Microbiome Center

The vaginal (and gut) microbiome

Role in fertility

Dr. Mariya Petrova

Fertility / Infertility

The global fertility challenge

- Fertility – Fertility refers to the ability of the male and female reproductive system to achieve conception resulting in a pregnancy.
- Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse
- Infertility is common, multifactorial, and increasingly understood as a systemic condition influenced by microbiomes across body sites.

Global infertility prevalence

Microbiome Center

Infertility is not a niche issue—it affects 1 in 6 people globally, with remarkably similar rates across high- and low-income countries.

Approximately **one in six** people have experienced infertility at some stage in their lives, globally.

17.5%

Estimated lifetime prevalence of infertility (95% confidence interval: 15.0, 20.3).

Lifetime prevalence is defined as the proportion of a population who have ever experienced infertility in their life.

12.6%

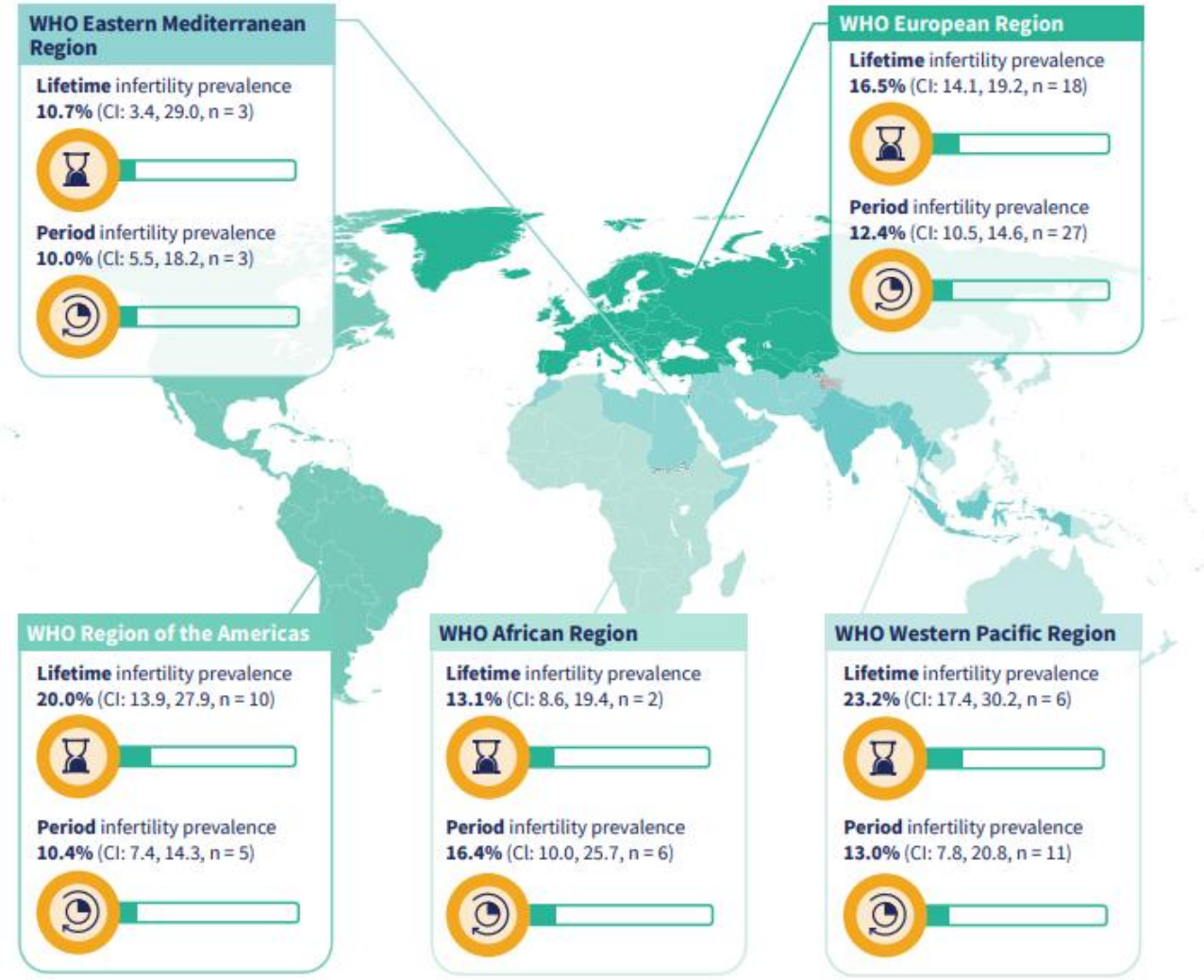
Estimated period prevalence of infertility (95% confidence interval: 10.7, 14.6).

Period prevalence is defined as the proportion of a population with infertility at a given point or interval in time, which may be current or in the past.

WHO Infertility Prevalence Estimates, 1990–2021. Published 2023

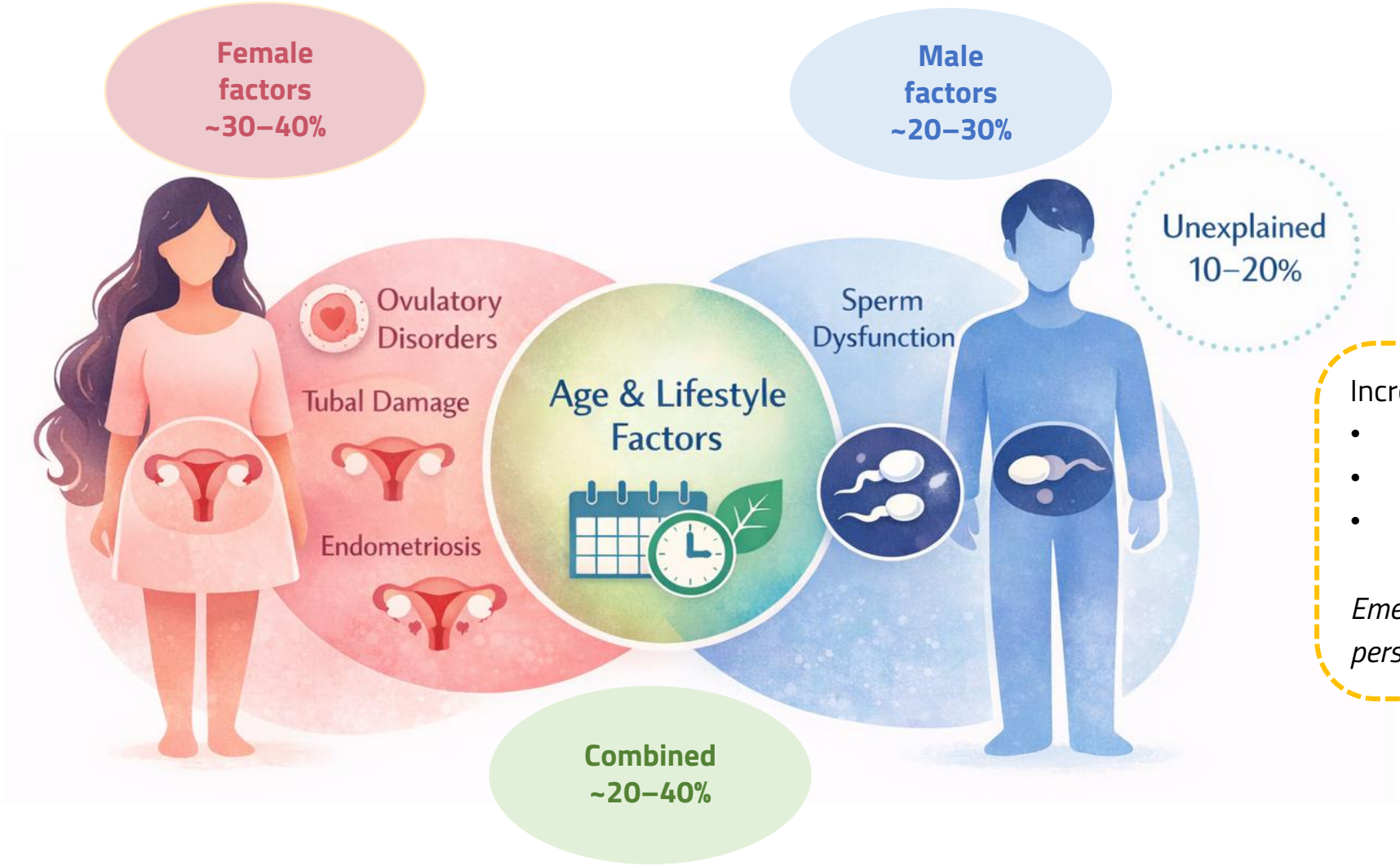
Global infertility prevalence

- ~48 million couples affected globally
- EU fertility rate: ~1.34 births/woman (2024)



WHO Infertility Prevalence Estimates, 1990–2021. Published 2023

Cause of infertility



Increasing interest in:

- Immune factors
- Inflammation
- Microbiome

Emerging field with strong clinical relevance for personalized approaches

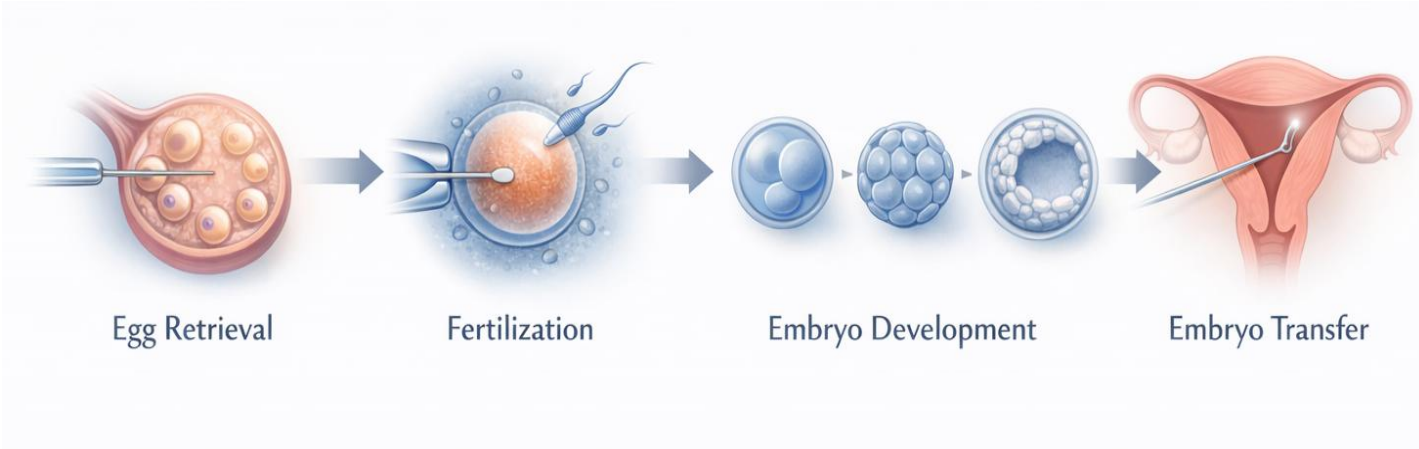
Carson et al 2021 JAMA doi:10.1001/jama.2021.4788
Narayanasamy et al 2025 Annals of Obsterics and Gynecology

In vitro fertilization (IVF)

What is IVF?

IVF is an assisted reproductive technology (ART) used to help people conceive.

- Eggs are collected from the ovaries
- Fertilization happens outside the body
- The resulting embryo is transferred into the uterus



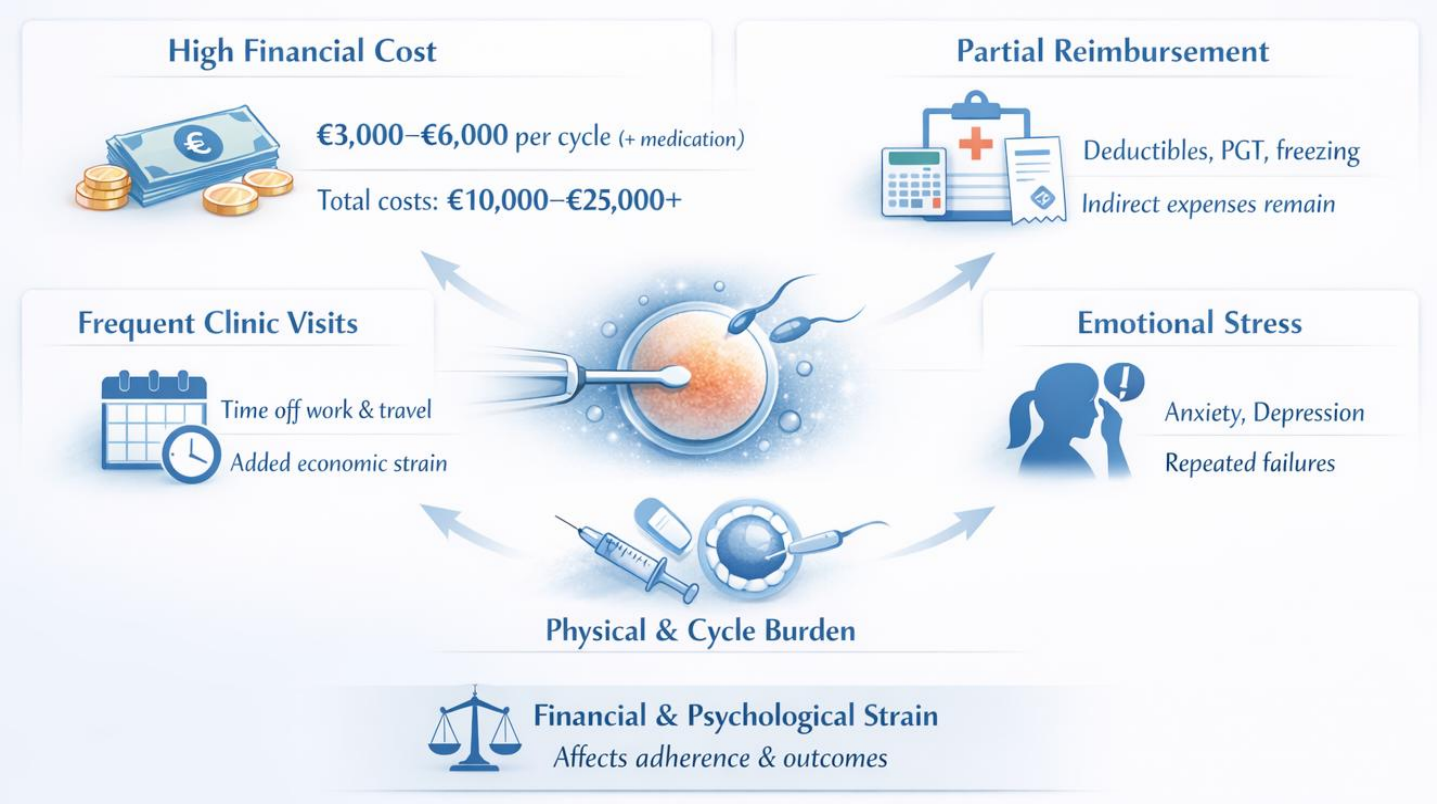
In vitro fertilization (IVF)

How common is IVF?

