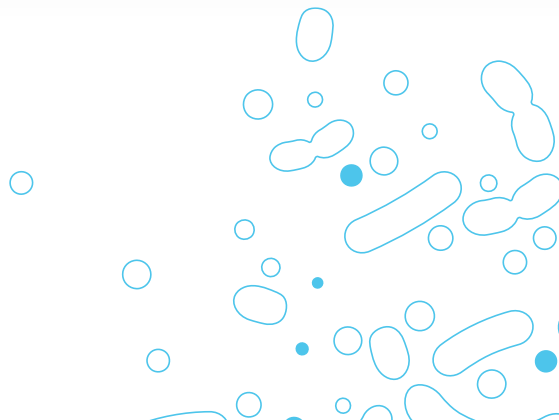


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# The Female Gut Microbiome: Lessons through life

Dr Emily Prpa PhD MSc





## In this session

### The Female Gut Microbiome

- Changes through the life course

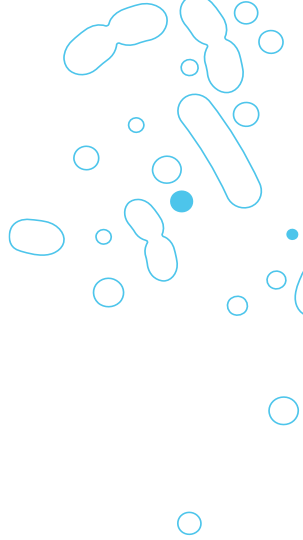
### Female Sex Hormones

- Gut microbiome interactions

### Key Life Stages

- Fertility
- Menopause

### Take-Home Messages

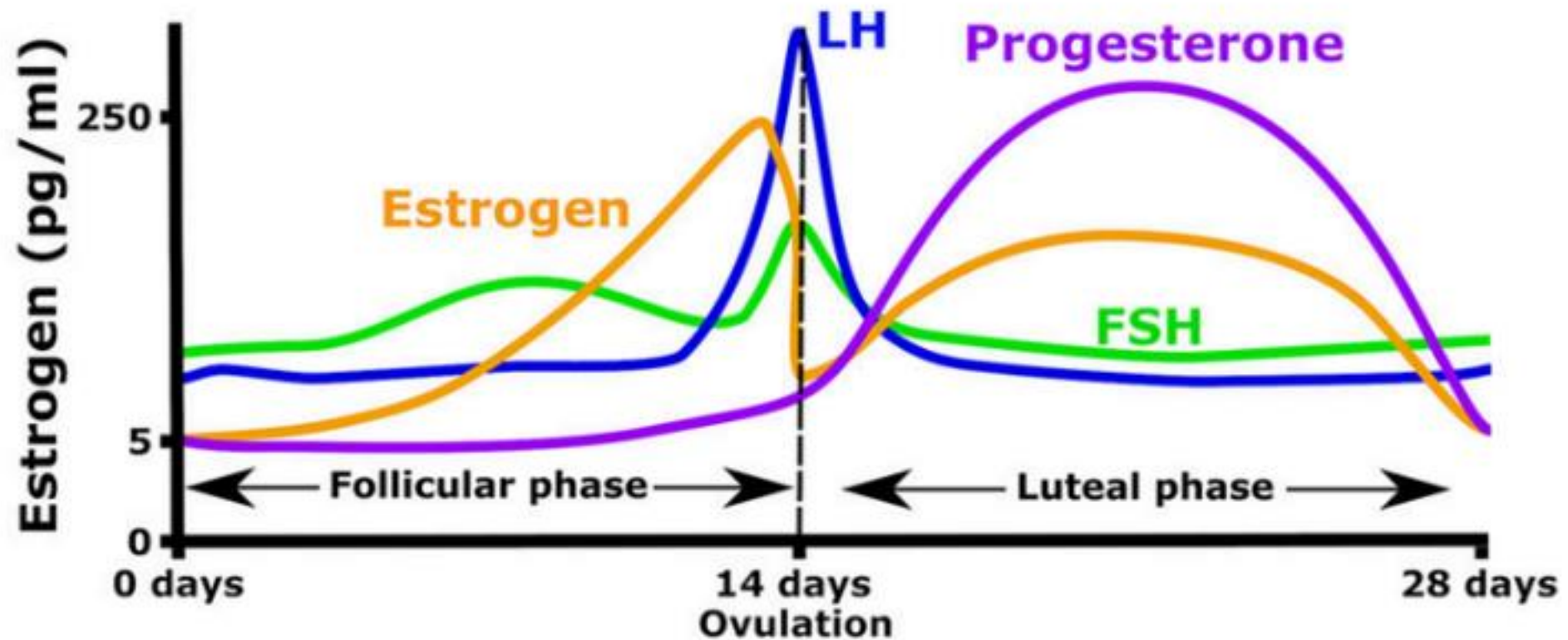




MIND THE GAP

# THE INNER POWER

Female hormone fluctuations



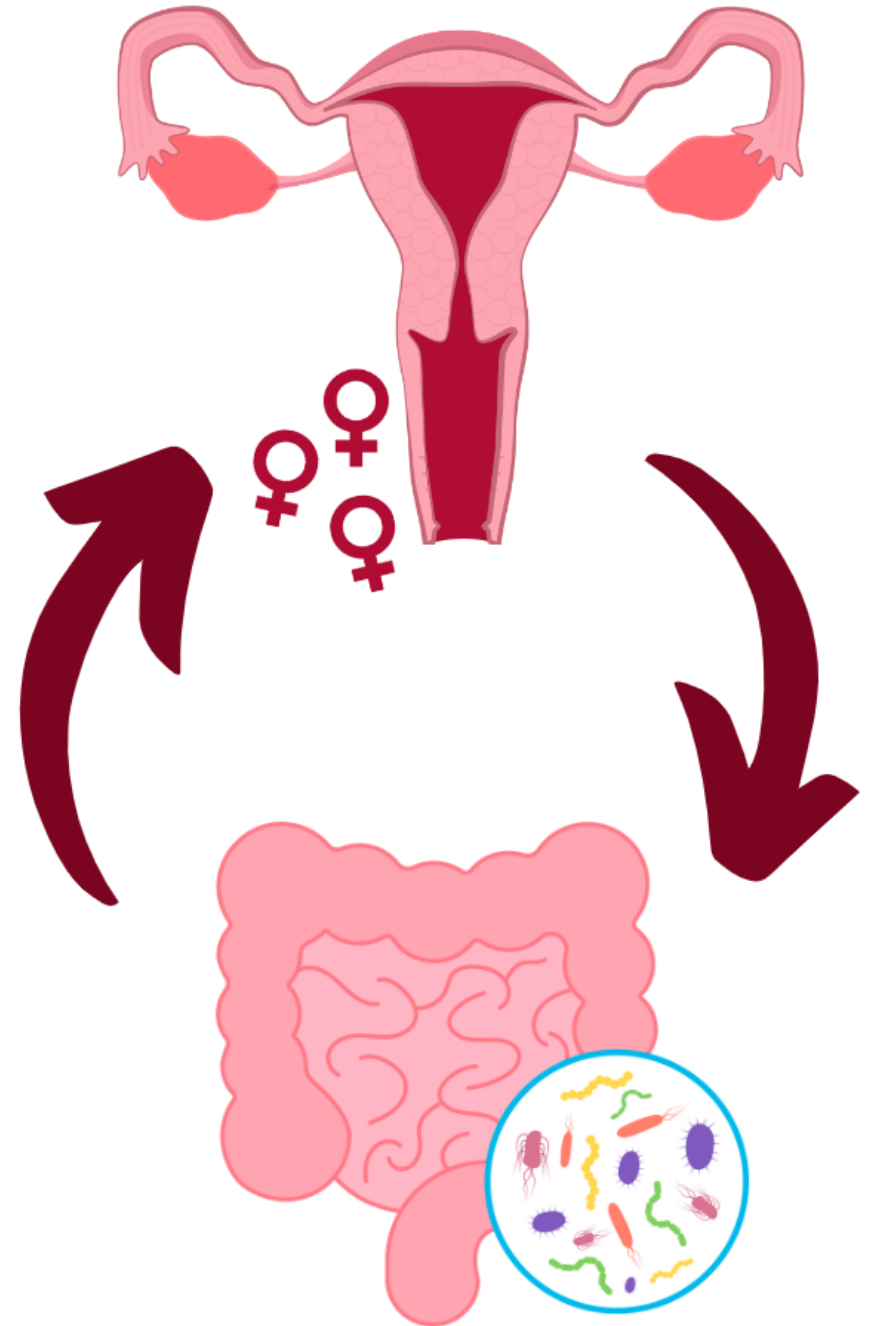
Chidi-Ogbolu & Baar (2019) *Front Physiol*, 9: 1834.

