

The Isala project: characterizing the female microbiome through citizen science

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ECCO XLII meeting

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The vaginal microbiome

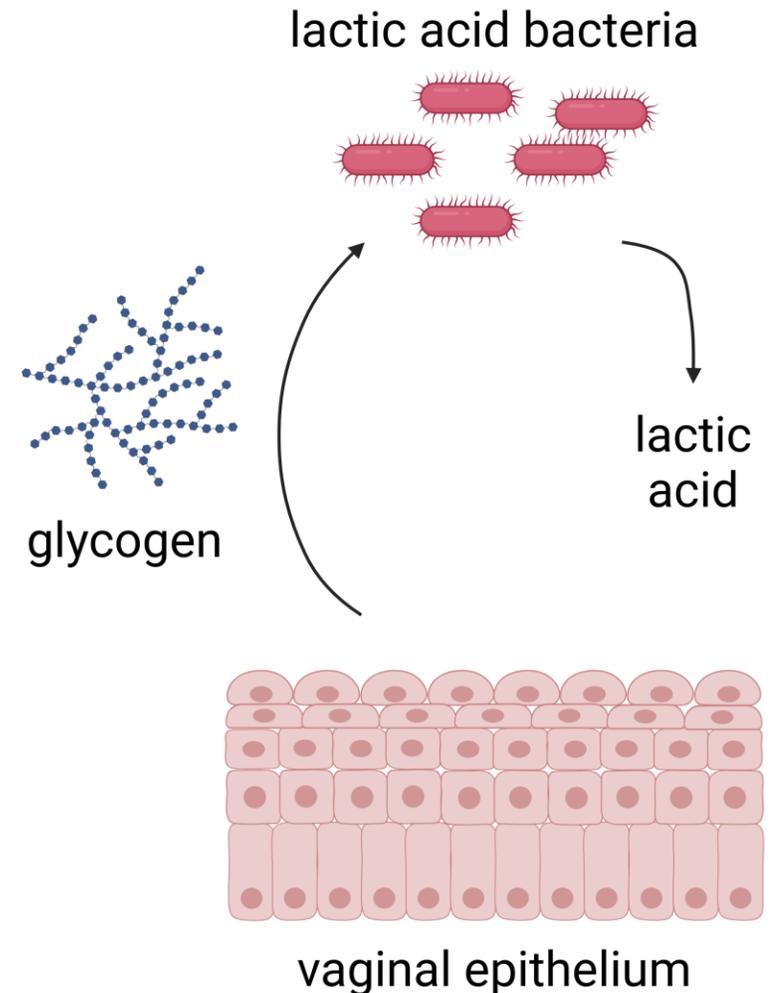
Community of mutualistic bacteria

- Host supplies glycogen as carbon source
- Community produces protective lactic acid
- Unique to *Homo sapiens*!

Composition strongly associated with health

~ *Lactobacillus* dominance reduces risk of:

- Bacterial vaginosis symptoms
- STDs
- Miscarriage and preterm birth



The vaginal microbiome

Fundamental questions unsolved

1. What determines the composition of the vaginal microbiome?
2. Where do vaginal bacteria come from?
3. Do vaginal bacteria interact with each other? How?

The vaginal microbiome

Problem with previous studies:

- Small-scale, clinical setting
- "Top down"

--> Citizen science project: Isala

- Large sample from general population
- Self-sampling
- Dialog with participants

Our inspiration



Isala Van Diest
1842-1916

CS challenges



Recruitment

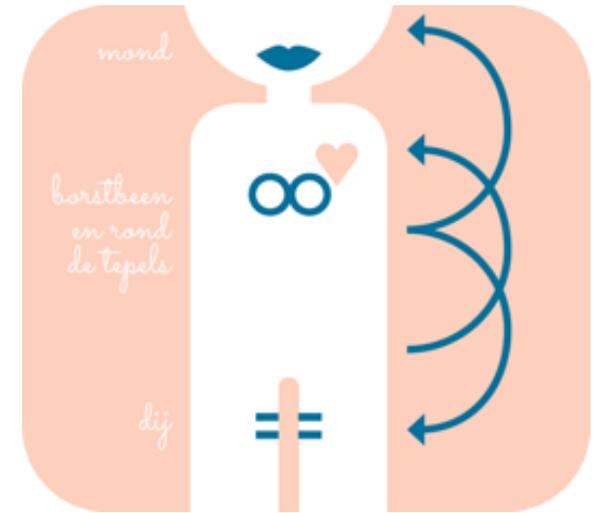
- Call for participants through regular and social media
- Professional website and promotional material
- Putting the project in a societal context
 - Tabboo on discussing vaginal health
 - Women's health research lagging behind



CS challenges

Communication

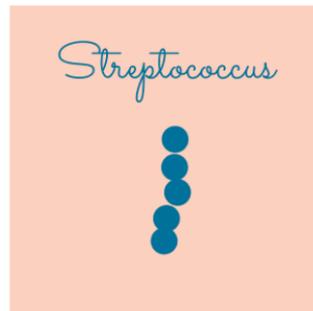
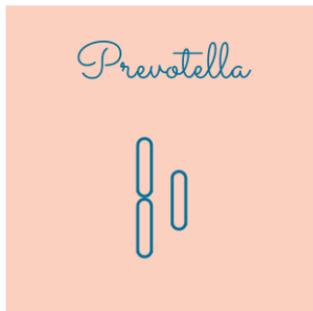
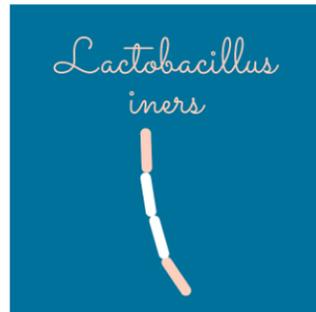
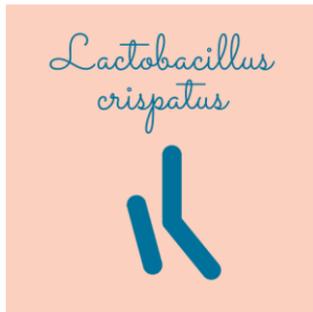
- Very clear instructions
- Sampling boxes professionally designed
- Engagement through email and social media
 - ~1,000 mails
 - ~200 social media posts
- Right "tone of voice"