- Around 5% of infertile couples use IVF
- IVF has resulted in >10 million births worldwide
- Up to ~12% of births in some countries involve assisted reproduction
- ~3% of births in the US (1 in 36 babies) are from IVF
- ~1 in 30 babies in the Netherlands is born via IVF
- Use of IVF is rapidly increasing globally, with >1.1million ART cycles annually in Europe alone

But IVF comes with economical and patient burden!

- €3,000–€6,000 per cycle in Europe
- Frequent clinic visits, stress, anxiety, hormonal stimulation, invassive procedure, etc.



The vaginal microbiome & fertility

Vaginal microbiome

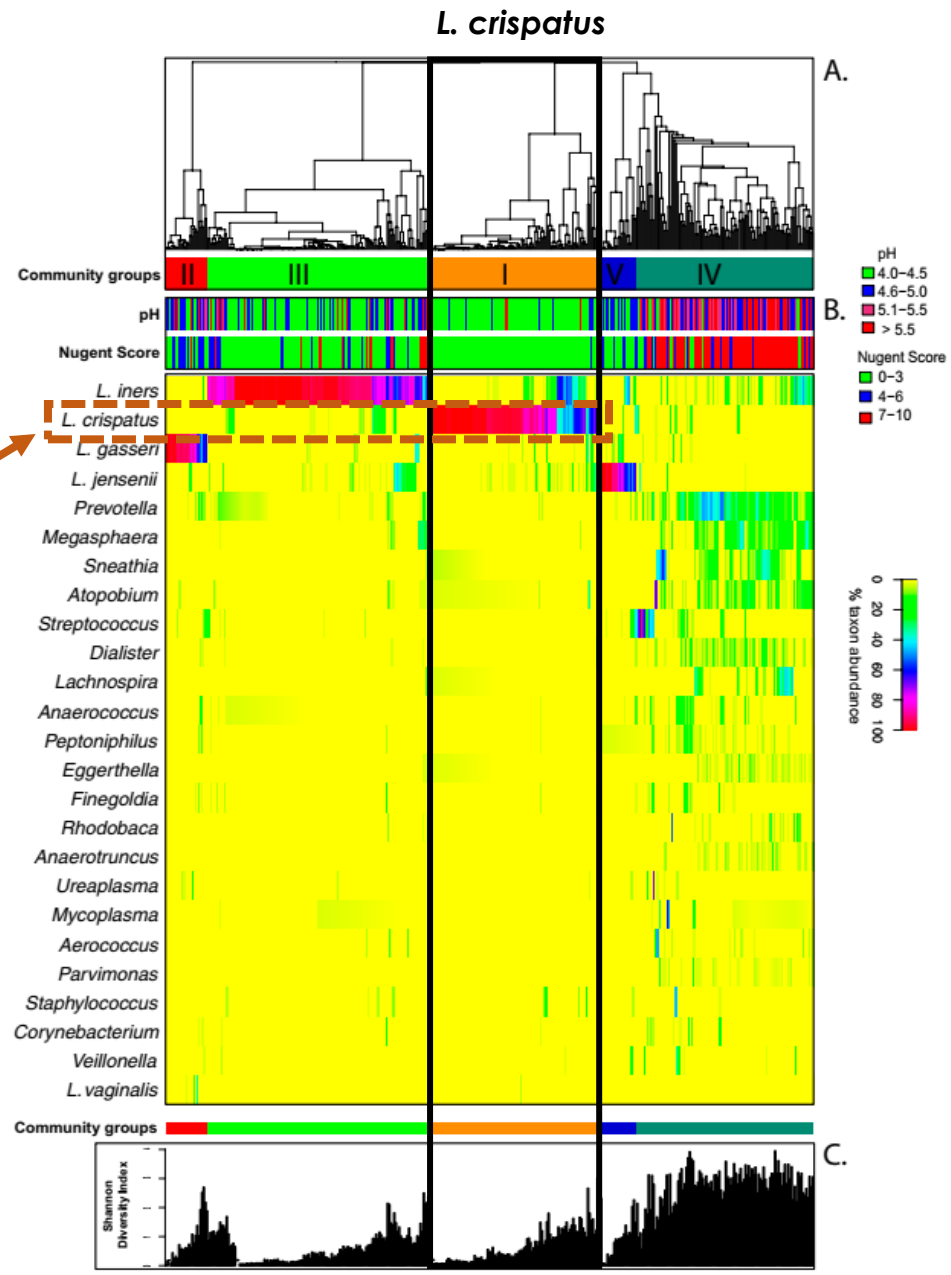
Optimal vaginal microbiota is:

- characterized with low diversity
- dominated by *Lactobacillus* species
- low pH between 3.8 -4.5

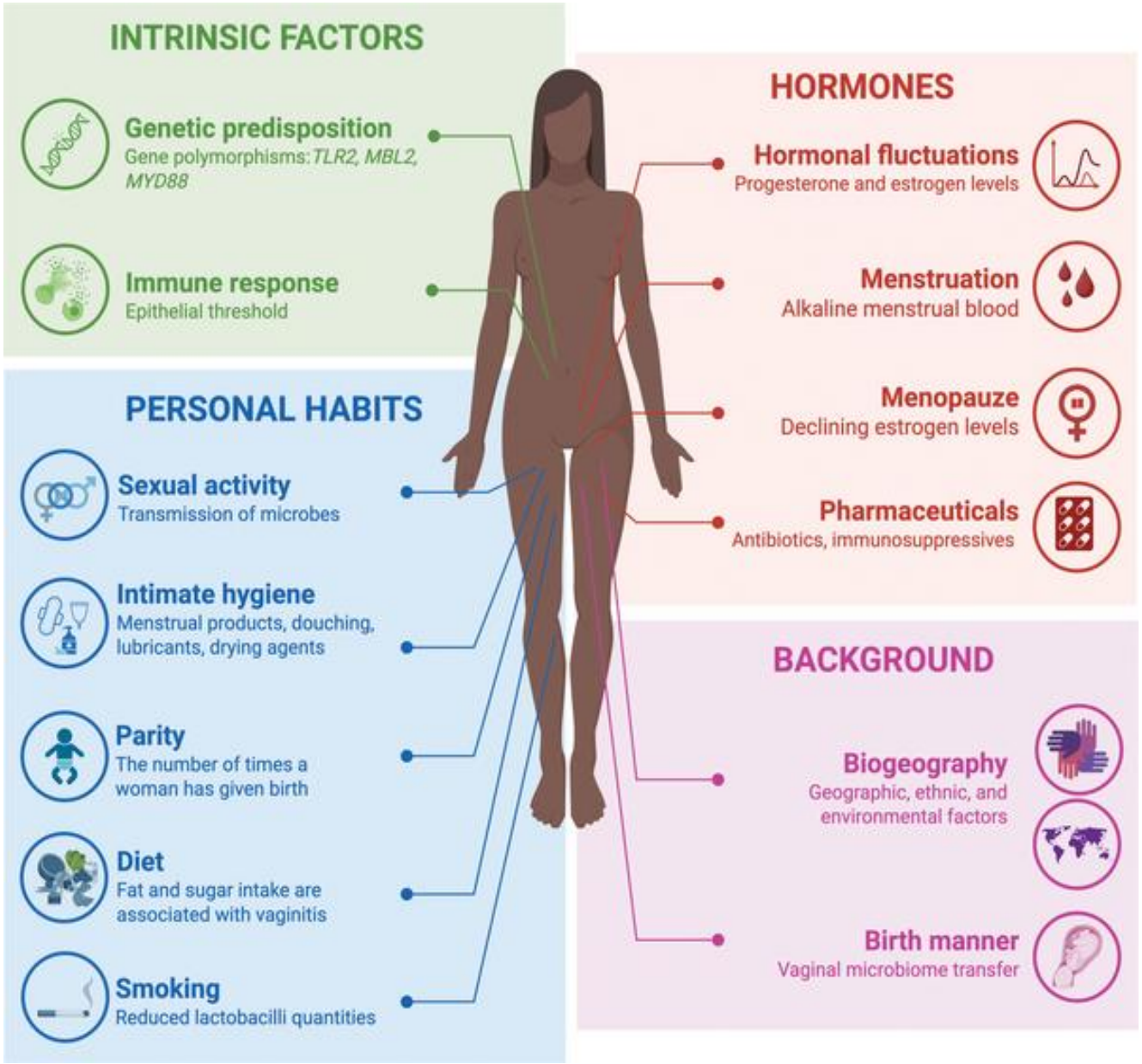
Community State Types[1].

- CST 1 – ***L. crispatus* dominated; most associated with health**
- CST 2 – *L. gasseri* dominated
- CST 3 – *L. inres* dominated; benefits under question
- CST 4 – high diversity, non-*Lactobacillus* dominated [2,3]
- CST 5 – *L. jensenii* dominated

Research has built ups since 2011 now each of the CST has been divided into subcategories



1. Ravel, J. et al. Proc Natl Acad Sci U S A 108, 4680–4687 (2011)
2. Verstraelen, H. et al. Journal of Lower Genital Tract Disease 26, 73 (2022)
3. Gajer, P. et al. Sci Transl Med 4, 132ra52 (2012)



Factors influencing the vaginal microbiome

Multiple factors can influence the composition of the vaginal microbiota over time.

The major contributors are:

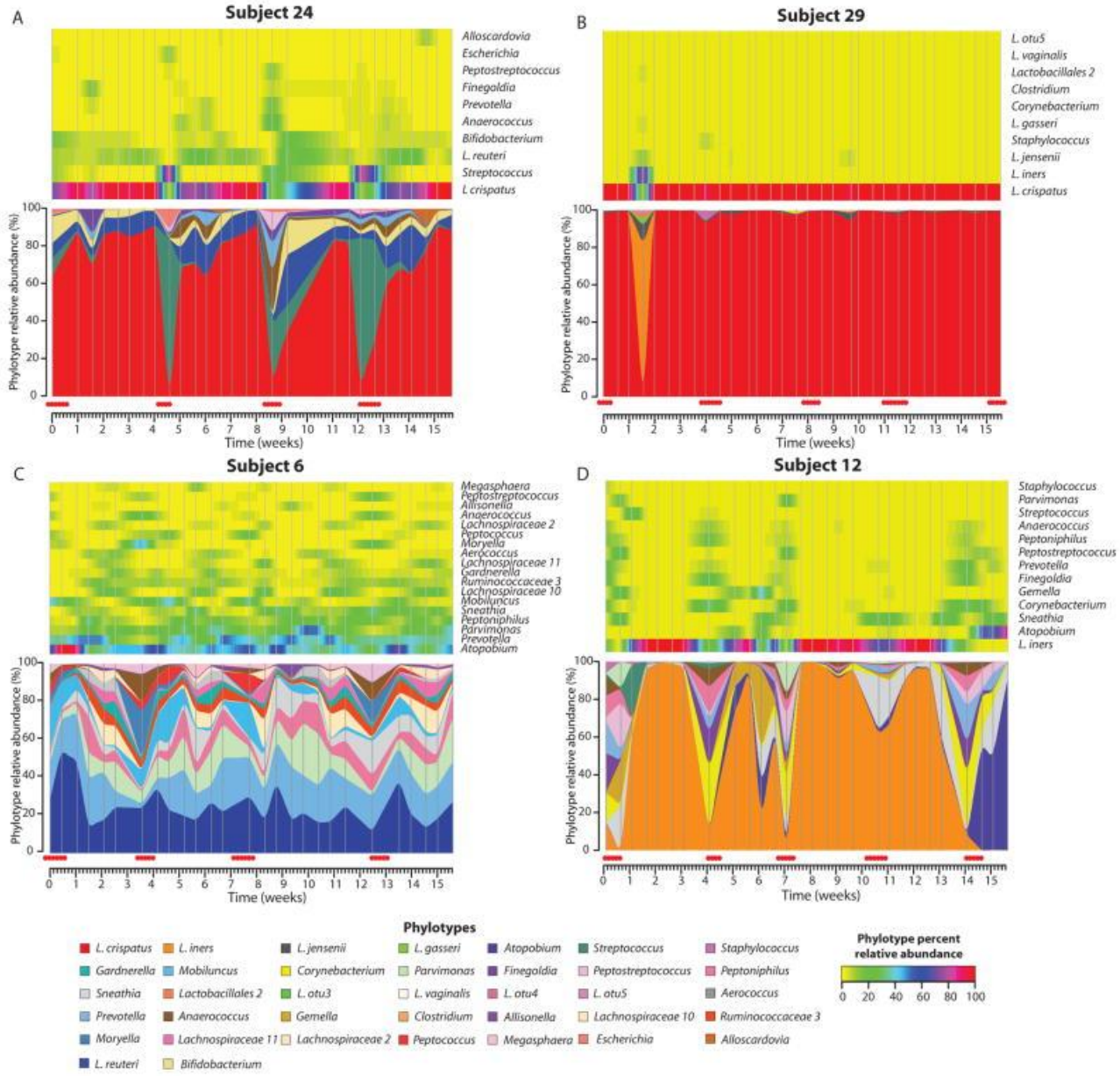
- Age
- Hormones
- Personal habits

Sillen et al 2025 Plos Pathogens https://doi.org/10.1371/journal.ppat.1013346

Vaginal microbiome during menstrual cycle

Menses is major disturbing factor during the menstrual cycle[1,2]:

- *L. crispatus* abundance declines during menses
- *L. iners* concentrations increase along with *Gardnerella vaginalis* and is the dominant species during menses
- There is certain “dynamic stability”: most women retain their typical state or alternate between states
- Alternation is aligned with menses.