# 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

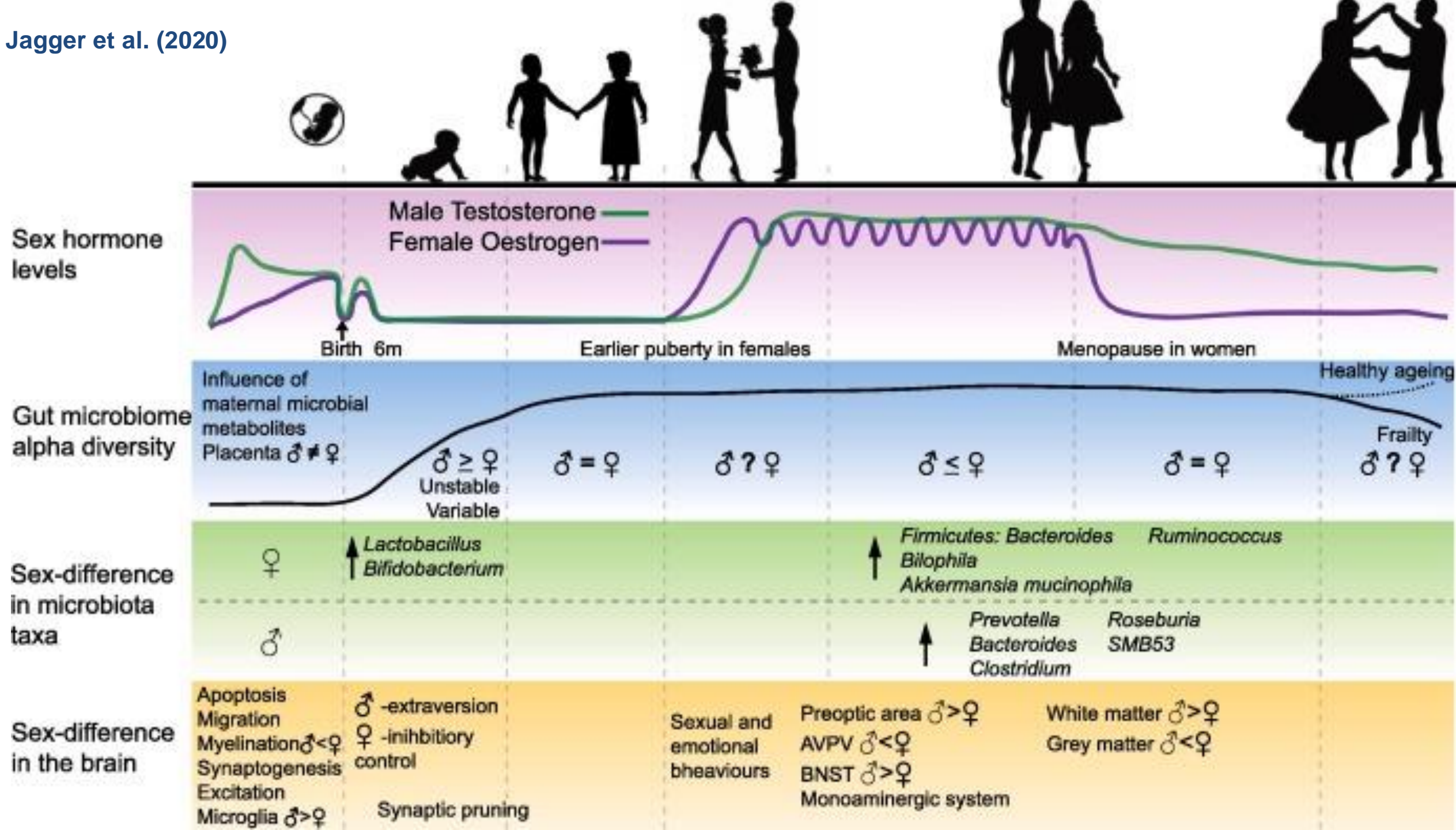
## “Microgenderome”