CS challenges

Communication

- Communicated individual results as profile/type



With Isala, we have found that this bacterium was dominant in the vagina of 1,398 women. That is about 43% of all participants that donated a sample.



What does this bacterium look like?

Lactobacillus crispatus is a fairly long rod of 2 to 11 micrometers in size with a thick wall. That's not that big when you know that 1000 micrometers fit into one millimeter. The name comes from the English 'curled, crisped'. This bacterium was first discovered by Brygoo and Aladame in 1953.



What does science already know about this bacterium?

Kind of a lot! This bacterium has a very extensive genome of about 2 million base pairs with more than 2000 genes, which means that this bacterium can make more than 2000 different proteins. She also seems to be well equipped to survive in a relatively wide variety of animal and human environments.



What is this bacterium doing in my vagina?

Lactobacillus crispatus is very often associated with a healthy vagina. This bacterium produces a lot of lactic acid and therefore ensures acidity in the vagina. In this way, this bacterium protects your vagina against infections or pathogenic bacteria and fungi. *Lactobacillus crispatus* also makes other molecules that act as natural antibiotics or protect against inflammation, but not all these molecules are well known. When researching a healthy vaginal microbiome, we often focus on lactic acid, but each strain of *Lactobacillus* also produces an array of protective or beneficial molecules for our health.

Unravelling these molecules is something that Isala's team is happy to work on in the future. For example, we already know that *Lactobacillus crispatus* has a very good and active immune system so that this bacterium can protect itself against bacteriophages. These are viruses that can make (healthy) bacteria sick.



Does this bacterium occur elsewhere?

Yes, *Lactobacillus crispatus* is also found in your gut and scientists have also found it in chickens. If you enter this bacterium in a search engine on the internet, you will probably come across a number of probiotics. After all, a lot of scientific research has already been done into the health effects of this bacterium.

CS challenges

Logistics

- Collaboration with Belgian post office
- Pilot study to verify sample quality
- Use of Qualtrics for questionnaire



Cross-sectional study

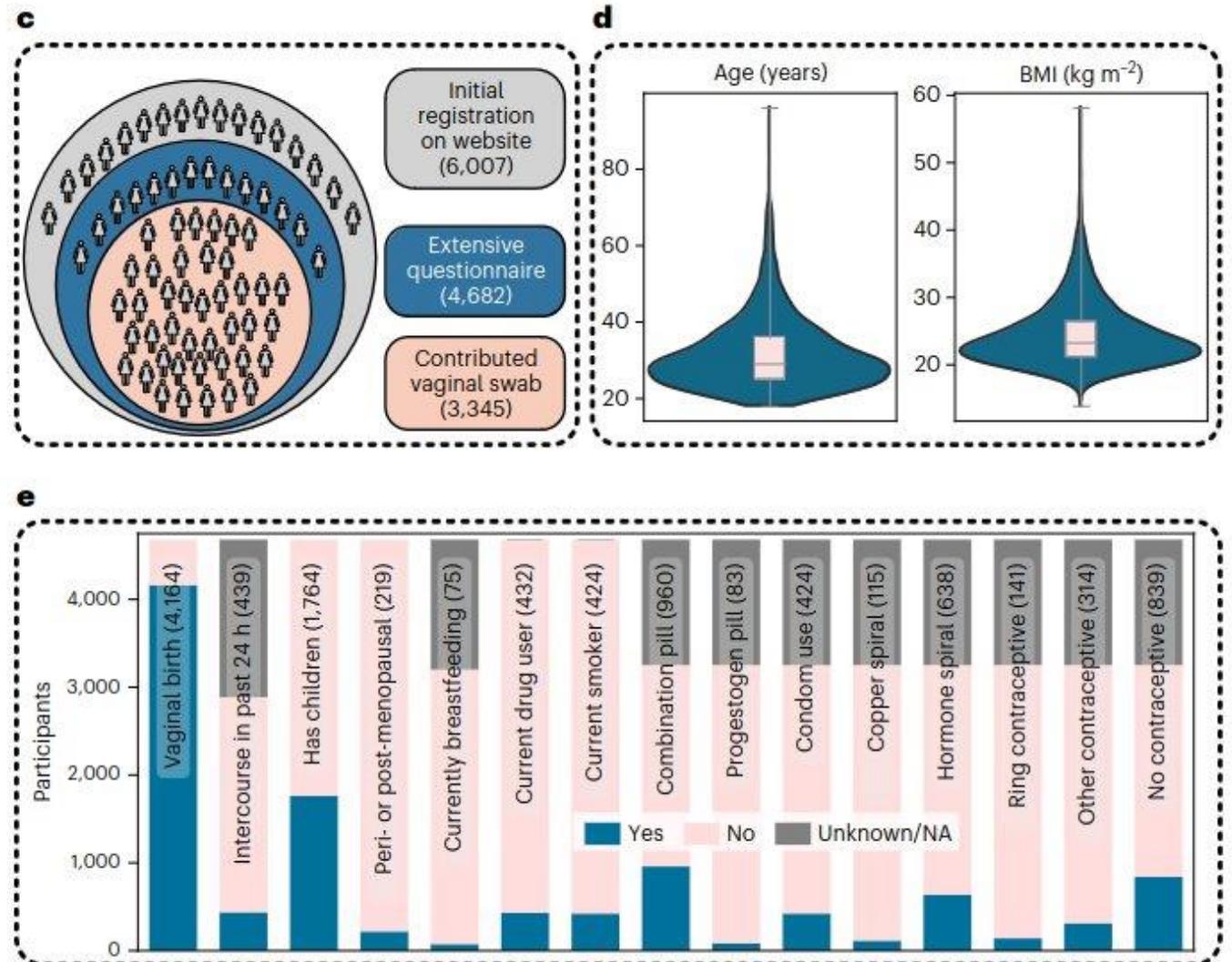
More than 6,000 women registered in 10 days!

