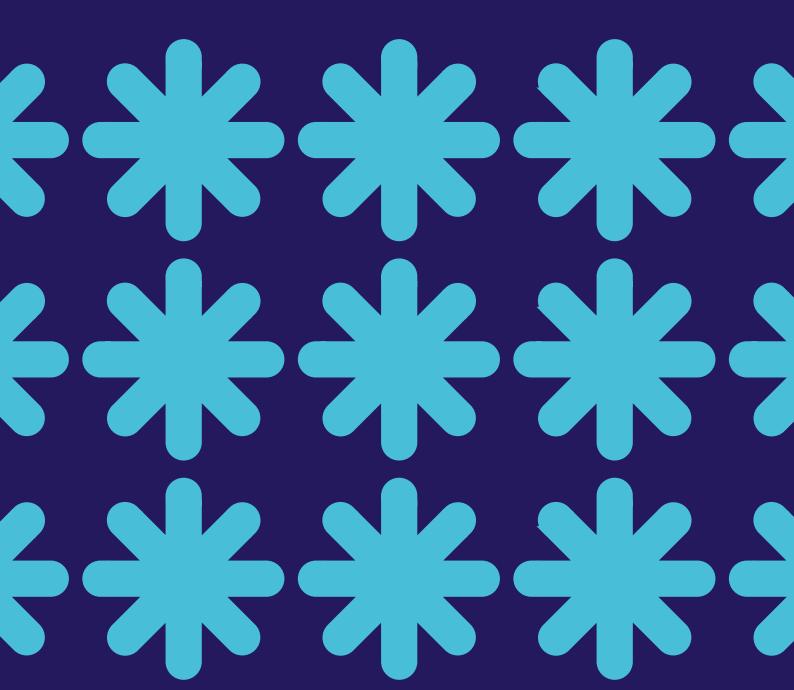


## Probiotics+ Women's Health



The widest range of benefits







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## **Women's Health and Microbiome**

The female gut and genito-urinary tract microbiota represent highly complex ecosystems that play a central role in women's health across their lifespan. These microbial communities are in constant communication, and this cross-talk impacts immunity, metabolism, hormone regulation, reproductive health, and susceptibility to infections.

The gut microbiome can act as a source of microorganisms that colonise the cervico-vaginal tract, either through transfer from the gastrointestinal tract or via maternal transmission during birth. In healthy women of reproductive age, the vaginal microbiome is typically dominated by *Lactobacillus* species, particularly *L. crispatus*, *L. gasseri*, *L. iners* and *L. jensenii*. These bacteria protect the vaginal environment by maintaining an acidic vaginal pH through the production of lactic acid and hydrogen peroxide, inhibiting pathogens and supporting mucosal defence. Based on the dominant species and pH values found in large cohorts of women, this composition has been divided into five community state types (CST I–V).

The microbial balance in both the gut and the genito-urinary tract may be affected by many factors, including antibiotics, high-sugar diet, digestive issues, stress, hygiene practices, sexual intercourse, and hormonal contraceptives. Disruption to either the gut or vaginal microbiome can lead to dysbiosis and increased risk of conditions including bacterial vaginosis, vulvovaginal candidiasis, urinary tract infections and inflammatory conditions

Women experience hormonal changes with age, and as they approach the menopause transition, oestrogen levels decline, potentially leading to symptoms and health challenges associated with menopause. There is growing evidence suggesting a bidirectional relationship between the gut microbiota and oestrogen, with the gut microbiota playing a key role in regulating oestrogen levels. One important mechanism involves  $\beta$ -glucuronidase, an enzyme produced by gut bacteria that deconjugates oestrogen metabolites excreted by the liver, allowing them to be reabsorbed into circulation through the enterohepatic pathway. Modulation of the gut microbiota may provide a promising strategy to support  $\beta$ -glucuronidase activity and overall women's health during the menopausal stages.