1. Gajer, P. et al. Sci Transl Med 4, 132ra52 (2012)
2. Verstraelen, H. et al. Journal of Lower Genital Tract Disease 26, 73 (2022)

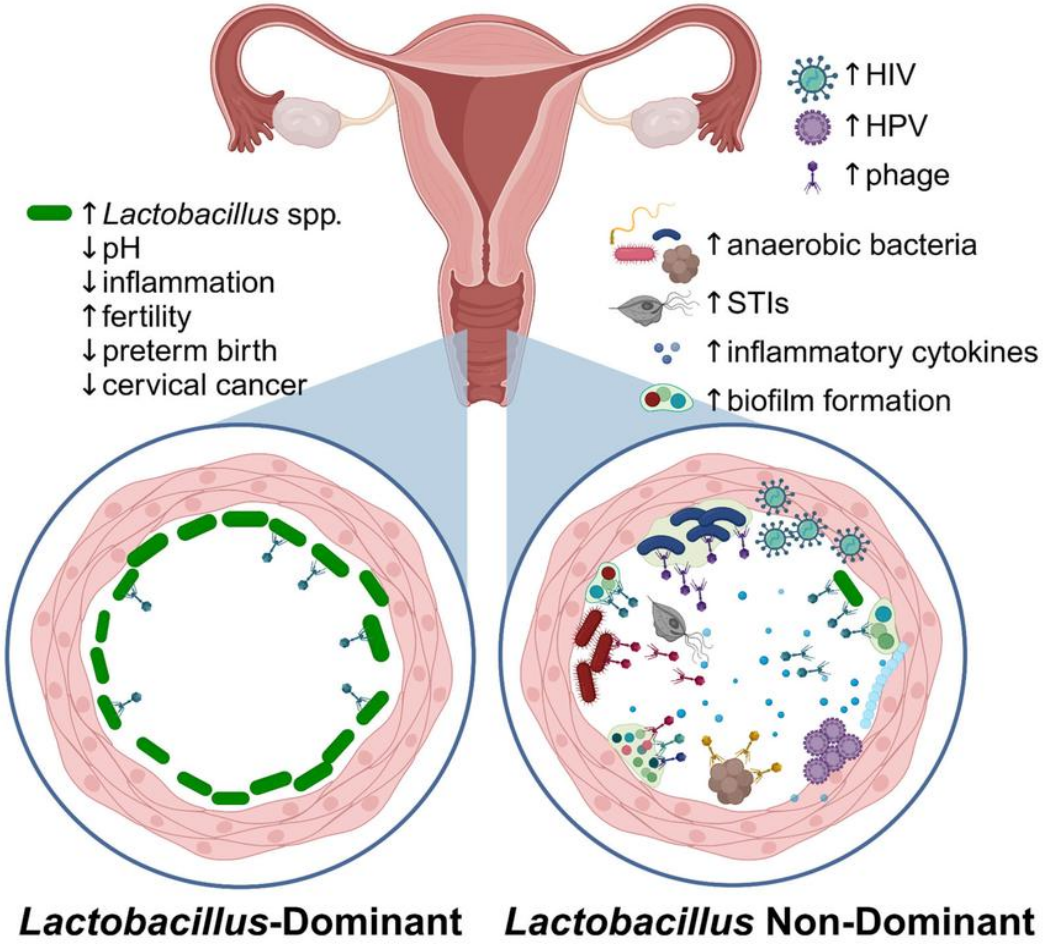
When balance breaks: Vaginal dysbiosis and disease

Bacterial vaginosis (BV)

- The most common vaginal dysbiosis
- 1 in 3 women worldwide may experience BV during their lifetime
- More than 50% of women report recurrent BV within a 1 year

BV is characterized with:

- Loss of *Lactobacillus spp.*
- Growth of anaerobic bacteria *G. vaginalis, A. vaginae, Prevotella spp.* and biofilm formation
- Increased vaginal pH above 4.5
- Increased local inflammation

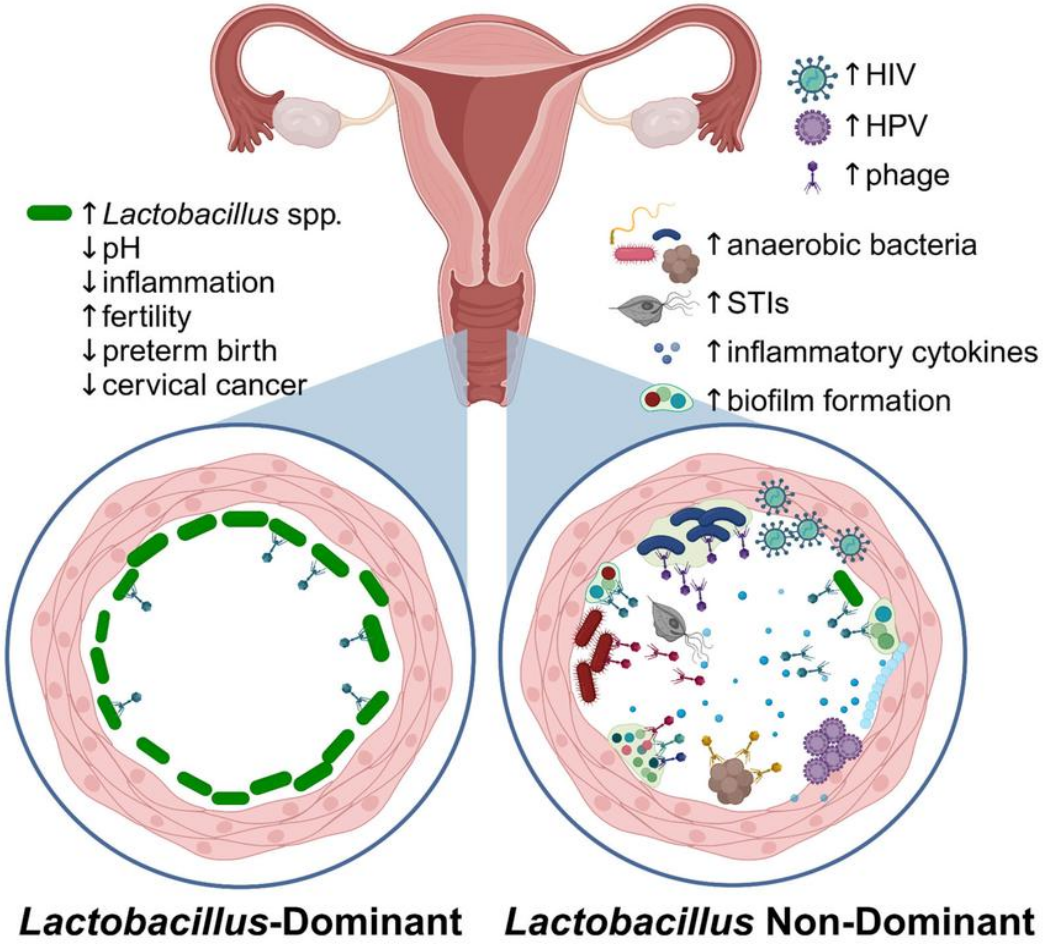


Orton et al 2025; https://doi.org/10.3390/microorganisms13020431

When balance breaks: Vaginal dysbiosis and disease

BV has been associated with an increased risk of:

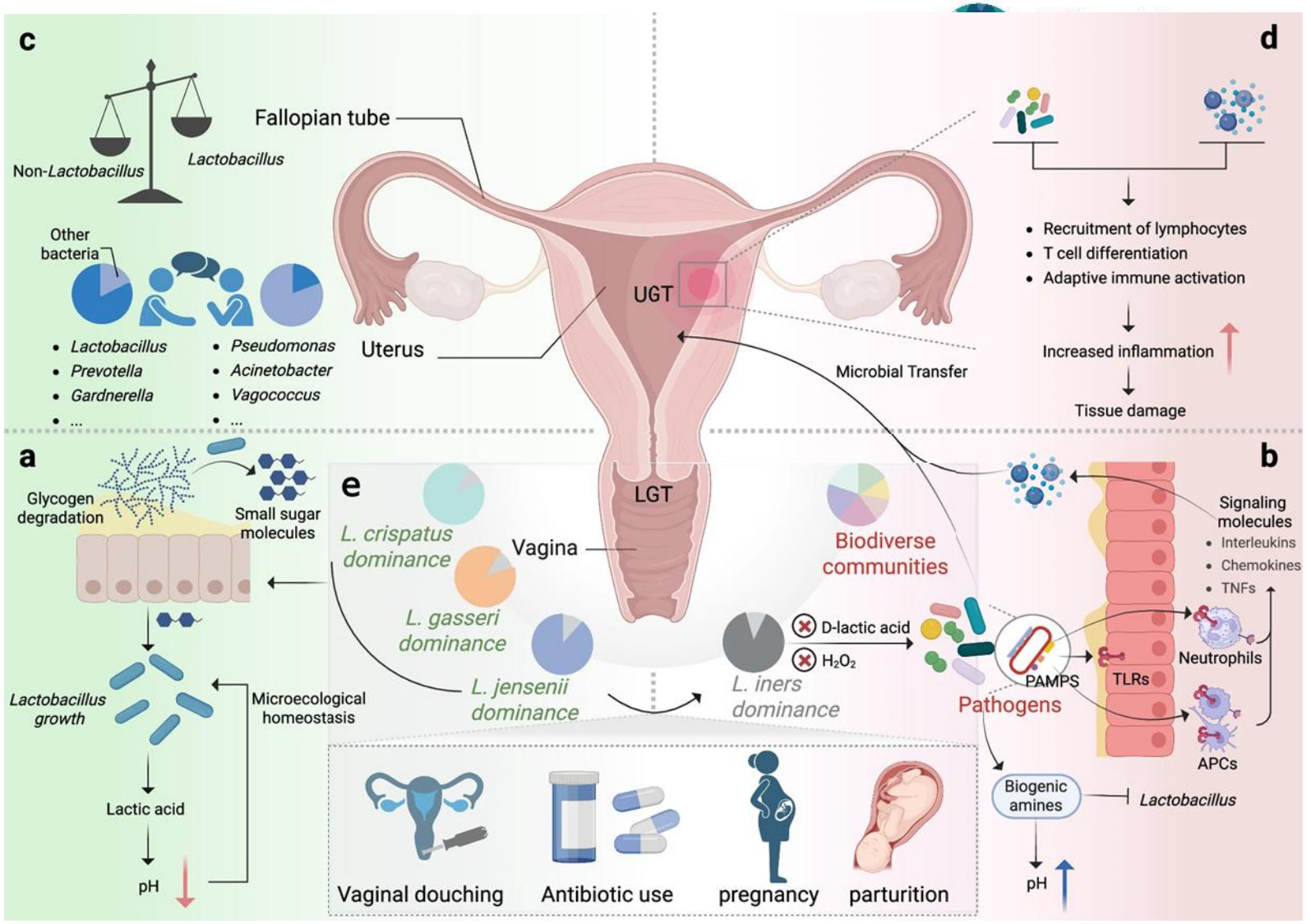
- STIs - *Chlamydia trachomatis, Neisseria gonorrhoeae,* HSV-2, HPV and HIV
- Pelvic inflammatory disease
- Urinary tract infections
- **Infertility and pregnancy outcomes**



Orton et al 2025; https://doi.org/10.3390/microorganisms13020431

Reproductive tract microbiota – the bigger picture

- Lower genital tract microbiota – vaginal health
- Upper genital tract microbiota – endometrial microbiota
- Role in fertility and healthy conception