Inclusion criteria:

- 18 years old
- Not currently pregnant

Representative sample?

- Huge age bias
- 10% identified themselves with a non-Belgian culture
- 5.4% below poverty level



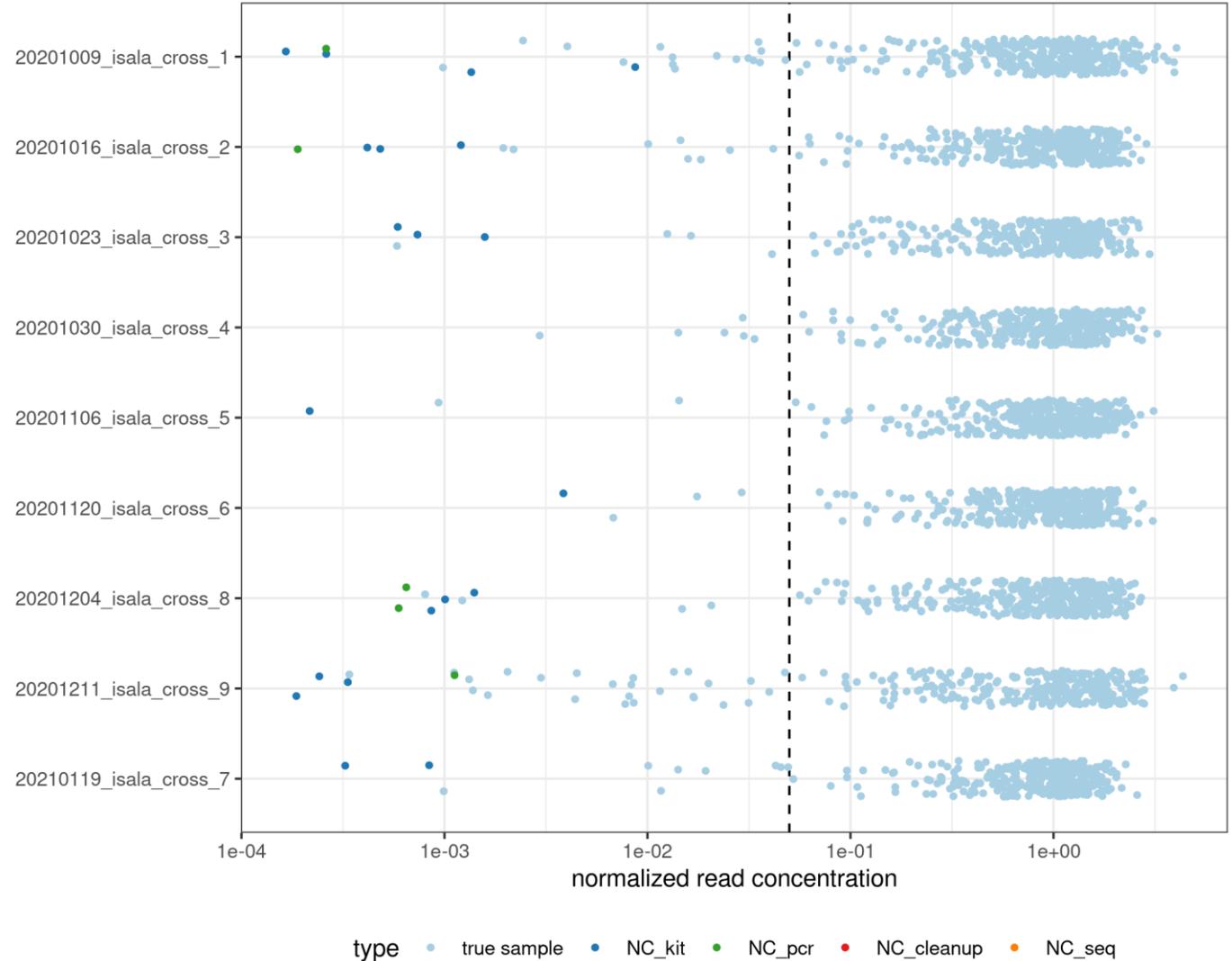
Cross-sectional study

The data: per participant:

- Two vaginal swabs --> 16S sequencing and culturing
- Very extensive questionnaire (139 questions):
 - Demographics: age, ethnicity, ...
 - Life history: children, pregnancies, ...
 - General health: BMI, diet, self-evaluated health, ...
 - Vaginal health: menstrual cycle phase, contraception, ...
 - Sexual lifestyle: recent intercourse, number of sexual partners, ...
 - ...