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

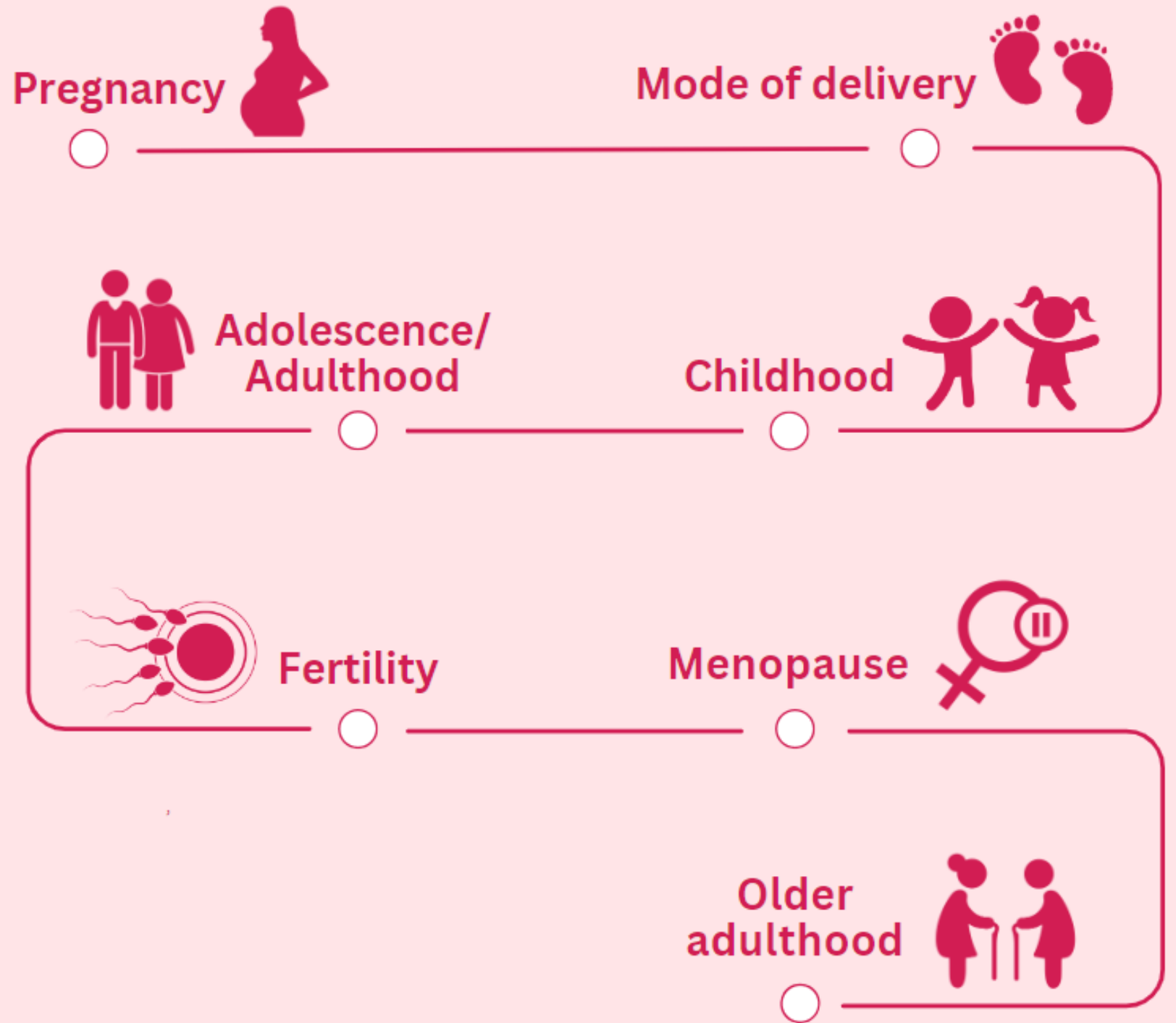
Vemuri et al. (2019) *Semin Immunopathol* 41(2): 265–275.

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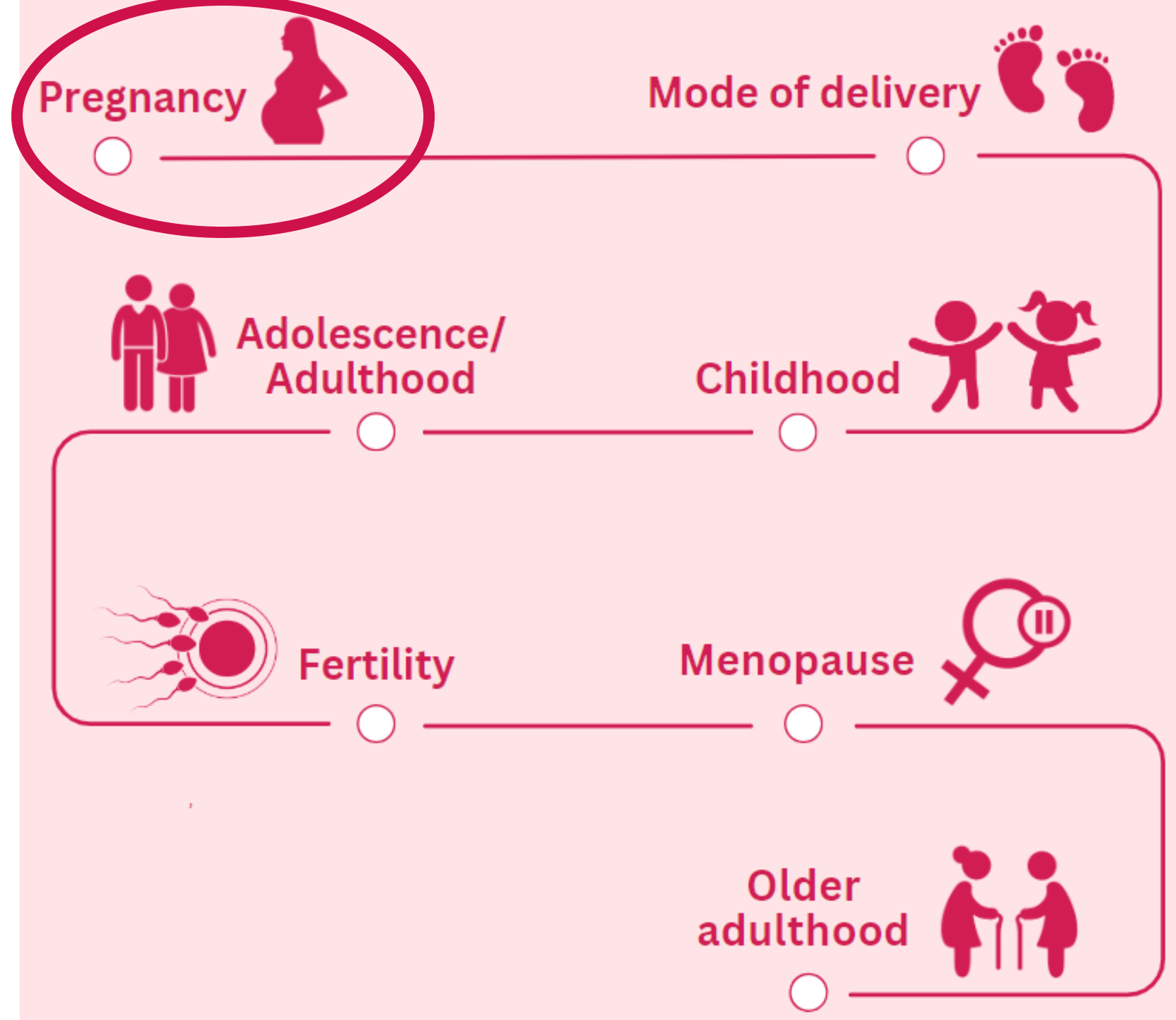