#### The Role of Probiotics in Women's Health

Probiotics play a significant role in supporting various aspects of women's health, including gut, immune, vaginal, and urinary health. They help restore and maintain a balanced gut and vaginal microbiome, contribute to immune modulation and support the gut–brain axis. Growing scientific evidence demonstrates their benefits in both prevention and management of gut and gynaecological conditions such as IBS, bacterial vaginosis, vulvovaginal candidiasis, urinary tract infections, and menopausal symptoms.

- 6 randomised placebo-controlled clinical studies with Lab4/Lab4P Probiotics supplementation showing benefits for women's health
- 2 studies on Irritable Bowel Syndrome (IBS) in individuals with IBS
  - 1 study on Candida albicans and other yeasts in IBS sufferers receiving antibiotics
- 2 studies on metabolic health in overweight/obese adults
  - 1 study on wellbeing, anxiety, and menopause-related symptoms in women aged 45 to 65 years



## Studies

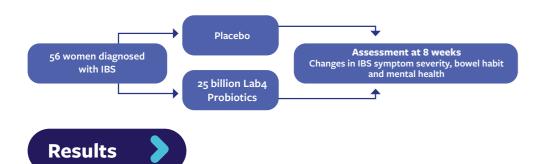
## The Evidence for Lab4/Lab4P Effectiveness for Women's Health

The Lab4 family of probiotics has demonstrated beneficial effects across various aspects of women's health, including irritable bowel syndrome, yeast overgrowth, anxiety, peri/menopausal symptoms, and overall wellbeing.

## Irritable Bowel Syndrome (IBS)

## The IBS in Women Study

This randomised, double-blind, placebo-controlled study was designed to confirm the beneficial effect of Lab4 Probiotics on IBS symptoms in women aged 18 to 40 years.



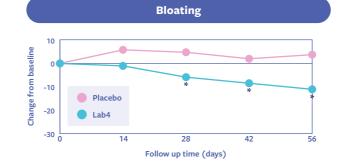
#### **IBS Symptoms**

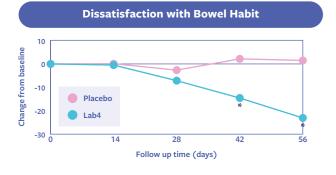
# During the 8-wee symptom scores with Lab4 Probio (\*P=0.0018), (² • Reductions ≥ 50 and by the end of the end

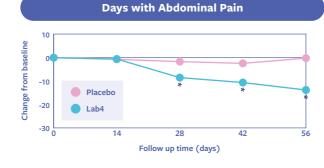
Follow up time (days)

- During the 8-week study, a significant reduction in total IBS symptom scores was observed in women supplemented with Lab4 Probiotics compared to those taking a placebo (\*P=0.0018), (\*P<0.0001).</li>
- Reductions ≥ 50 points are considered clinically meaningful and by the end of this study 63% of the women taking Lab4 Probiotics achieved this level of reduction in symptom severity (compared to only 4% in the placebo group).

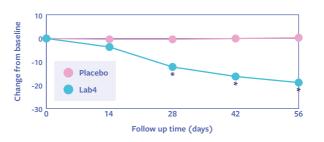








#### Abdominal pain



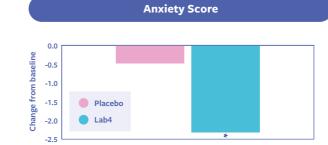
 In the Lab4 Probiotics group, the reduction in the IBS-symptom severity score was associated with significantly fewer days with abdominal pain, reduced pain and bloating severity, and improvements in bowel habit satisfaction and overall well-being and quality of life.

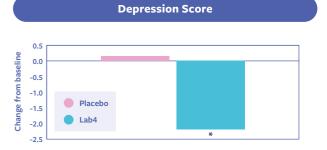
#### **Bowel Habits**



- The proportion of women with normal stool consistency in the Lab4 group was significantly higher than in the placebo group (\*P=0.0106).
- The Lab4 group experienced fewer loose stools (\*P=0.0311).