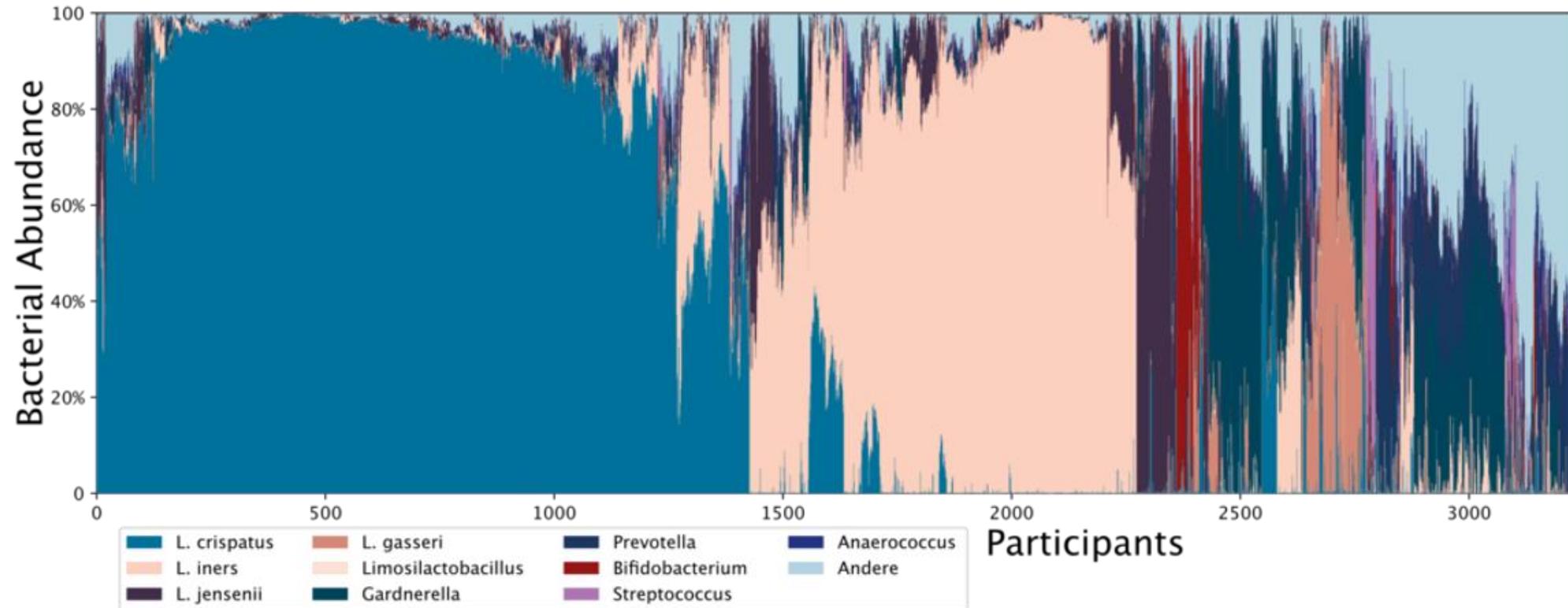
Cross-sectional study

High sample quality



Cross-sectional study

Overview of profiles:



Cross-sectional study

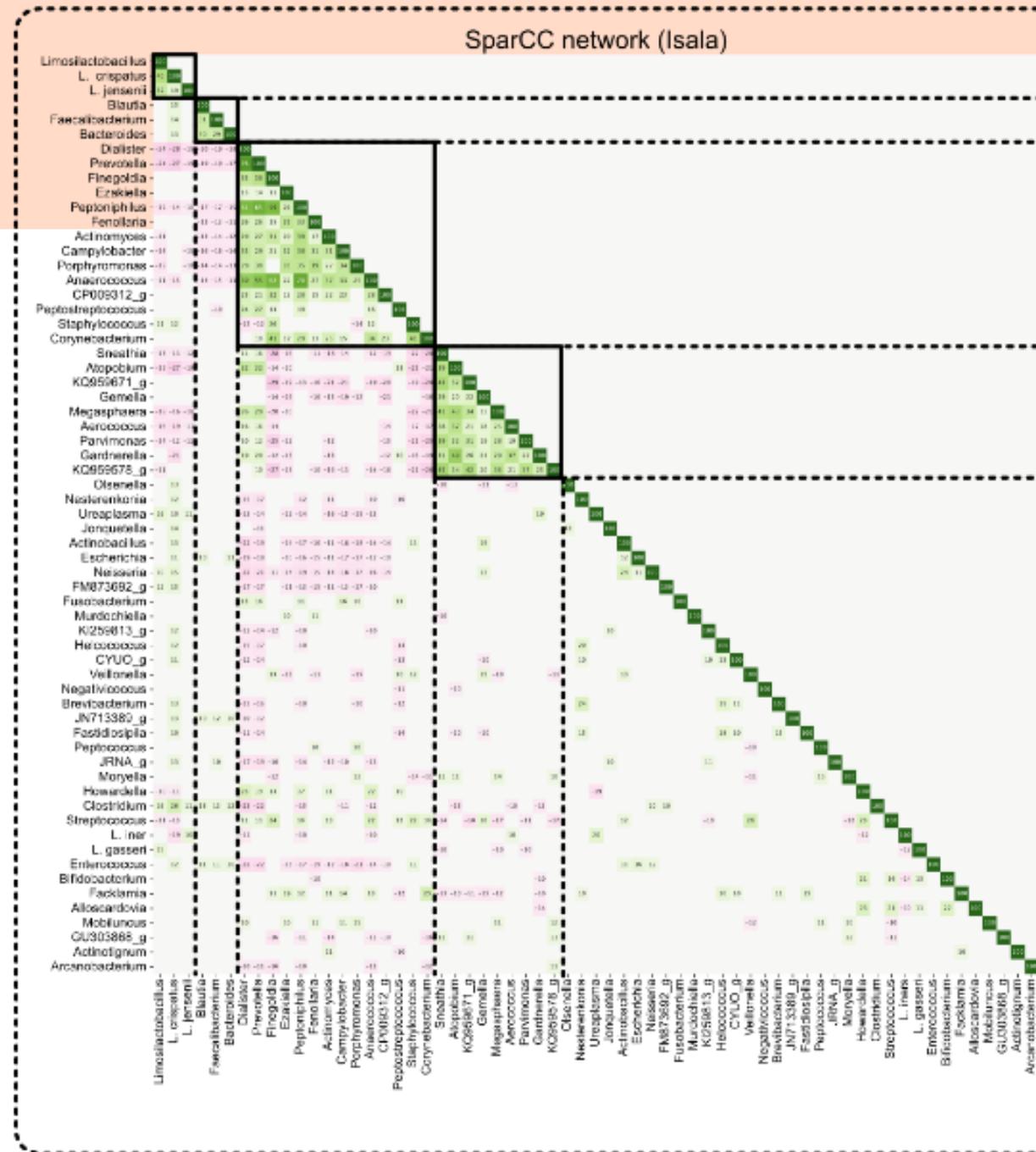
Covariates explaining most microbiome variance:

