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The Female Gut Microbiome: Lessons through life

Dr Emily Prpa PhD MSc

In this session

The Female Gut Microbiome

- Changes through the life course

Female Sex Hormones

- Gut microbiome interactions

Key Life Stages

- Fertility
- Menopause

Take-Home Messages

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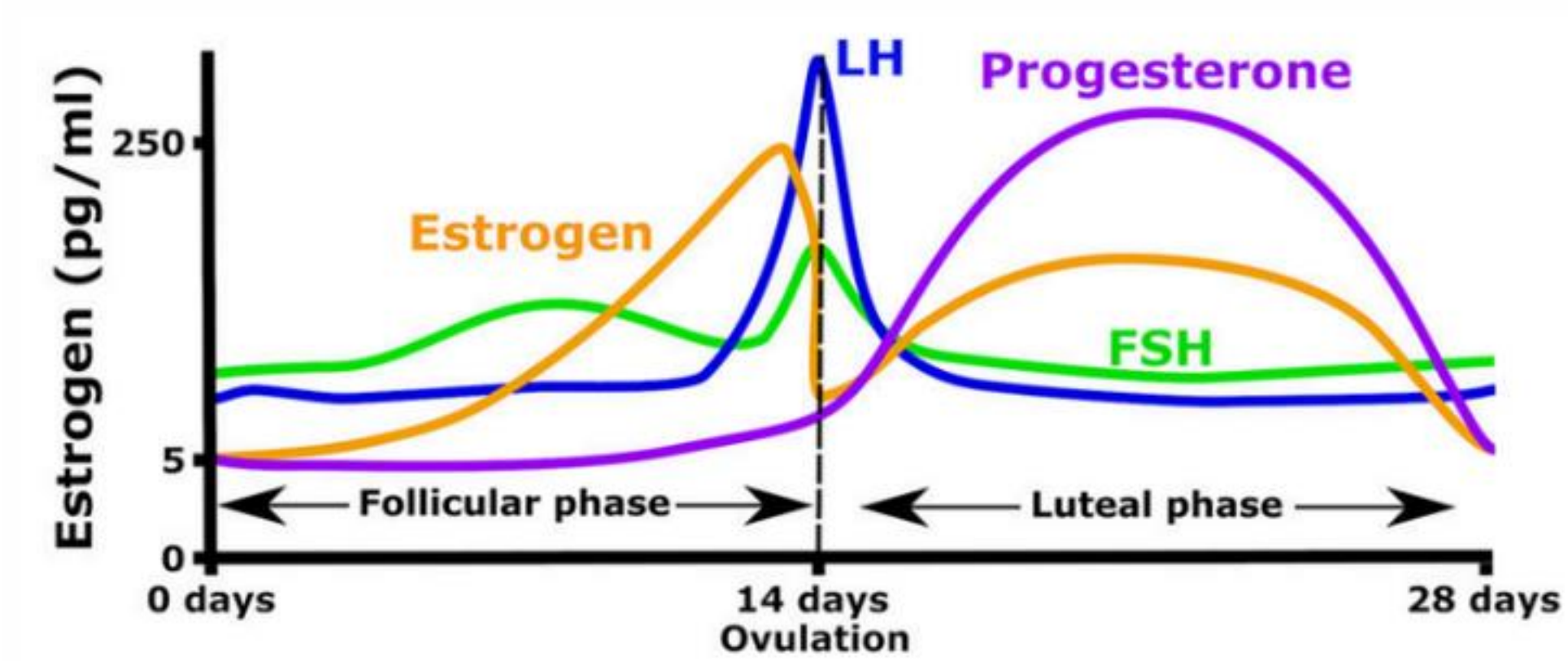
MIND THE GAP

THE INNER POWER

Female hormone fluctuations



Chidi-Ogbolu & Baar (2019) *Front Physiol*, 9: 1834.

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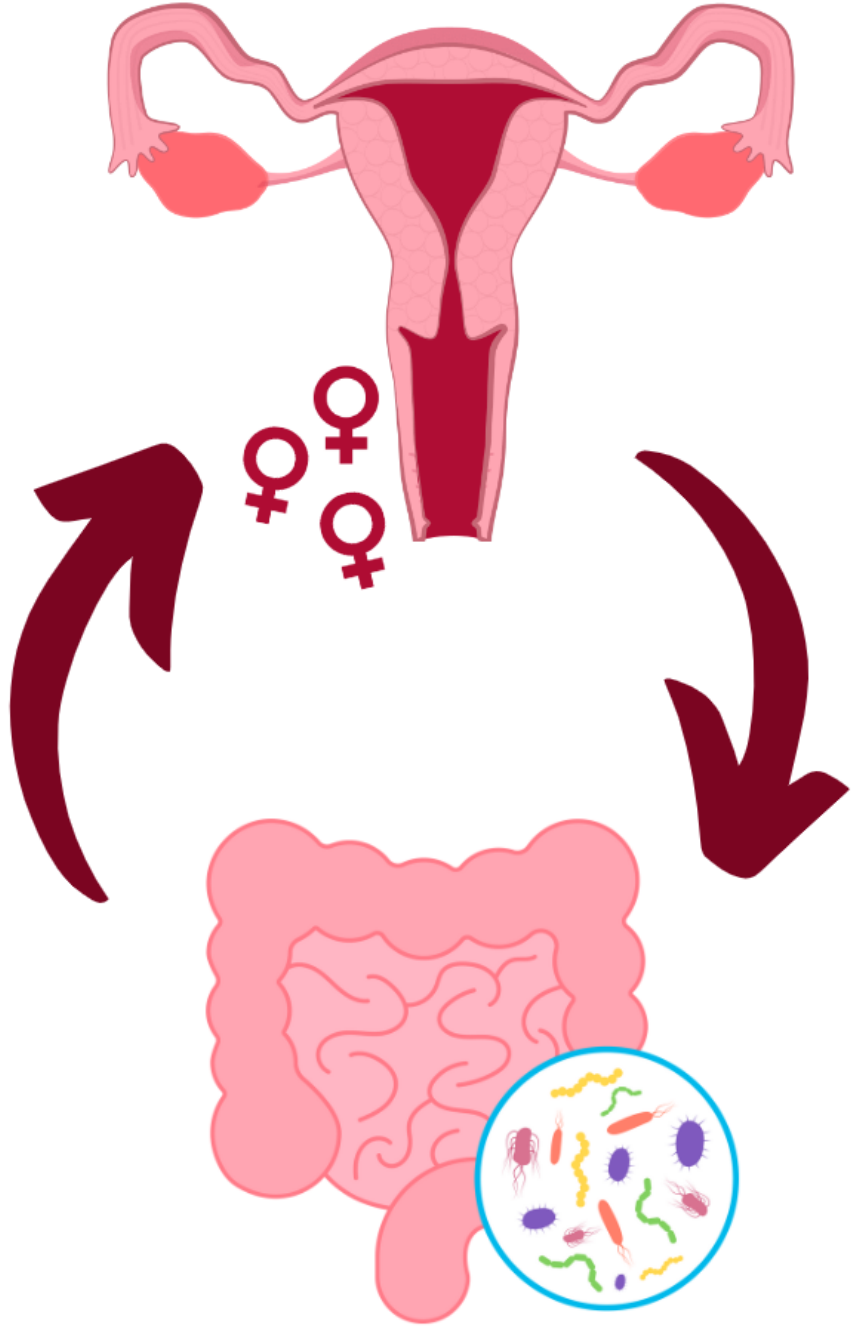
The Oestrobolome