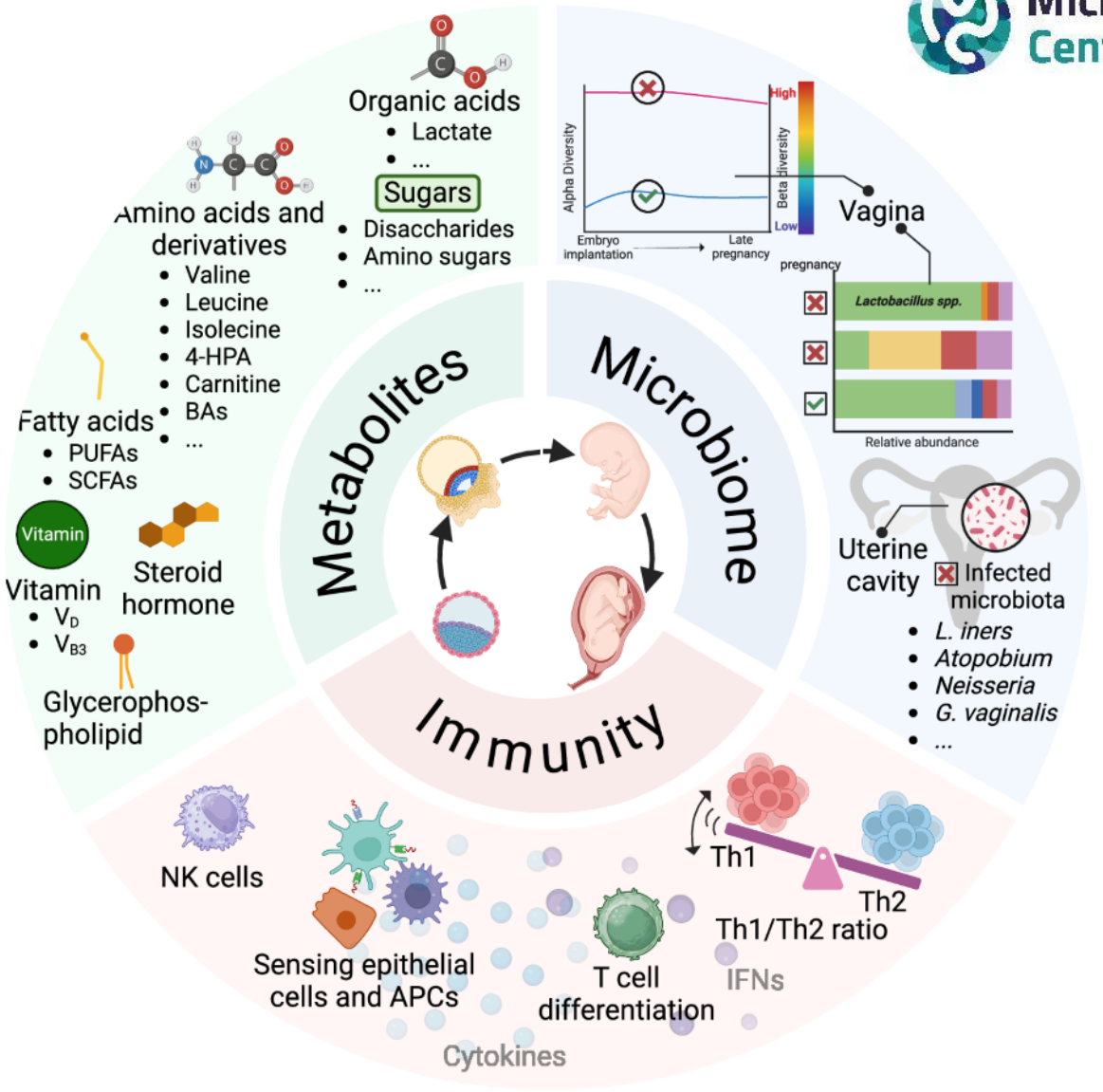


Cheng et al, 2025 npj Biofilms and Microbiome

Cheng et al 2025; https://doi.org/10.1038/s41522-025-00839-y

Successful conception & healthy pregnancy

- It is not only about “who is there”
- Alterations in the microbiota lead to metabolites changes affecting conception and pregnancy
- Alteration in the microbiota leads to immune dysregulation affecting conception

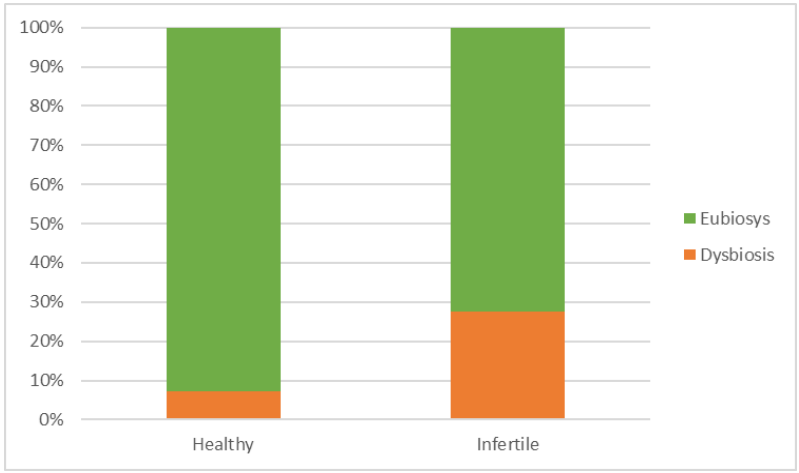


Cheng et al, 2025 npj Biofilms and Microbiome

Vaginal microbiota role in fertility

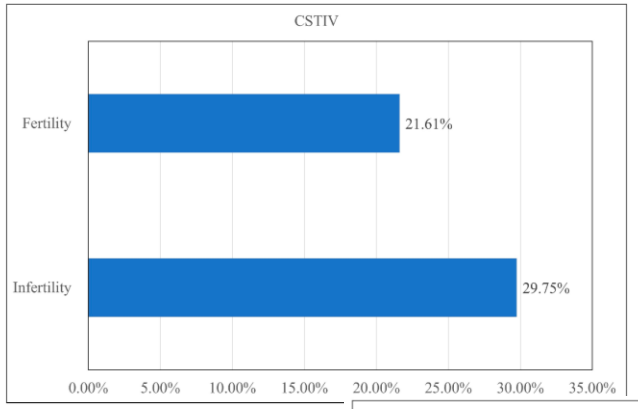
Culture-based study on fertility found higher prevalence of vaginal dysbiosis in infertile women compared to healthy controls [1,2].

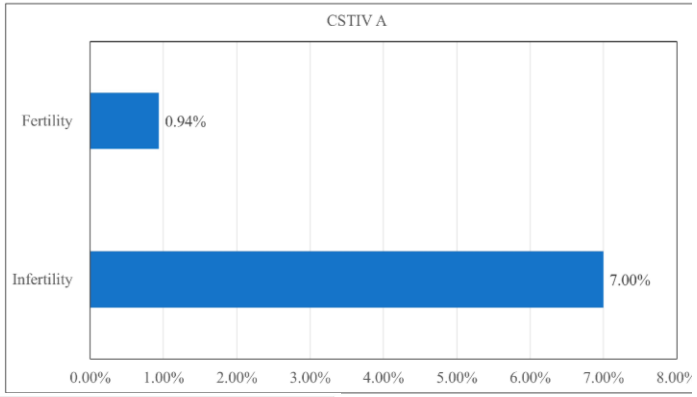
- Only 3.5% of infertile women had *Lactobacillus* species.



Lactobacillus spp. more abundant in fertile patients than infertile patients[3]. Infertile women had:

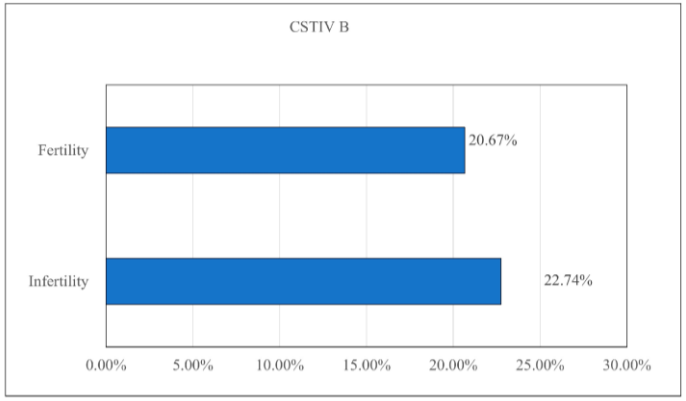
- ↓ *Lactobacillus* abundance
- ↑ CST IV dysbiosis - ↑ *Prevotella*, ↑ *Gardnerella*





Fertile women showed:

- stronger *Lactobacillus* dominance
- lower diversity



1. Babu, G. et al. J Clin Diagn Res 11, DC18–DC22 (2017)
2. Haahr, T. et al. Hum. Reprod. 31, 795–803 (2016)
3. Chen et al. Diagnostics 10.3390/diagnostics15192544

Vaginal & Endometrial microbiota role in IVF and embryo transfer

Compared with HC and women with successful implantation (IS), women with implantation failure (IF) showed:

- Lower levels *of Lactobacillus*
- Higher levels of *Gardnerella*

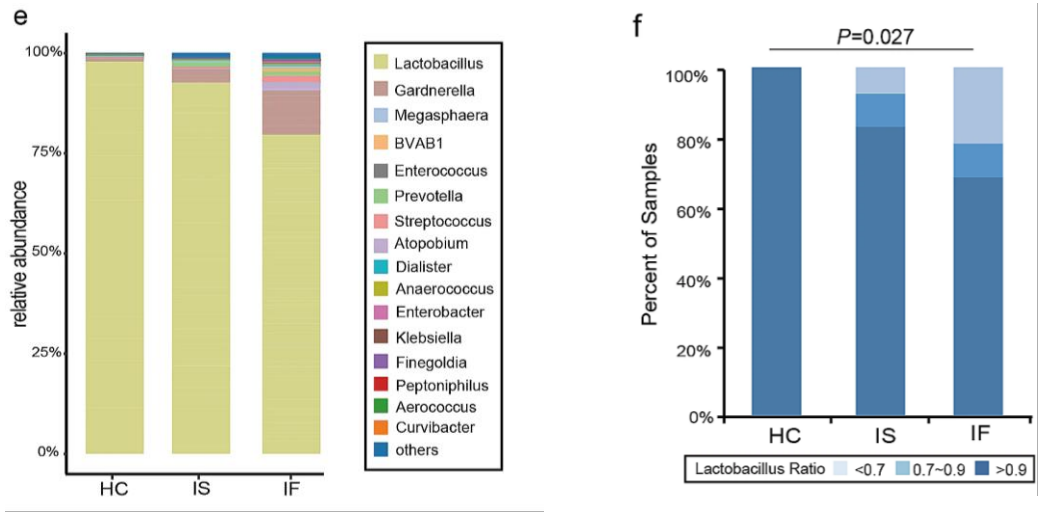
In healthy women and women with successful implantation:

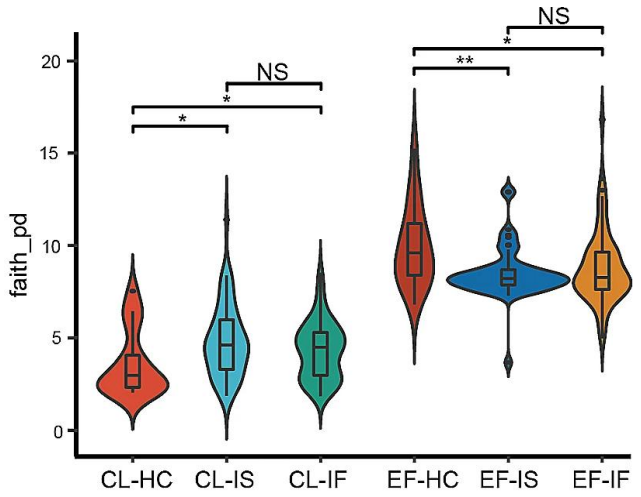
- Most samples contained >90% Lactobacillus

In women with implantation failure:

- Fewer women had Lactobacillus-dominated microbiota
- More samples had <70% Lactobacillus

Higher microbial diversity found in women with implantation failure – *Gardnerella, Sphingobium, Corynebacterium, Ralstoni, Enterobacter, Enterococcus*





1. Su et al 2024 Spring Nature https://doi.org/10.1186/s12958-024-01274-y

Vaginal microbiota and inflammation in IVF[1]

28 women completing IVF cycle:

- 14 with unexplained infertility
- 14 with male factor infertility (MFI)

Women with male factor infertility (MFI) had:

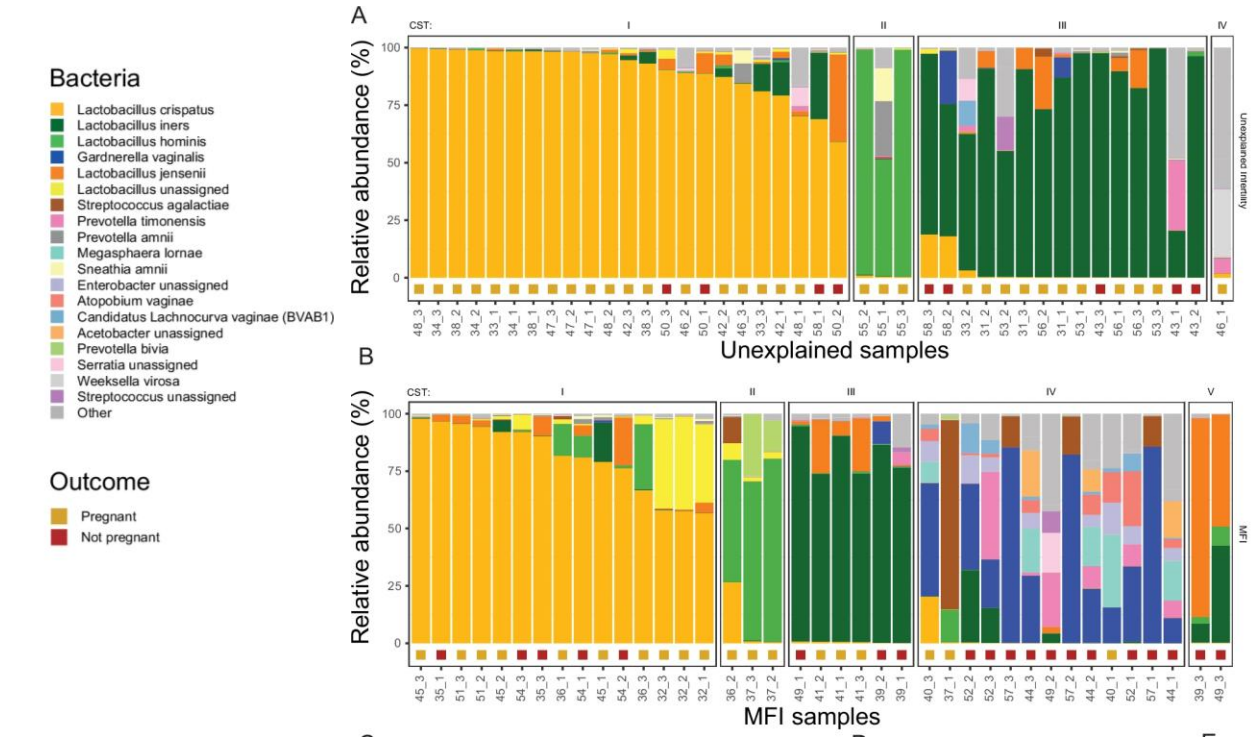
- higher vaginal microbial diversity
- than women with unexplained infertility

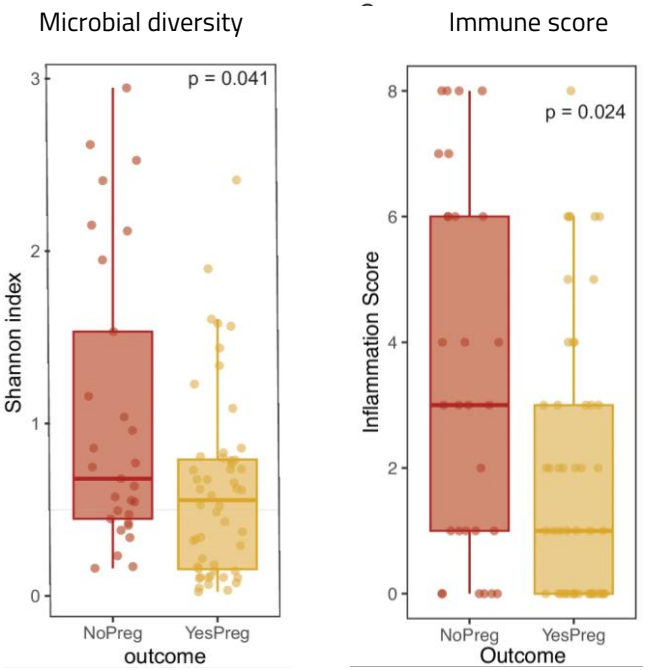
Women with a CST I microbiome (*L. crispatus*) had the highest pregnancy rates.