#### **Anxiety, Depression and IBS-related behaviour**





#### **Avoidance and Control Behaviour**



- Significant reductions in both anxiety and depression scores were observed in the group taking Lab4 Probiotics compared to the placebo group (\**P*=0.0002 and \**P*<0.0001, respectively).
- Lab4 supplementation significantly reduced IBS-related avoidance and control behaviour, such as food anxieties and the avoidance of social situations (\*P=0.0002).

## Conclusion

Lab4 Probiotics supplementation plays a beneficial role in the management of IBS in women, including improvements in IBS symptoms, bowel habits, anxiety, and depression.



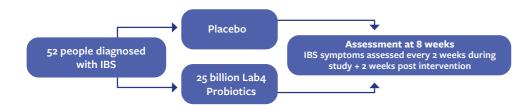
Scan for more info



## The Sheffield IBS Study

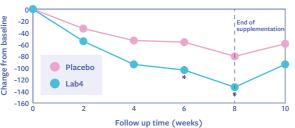
This randomised, double-blind, placebo-controlled study investigated the effect of supplementation with Lab4 Probiotics on the symptoms of IBS.

The participant cohort comprised 86% women. The study was conducted by Sheffield University Medical School in the UK.



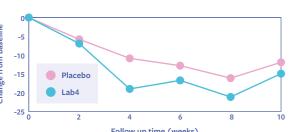


#### **Total IBS Symptom Severity Score**



Participants taking Lab4 Probiotics showed significant reduction in total IBS symptoms compared to placebo (\*P<0.05), including:

- days with pain
- dissatisfaction with bowel habit
- severity of pain days with bloating
- quality of life

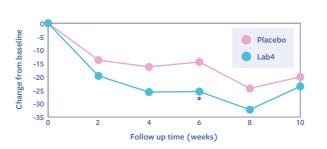


#### **Abdominal Pain**



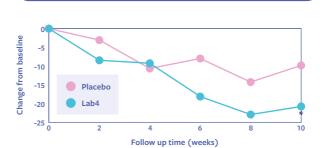
Follow up time (weeks)

#### **Dissatifaction with Bowel Habit**

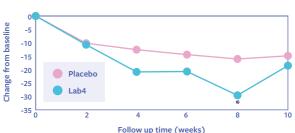




#### Days with Pain



## Quality of Life



 $\bullet$  The days with pain and days with bloating both reduced in the group taking the Lab4 Probiotics.

• Dissatisfaction with bowel habits decreased significantly and quality of life significantly improved in the Lab4 Probiotics group.

## Conclusion





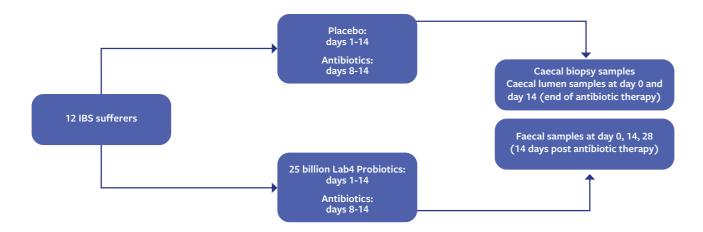


## Antibiotics & Yeasts

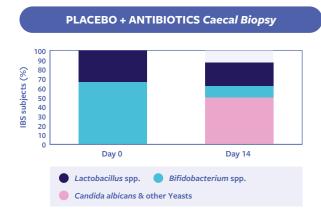
## Reduction in Candida albicans and other yeasts



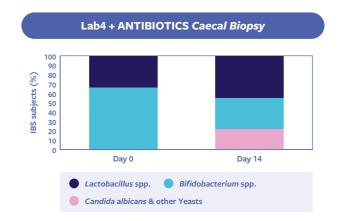
This study assessed the effect of Lab4 Probiotics on the composition of the microbiota in IBS sufferers receiving antibiotic therapy. Women comprised 75% of the participant cohort. The study was conducted by Cambridge University/Addenbrooke's Hospital in the UK.