- A unique collection of microbes within the gut microbiome, capable of metabolising and regulating circulating oestrogen levels.
- ‘Recycles’ oestrogen by enabling it to re-enter circulation.
- This reactivation of oestrogen is achieved via excretion of the beta-glucuronidase enzyme which is produced by certain types of gut bacteria, e.g., *Bacteroides* and *Firmicutes.*



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Battle of the sexes

“Microgenderome”

Refers to the sex-related differences in the gut microbiota, and how they interact with sex hormones and the immune system.

Vemuri et al. (2019) *Semin Immunopathol* 41(2): 265–275.

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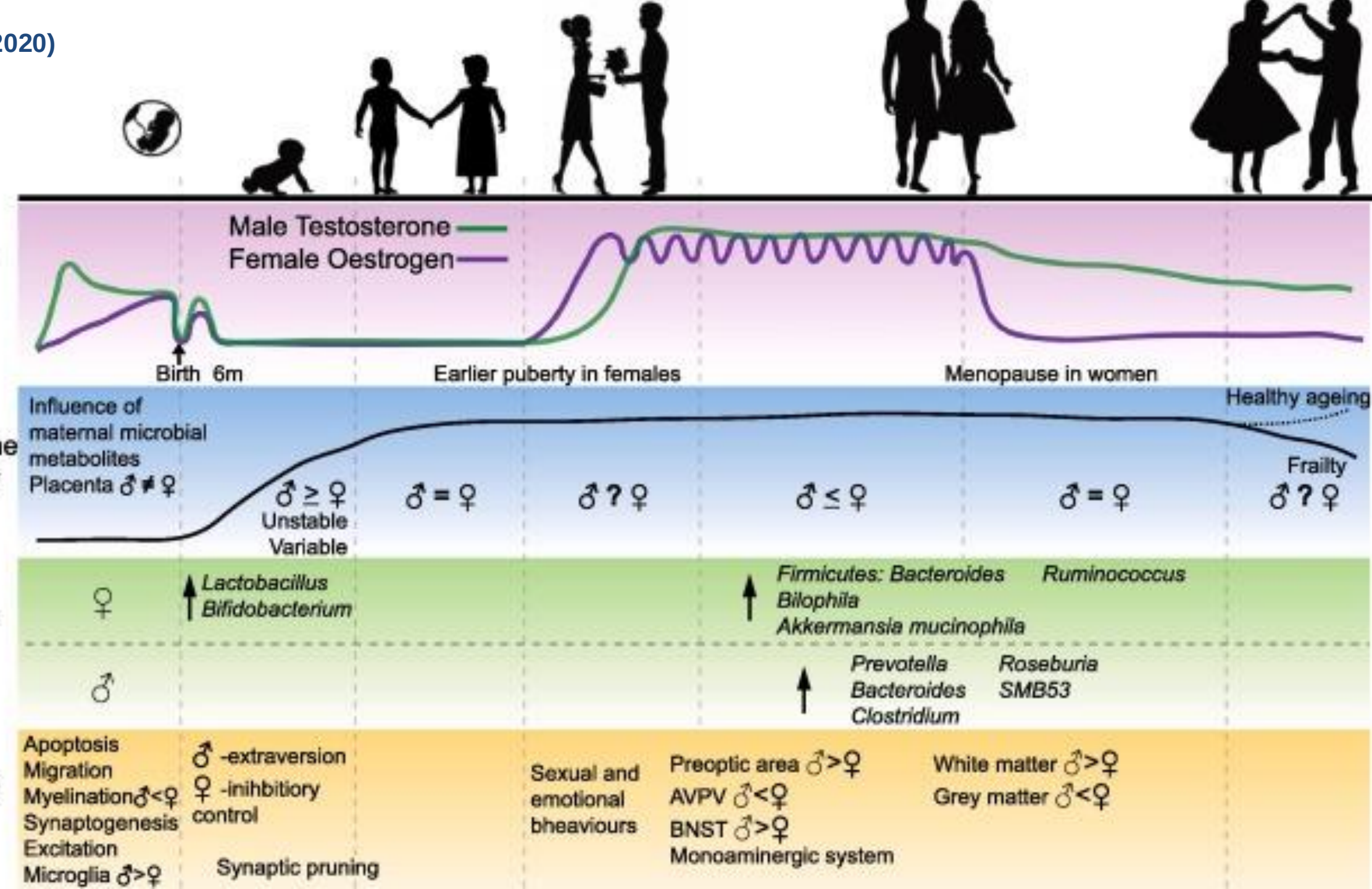
Jagger et al. (2020)



