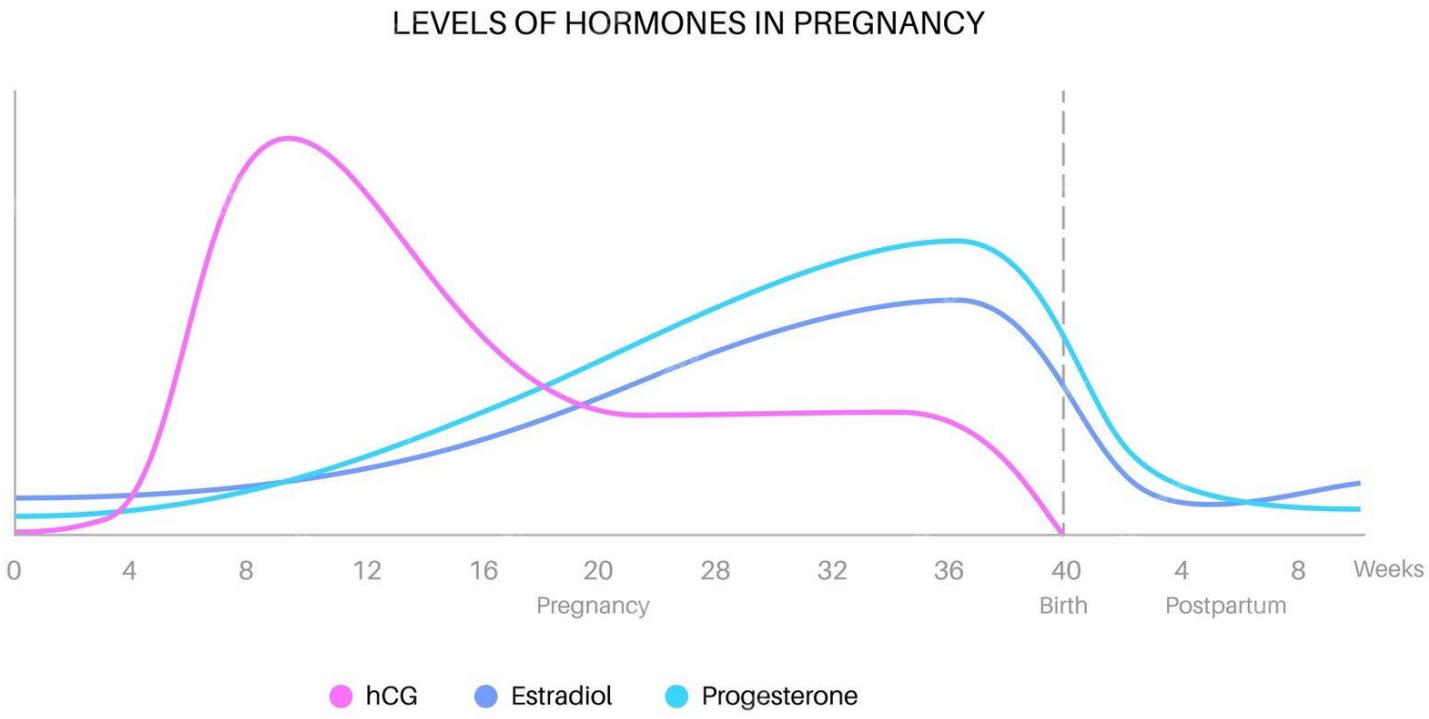
The Reproductive Years
Hormonal transitions: Menstrual cycle

Hormonal transitions, including during the menstrual cycle, impact brain structure and function.

(Bankstrom et al, 2014).