1. Age (1.2%):
 - - association with *L. crispatus/jensenii*
2. Having had children (1.2%)
 - - association with *L. crispatus/jensenii*
 - + association with *L. gasseri*
3. Phase of the menstrual cycle (0.7%):
 - + association between luteal phase and *L. crispatus/jensenii*
4. Recent sexual intercourse (0.3%)
 - + association with *Streptococcus*, *Staphylococcus* and others

Cross-sectional study

Four "modules" of intercorrelated taxa:

1. *L. crispatus* module
2. *Bacteroides* module
3. *Anaerococcus* module
4. *Gardnerella* module

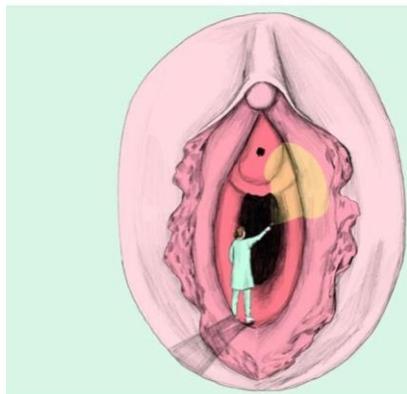


Cross-sectional study

ds De Standaard

ONDERZOEK

De vagina: iedereen kent de weg, niemand de bewoners



© Jip van den Toorn



Grootste vaginale burgeronderzoek in Vlaanderen: "Vooral goed nieuws"

vrt NWS



Foto: Unsplash Timothy Meinberg

Vlaamse vagina is gezonder dan gedacht: "Gezonde voeding speelt grote rol"

eos WETENSCHAP

Gezondheid

Het vrouwelijk microbioom in kaart gebracht



U Universiteit van Vlaanderen

Waarom lijkt je vagina op een potje yoghurt?

prof. dr. Sarah Lebeer

Universiteit Antwerpen ▶ Afspelen

DeMorgen.

Donderdag 24/06/2021

◆ Nieuws Gezondheid

Grootschalig onderzoek naar vaginale gezondheid van Belgische vrouwen: dit zijn de conclusies



The Brussels Times

Nine in ten women in Belgium suffer from their period, large-scale study finds

Friday, 25 June 2021

By Lauren Walker

HLN NINA ABONNEREN LOGIN



Meer dan 73 procent van de vrouwen maakte zich al eens zorgen over hun vaginale gezondheid. © Polina Zimmerman via Pexels

Belgische wetenschappers achterhalen voor het eerst hoe een gezond vaginaal

Flair

oef, het gaat goed met de



foef

Facts, figures & tips voor een gezonde vagina

Groot vaginaonderzoek: wie zijn de bewoners en zijn ze gezond?