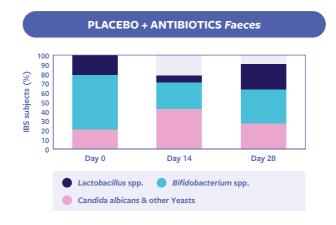


- Significant increases in the detection of Candida albicans (C. albicans) and other yeasts were recorded on Day 14.
- Decreases in the detection of bifidobacteria and lactobacilli were also observed on Day 14.

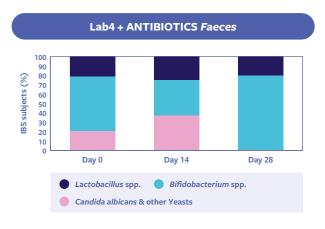


• Detection of C. albicans and other yeasts was reduced on Day 14 compared to the placebo group.





• The proportion of IBS sufferers harbouring *C. albicans* and other yeasts was increased on Day 14 and on Day 28 (14 days after the end of antibiotic treatment)



- Detection of C. albicans and other yeasts was reduced on Day 14 compared to the placebo group.
- C. albicans and other yeasts were not detected on Day 28.

## Conclusion

In this unique, small, and invasive study, supplementation with Lab4 Probiotics prior to and during antibiotic therapy helped to protect against overgrowth of C. albicans and other intestinal yeasts.

Colonisation of the intestinal epithelium by C. albicans can trigger an inflammatory response, and difficulty in eliminating this colonisation may result in a chronic inflammatory state.



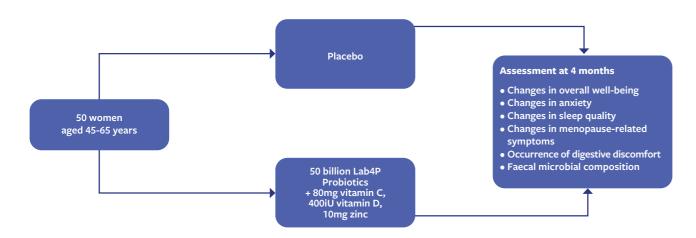


## Peri/Menopause & Well-being

## **The ProWome Study**

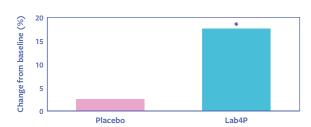


This randomised, double-blind, placebo-controlled study investigated the effect of Lab4P Probiotics in combination with vitamins C & D, and zinc on symptom management and overall health in women aged 45 to 65 years.

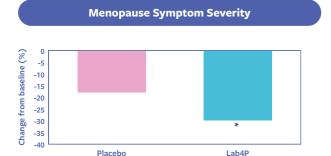


## Results 🔪

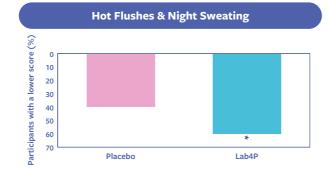
#### **Overall Wellbeing Score**



 During the 4-month study, a 17.1% significant improvement in overall wellbeing was observed in the Lab4P Probiotics group compared to placebo (\*P=0.0142).



 A significant 18.5% reduction in menopause-related symptom scores was observed in the Lab4 Probiotics group compared to placebo (\*P=0.0327).



• There was a significant improvement in hot flushes/night sweating in women taking the Lab4P Probiotics intervention (\*P=0.0225).

#### Anxiety



 Women in the Lab4P Probiotics group showed a 40% reduction in anxiety compared to those in the placebo group (\*P=0.0026).