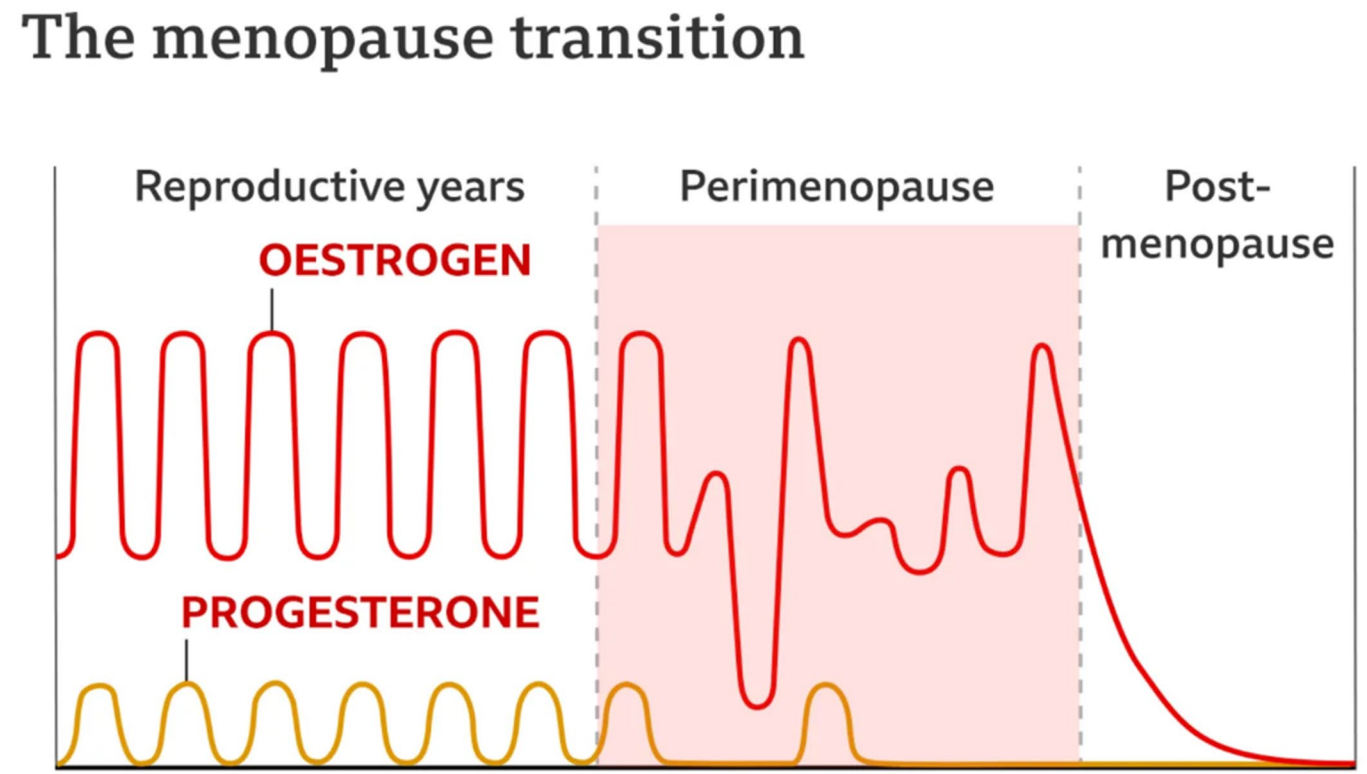


Pregnancy and Postpartum



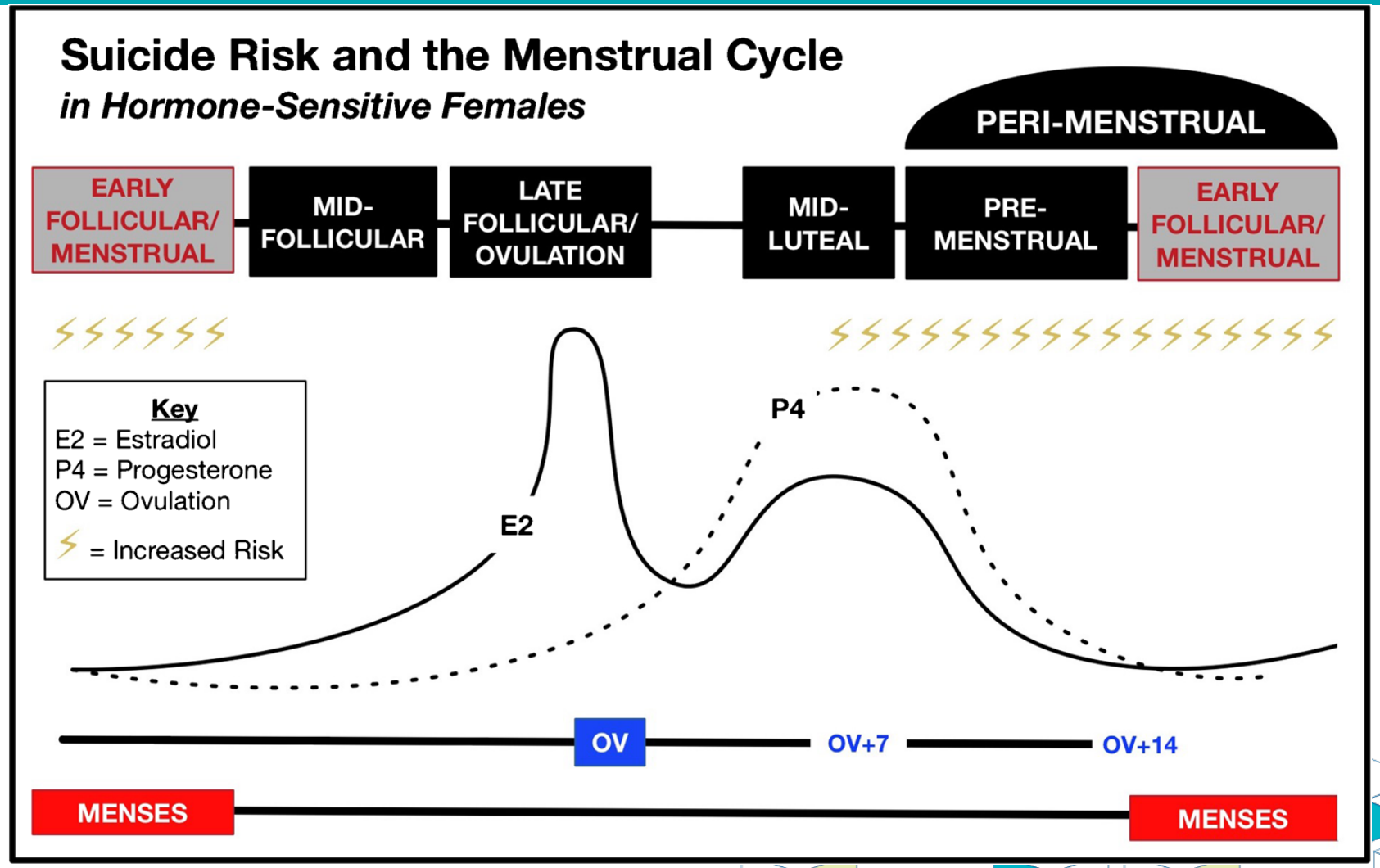
- Increased risk of anxiety, depression and psychosis.
- Birth trauma
- Post delivery – lowering of estrogen levels can precipitate return of various symptoms (e.g. ADHD, Anxiety, Depression, OCD, Psychosis),
- Coincides with a large shift in role and life demands, significantly worsening functioning – high risk of PND/anxiety.