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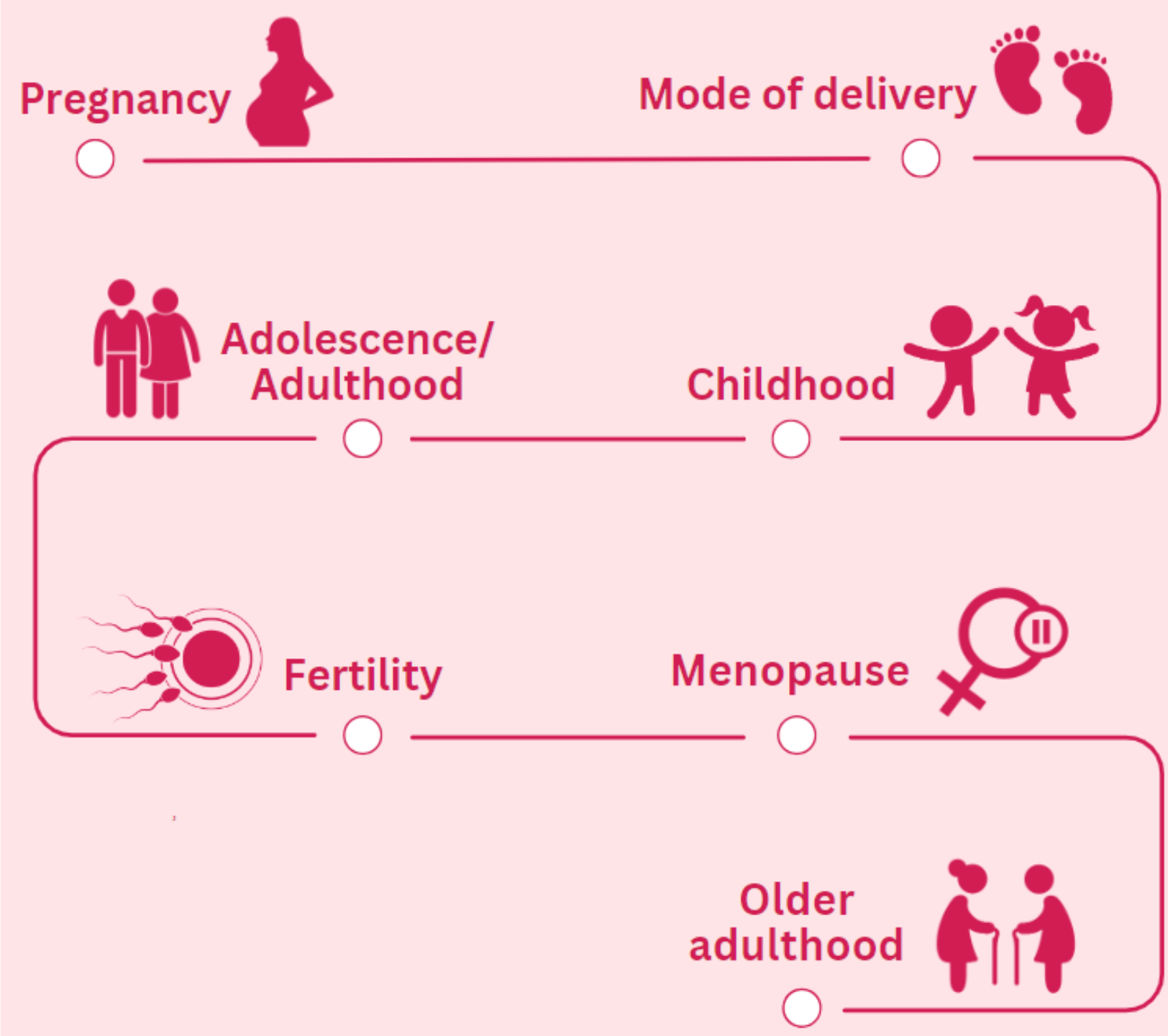

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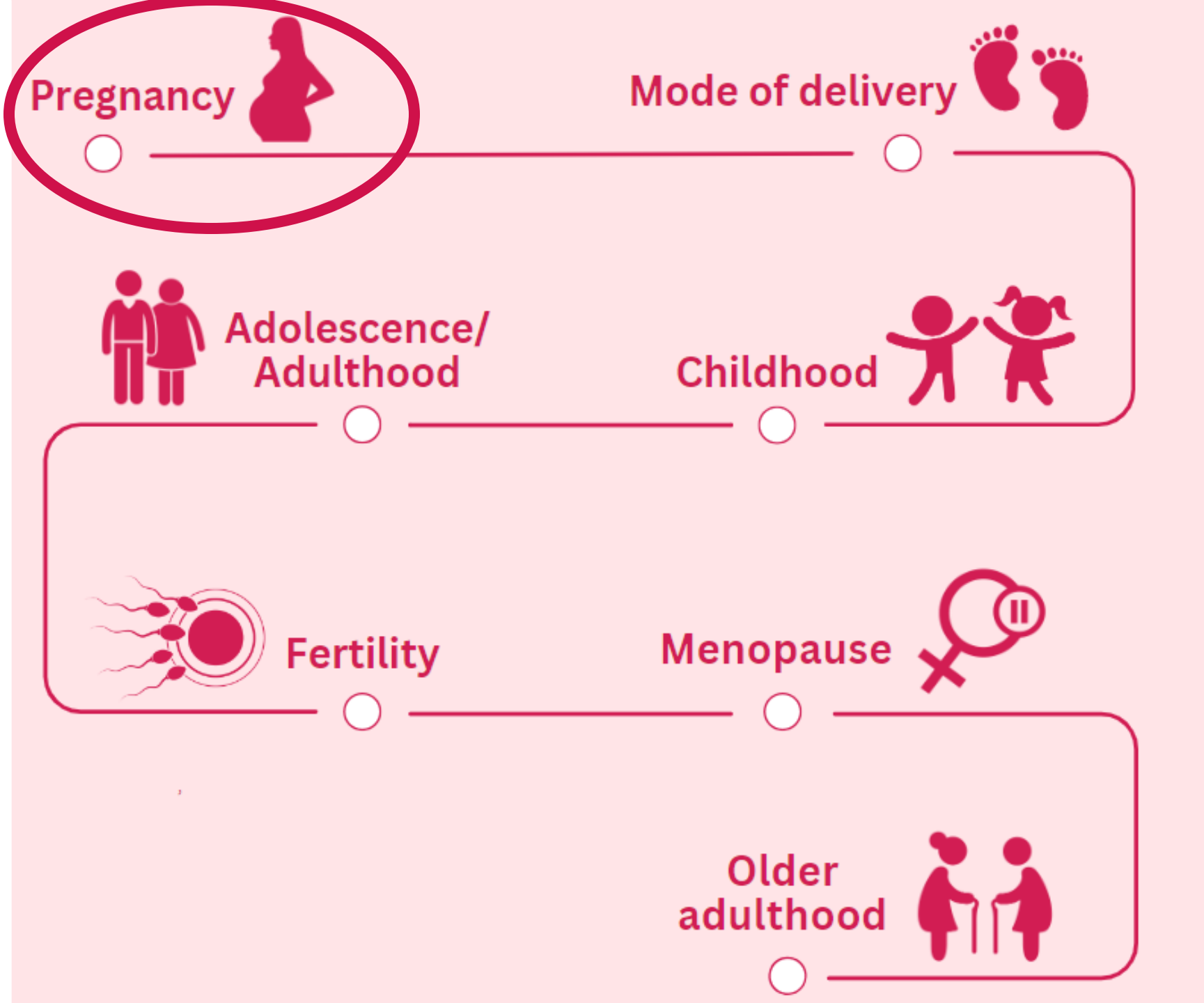

