

A pair of hands is shown from the bottom, holding a collection of pills. The pills are arranged in a roughly triangular shape, with several pink round tablets and a few orange capsules. The background is a solid, light pink color. The hands are positioned as if presenting the pills. A white rectangular box is overlaid on the top left of the image, containing text.

AN INTRODUCTION TO **THE VAGINAL MICROBIOME**

Understanding the science behind
the vaginal microbiome - a
whitepaper by Labskin.

LABSKIN

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AN INTRODUCTION TO THE VAGINAL MICROBIOME

Research into the vaginal microbiome and how it affects the overall health of women has accelerated over the last decade.

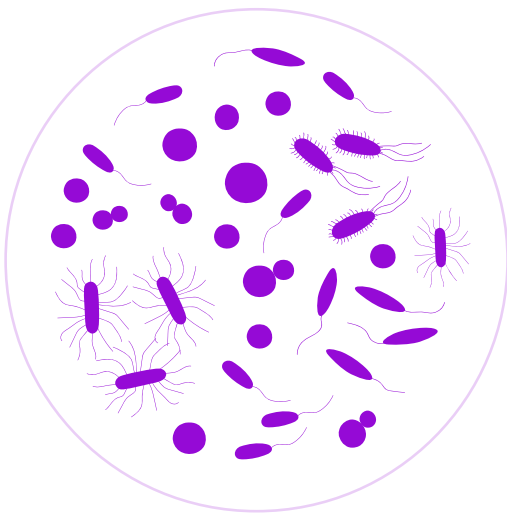
As scientists, academics, and medical experts gain knowledge of the vaginal microbiome, more evidence shows how an imbalance of the vaginal microflora can cause disease, infections, and fertility problems in women¹. This paper aims to explain what the vaginal microbiome is, the characteristics of microorganisms that colonise the vagina, and how it affects the overall health of women.

You will learn about the history of the vaginal microbiome, and discover how the exponential rise in research over the last decade is transforming how diagnostic tests and treatments are

developed. It becomes clear how different the vaginal microbiome is to other microbiomes of the human body in terms of bacteria, fungi, and viruses present, and the impact this has on the body's ability to fight infection and disease.

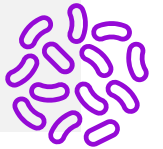
Technological advancements and breakthroughs are explored to learn how new products and treatment solutions are being developed with the advent of human skin equivalent (HSE) models that mimic the vaginal microbiome. Along with the demand for microbiome friendly intimate care products.

Finally, the future of vaginal microbiome research will be investigated to determine how advanced diagnostic tools and treatment solutions will become more accessible, save time, and improve cost efficiency.



95%

Estimated percentage of the Lactobacillus genera of bacteria that makes up normal vaginal flora.



4.5

Estimated pH balance of a healthy vagina (same as wine and tomatoes)





WHAT IS THE VAGINAL MICROBIOME?

An ecosystem of bacteria, yeasts, viruses, fungi, and other microorganisms colonise the vagina, and together make up what is known as the vaginal microbiome.

Playing a significant role in women's overall health, a balanced vaginal microbiome protects the vagina from pathogens and anaerobic bacteria, to prevent infections and other diseases. Although there are more than one million bacterial genes, representing over 300 different species of bacteria in the vagina³, it is predominantly dominated by *Lactobacillus*.

Lactobacilli produce lactic acid to maintain a low, acidic pH within the vagina, and inhibit the growth of unwanted pathogens such as *Candida*, *E. coli*, *Gardnerella vaginalis*, and *Atopobium Vaginae*. (3) However, genes, ethnicity, and

the physiological status of the vagina can also affect the balance of the vaginal microbiome⁴.

THE HISTORY OF VAGINAL MICROBIOME RESEARCH

Back in 1982, Albert Döderlein, a German obstetrician and gynaecologist was the first to discover a large gram-positive bacterium found in the vagina, vaginal bacillus⁵. (5) Further studies have shown several kinds of vaginal communities exist in healthy women, composed of different bacterial species depending on ethnicity and physiological states. Usually, they are dominated by one of four common Lactobacillus:

- L. crispatus
- L. iners
- L. gasseri
- L. jensenii

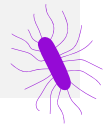
While other vaginal community state types have lower proportions of lactic acid bacteria, and higher proportions of strictly anaerobic organisms⁶.