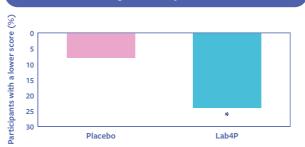
Significant improvement in anxiety-related heart discomfort was also

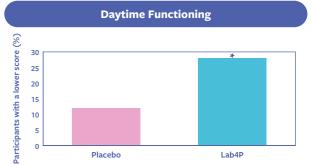
Lab4P

Placebo

**Anxiety-related Heart Discomfort** 

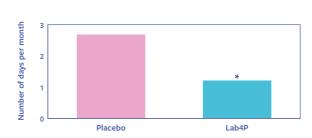
#### Daytime Sleepiness





• Significant improvements were observed in both daytime sleepiness (\*P=0.0075) and daytime functioning (\*P=0.0422).

#### Indigestion



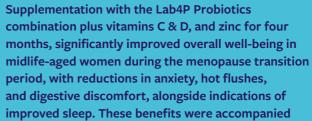
• Women in the Lab4P Probiotics group reported 55% fewer days with indigestion (\*P=0.0041).

#### Stomach Pain



 $\bullet$  40% fewer days with stomach pain was also observed (#P=0.0700).

#### Conclusion



by a reduction in *Blautia* bacterial species, which have previously been linked to hot flushes and sleep disturbances.







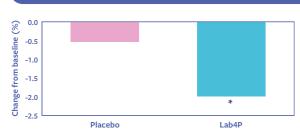
## The Promagen and Probe Studies 🔪



A subgroup analysis of peri- and menopausal women aged 45 to 65 years, from two randomised, placebocontrolled clinical studies<sup>1,2,</sup> was conducted to investigate the effects of Lab4P Probiotics on menopause-related physical changes, metabolic health, quality of life, and cognition.



#### **Body Weight**



• Lab4P Probiotics supplementation resulted in significant weight loss compared to placebo (\*P=0.0211).

#### **Waist Circumference**

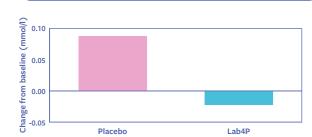


## **Hip Circumference** -1.0 -1.5 -2.0

Placebo

• Significant reductions in waist and hip circumferences were also observed in the Lab4P group (\*P<0.0001 and \*P=0.0010, respectively).

#### **Total Cholesterol**

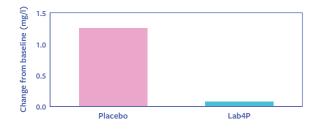


#### **Graph for LDL-Cholesterol**

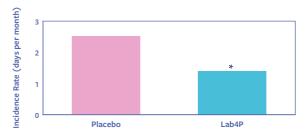


• Women taking Lab4P Probiotics showed reduced levels of total cholesterol, LDL-cholesterol (#P=0.0847), and inflammation compared to placebo.

#### **C-Reactive Protein**



#### **Total Upper Respiratory Tract Infection (URTI) Symptoms**

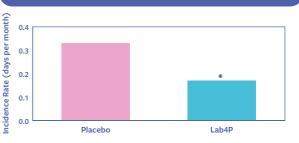


- A significant 44.5% reduction in the incidence of total URTI symptoms was observed in women taking Lab4P Probiotics compared to those taking placebo (\*P=0.0146).
- $\bullet$  The URTI symptoms included cough, sneezing, runny nose, blocked nose, and sore throat.

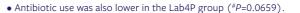
#### Headache



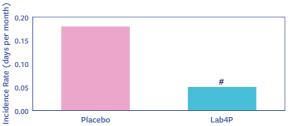
#### **Muscle Ache**



#### • A significant 50% reduction in headache (\*P=0.0112) and a 48.5% reduction in muscle ache (\*P=0.0227) were observed in the Lab4P group compared to the placebo group.