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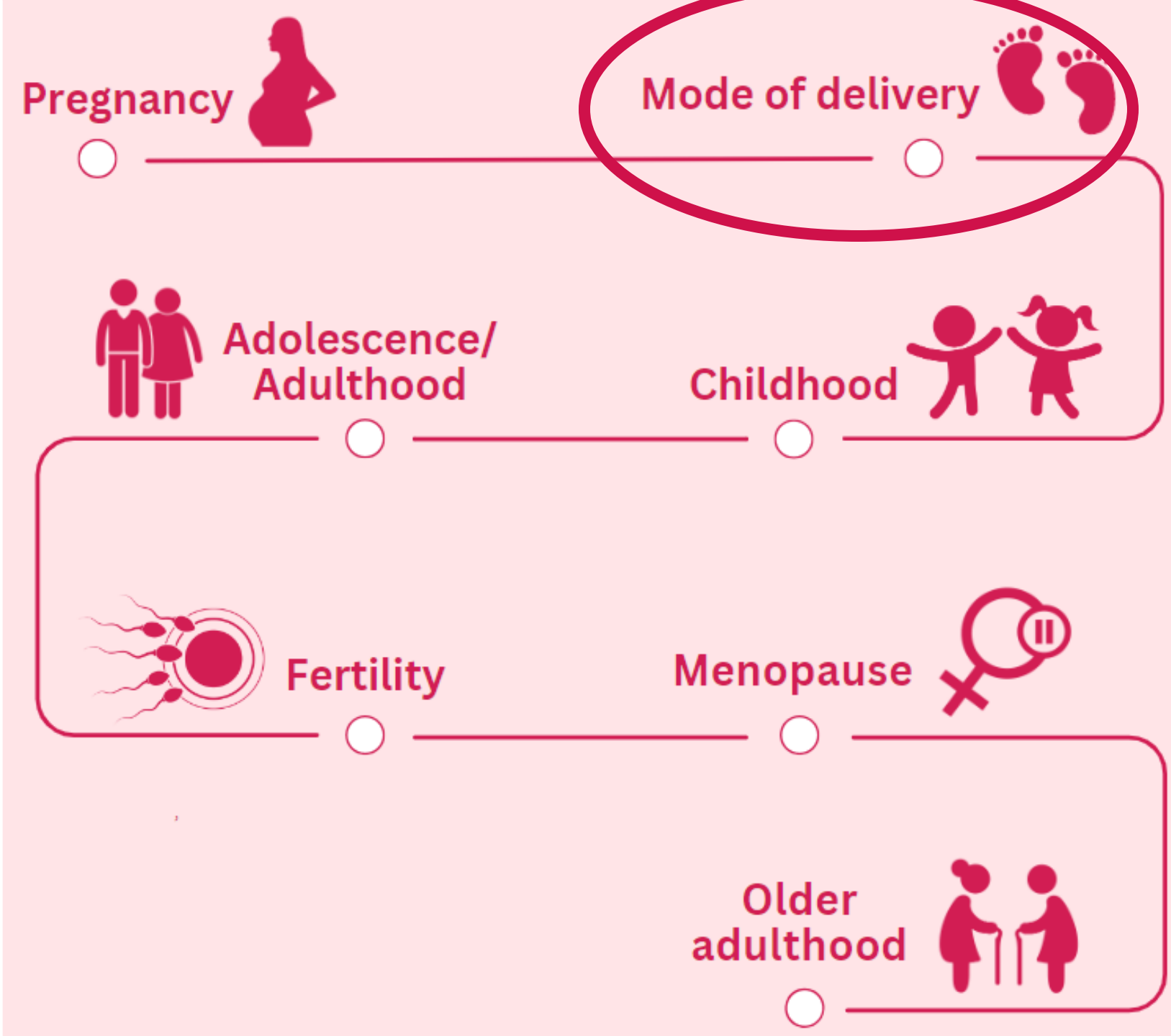

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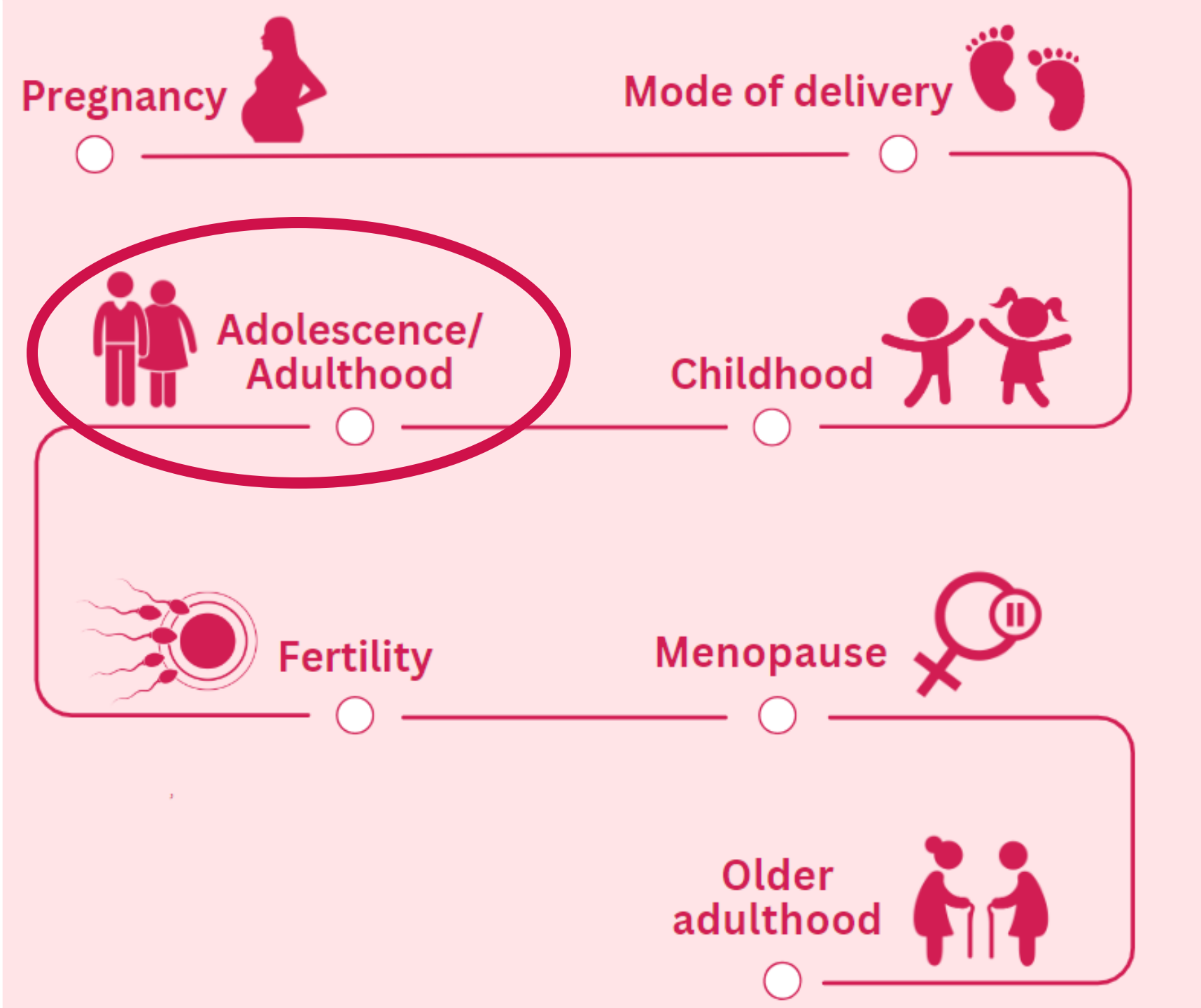