# The Female Gut Microbiota

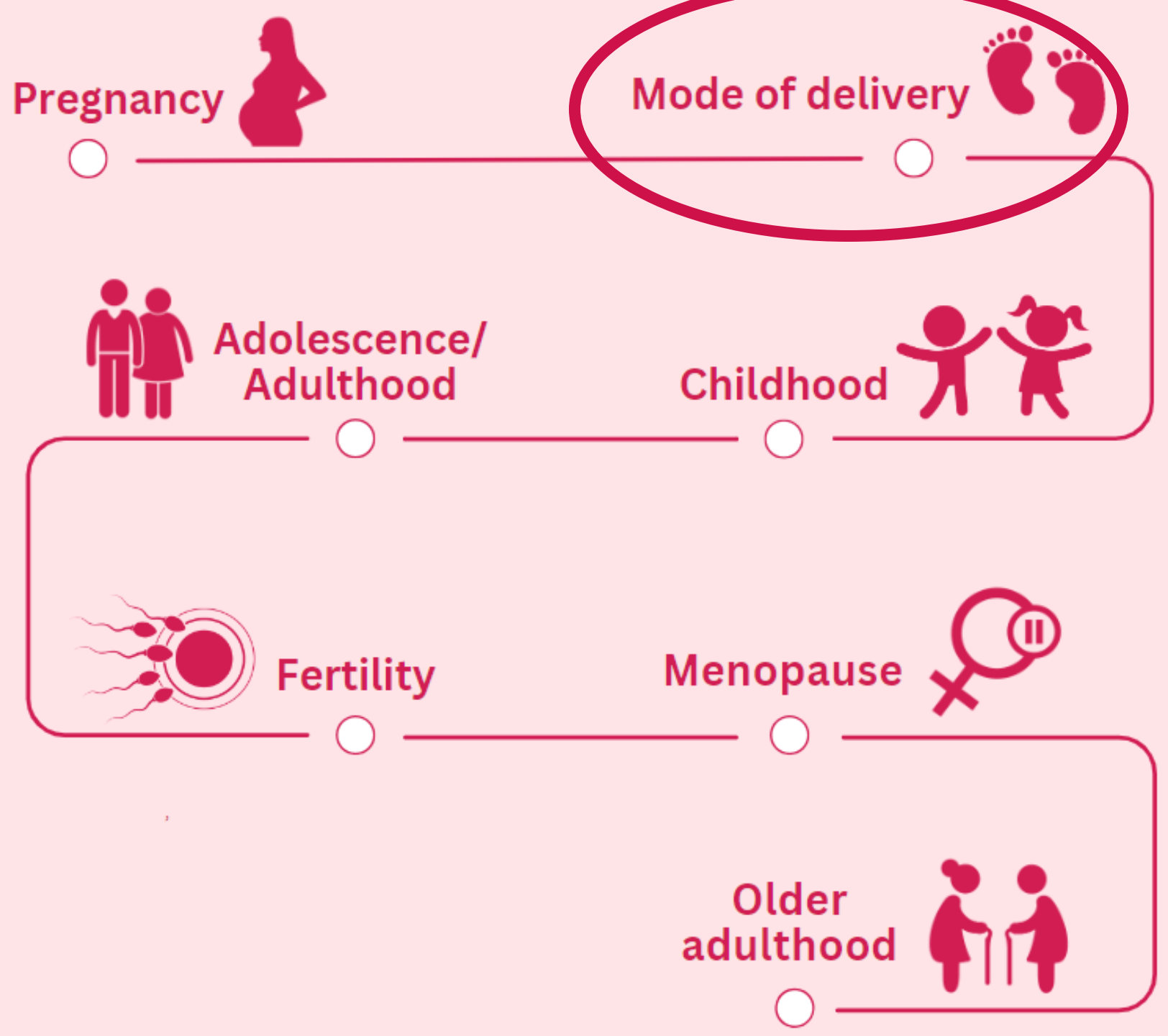




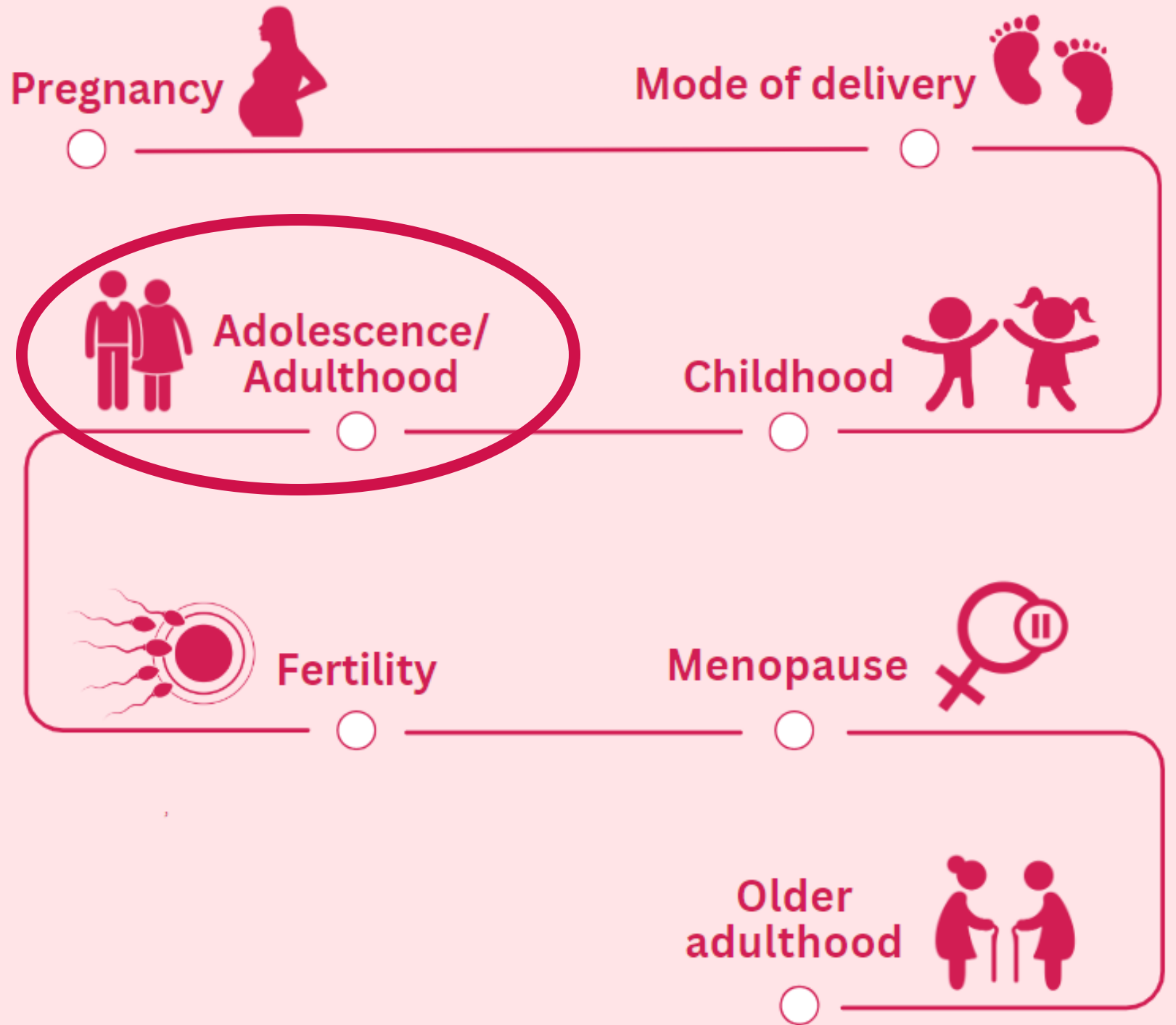
# The Female Gut Microbiota



# The Female Gut Microbiota