Women who became pregnant had:

- lower vaginal microbiome diversity
- more stable microbiota

Women who became pregnant had lower genital inflammation scores compared with women who did not become pregnant (cytokines measured IL-1β, IL-6, TNF-α, IL-8, IL-17)

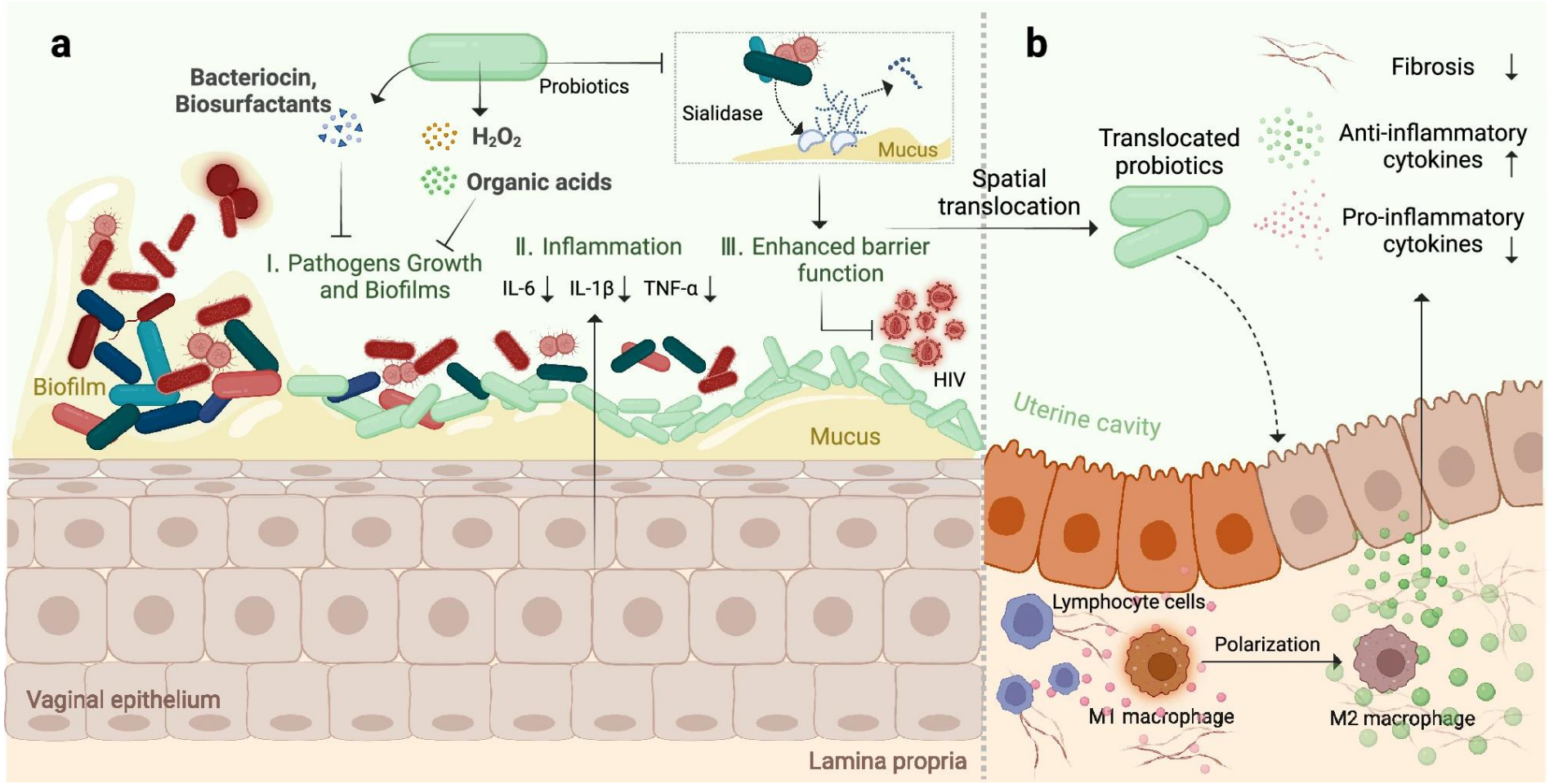




1. Bar et al 2025 NPJ Biofilm and Microbiomes; https://doi.org/10.1038/s41522-025-00732-8

Vaginal suppositories

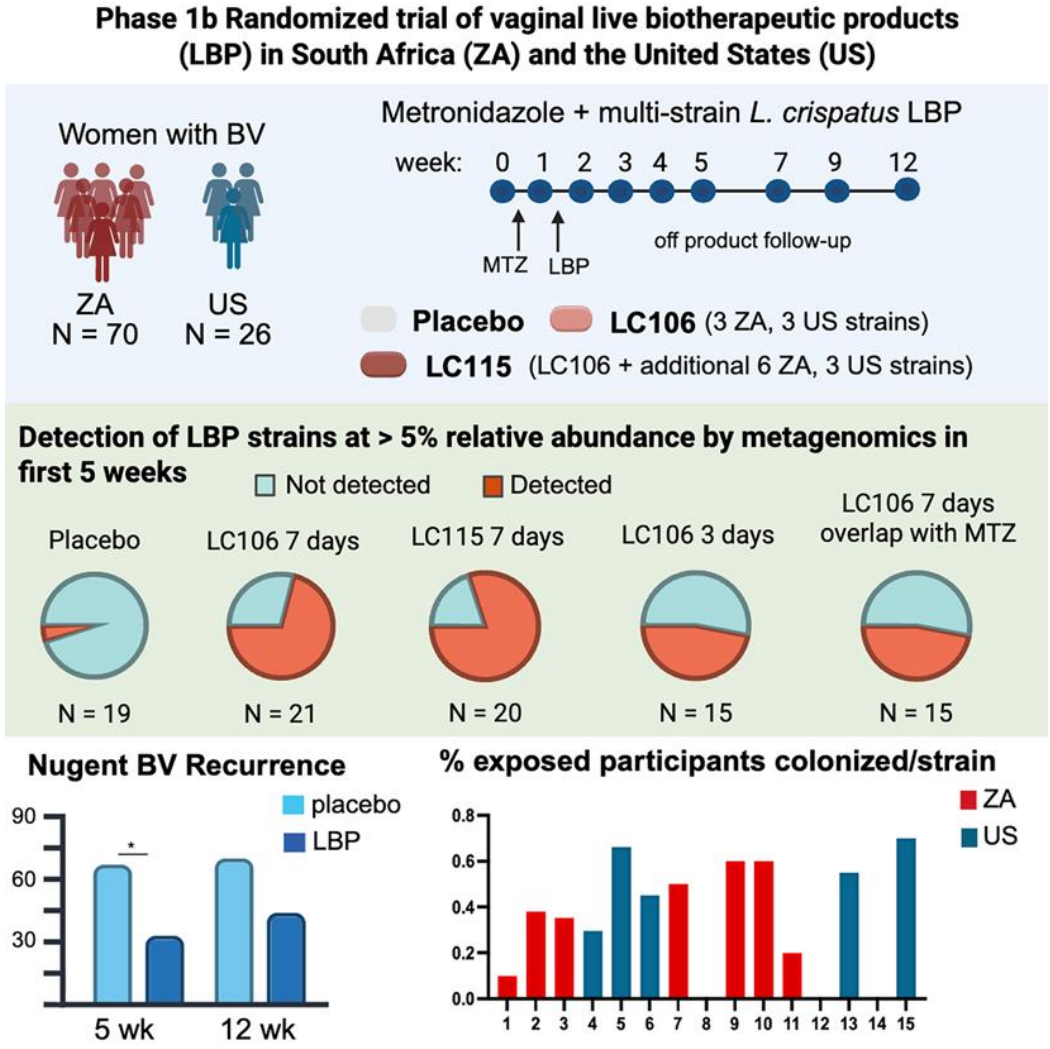
Probiotics potential in the vaginal niche



Cheng et al, 2025 npj Biofilms and Microbiome

The VIBRANT study – the potential of *L. crispatus* for BV

- Phase 1 RCT in US & South Africa
- Multi-strain vaginal *Lactobacillus crispatus* LBPs colonized 66% of participants
- Colonization persisted for up to 12 weeks following only 3–7 days of dosing
- The same three strains most frequently colonized participants in the US and South Africa
- Study products reduce risk for recurrent BV and are safe and well tolerated



1. Potloane et al 2026 Cell Host & Microbe https://doi.org/10.1016/j.chom.2026.02.016

Microbiome Center vaginal suppositories

Contains three active strains:

- *Lactobacillus crispatus* SP28 ($2.5x10^9$ cfu/piece)
- *Lactobacillus crispatus* LCR01 ($2.5x10^9$ cfu/piece)
- *Lactobacillus acidophilus* La02 ($2.5x10^9$ cfu/piece)

Matrix from cacao butter with coconut butter.

Available as 30 vaginal suppositories for EUR 81,-

Includes leaflet with clear instructions

Case report 1: IVF

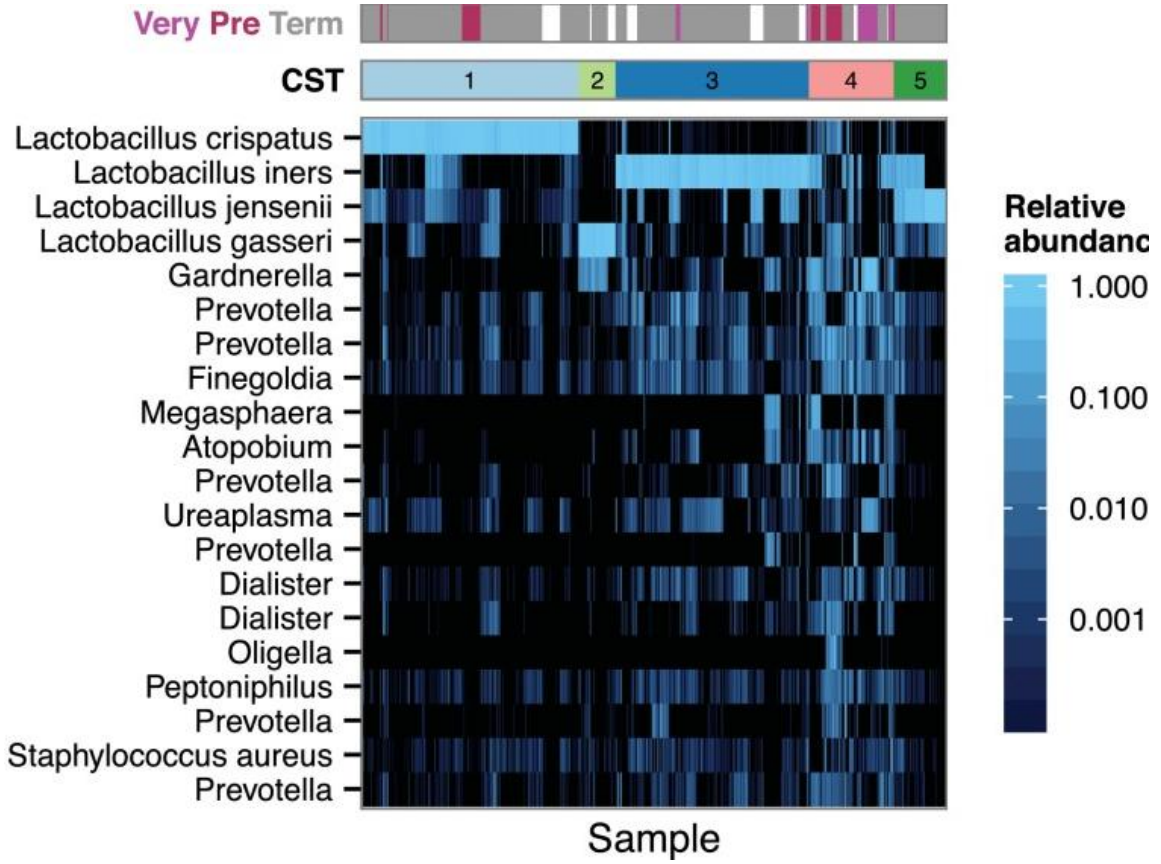
- Woman 35 years old
- Since 2015 stress-related disturbance of cycle, endometriosis, failed intrauterine insemination and two IVF attempts (low yield). Over 4 years of unfulfilled pregnancy wish.
- Estrogen breakdown problem
- After low-dose naltrexone (LDN) with exorphin-free diet, recovery of stress and immune system. Improvement of methylation with B vitamins and NAC.
- IVF yield suddenly very good (17 oocytes), 6 months after setting LDN pregnant. Labor after 38 weeks with cesarean section, son in 2020.