N Het Nieuwsblad

Cross-sectional study

Resource | [Open access](#) | Published: 26 October 2023

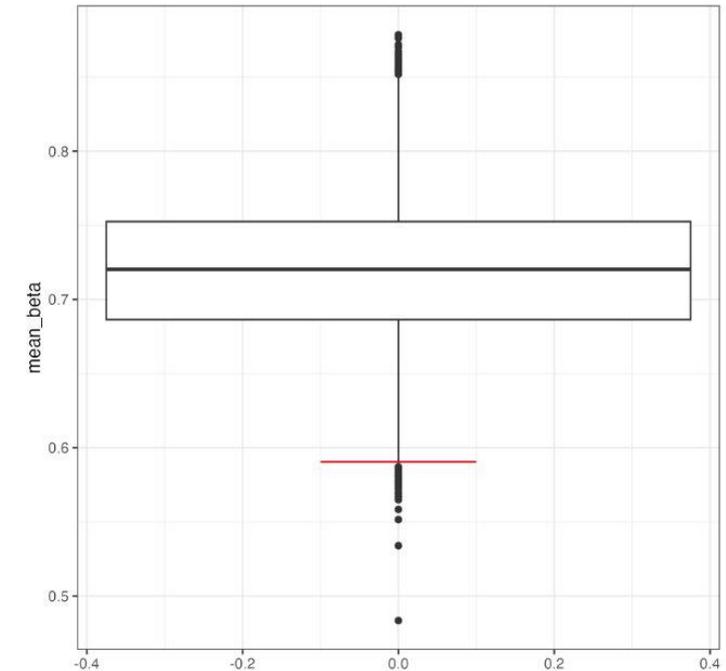
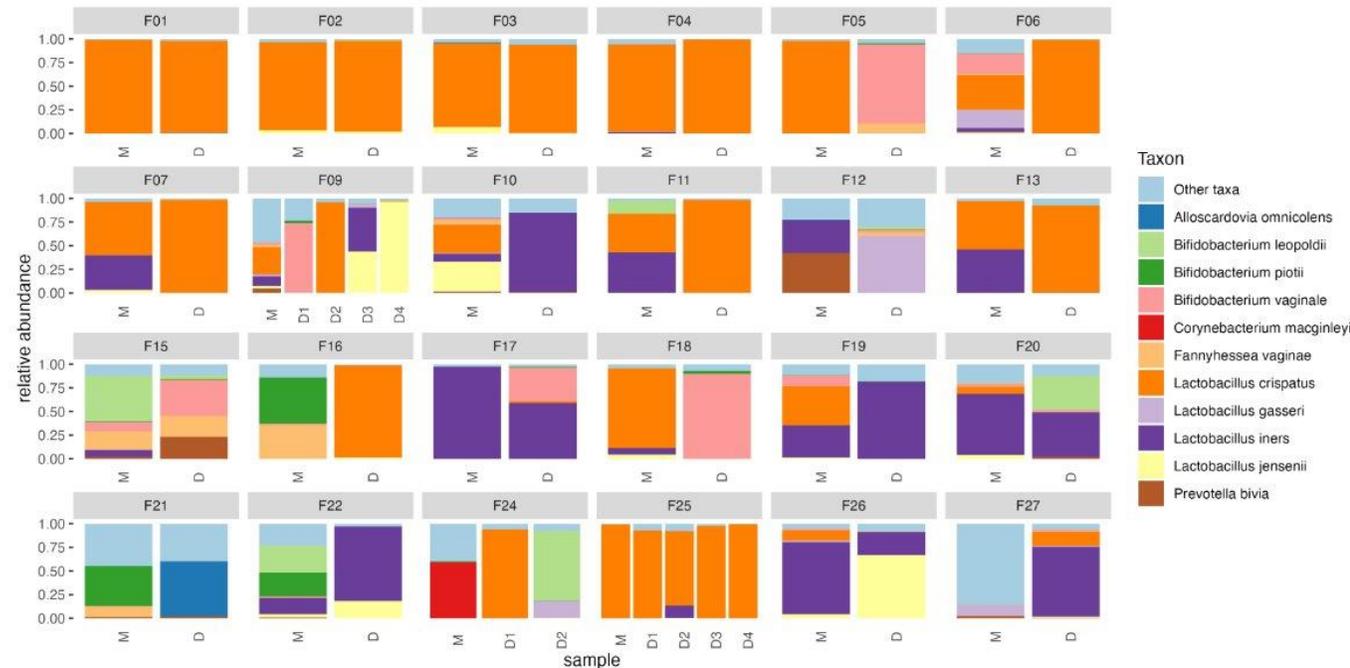
A citizen-science-enabled catalogue of the vaginal microbiome and associated factors

[Sarah Lebeer](#) , [Sarah Ahannach](#), [Thies Gehrmann](#), [Stijn Wittouck](#), [Tom Eilers](#), [Eline Oerlemans](#), [Sandra Condori](#), [Jelle Dillen](#), [Irina Spacova](#), [Leonore Vander Donck](#), [Caroline Masquillier](#), [Camille Nina Allonsius](#), [Peter A. Bron](#), [Wannes Van Beeck](#), [Charlotte De Backer](#), [Gilbert Donders](#) & [Veronique Verhoeven](#)

[Nature Microbiology](#) **8**, 2183–2195 (2023) | [Cite this article](#)

14k Accesses | **20** Citations | **82** Altmetric | [Metrics](#)