Advances in technology have now led to the culmination of data on the vaginal microbiome such as the Human Vaginal Non-Redundant Gene

Catalog, or VIRGO. New diagnostic tests and treatments can now be investigated as this tool includes the sequences of over one million genes in bacteria, viruses, and fungi that are active in the vagina⁷.

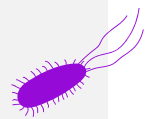
300

Approximate number of different species of bacteria in the vagina.



1 million

The number of bacterial genes in the vagina.





WHAT DOES THE VAGINAL MICROBIOME DO?

Similar to other microbiome areas such as the gut, skin, and scalp, the vaginal microbiome is unique to each individual.

However, its main objective is to prevent infection and maintain vaginal health. Race, ethnicity, hygiene, and behaviours all heavily influence the composition of a woman's vaginal microflora, leading the microbiome to continuously fluctuate throughout a woman's life due to hormonal and lifestyle changes.

Many studies have taken place to investigate the effects of the vaginal microbiome on successful reproduction, as an imbalance of vaginal microflora has been shown to increase the risk of infertility,

miscarriages, and preterm births⁸.

Interestingly, a woman's vaginal microflora can determine the skin microbiome of a newborn baby during birth, as microbes pass onto the baby's skin during delivery. Whereas with a caesarean birth, the mother's stomach microflora can be found instead⁹.

Vaginal dysbiosis, an imbalance of the vaginal microbiome, can occur under a range of circumstances and reduce the protective defences of Lactobacilli through:

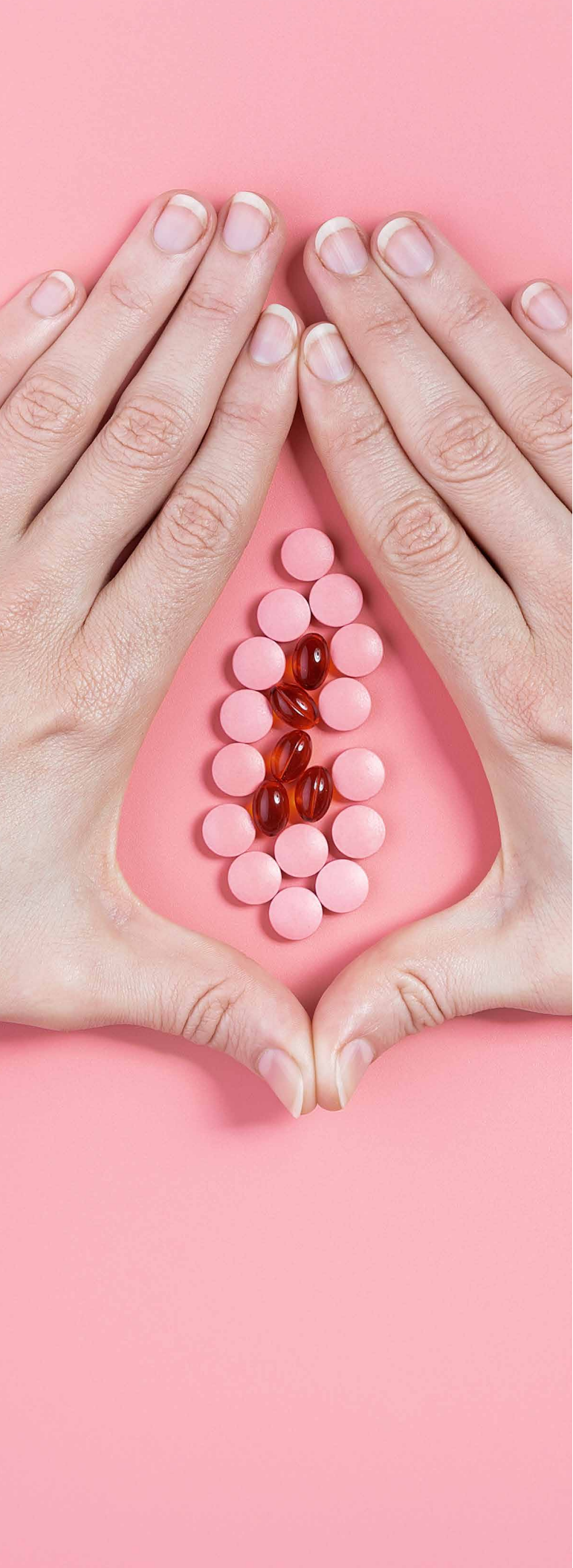
- Antibiotics
- Hormonal changes
- Sexual activities
- Douching
- Bacterial vaginosis (BV)