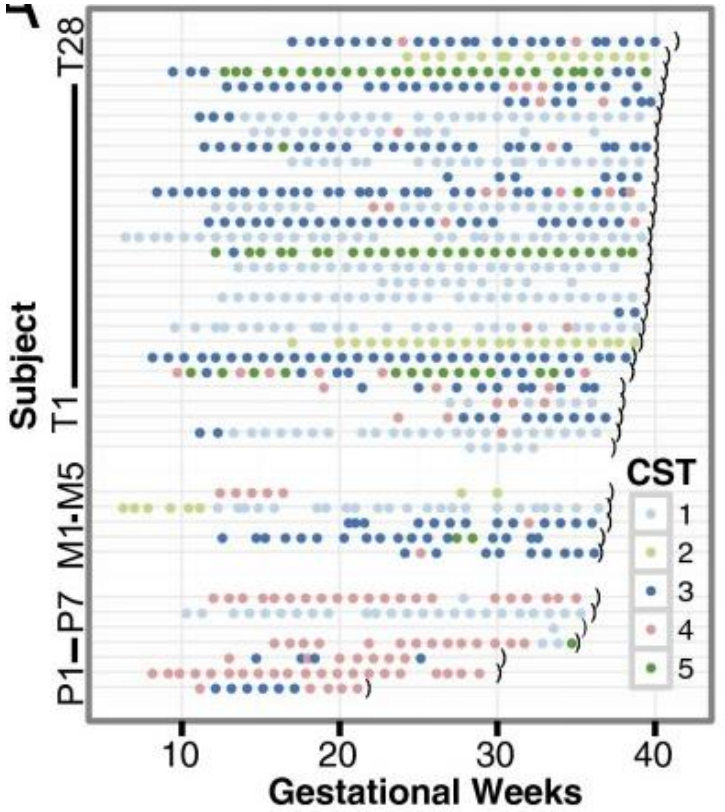
- For second pregnancy again setting up LDN from April till June 2020 with methylation support.
- From June also used vaginal suppositories. Also around embryo transfer.
- **Immediately pregnant**!

The vaginal microbiome & pregnancy outcomes

Preterm is associated with highly diverse vaginal microbiome[1]

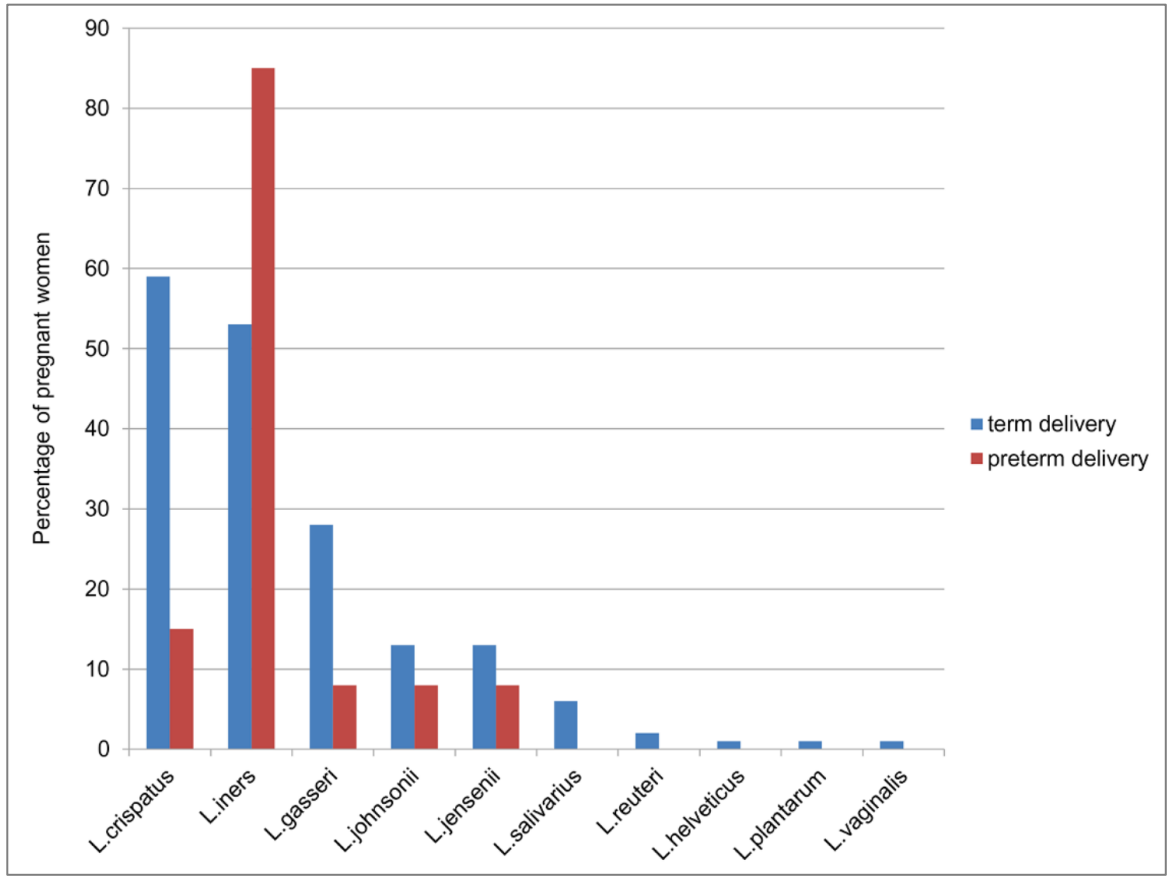
- Microbiome is relatively stable during pregnancy
- Healthy term pregnancy is associated with *Lactobacillus-dominated* vaginal microbiota (low diversity)
- Non- optimal microbiota (CSTIV) is associated with inflammation and adverse pregnancy outcomes

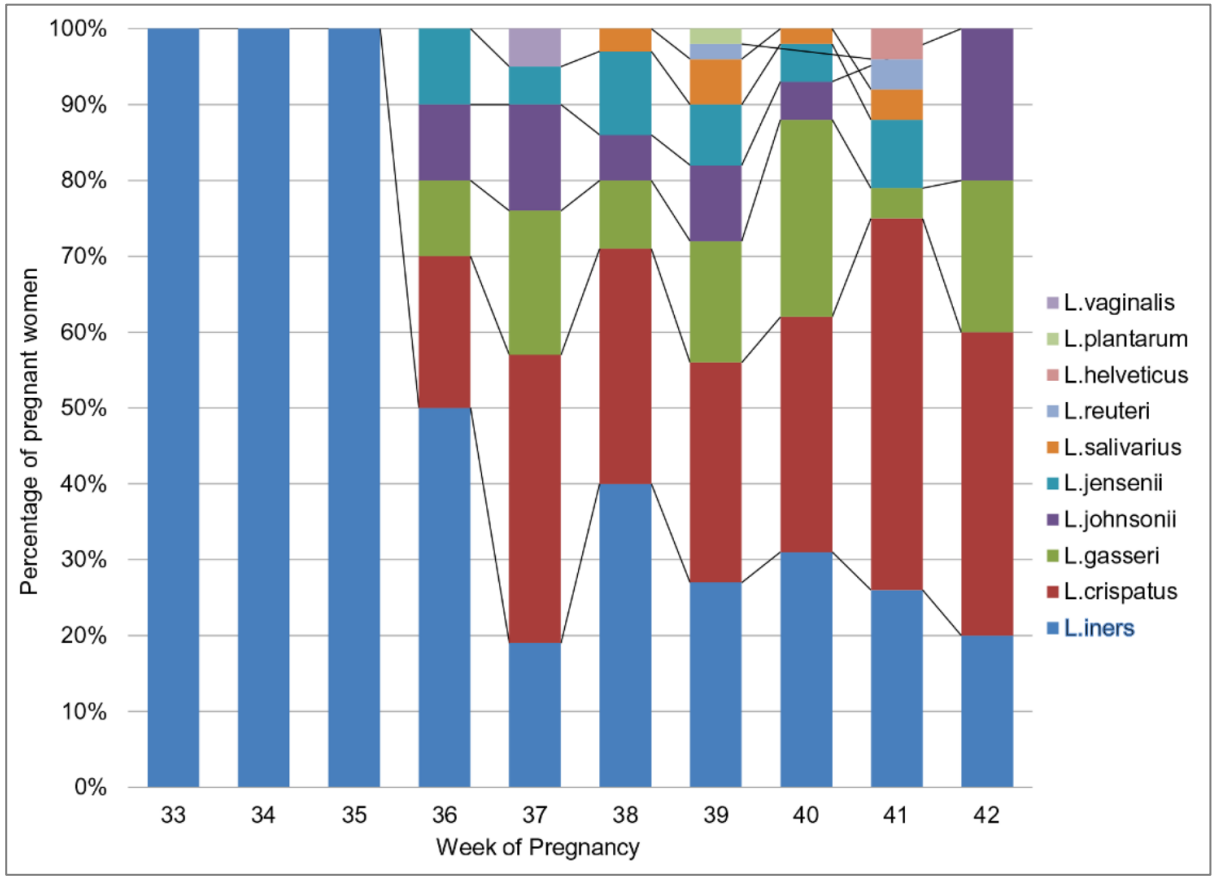




1. DiGiulio, D. B. et al. Proc Natl Acad Sci U S A 112, 11060–11065 (2015)

L. iners more often preterm delivery, *L. crispatus* most often term delivery[1]

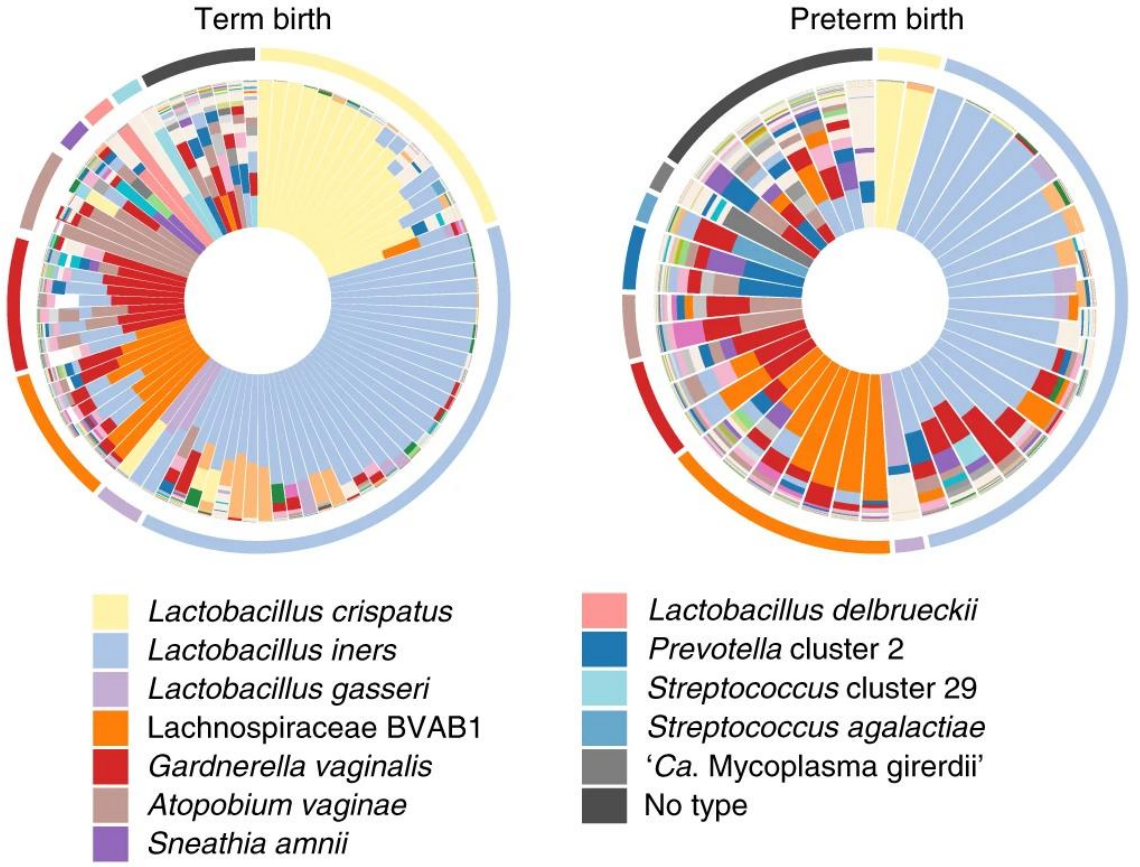




1. Petricevic, L. et al.Sci Rep.4,.5136.(2014)

Bacterial taxa associated with preterm birth [1]

- Women who delivered preterm exhibited significantly lower vaginal levels of *L. crispatus*
- Higher abundance of bacterial vaginosis–associated species (e.g. *BVAB1, Sneathia amnii, TM7-H1* and *Prevotella* spp.) was strongly associated with an increased risk of preterm birth.
- Preterm-birth-associated taxa were correlated with proinflammatory cytokines in vaginal fluid.