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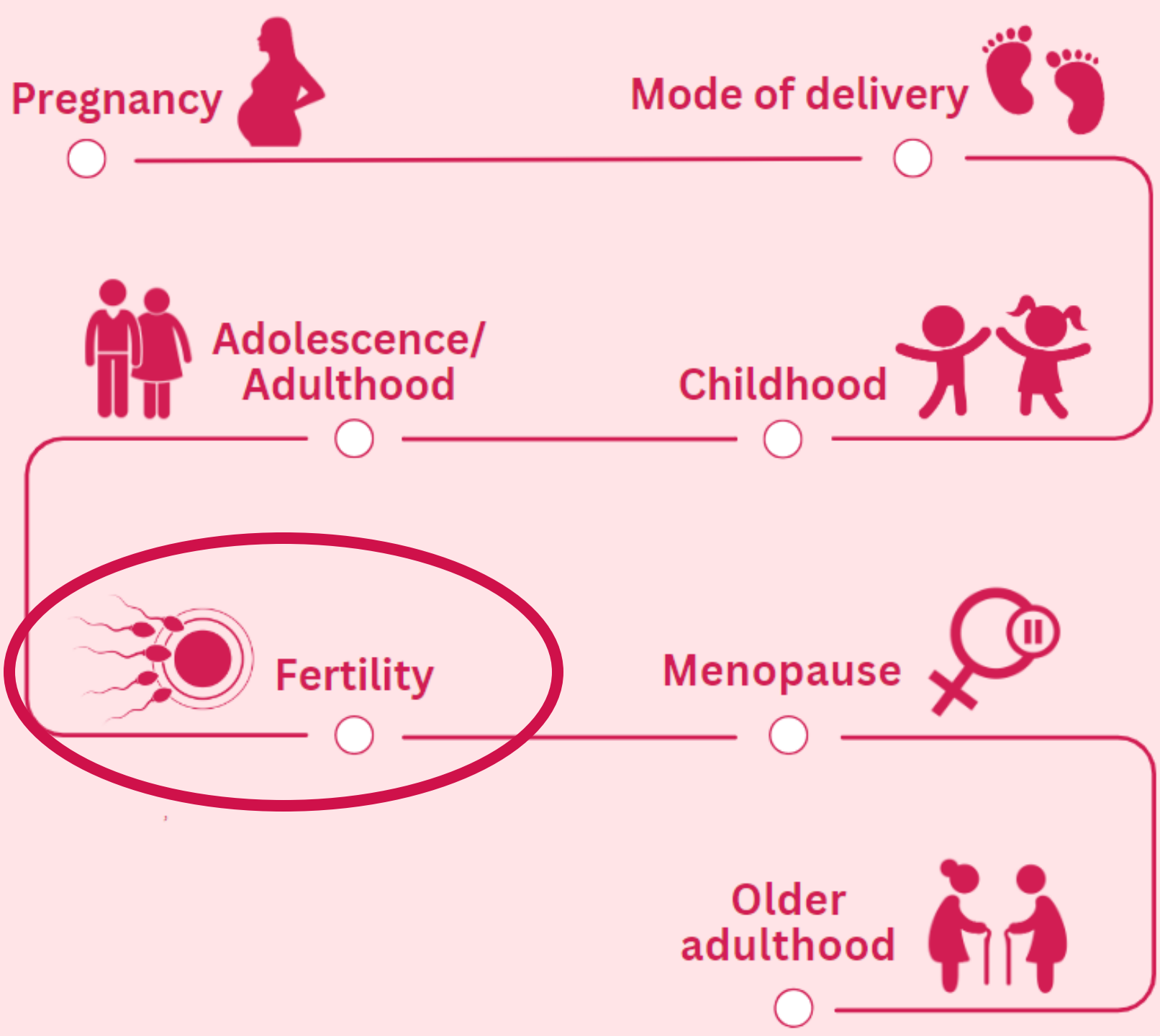