Mother-daughter pairs

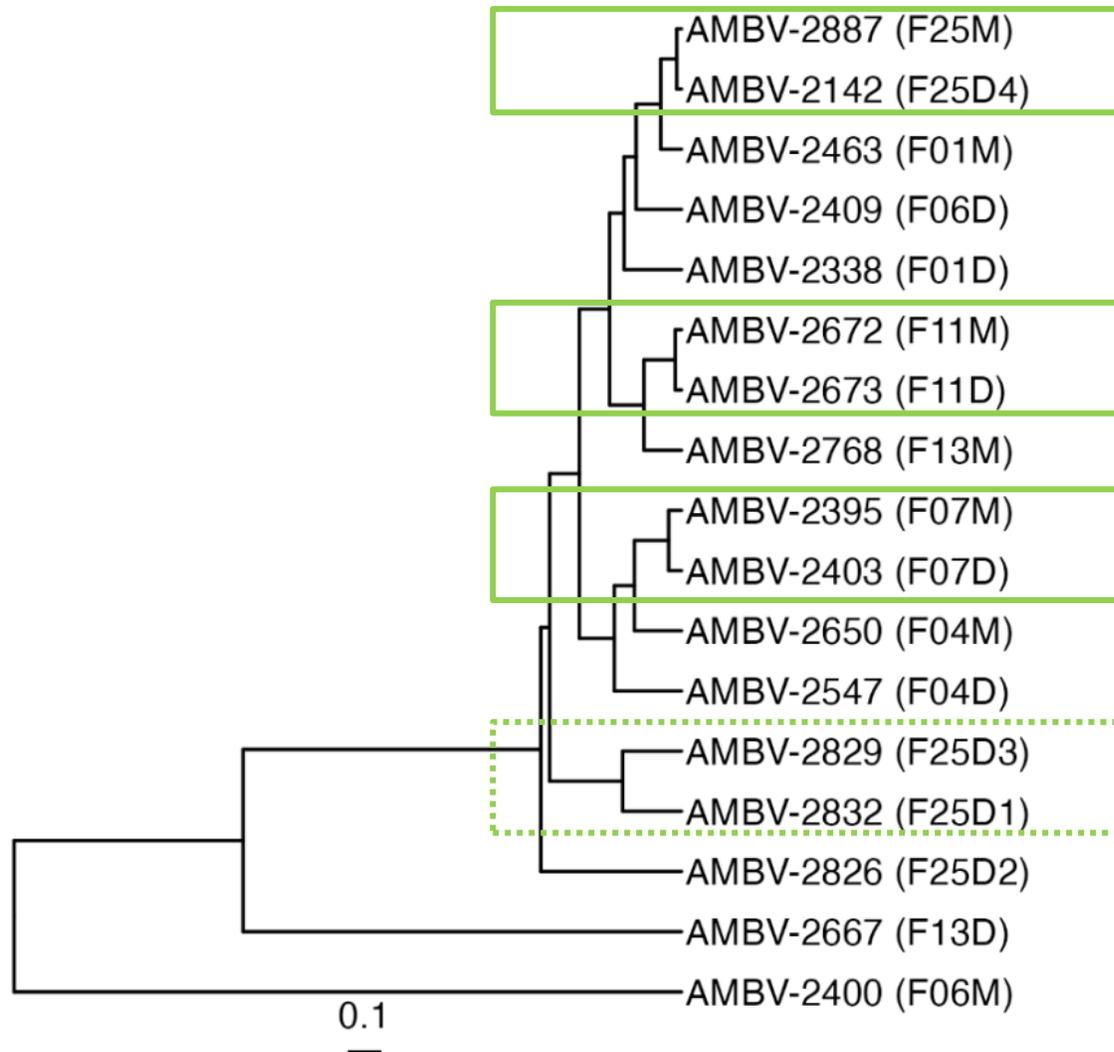


24 families where at least the mother and one daughter participated:

Daughters are more similar to their mothers (41%) than to random mothers (28%)

Erreygers, Pinedo-Bardales, Allonsius et al., in preparation

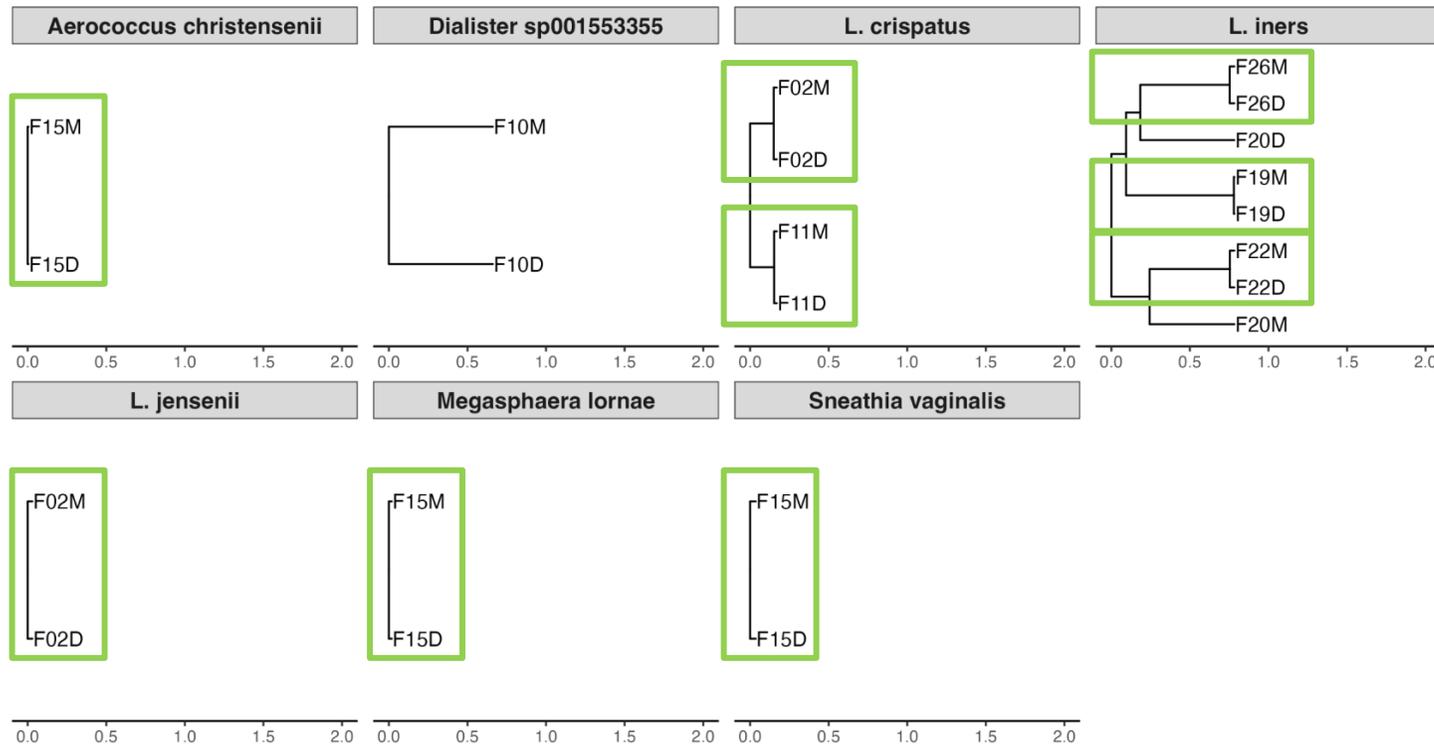
Mother-daughter pairs



L. crispatus isolates

- Whole-genome sequenced
- Clustering on ANI matrix
- 7 families with multiple isolates
 - 3 of them show "strain sharing"!
 - ANI of ~ 99.9%