Perimenopause and Menopause



[BBC link]

Suicide Risk and the Menstrual Cycle – an Ode to estrogen



- PMDD
- ADHD
- Schizophrenia
- PTSD
- BPD

Sarah A. Owens & Tory Eisenlohr-Moul 2018

Hormonal Contraception

1. **the “chemical menopause”**

2. Increases depression, suicidality and self-harm in a significant proportion of women.

3. Synthetic ethinylestradiol is 100 - 200fold more potent than natural estradiol.

Take a thorough history - *It is important to identify women with history of PMDD or other mood disorders when providing contraceptive counselling.*

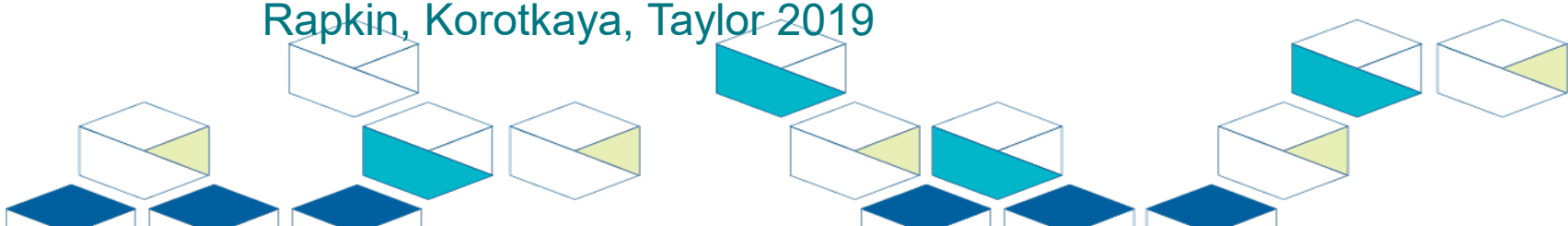
Ask about -

1. *severe premenstrual symptoms,*
2. *PMDD,*
3. *mood or anxiety disorder (current or past),*
4. *postpartum depression,*
5. *sensitivity to progestins*
6. *prior use of antidepressants.*

*- Those with **risk factors** should undergo a more thorough current and past psychiatric history*

*- **Encourage reporting new or worsening** mood symptoms during counselling.*

Rapkin, Korotkaya, Taylor 2019



Hormonal Treatments

"Hormonal Problems do well with Hormonal Treatments"

1. First line: PMDD Treatment

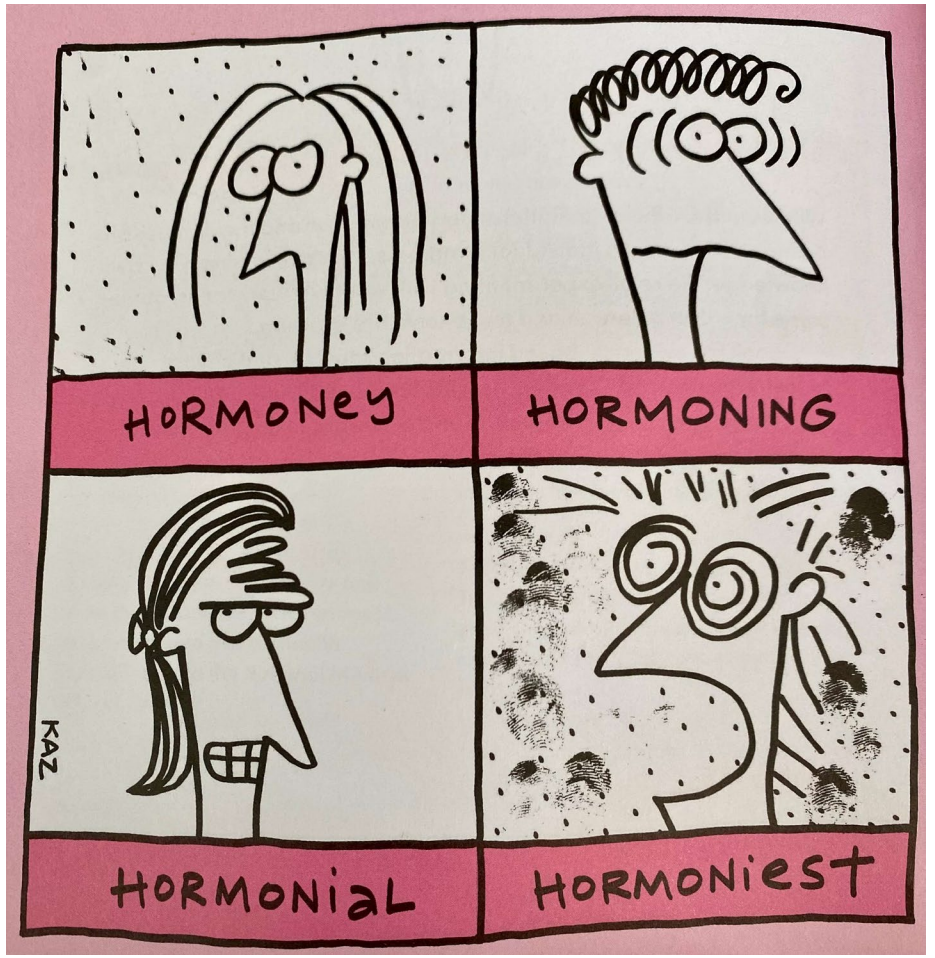
Oral Contraceptive Pill (OCP) continuous