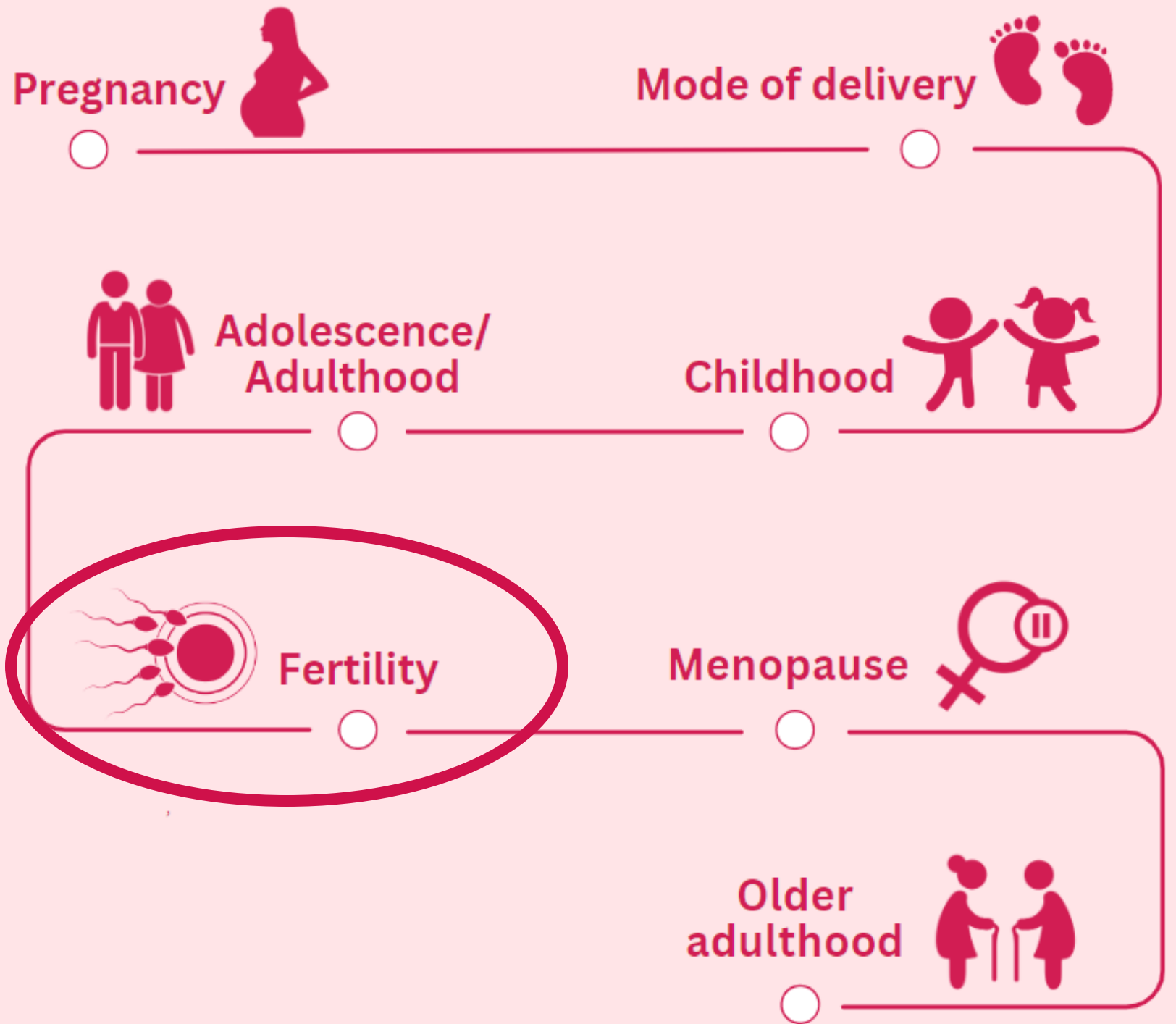
# The Female Gut Microbiota



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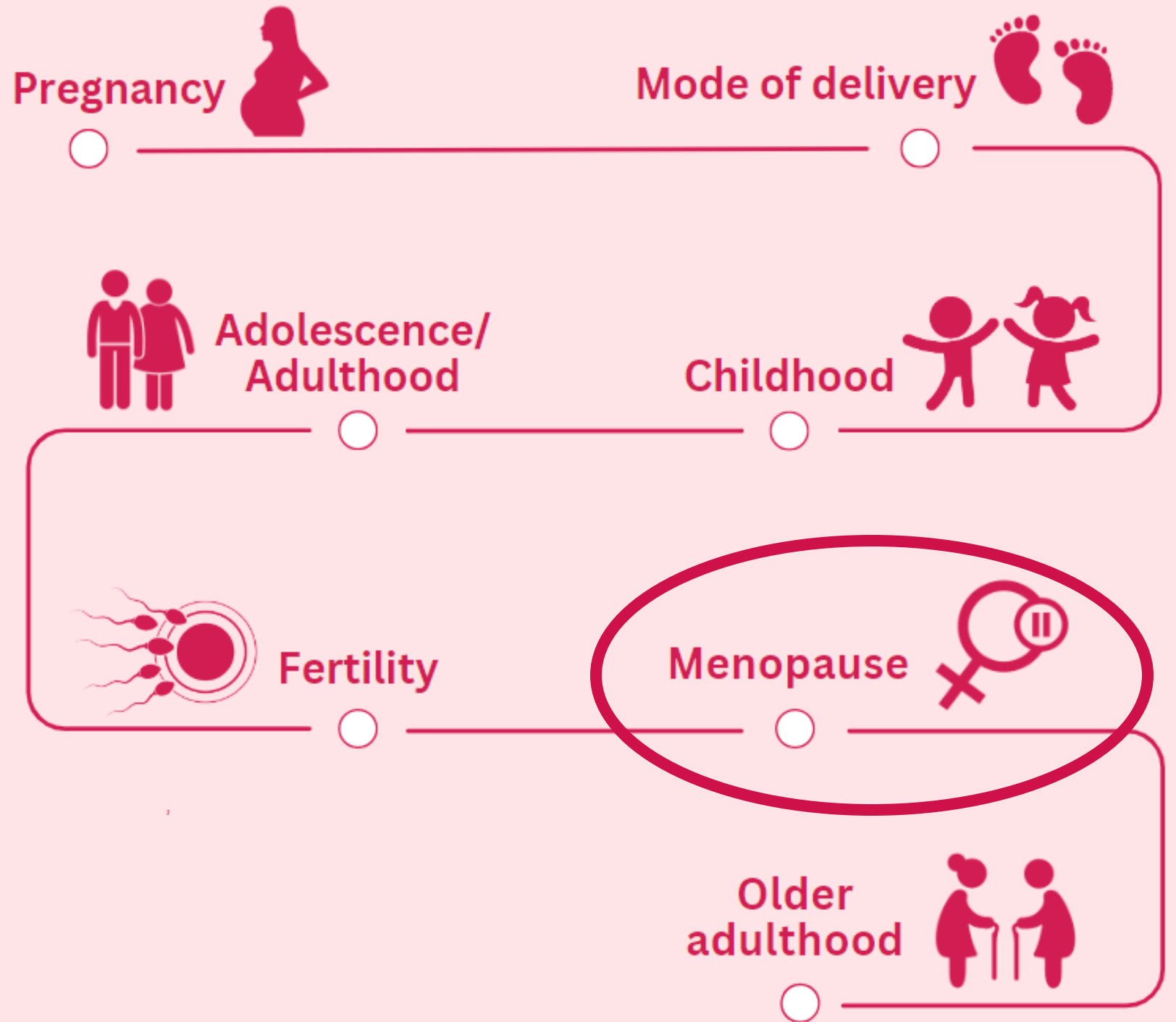
# The Female Gut Microbiota