Mother-daughter pairs



Genomes assembled from metagenomes

- 8 families with multiple MAGs (of same species)
 - 6 of them show strain sharing
 - ANI of ~ 99.9%

Conclusions

Fundamental questions on vaginal microbiome:

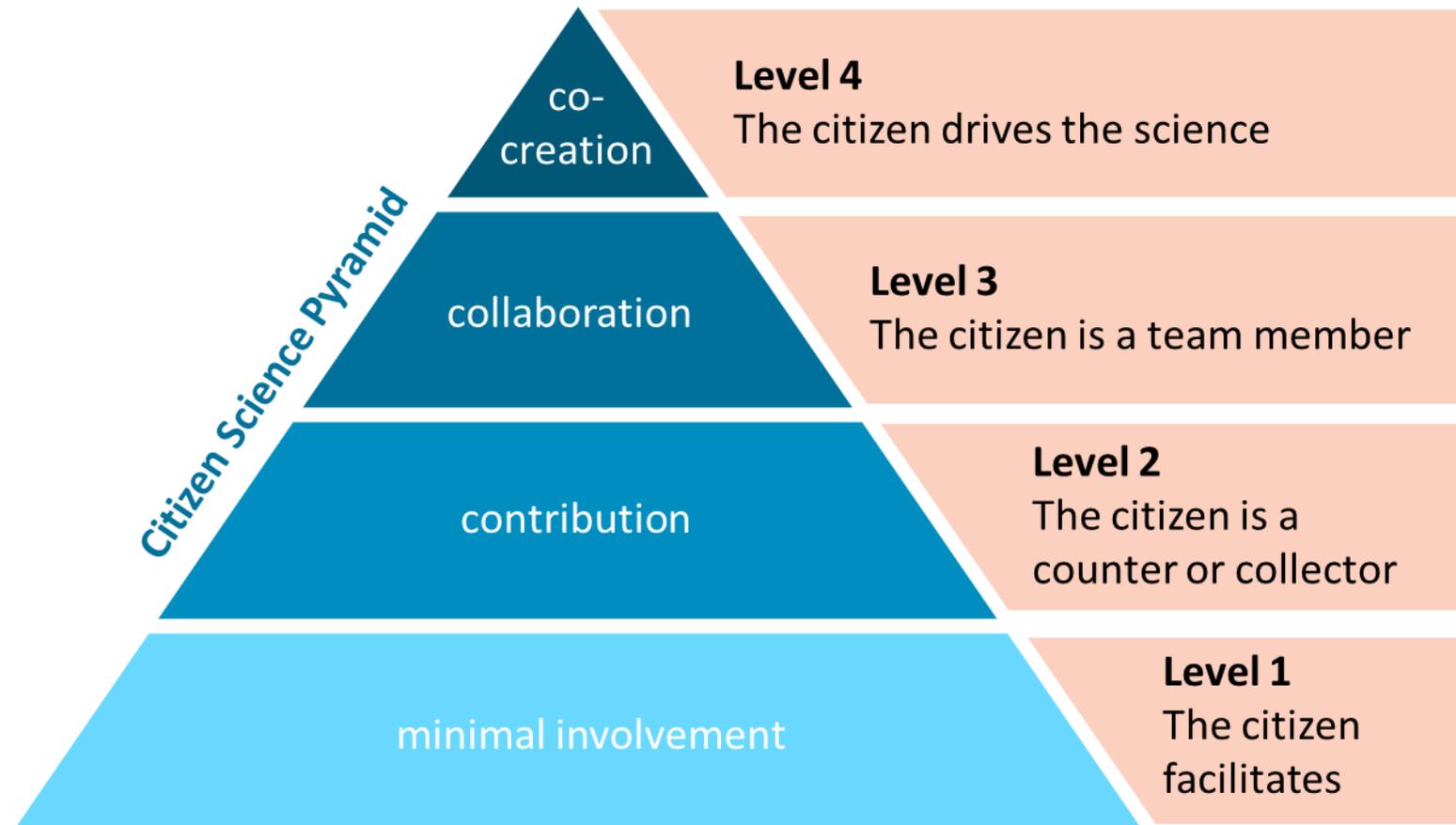
- What determines the composition of the vaginal microbiome?
 - No variables that we measured in Isala
 - Some degree of heritability --> Genetics? Immune system?
- Where do vaginal bacteria come from?
 - Frequent mother/daughter strain overlap with some accumulated differences --> From the mother at birth?
- Do vaginal bacteria interact with each other? How?
 - Possibly! *L. crispatus* module with *L. jensenii*, *L. vaginis* and *L. coleohominis*

Conclusions

Citizen science can be an effective tool to:

- Set up large-scale studies with high-quality data
- Increase societal impact of studies
- Increase societal relevance of studies

Citizen Science



Adapted from Gijssels, Huyse and Hoyweghen, 2019



Prof. Sarah
Lebeer



Dr. Sarah
Ahannach



Dr. Thies
Gehrman



Dr. Stijn
Wittouck



Prof. Gilbert
Donders



Prof. Veronique
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Ines
Tuyaearts



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Leonore
Vander Donck



lebeerlab.com
isala.be/en

#LetsSwab
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