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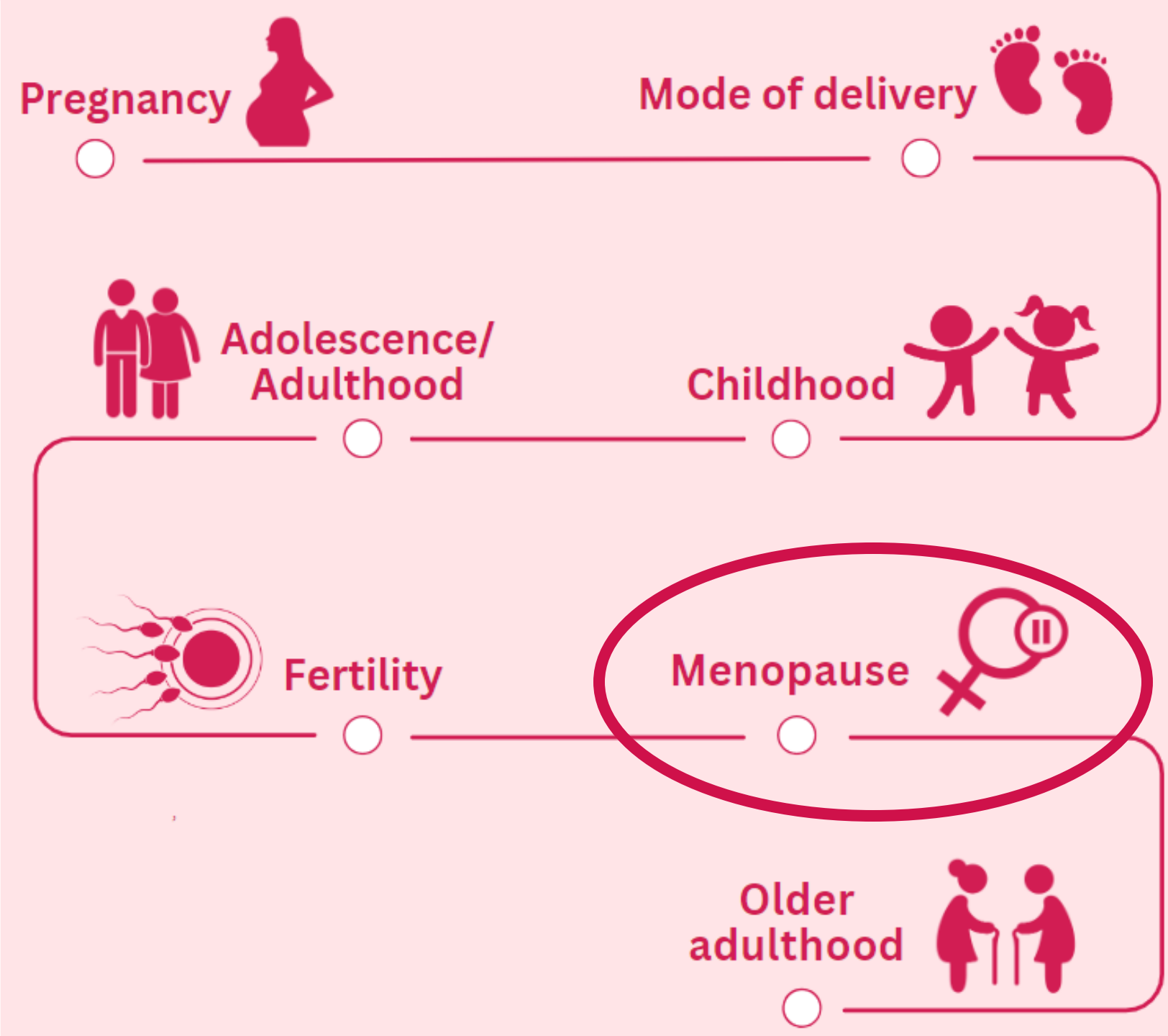

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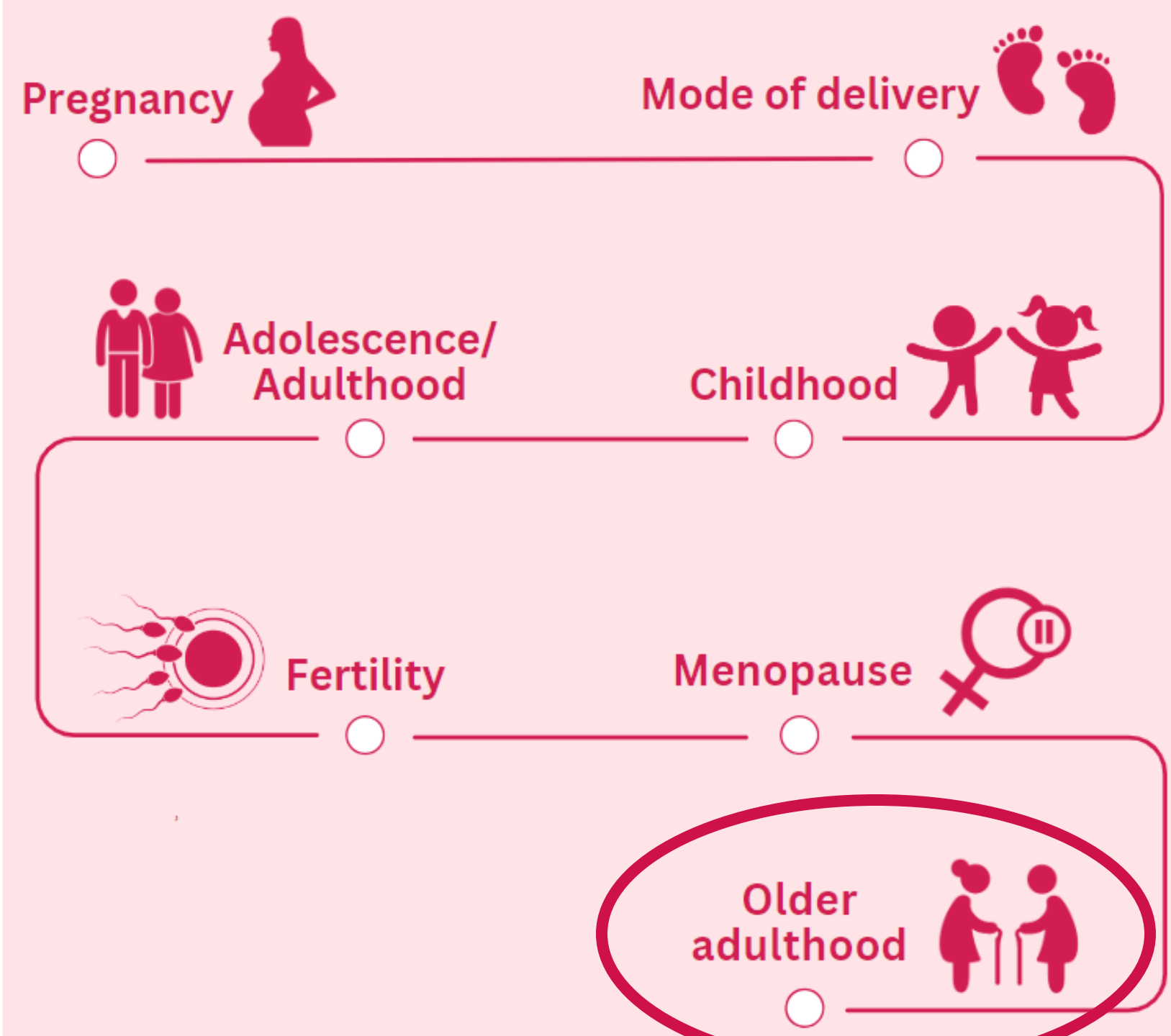

REPRODUCTIVE HEALTH

The ability to conceive. Diet & lifestyle factors can affect fertility.