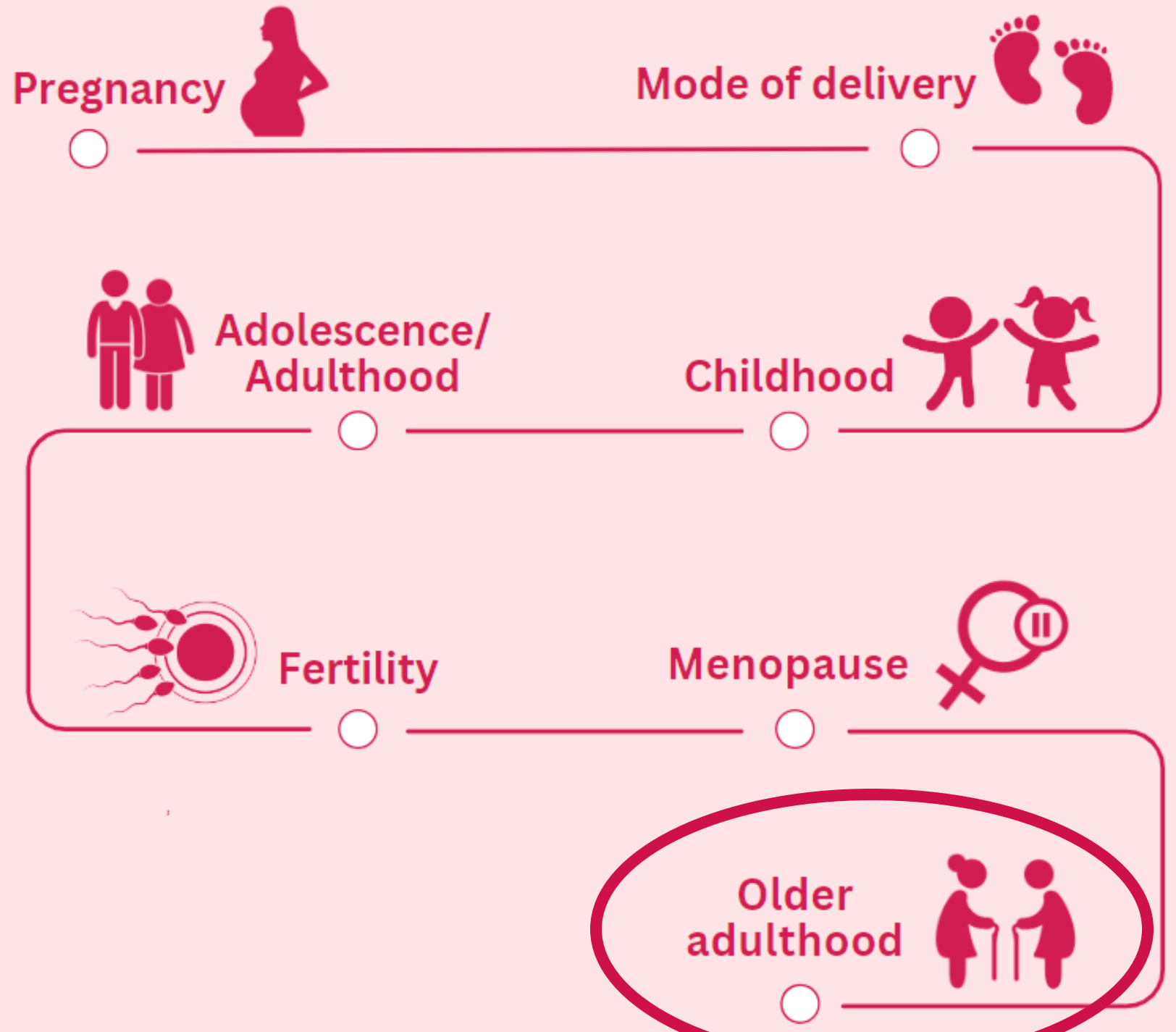
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# The Female Gut Microbiota