Antibiotics are designed to destroy bacterial infections in the body. Unfortunately, they also kill the good lactobacilli bacteria which protect the vagina from yeast and urinary tract infections. Changes in hormonal activity as a woman ages also affects the vaginal microbiome, as oestrogen helps maintain the amount of lactobacilli within the vagina¹⁰. Pregnant or pubescent females experience higher amounts of oestrogen, which prevents

imbalances. Whereas menopausal women experience a decline in oestrogen levels as they age, encouraging vaginal dysbiosis to occur. Once an imbalance in the vaginal microbiome occurs, women are more likely to suffer from urogenital disorders, such as:

- Bacterial Vaginosis (BV)
- Sexually transmitted infections
- Yeast infections
- Urinary tract infections





VAGINAL MICROBIOME AND VAGINAL DISEASES

Due to race, age, and hormonal changes, no two women have the same vaginal microbiome.

This creates many challenges when diagnosing and treating various types of vaginal disease. However, with the latest technologies, new ways of assessing the vaginal microbiome and changes that occur when infections take place are opening up a wider realm of research for products that can treat infections, or prevent them from ever taking place¹¹.

Treating vaginal disease or infections can be difficult at times, as symptoms can vary between individuals. One of the most important factors to consider is a focus on the right diagnosis to successfully treat the condition, especially with ailments such as:

- Bacterial vaginosis (BV)
- Candida or yeast infections
- Trichomoniasis
- STDs including chlamydia, genital herpes, and gonorrhoea

Diagnosing and treating BV in particular has its own challenges, despite the number of oral and intravaginal treatments available. Failing to re-establish a healthy vaginal microbiome after initial infection and treatment can lead to recurring infections in up to 50% of patients¹².

Globally, the prevalence of BV is between 23% – 29% of the female

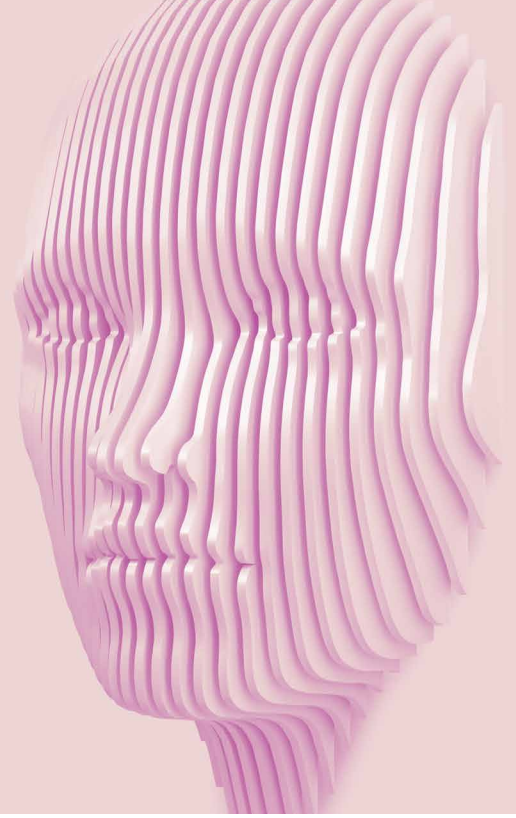
population, while the estimated cost of treating this condition is US \$4.8 billion per year¹³. Therefore, prevention and sustainable treatment strategies are urgently needed to decrease the burden of BV on women, and prevent adverse health outcomes.

\$4.8 Billion

Estimated cost of treating bacterial vaginosis (BV) yearly.



VAGINAL MICROBIOME AND TECHNOLOGY ADVANCEMENTS



Accelerating discovery into new diagnostic testing and treatment solutions.

Developing treatments for vaginal infections has accelerated as technology has progressed. Instead of focusing on molecular and culture-independent approaches to identify the bacteria associated with BV and other infections, researchers can now take advantage of various types of sequencing technology, including:

- Next generation genome sequencing
- Single-cell genome sequencing
- rRNA sequencing technology¹⁴

Genetic factors, physiological conditions, and environmental

exposures all affect the vaginal microbiome. But, sequencing technology combined with human skin equivalent testing (HSE) innovations that replicate the vaginal microbiome opens up the market for faster, more reliable, and targeted intimate care products and treatments¹⁵.

To fully understand the vaginal ecosystem, species and strain level analyses combined with a multitude of other approaches are necessary to fully determine what intimate care products and treatments are not only safe to use, but avoid disrupting the vaginal microbiome. That's why


cosmetic and medical companies are increasingly using innovative HSE technology, as testing capabilities have improved to such a degree that it's now possible to accurately mimic the vaginal microbiome in a laboratory setting.