FERTILITY

The inability to become pregnant after 12+ months of regular unprotected sex.

INFERTILITY

Unable to conceive following a successful pregnancy.

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FEMALE INFERTILITY & GUT MICROBIOME

- **Gut dysbiosis** can promote **inflammation** and immune dysregulation which can influence reproductive health.
- Gut **dysbiosis** has been linked to both **male** and **female infertility**.
- A **causal** link between dysbiosis and infertility is **not established**.

- The gut microbiota has been implicated in conditions such as **PCOS** and **endometriosis** which are **risk factors** for **infertility**.

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Probiotics

PCOS

- Worldwide 8–13% of reproductive-aged women affected with 70% undiagnosed.
- Lower levels of lacotobacilli and bifidobacteria observed.
- SRMAs conclude probiotics and synbiotics can have a positive effect.
- Different strains may support different symptoms.
    - Improve testosterone levels, inflammation, metabolic parameters.

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Li et al. (2023) *Crit Rev Food Sci Nutr* 63(4): 522–538.
Angoorani et al. (2023) *Front Med* 10: 1141355.
Cozzolino et al. (2020) *Eur J Nutr* 59(7): 2841–2856.
Calcaterra et al. (2023) *Nutrients* 15(14): 3144.
Mukherjee et al. (2023) Metabolites, 13(1), 129.

Probiotics

Endometriosis

- 10% (190 million) of reproductive age women and girls globally, and up to 50% of women who are infertile.
- Oestrogen levels, immunity or inflammation which are modulated, at least in part, by the gut microbiota, may play a role.
- Limited research suggests the beneficial effects of *Lactobacillus* administration on endometriosis-related pain.

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Qin et al. (2022) *Front Cell Infect Microbiol* 12: 1069557.
Salliss et al. (2021) *Hum Reprod Update* 28(1): 92–131.
Jiang et al. (2021) *Int J Mol Sci* 22(11): 5644.
Khodaverdi et al. (2019). *Int J Fertility & Sterility* (3):178.

Postpartum Depression

- 10-15% of women suffer from PPD.
- Maternal depression is very complex and is influenced by various bidirectional factors.
- Differences in gut microbiota are evident between pregnant women with PPD and those without PPD.
- Microbial-derived metabolites including those associated tryptophan metabolism are altered.
- Limited but promising evidence shows the effectiveness of microbial-related therapies to reduce PPD.

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Zhang et al. (2023) *Ann Gen Psychiatry* 22(1), 36.
Liu et al. (2020) *J Agric Food Chem* 68(47): 13697–13710.
Halemani et al. (2023). *J Global Health*, 13.
Desai et al. (2021). *Front in psychiatry*, *12*, 622181.

Gut-Vagina Axis

The World's Largest Citizen Science Study Into The Vaginal Microbiome

In Belgium, over 6000 women have already registered to take part.

STUDY HIGHLIGHTS

Largest study on vaginal microbiome in the world!

Over

6000

women participated in Isala

We found

10 types

based on the most important bacteria

80%

has mainly lactic acid bacteria

2000

Already more than 2000 cultured vaginal bacteria, and still counting

High-tech analysis of nearly

4500

swabs, and still counting

Determination of factors influencing the vaginal microbiome

Let's go international with sisterhood projects

LAURA

Inspired by isala.be

MARIE

Inspired by isala.be

Base for novel diagnostics and therapeutics

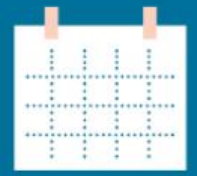
Awarded for clear science communication

INFLUENCING FACTORS

Your age and stage of life

Use of period products

Use of hormonal contraceptives



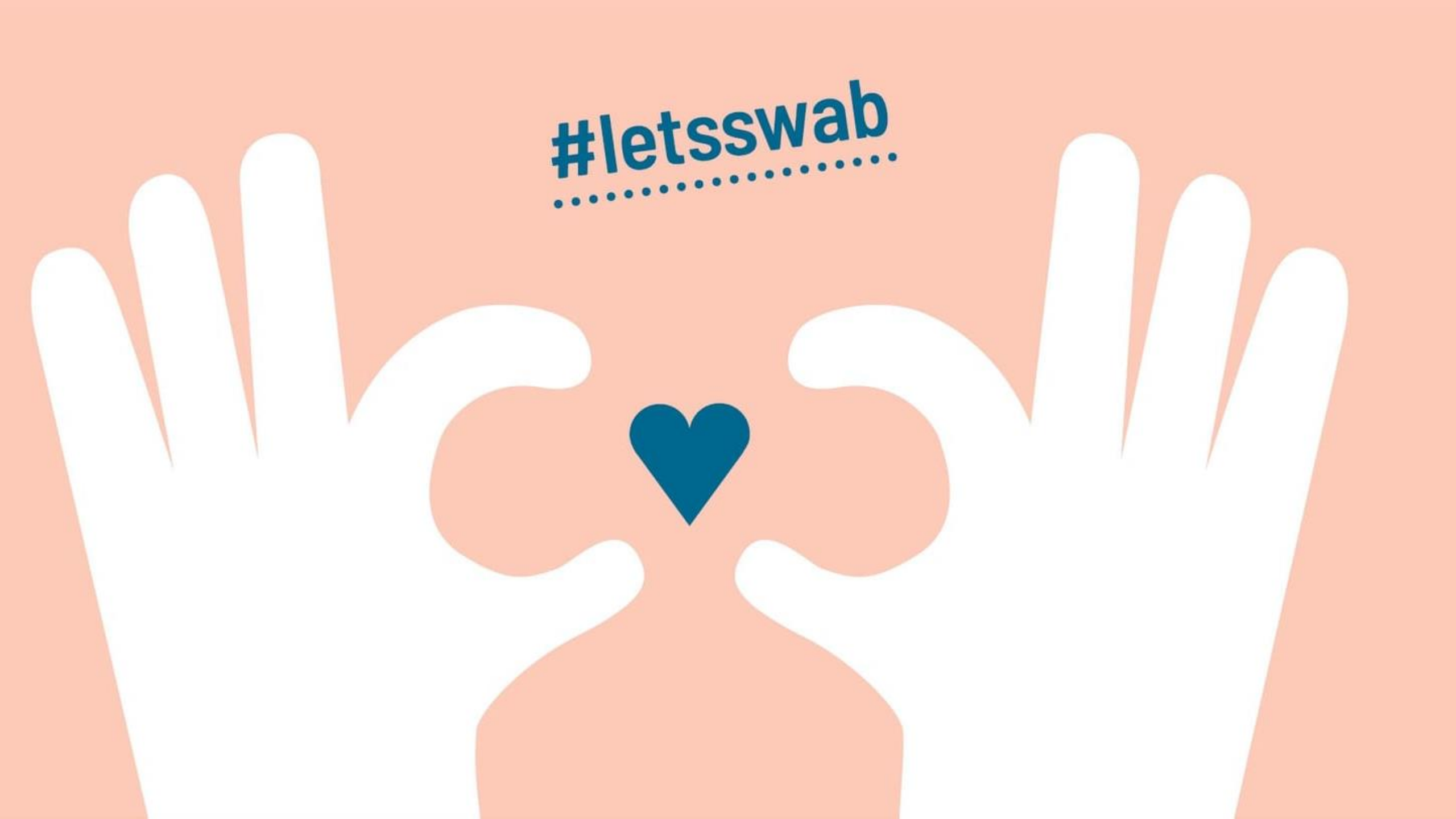
The natural course of your menstrual cycle