# The Female Gut Microbiota





# REPRODUCTIVE HEALTH

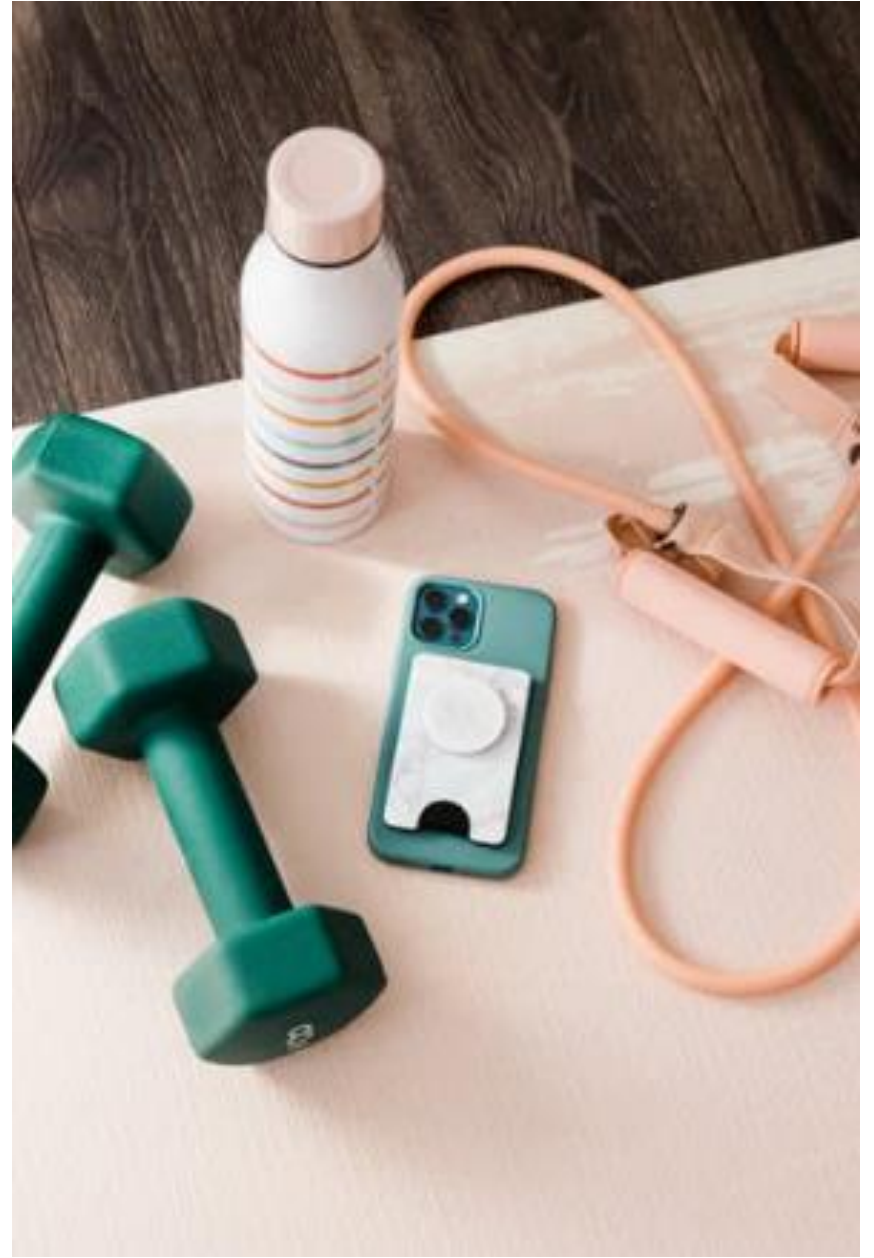
The ability to conceive. Diet & lifestyle factors can affect fertility.

**FERTILITY**

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

**INFERTILITY**

Unable to conceive following a successful pregnancy.







# 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**.



# Probiotics



## PCOS

- Worldwide 8–13% of reproductive-aged women affected with 70% undiagnosed.
- Lower levels of lactobacilli 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.



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.



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



women participated in Isala

We found



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



Inspired by isala.be



Inspired by isala.be

Base for novel diagnostics and therapeutics



Awarded for clear science communication



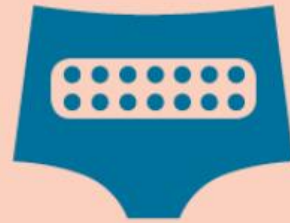


# INFLUENCING FACTORS

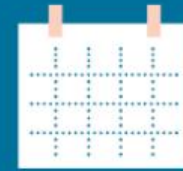
Your age and stage of life



Use of period products



Use of hormonal contraceptives



The natural course of your menstrual cycle

Whether you have children or not



Sexual activity

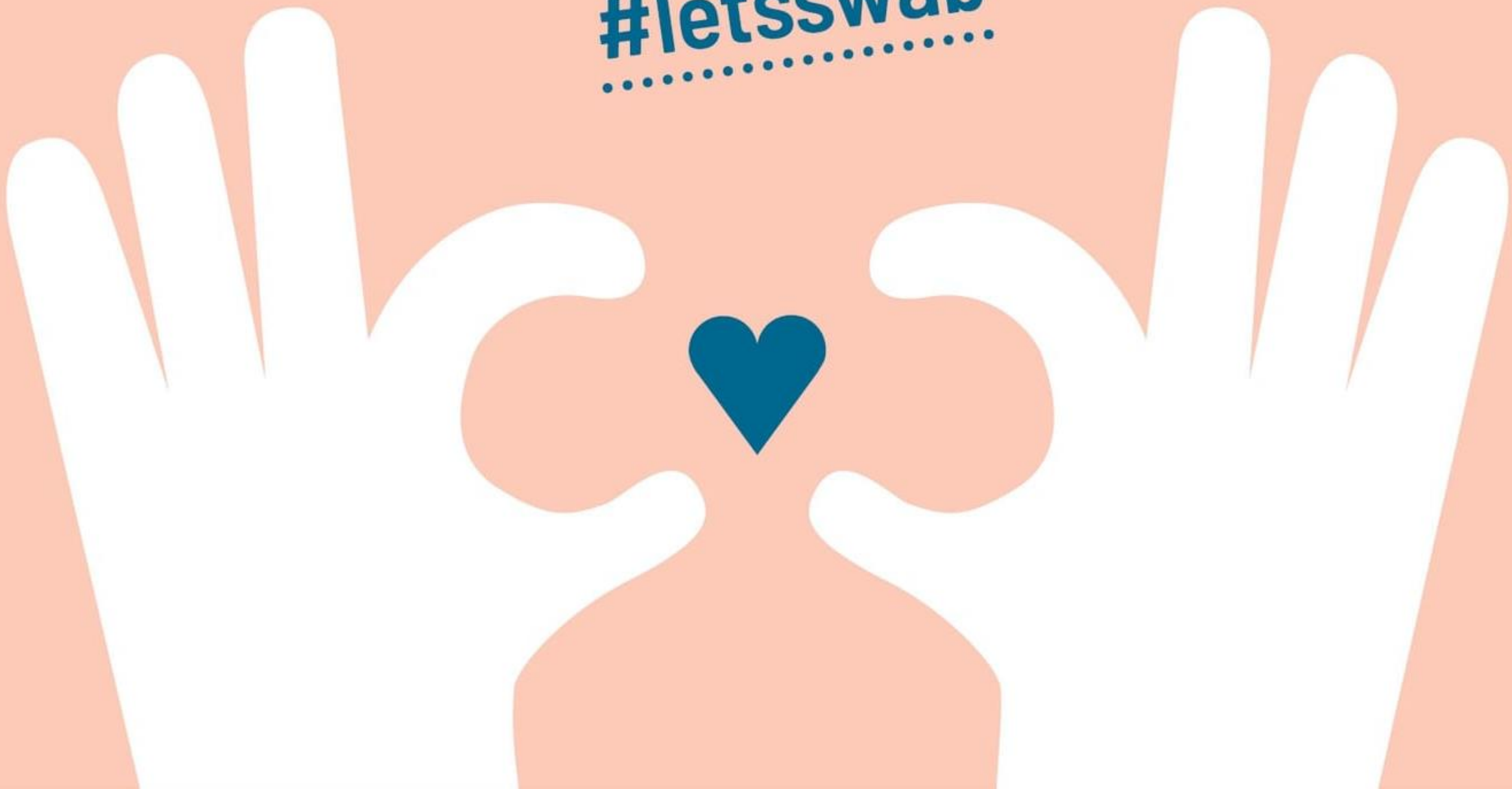


Some foods and drinks have a positive impact...