1. Fettweis, et al. 2019 Nature Medicine https://doi.org/10.1038/s41591-019-0450-2

The gut microbiome & fertility

Gut dysbiosis and effect on female fertility

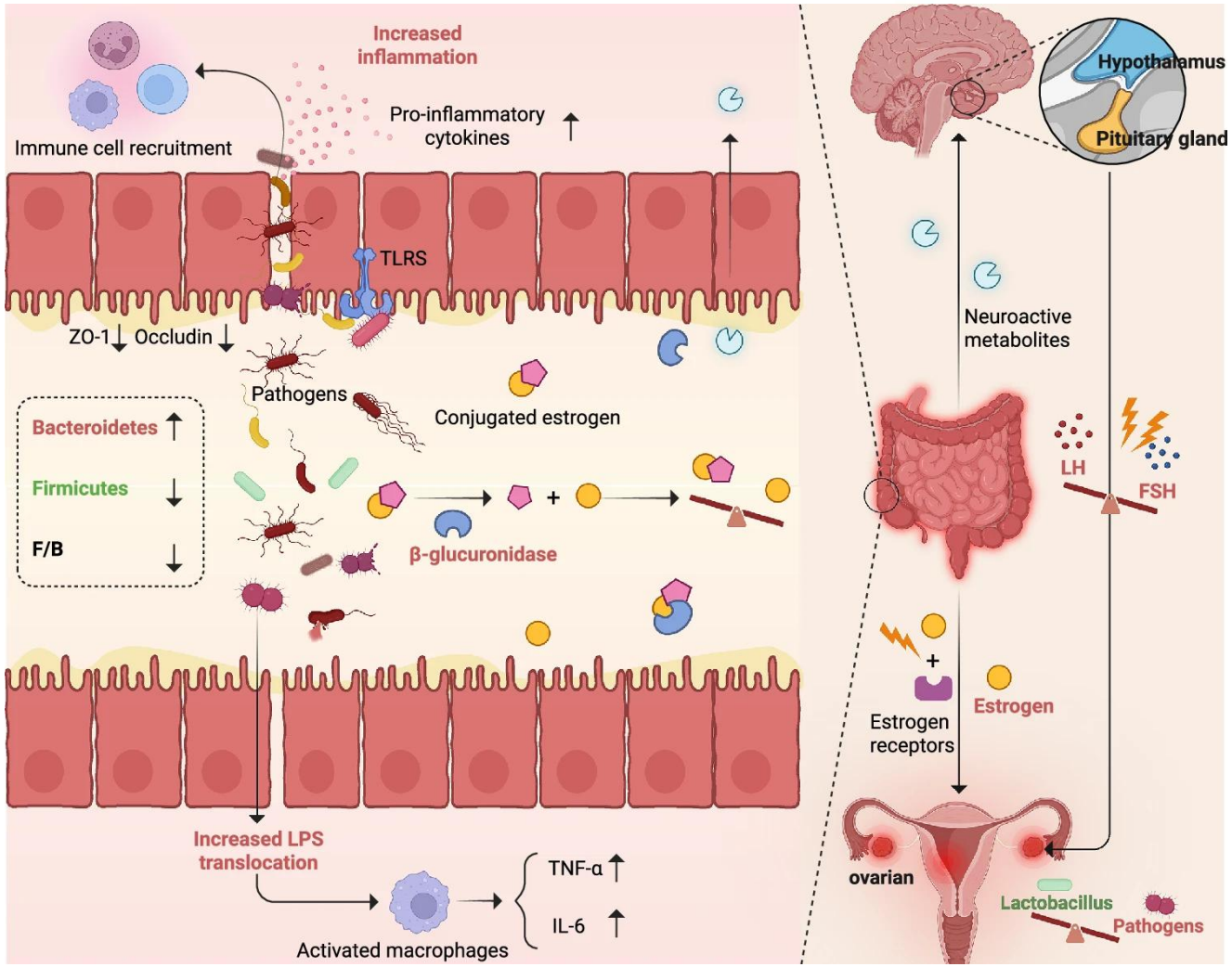
1. Hormonal regulation → regulate estrogen metabolism.

Dysbiosis → altered estrogen circulation. Important for:
- Ovulation
- Endometrial receptivity

2. Immune modulation

3. Metabolic control

Gut dysbiosis linked to:
- PCOS
- Endometriosis
- obesity-related infertility
- systemic inflammation



Cheng et al, 2025 npj Biofilms and Microbiome

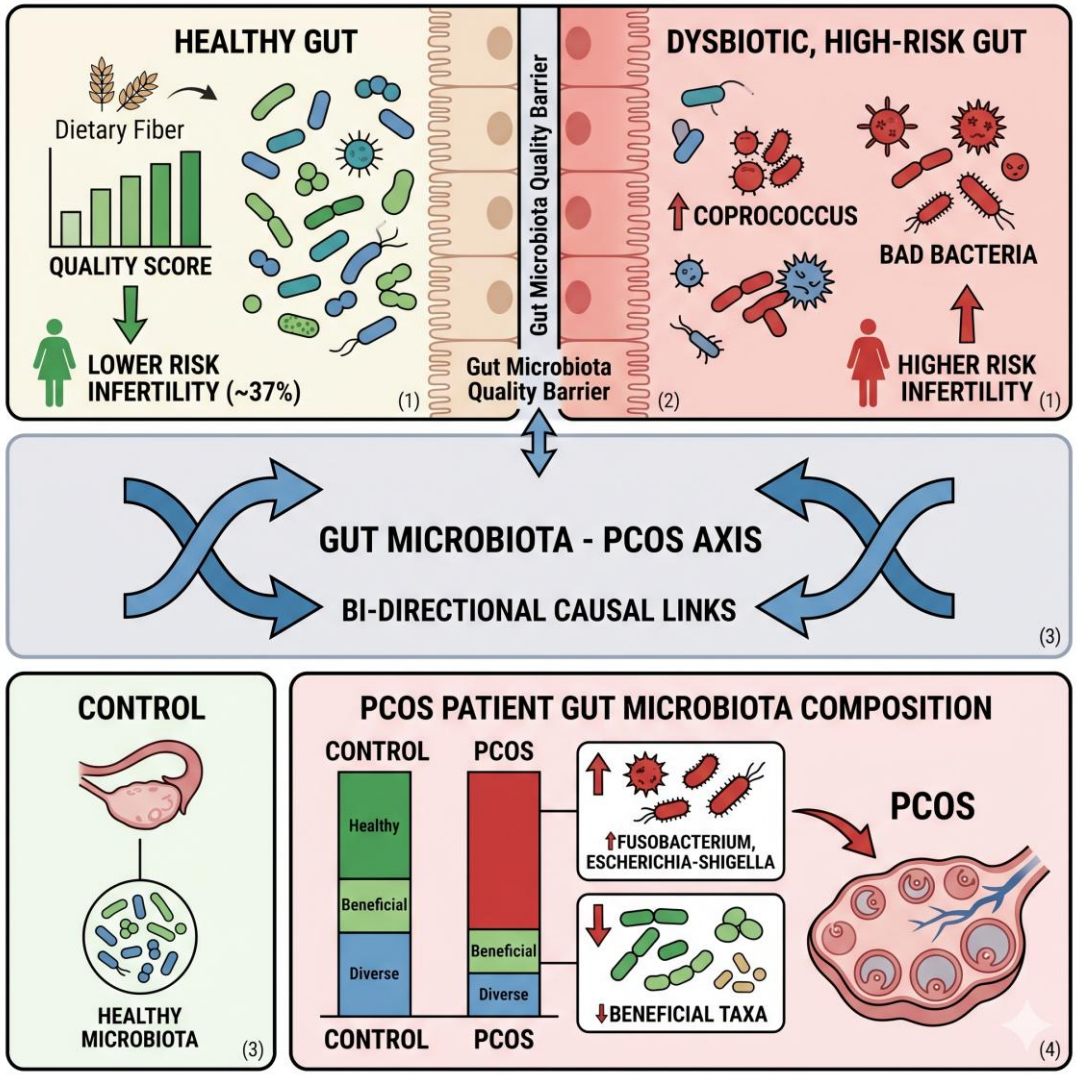
Gut dysbiosis and effect on female fertility

- Lower “gut microbiota quality score” → higher infertility risk. Women with healthier microbiota profiles had:~37% lower risk of infertility (based on population study)[1]

- Specific gut bacteria associated with increased infertility risk e.g. *Coprococcus2* → ↑ infertility risk[2]

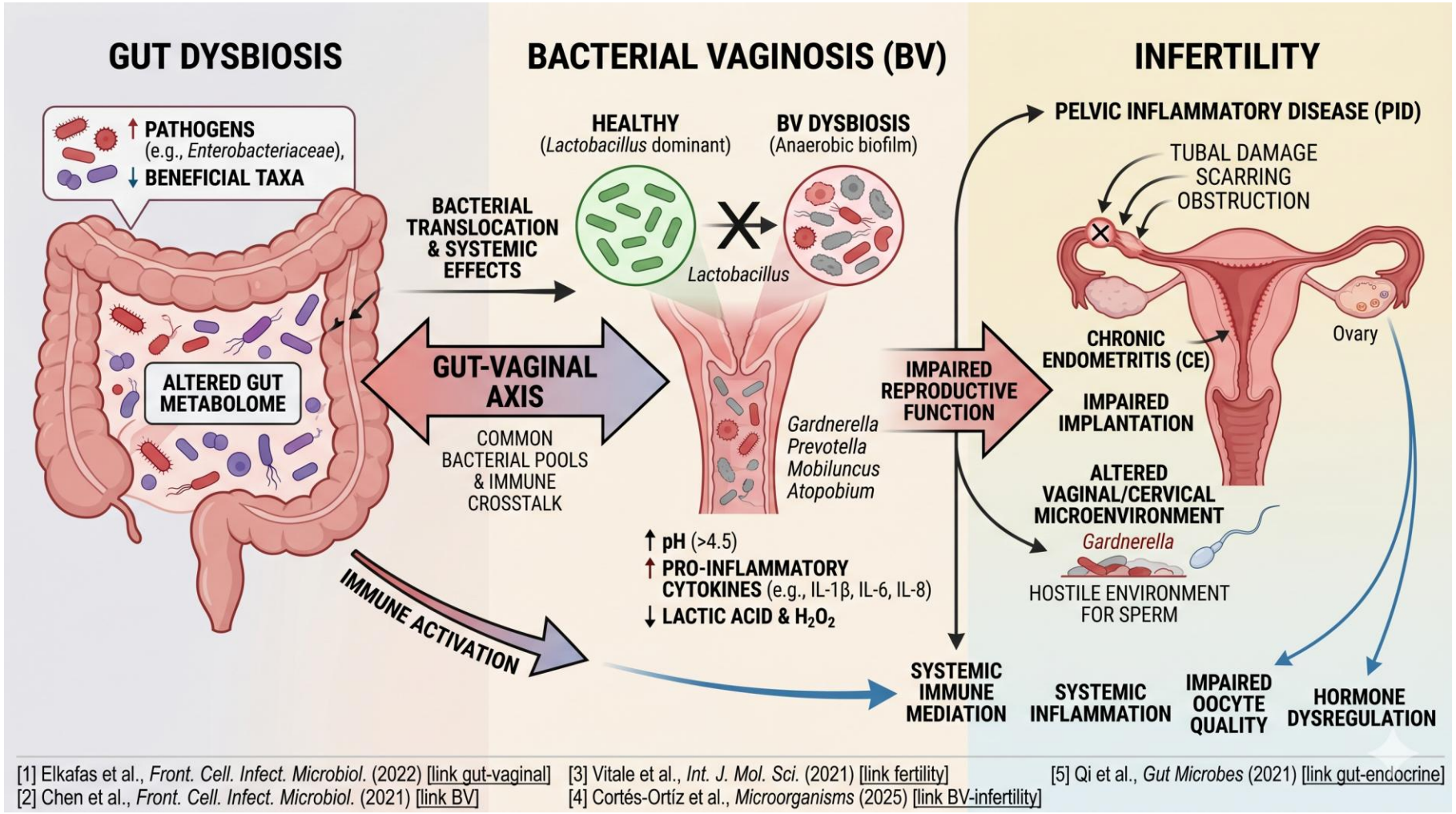
- Bi-directional causal links between gut microbiota and PCOS[3]

- PCOS patients show distinct gut microbiota composition
- ↑ *Fusobacterium*, *Escherichia-Shigella*
- ↓ Beneficial taxa [4]



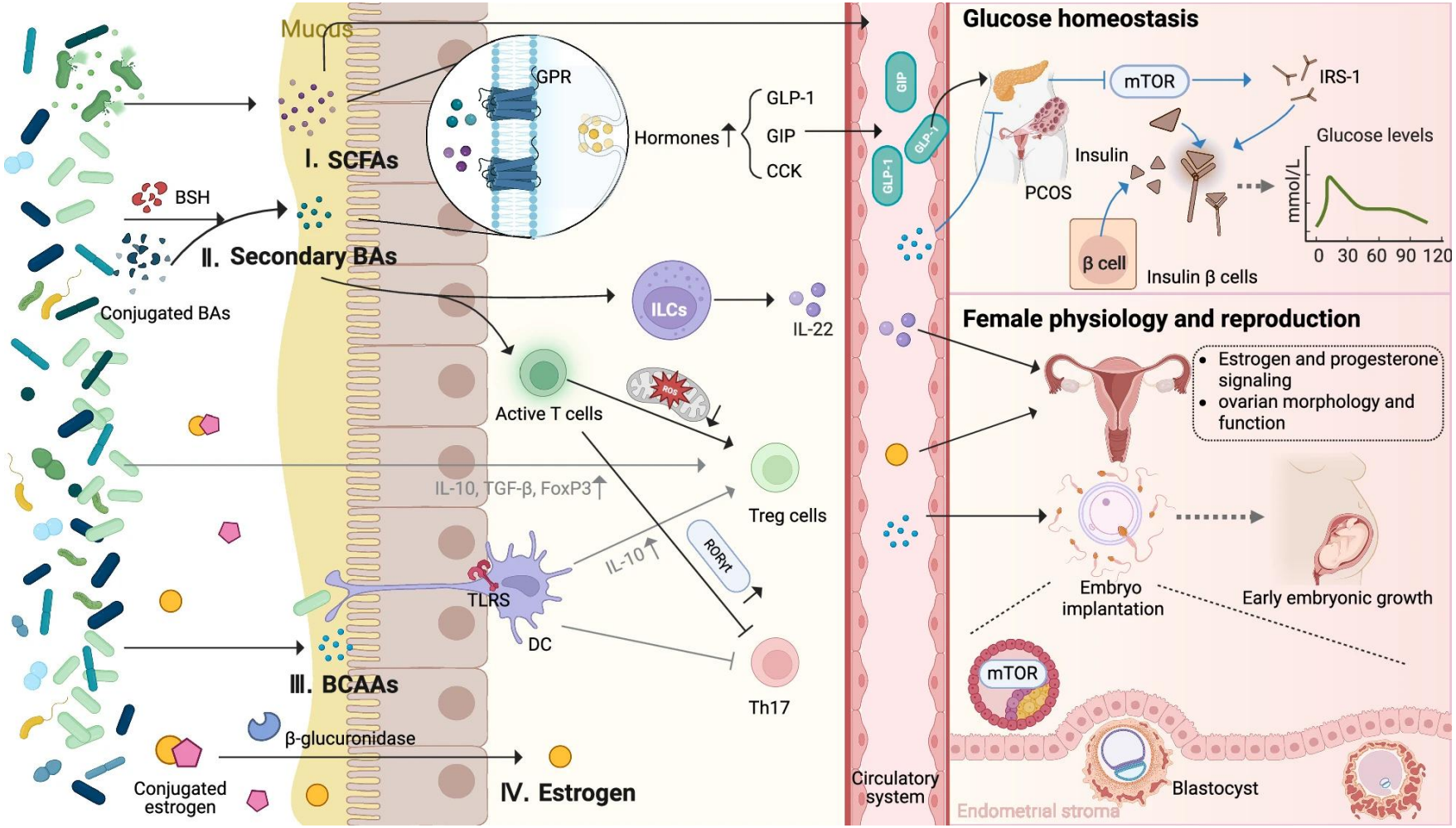
1. Zhang et al, 2025 Front Nut doi: 10.3389/fnut.2025.1583805
2. Liang et al 2023 Front Endocrinol https://doi.org/10.3389/fendo.2023.1164186
3. Mao et al 2024 Acta Obstet Gynecol Scand doi: 10.1111/aogs.14957.
4. Yang et al 2024 eClinical Medicine DOI: 10.1016/j.eclinm.2024.102884