Whether you have children or not

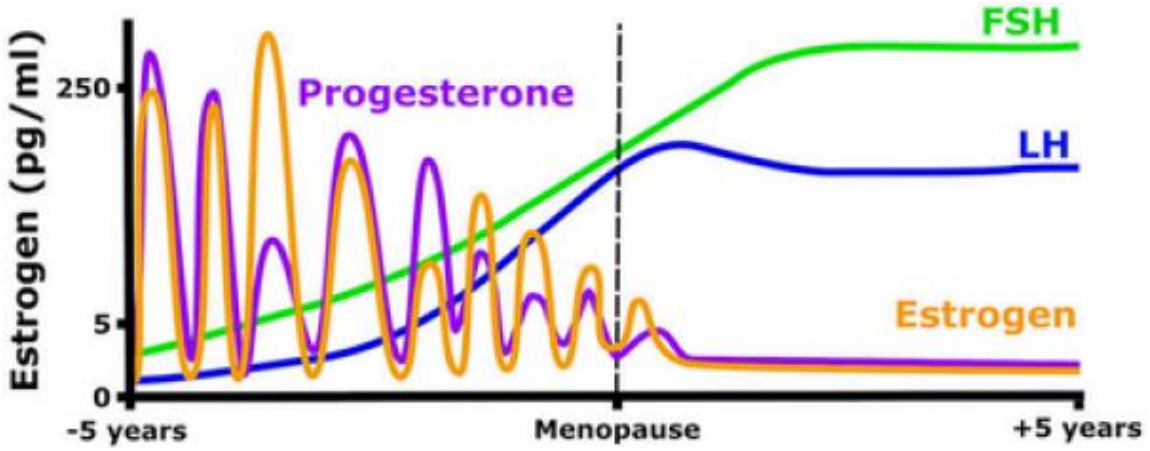
Sexual activity

Some foods and drinks have a positive impact...

.... others appear less positive


#letsswab

MENOPAUSE



Chidi-Ogbolu & Baar (2019) *Front Physiol*, 9: 1834.

Perimenopause

The transition to menopause, characterised by erratic menstrual cycles.

Menopause

Absence of menses for 12 consecutive months, marking a significant change to hormones.

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MENOPAUSAL SYMPTOMS

Irregular menstrual cycles

Hot flushes

Sleep disturbances

Incontinence

Low mood

Night sweats

Muscle and joint pain

Sexual dysfunction

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MENOPAUSE & GUT MICROBIOME

Postmenopausal women have **lower** gut microbiome **diversity**.

The gut microbiome becomes **more similar** to the **male** gut microbiome.

Decrease in **short-chain fatty acid** (SCFA) producing bacteria.

Via the **oestrobolome**, gut microbes can **reactivate** and help retain sex hormone levels in postmenopausal women.

Research suggests **HRT** reduces gut microbiota **dysbiosis**.

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Probiotics Post-menopause

- **SRMA**: Overweight and obese postmenopausal women. Probiotics supplementation reduced insulin, HOMA-IR and TNF-α.

  Li et al. *Probiotics Antimicro* 15.6 (2023): 1567-1582.

- **RCT** (n=66): 6-week probiotic yoghurt intervention significantly lowered anxiety and stress scores, but not sleep quality.

  Shafie et al. *Nutrition ESPEN*, *50*, (2022) 15-23.

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Randomized Controlled Trial > Int J Food Sci Nutr. 2022 Aug;73(5):693-704.
doi: 10.1080/09637486.2022.2048360. Epub 2022 Mar 9.

Effects of prebiotic-rich yogurt on menopausal symptoms and metabolic indices in menopausal women: a triple-blind randomised controlled trial

Mehrnaz Shafie [1], Aziz Homayouni Rad [2], Mojgan Mirghafourvand [3]

Over 6 weeks, 100 g of prebiotic-rich (inulin) yogurt daily improved:

- Menopausal symptoms ($p < 0.001$)
- Anxiety scores ($p < 0.001$)
- Depression scores ($p = 0.003$)
- Vasomotor ($p < 0.001$)
- Low-density lipoprotein ($p = 0.028$)

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By 2039 there will be ~1.2 billion menopausal and postmenopausal women.

It is necessary to develop innovative strategies to improve health for what can be up to 1/3 of a woman’s life.

“MENOWASHING”

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Diet & Lifestyle Advice

Fibre-rich

Omega-3

Limit sat fat

Sleep

Exercise

Mindfulness

TAKE HOME MESSAGES

- A **bi-directional relationship** exists between the gut microbiome and female sex hormones.
- Sex hormones fluctuate throughout a woman's life. The oestrobolome is a **unique collection of microbes within the gut microbiome** which can recycle oestrogen.
- Lower gut microbiota **diversity and dysbiosis** are common features of PCOS. Emerging research highlights the potential role of probiotics and synbiotics to help treat PCOS.
- Postmenopausal women have lower gut microbiome diversity and **decreased abundance of gut microbial beta-glucuronidase**, the enzyme involved with the oestrobolome.
- **Diet and lifestyle choices** can support female health throughout life by supporting the gut microbiota.

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Female Gut Health
New Resource

Discover the relationship between the **gut microbiome** and **female sex hormones** with a focus on key life stages:

- Puberty
- Fertility
- Pregnancy
- Menopause

Email science@yakult.co.uk for a PDF or free hardcopies

Thank you

My colleagues at Yakult Group in Europe

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