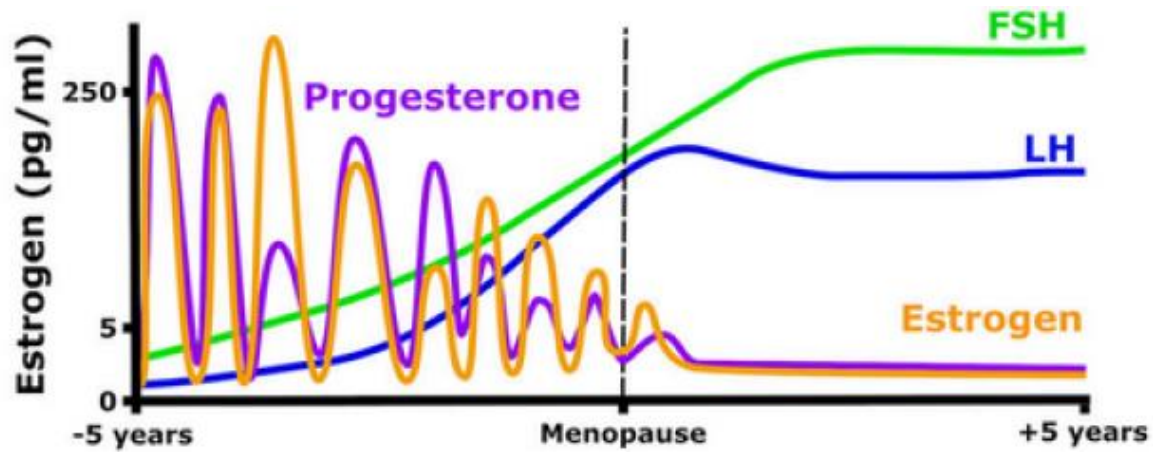
.... others appear less positive

**#letsswab**





# MENOPAUSE



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

The transition to menopause, characterised by erratic menstrual cycles.

**Perimenopause**

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

**Menopause**



# MENOPAUSAL SYMPTOMS



Irregular  
menstrual cycles



Hot flashes



Sleep disturbances



Incontinence



Low mood



Night sweats



Muscle and  
joint pain



Sexual  
dysfunction



# 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**.

# Probiotics Post-menopause

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

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.



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 <sup>1</sup>, Aziz Homayouni Rad <sup>2</sup>, Mojgan Mirghafourvand <sup>3</sup>

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 ( $p = 0.028$ )





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.

# 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

### Menstruation

The gut microbiome plays a role in the menstrual cycle, and vice versa. Menstrual cycles vary between women; however, on average, it lasts 28 days and includes 3 main phases: Follicular phase, Ovulation, and Luteal phase.

Oestrogen peaks about midway through the cycle, which causes an increase in oestrogen hormone, triggering ovulation. Progesterone levels then rise to support a fertilised egg. After ovulation, progesterone and oestrogen levels drop, and menstruation begins (see Figure 1).

Sex hormone fluctuations can also be associated with menstrual pain sensitivity and symptoms. Changes in the gut microbiome throughout the menstrual cycle may be associated with premenstrual syndrome (PMS); however, more research is needed in this area.

If the gut microbiome is imbalanced, this may lead to an imbalance in sex hormones. Cyclical changes in the gut microbiome can impact oestrogen levels as gut health and microbial diversity can influence excretion and recirculation of oestrogen.

Figure 1. Hormonal fluctuation throughout the menstrual cycle.<sup>46</sup>  
Chidi-Ogbolu & Bear (2019) Front Physiol

### IBS Spotlight

Sex hormones (oestrogen and progesterone) may modulate and influence the gut microbiome. Women with IBS are more likely to suffer than men.<sup>44,45</sup> Correlations exist between worsened IBS symptoms and phases of the menstrual cycle, possibly due to elevated progesterone during menstruation,<sup>46</sup> highlighting the potential role of sex hormones in this condition.

IBS incidence tends to decline in older women. This may be due to menopause-related reduction in oestrogen.

Visceral sensitivity is a characteristic of IBS. Oestrogen is thought to regulate visceral sensitivity as well as gut motility, which are characteristic of IBS.

Find out more at: [yakult.co.uk/HCP](http://yakult.co.uk/HCP)  
Contact us: [science@yakult.co.uk](mailto:science@yakult.co.uk)

@yakultscience\_ukie  
Yakult Science for HCPs in UK & Ireland

## The Female Gut Health Guide

### Lessons Through Life

A Guide for HCPs

Find out more at [yakult.co.uk/HCP](http://yakult.co.uk/HCP)

### The Gut Microbiota and Reproductive Health

Polycystic ovary syndrome (PCOS) and endometriosis are reproductive conditions which are more prevalent in females, and may be influenced by alterations in the gut microbiota.

#### PCOS

PCOS is a common condition which affects how a woman's ovaries work. Approximately 8-13% of women of reproductive age struggle with PCOS and up to 70% of affected women remain infertile.<sup>47</sup> The exact cause is unknown, however it is often hereditary, and is associated with insulin resistance.

- Fertility issues
- Excessive hair growth
- Weight gain

#### microbiota associated with PCOS?

Oestrogen (a predominant male sex hormone) is one of the main signs of PCOS. The gut microbiota plays a role in regulating this hormone.<sup>48</sup> Lower gut microbiota diversity and lower microbial biomass are common features of PCOS.<sup>49,50</sup> Gut dysbiosis increases intestinal permeability, which is associated with elevated androgen production and inflammation which can lead to PCOS. A number of systematic reviews and meta-analyses have investigated the role of probiotics and synbiotics (probiotics and prebiotics combined) to help treat PCOS. It remains difficult to identify optimal probiotic strains, Lactobacillus and Bifidobacterium are commonly used in studies.

Research suggests that probiotics or synbiotics may improve insulin sensitivity, decrease inflammation, and improve insulin resistance and blood glucose levels in women with PCOS, in turn improving fertility outcomes for some people. Much more research needs to be done, but taking a probiotic with a Lactobacillus strain may support fertility outcomes for some people - in addition to a diet rich in fruit, vegetables, nuts, seeds, and wholegrains to promote a healthy gut microbiome.<sup>51</sup>

Ro Huntriss RD  
Founder of Fertility Dietitian UK  
and author of 'Gastrointestinal Health: Healthy Fertility'

Find out more at: [yakult.co.uk/HCP](http://yakult.co.uk/HCP)  
Contact us: [science@yakult.co.uk](mailto:science@yakult.co.uk)

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# Thank you

My colleagues at Yakult Group in Europe

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