- "Zoely" Oral Contraceptive Pill– a natural estradiol and nomegestrol acetate
- OCP plus Estradiol

2. Hormonal treatments:

Progesterone (micronized) plus transdermal estradiol

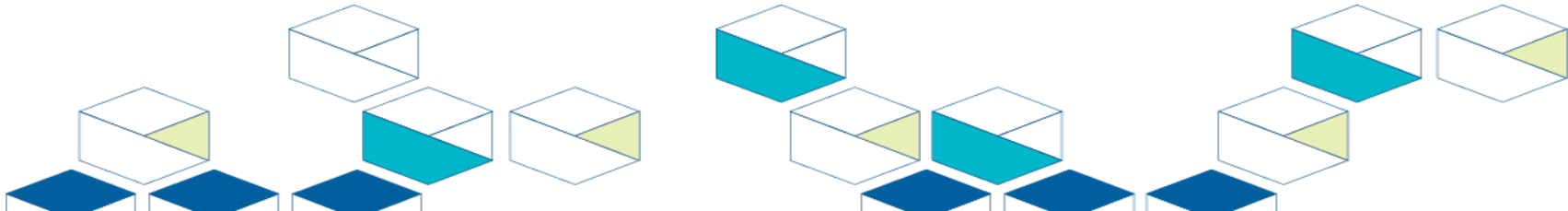
This settles the hormonal fluctuation on a central nervous system level.