#### **Antibiotics**

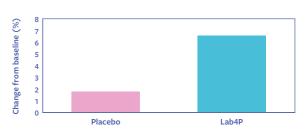


#### **Quality of Life**



- The Quality of Life questionnaire covered five domains: general wellness, state of health, state of energy, state of mood and
- An improvement in the Quality of Life score was observed in women supplemented with Lab4P Probiotics compared to the placebo group (#P=0.0582)

#### **Accuracy (% Correct Answers)**



• Lab4P Probiotics supplementation indicated an improvement in mental agility, as measured by the Stroop Colour and Word

#### Conclusion



Lab4P Probiotics supplementation may provide a supportive strategy for managing health and wellbeing in women aged 45 to 65 years, a group typically undergoing the menopausal transition. Clinical evidence suggests benefits across weight management, metabolic health, immune function, quality of life, and cognition.

<sup>1</sup>Michael DR et al. 2020. A randomised controlled study shows supplementation of overweight and reduces bodyweight and improves well-being. Sci Rep

 $^{2}$ Michael DR et al. 2021. Daily supplementation with the Lab4P probiotic consortium induces significant weight loss in overweight adults. Sci Rep 11(1):5.





## In vitro Evidence for Anti-Candida Effects of Lab4 strains



Candida albicans is an opportunistic pathogen with the ability to cause vaginal candidiasis, affecting up to 75% of women during their lifetime. This in vitro study aimed to investigate the activity of two probiotic strains from our latest Lab4G consortium against Candida albicans.

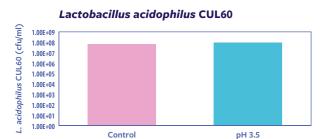
## Results

#### **Functional Genomic Screening**

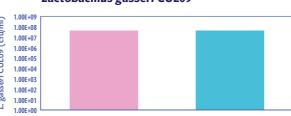
Gene	EC Number	Proposed relevance	L. acidophilus CUL60	L. gasseri CUL09
L-Lactate dehydrogenase	1.1.1.27 1.1.2.3	Acid tolerance/lactate production	<i>'</i>	<b>√</b>
D-Lactate dehydrogenase	1.1.1.28	Acid tolerance/lactate production	1	✓
Pyruvate oxidase	1.2.3.3	Hydrogen peroxide production	✓	✓
Na+/H+ NhaA antiporter		Acid tolerance	✓	
Enolase	4.2.1.11	Adherence	✓	✓
Fibronectin-binding protein		Adherence	1	

• Lactobacillus acidophilus CUL60 and Lactobacillus gasseri CUL09 harbour genes associated with survival in the vaginal tract and the ability to inhibit the growth of C. albicans.

#### **Acid Tolerability**

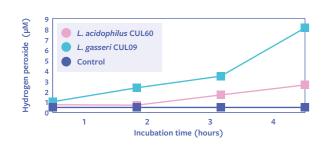


## Lactobacillus gasseri CUL09



• Both Lactobacillus acidophilus CUL60 and Lactobacillus gasseri CUL09 demonstrated tolerance to acidic pH, a key factor for survival in the vaginal tract.

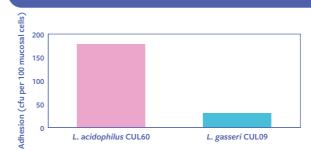
#### **Hydrogen Peroxide Production**

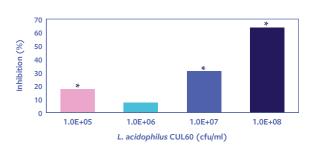


• Lactobacillus acidophilus CUL60 and Lactobacillus gasseri CUL09 produced hydrogen peroxide, a recognised inhibitor of *C. albicans* cell growth.



#### **Mucosal Adhesion**



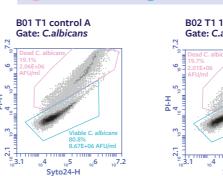


• Both strains adhered to mucosal cells, with Lactobacillus acidophilus CUL60 showing the highest level of adhesion.