Gut dysbiosis is linked with bacterial vaginosis, bacterial vaginosis is linked with female infertility



[1] Elkafas et al., *Front. Cell. Infect. Microbiol.* (2022) [link gut-vaginal]
[2] Chen et al., *Front. Cell. Infect. Microbiol.* (2021) [link BV]
[3] Vitale et al., *Int. J. Mol. Sci.* (2021) [link fertility]
[4] Cortés-Ortíz et al., *Microorganisms* (2025) [link BV-infertility]
[5] Qi et al., *Gut Microbes* (2021) [link gut-endocrine]

Probiotics potential in the gut to improve women's reproductive health



Cheng et al, 2025 npj Biofilms and Microbiome

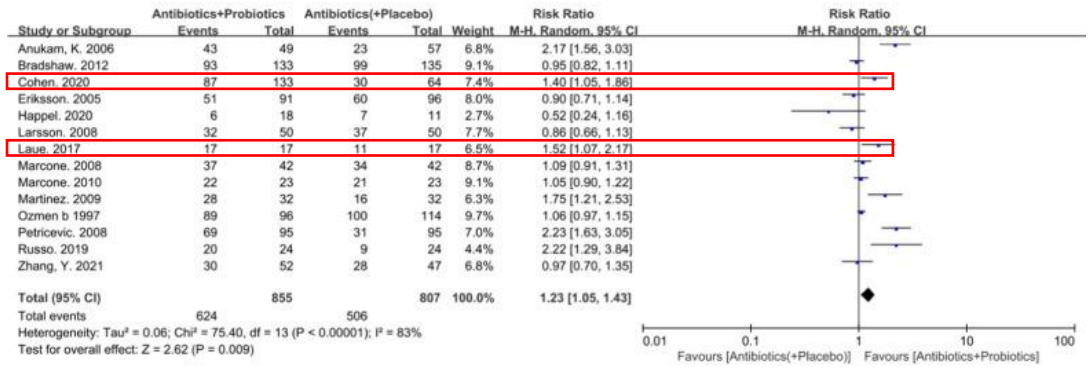
Probiotics for bacterial vaginosis

Several meta-analyses on probiotics for treatment of bacterial vaginosis are published.

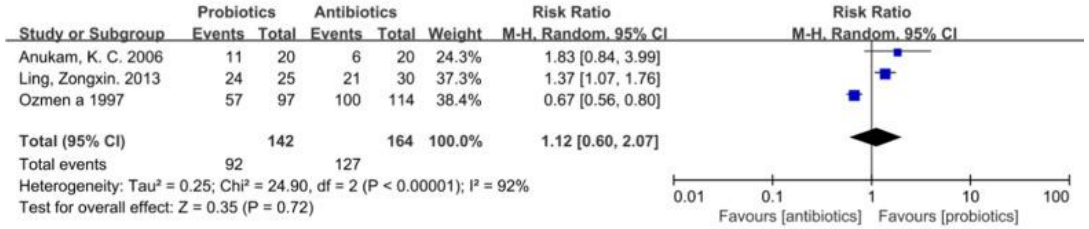
One meta-analaysis from 2022 includes 14 studies with 2093 participants[1]:

- Antibiotics + probiotics are somewhat better than antibiotics alone (RR: 1,23)
- Probiotics are much better than placebo (RR 15,2)
- Half of studies used oral administration
- Only 2 studies use a *L. crispatus* strain

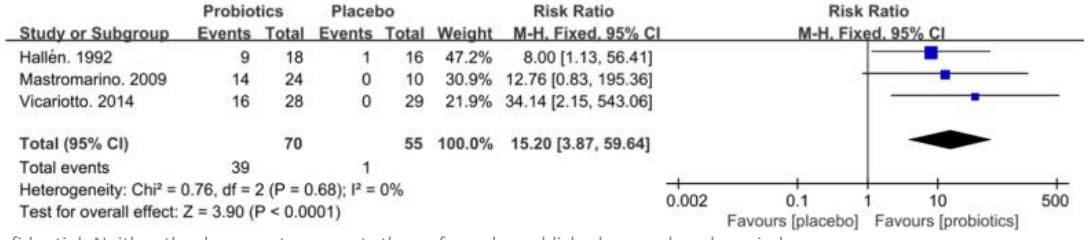
A. Antibiotics + Probiotics/Antibiotics (+Placebo)



B. Probiotics/Antibiotics.



C. Probiotics/Placebo.



1. Chen, R. et al. Reprod Health 19, 137 (2022)

Case report 2: VVC + BV

- Woman 22 years old
- Alternating vaginal complaints due to candida or due to bacterial vaginosis
- Was prescribed vaginal suppositories

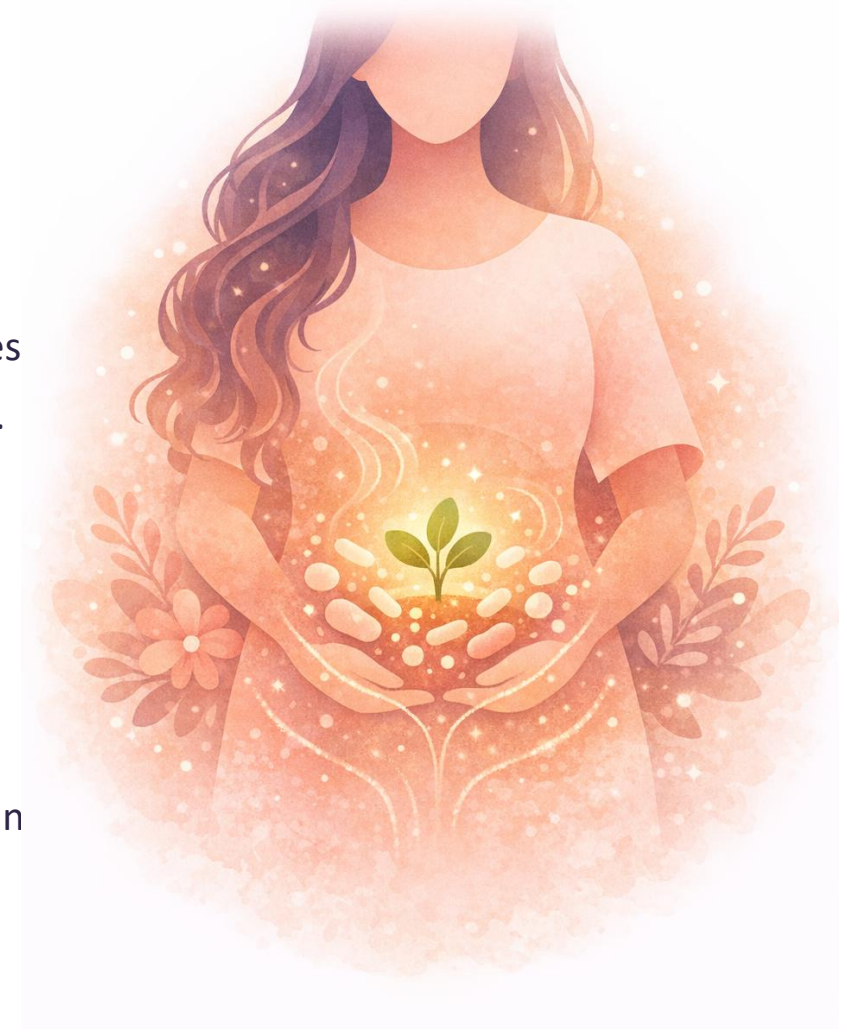
- Were they easy to use?
  - *“There seems to be some kind of coating over them that makes it easy. It doesn't hurt either.“*
- Did you experience any side effects?
  - *“I did not experience any side effects.”*
- Have they had the desired effect?
  - *“The suppositories often had the desired effect, especially with vaginal yeast infections. With bacterial infections, it seems to come back more quickly.”*

Conclusions

- Infertility is common
- Both male and female infertility play a role

- The vaginal microbiome influence the female fertility
- Vaginal dysbiosis is linked to lower pregnancy rates
- *L. crispatus* dominated vaginal microbiome is linked to highest fertility rates
- It is not only about “who is there?” but also about “what are they doing?”. Example: inflammation.
- *L. crispatus* dominance is also linked to lower rates of preterm delivery

- *L. crispatus*-containing vaginal suppositories have been shown to improve pregnancy rates.
- The gut microbiome influences reproduction both directly and via the vagin microbiome
- Treating gut dysbiosis simultaneously can be helpful



In case of any questions contact

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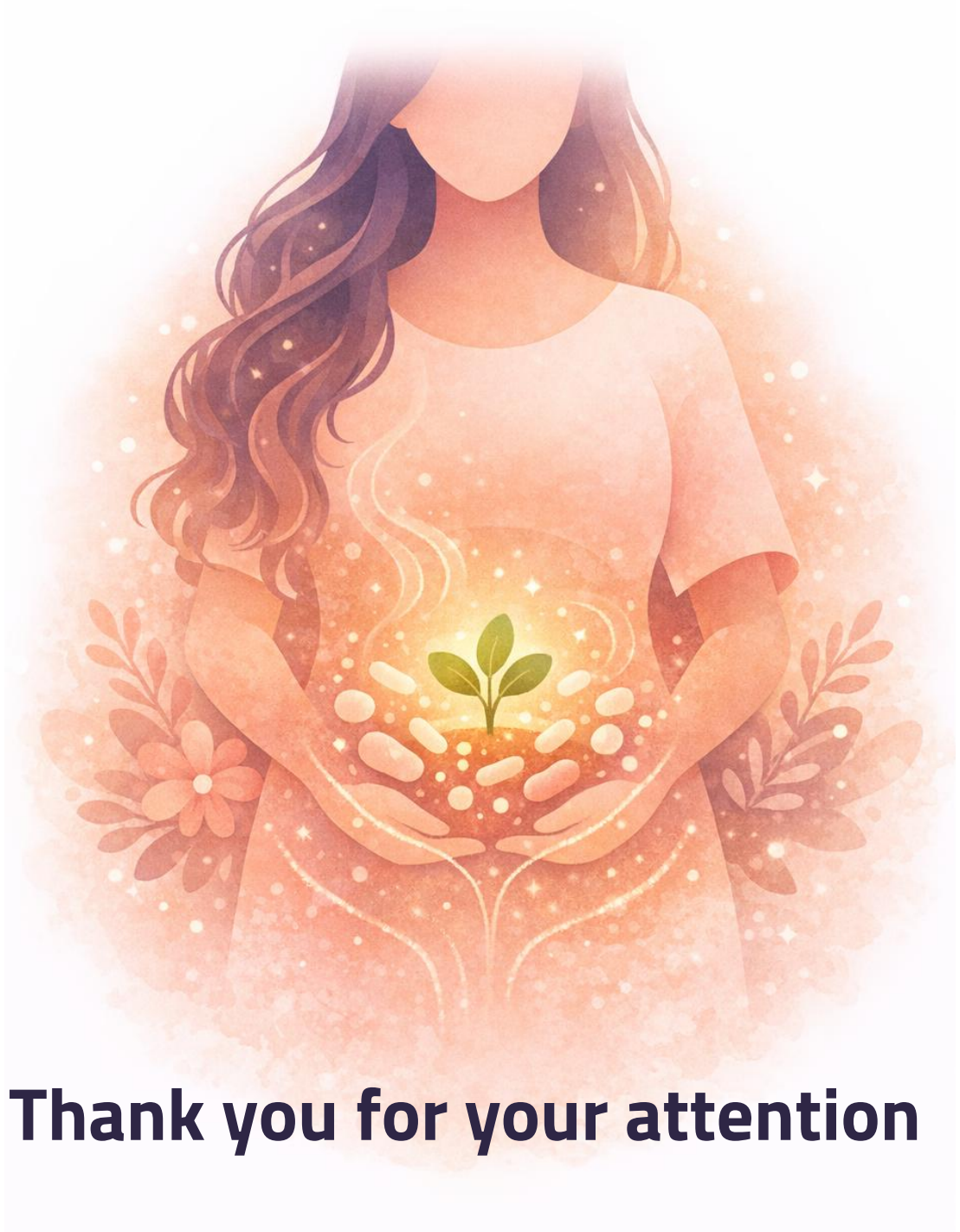

Thank you for your attention