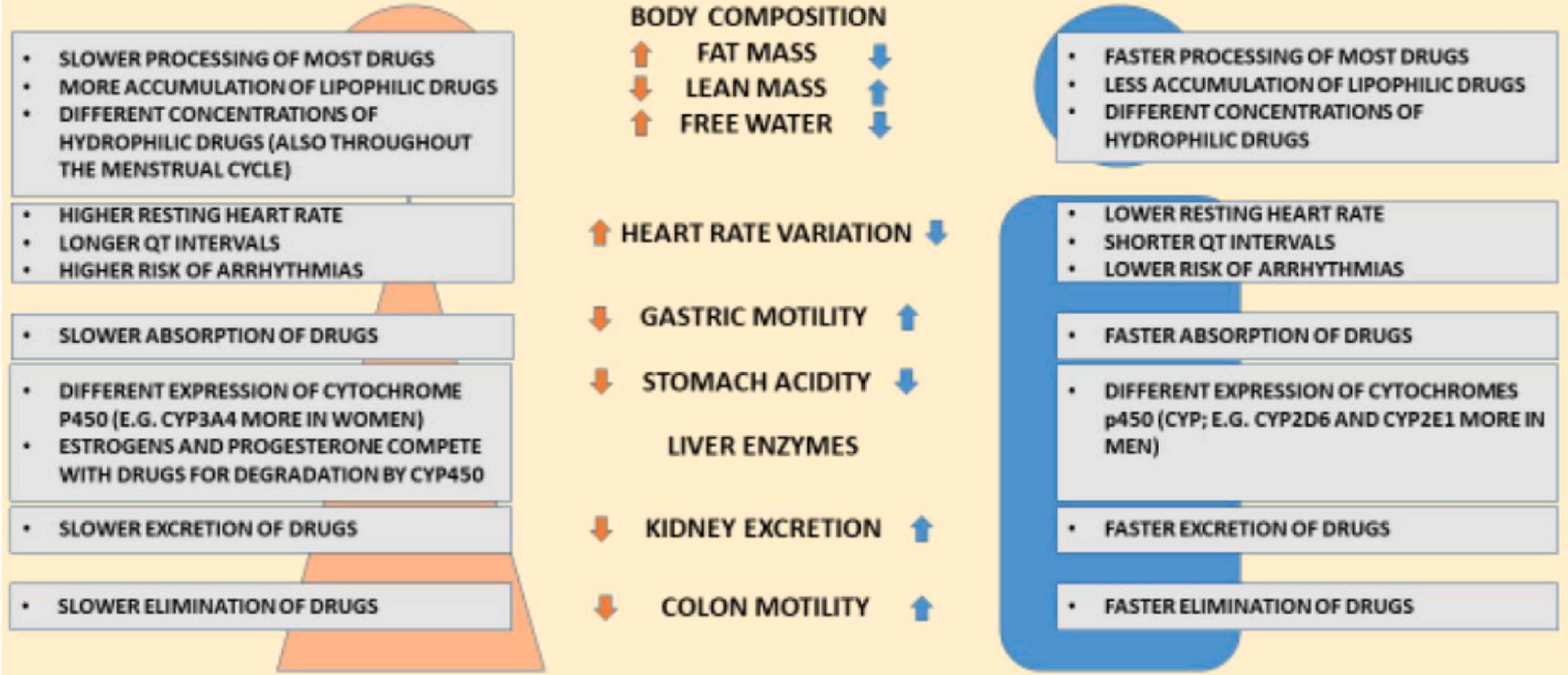
Onset of Schizophrenia and Estrogens

- Solid evidence that estrogens are one of the influencing factors in schizophrenic psychosis, impacting on brain development and functioning.
- Physiologically higher levels of estrogens may lead to slightly lower overall incidence and later age of onset, with second peak after menopause.
- Lower levels of estrogen when premenstrual, and after menopause – more severe symptoms.
- Patients with developing psychosis may have hypothalamic - pituitary-gonadal dysfunction with low production of estrogens and testosterone.

Kulkarni 1996



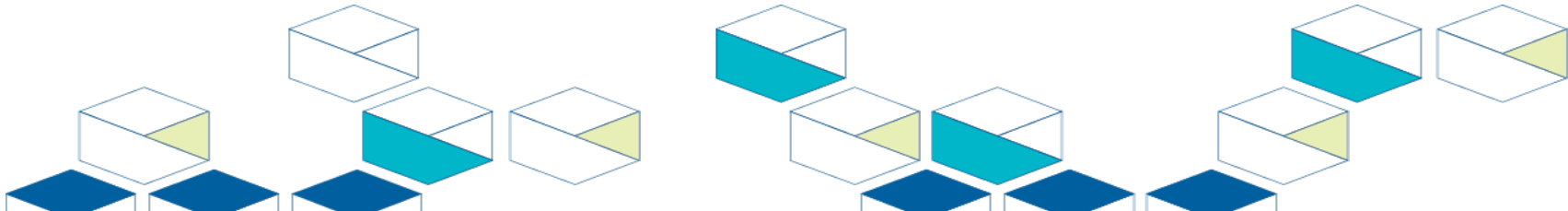
SEX DIFFERENCES IN DRUG PROCESSING



Women tend to have smaller body size and more fat tissue than men, which affects drug distribution, and smaller kidneys, which leads to slower drug elimination. Liver enzymes may behave differently because of oral contraception and some hormone therapy. Women's heart rhythms are different from men's (longer Q-T interval), which makes women more susceptible to fatal heart disturbances, called arrhythmias.