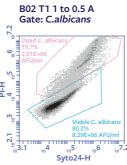
Viable C. albicans

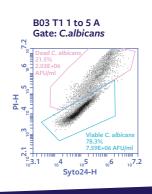
• Increased concentration of Lactobacillus acidophilus inhibited C. albicans adhesion to buccal epithelial cells (BEC) by up to 63.7%.

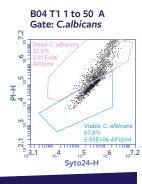
#### Inhibition of Candida albicans



Dead C. albicans







• The combination of Lactobacillus acidophilus CUL60 and Lactobacillus gasseri CUL09 strongly inhibited the growth of C. albicans, as demonstrated by flow cytometry analysis of yeast survival in the presence of the probiotic strains.

## Conclusion

In vitro studies demonstrate that Lab4 strains inhibit Candida albicans through multiple mechanisms, supporting their potential role in maintaining vaginal health by limiting Candida colonisation and overgrowth.











## A multitude of benefits

- Lab4 Probiotics has shown simultaneous benefits on digestive health, immune function, athletic performance, gut-brain axis, and alongside antibiotic use
- Lab4P Probiotics has shown benefits in relation to metabolic and women's health, as well as entraining all the benefits identified for the original Lab4 consortium
- The Lab4 consortia are adapted to the human gut with demonstrable ability to survive stomach acidity and bile acids and to colonise epithelial tissue and mucous
- Shelf-life up to 24 months in ambient conditions\*

## **Why Lab4 Blends Work**

#### One body system

The gut and hence the microbiome are extensively connected to almost all of the other physiological systems of the body, this includes the immune system, endocrine system, brain and central nervous system, and metabolic physiology.

#### **Proxies for microbes**

Consequently, as proxies for our microbiome, effective probiotics could also impact beneficially on these distant physiologies – and these benefits may be manifest simultaneously as the intestinal health benefits outlined above.

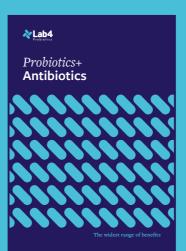
#### **Bacterial colonisation**

Lab4 contains Lactobacillus acidophilus (two strains) as well as Bifidobacterium animalis subsp. lactis and Bifidobacterium bifidum. The Lactobacilli are dominant colonisers of the sparsely populated small intestine and the Bifidobacteria constitute a significant population in the distal small intestine and are also present throughout the large intestine.

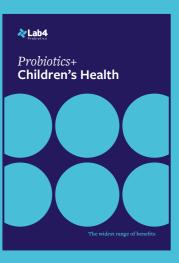
#### High dose

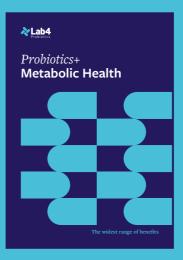
Over the past 30 years it has become evident that higher doses of effective probiotic strains produce faster, greater and more consistent effects and benefits. In all clinical studies on adults performed to date, Lab4 has been supplemented at 25 billion a day. This is why we have seen a broad range of consistent health benefits across a wide range of conditions and particularly with intestinal health.

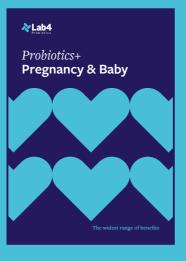
### See our other Guides

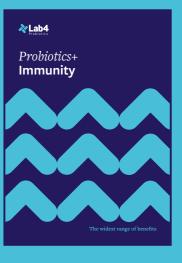












## **Lab4 Specification**

Lab4 Probiotic blends are available as freeze-dried concentrated powders at various concentrations. Please contact us for more details at <a href="mailto:info@lab4probiotics.co.uk">info@lab4probiotics.co.uk</a> or on 01639 825100 <a href="https://www.lab4probiotics.co.uk">www.lab4probiotics.co.uk</a>

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<sup>\*</sup>In powder and capsule products produced and packed appropriately





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