Systems biology will also play a significant role in the future of understanding the vaginal microbiome as more advanced AI and bioinformatic tools are developed¹⁶, in conjunction with:

- Metagenomics
- Transcriptomics
- Proteomics
- Metabolomics

Knowledge of the individual strains of bacteria commonly found in the vaginal microbiome, along with how and why it differs between women at various stages of life is continuously progressing. It will continue to do so to meet the demand for microbiome friendly feminine hygiene and intimate care products.





FEMININE HYGIENE AND INTIMATE CARE PRODUCT MARKETS

There is increasing demand for vaginal microbiome friendly products.

As consumers become more aware of the importance of vaginal microbiome friendly products in preventing disease and infections, the markets for feminine hygiene and intimate care products are dramatically increasing year on year across the globe. As of 2019, the feminine hygiene products market stood at USD 39.73 billion, and is expected to grow to USD 51.13 billion by 2027 with a CAGR of 4.6%¹⁷.

Cosmetic and skin-care companies are rising to meet this demand by partnering with research and academic companies to test and validate their products, as consumers become more self-aware of how using the wrong type of products can induce infections such as yeast and urinary tract infections.

As consumer knowledge continues to expand with the advent of microbiome friendly products for the skin, scalp, gut, and other microbiome regions of the body¹⁸, so too will the demand for vaginal microbiome friendly products, such as:

- Menstrual hygiene products
- Deodorizing wipes
- Washes
- Bathing products
- Reusable and disposable intimate care products
- Targeted probiotics for vaginal health

\$39.73 billion

As of 2019, the feminine hygiene products market.

\$51.13 billion

Expected growth in the market by 2027.

Traditionally, vaginal care product development backed up by clinical and efficacy testing standards can take years due to fluctuating research material and the sheer amount of data to be deciphered about the vaginal microbiome. However, these challenges can now be overcome with

solutions that reduce research & development (R&D) costs and the time it takes to bring new products to market that comply with regulatory, safety, and efficacy standards¹⁹.

THE FUTURE OF THE VAGINAL MICROBIOME

Although the vaginal microbiome is still in its infancy in terms of research, technological advancement and reductions in the cost of analysis has opened up a world of opportunities for cosmetic, skin care, and medical companies. Preventing or treating vaginal disease and infection is of the highest priority, due to the extremity of problems that can occur from vaginal dysbiosis. Closely followed by the growing demand for feminine care products that can alleviate symptoms of thrush, urinary tract infections, and prevent toxic shock syndrome (TSS) from occurring.

Further research is taking place regarding the pathogenesis of bacterial vaginosis, ways to optimize BV treatments, and the roles of sexual transmission and endogenous infection in BV epidemiology²⁰. When studied in tandem with the vaginal microbiome, cosmetic, skin care, and

medical companies will have an overview of the effects of intimate care products on the vaginal microbiome, and provide more targeted products to females depending on their age, ethnicity, hormonal, and lifestyle factors.

Early diagnoses and better treatment solutions can be achieved by swabbing the vaginal microbiome to examine disease markers that could potentially discover the susceptibility of women to certain infections. Especially when combined with better AI diagnostic and big data tools.

Now that animal testing on cosmetics and skin care products has increasingly been diminished across the globe²¹, the technological breakthrough of human skin equivalent (HSE) models will be at the forefront of vaginal microbiome research. Clinical trial participant numbers can be cut in half by cloning gathered data to replicate multiple test subjects, ensuring the time, and cost to bring safe and validated products to market is reduced.

LABSKIN'S 3D MODEL FOR TESTING THE VAGINAL MICROBIOME

Labskin researchers and scientists have worked tirelessly over the last decade to develop a commercial lab-grown, full-thickness human skin equivalent that mimics the vaginal microbiome, and assists in determining the impact of cosmetics, pharmaceuticals, and skincare products on the body's microbiota. While similar living skin equivalents have existed for decades, Labskin's 3D model is the first with the capability of colonising skin microflora, ensuring the most accurate results from tests without the need for animal testing or expensive and time-consuming human trials.

Labskin makes this technology available to both commercial and research institutions and encourages working together on projects to advance the knowledge of how the vaginal microbiome works. Labskin AI technology gives the capabilities to create a repository of data and predictive analysis, supporting industry and academia in the creation of rapid and ethical discoveries and strategies for new products and medical advancements.

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