Factors to ask about when you assess women

1. **Exposure to** domestic, family and sexual violence and trauma.
2. Place in the **reproductive life cycle –** impact on them?
3. Any female/gender related **comorbidities**
4. Periods of increased risk and **populations** at increased risk



Hormonal Sensitivity: Relation to Reproductive Events

PMS/PMDD
Depression and the oral contraceptive pill
Postnatal depression
Perimenopausal depression
Emotionally unstable personality disorder/complex PTSD
Relapses of psychosis related to estradiol fluctuations

FIONA STANLEY FREMANTLE HOSPITAL GROUP

WOMEN'S MENTAL HEALTH REPRODUCTIVE HISTORY

SURNAME	UMRN	
GIVEN NAMES	DOB	GENDER
ADDRESS		POSTCODE
	TELEPHONE	

Staff name: _____ Delegation: _____ Ward: _____

Menstrual? ☐ Yes ☐ No – please move to Menopausal section

Menstrual cycle *Tick relevant box.*	☐ Regular ☐ Irregular ☐ Amenorrheic ☐ Unsure If irregular – ☐ Primary ☐ Secondary	
	Date of last menstrual cycle?	
	Cycle duration?	
	Length of menstruation?	
	Flow? (rate 1-5) *Scale: 1. Mild …5. Severe*	
	Pain? (rate 1-5) *Scale: 1. Mild …5. Severe*	If dysmenorrhea – ☐ Primary? ☐ Secondary?

Premenstrual symptoms *Indicate duration.*	Emotional Symptoms	
	Physical Symptoms (e.g. headache, fatigue, joint or muscle pain, weight gain, breast tenderness, acne).	
	Suicidal thoughts	
	Impact on function (rate 1-5) *Scale: 1. Minimal …5. Severe*	

Menopausal	**Perimenopausal?** ☐ Yes ☐ No ☐ Unsure **Postmenopausal?** ☐ Yes ☐ No ☐ Unsure **Menopausal?** ☐ Yes ☐ No ☐ Unsure If experiencing symptoms related to peri / post menopause, detail below and note frequency: Physical: Vasomotor: Mood: Genitourinary:

Pregnancy history	**Is the patient pregnant?** ☐ Yes ☐ No ☐ Unsure				
	Is the patient postpartum *(up to 12 months)*? ☐ Yes ☐ No **If yes, was the outcome of this pregnancy a live birth?** ☐ Yes ☐ No				
	Is the patient currently breastfeeding and/or lactating? ☐ Yes ☐ No				
Previous pregnancies	Year	Duration	Outcome	Complications	Mental Health
Date	Name			Signature	

1. **Orientation provided with every RMO** term on how to use the form, trauma informed approach to taking a reproductive history.

2. **Prompts for further enquiry** and investigation, referral to in-house GP, psychoeducation, cycle tracking –
   - Amenorrheic ▢
   - Irregular ▢
   - Unsure ▢

THANK YOU FOR YOUR ATTENTION

Dr Kiri von Klier, M.D

Child and Adolescent Psychiatrist and Psychotherapist
(Germany)
Clinical Research Lead - Mental Health
South Metropolitan Health Service

Specialist in Women's Mental Health
Cockburn Health- Women's Mental Health Service

Adjunct Senior Clinical Lecturer
University of Western Australia (UWA)

Honorary Research Associate
The Kids Research Institute, Perth Children's Hospital