Lab4 Probiotics

Probiotics+ Antibiotics

The widest range of benefits

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Contents

Microbiologists Dr. Nigel Plummer and Dr. Sue Plummer established Cultech Ltd in 1994 with the vision for a company with research at its heart.

Adverse Effects of Antibiotics on The Microbiome and Disease Implications

The discovery of antibiotics and their subsequent impact in reducing mortality and suffering from infectious disease was arguably the single most important advancement in human healthcare in the 20th century.

However, while antibiotics effectively treat bacterial infections, they can also significantly disrupt the gut microbiome - the complex community of microorganisms residing in our digestive tract. This disruption, known as dysbiosis, occurs because antibiotics target both harmful and beneficial bacteria, leading to a reduction in microbial diversity, and often 'overgrowth' of 'undesirable' types of bacteria. This can result in:

- **Antibiotic Associated Diarrhoea** (AAD), including cases caused by *Clostridium difficile* (*C. difficile*) and increased susceptibility to other infections, which may not be limited to the gut. A key reason for this is that the beneficial bacteria have the ability to reduce the infectivity of intestinal pathogens - an effect that is lost when their numbers are reduced.
- **Gastrointestinal Issues:** The dysbiosis caused by antibiotics can trigger symptoms of Irritable Bowel Syndrome (IBS), such as bloating, abdominal pain, and altered bowel habit (constipation and/or diarrhoea). These symptoms often arise weeks or even months following antibiotic use, leading to the underestimation of a possible link.
- **Long-Term Health Implications:** Changes in the gut microbiome have been associated with an increased risk of developing chronic conditions such as allergies, obesity, and inflammatory bowel diseases. This risk is more apparent in early life (0-16 years) and with increased frequency of antibiotic use.

- 5 randomised placebo-controlled studies related to antibiotic use
- 1 study on antibiotic associated *Clostridium difficile* diarrhoea in hospitalised patients
- 2 studies on gut microbiota disruption during and following antibiotic therapy
- 2 studies on antibiotic resistance following antibiotic use

Studies

The Evidence for Lab4/Lab4S Effectiveness During and Following Antibiotic Use

Antibiotic Resistance

Whilst not a disease itself, antibiotic resistance is possibly the biggest global threat to human healthcare in the 21st century. The prevalence of resistance is widespread, with an estimated 700,000 deaths annually due to resistant infections, a figure that the World Health Organisation (WHO) predicts will rise to 10 million deaths annually by 2050.

Each course of antibiotics can disrupt the gut microbiome, often leading to an increase in antibiotic-resistant bacteria. Individuals with frequent antibiotic exposure tend to harbour higher levels of resistance genes within their microbiota, potentially elevating their risk of infections caused by resistant pathogens. Currently, the only measures available to reduce the progression of antibiotic resistance are around restriction of use, whether this is limitation of antibiotics for agricultural use, or reducing prescriptions for self-limiting viral infections.

Emerging evidence indicates that certain probiotics may be effective in reducing levels of antibiotic resistance in the 'regrowth microbiota' when used in conjunction with antibiotics.

Probiotics and Antibiotics

Antibiotics taken orally, will almost always have a devastating effect on the fragile and low numbered but highly functional microbiota of the small intestine, whilst often having a less significant impact on the vast bacterial population that make up the large intestinal microbiome. The result is that bacteria sensitive to the antibiotic are reduced or eradicated, allowing the resistant bacteria and microbes unaffected by the antibiotic (e.g. yeasts) to overgrow and thrive.

When probiotics are taken alongside and preferably also following a course of antibiotics, they help to 'fill the colonisation gaps' left by the bacteria killed by the antibiotics. Although, this effect is likely to be temporary – since probiotics can also be killed by the antibiotic - the benefit is maintained through daily supplementation throughout the antibiotic treatment course. The result, particularly in the small intestine, is a significant mitigation of collateral damage to the microbiota.

Lab4/Lab4S Probiotics and Antibiotics

A unique combination of *Saccharomyces boulardii*, the most researched probiotic yeast for the prevention of antibiotic associated infections, alongside Lab4, the multi-strain bacterial probiotic clinically shown to reduce antibiotic associated dysbiosis.

Lab4 and Lab4S Probiotics have been shown to reduce total antibiotic resistance in the re-growth microbiota.

The Evidence for *Saccharomyces boulardii*

***Saccharomyces boulardii* (*S. boulardii*) is the world's most studied probiotic for use alongside antibiotics. Various meta-analyses (Table 1) have shown the following effects alongside antibiotics:**

- Reduction in AAD caused by *C. difficile* and other pathogens
- Reduction in numbers of opportunistic pathogens in the re-growth microbial population following antibiotics

Table 1

Reference (Meta-Analysis)	Population	No. of RCTs (Participants)	AAD Incidence Control Group	AAD Incidence S. boulardii Group	Risk Ratio (95%CI)	Number Needed to Treat (NNT)	Outcome
Szajewska H & Kołodziej M. (2015)	Adults & Children	21 (4,780)	18.7%	8.5%	0.47 (0.38–0.57)	10	Significant reduction in AAD risk; effective in both age groups
Guo Q *et al* (2019)	Children	9 (3,165)	21%	8%	0.36 (0.24–0.54)	8	Significant reduction in AAD risk; supported by Cochrane subgroup analysis
McFarland LV (2010)	Adults	10 (1,858)	19.2%	9.3%	0.47 (0.35–0.63)	10	Significant reduction AAD risk

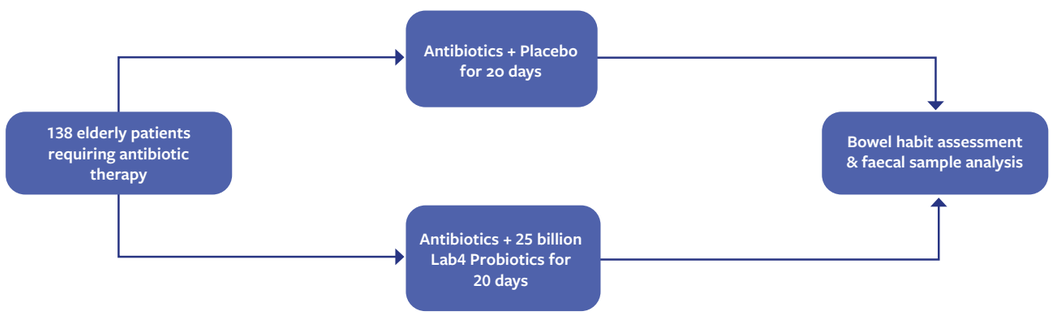
The Evidence for Lab4

Lab4 has shown the following benefits when used alongside antibiotics:

- Reduction in *C. difficile*-associated diarrhoea
- Reduction in populations of opportunistic pathogens, including enterobacteria, enterococci, staphylococci and *Candida albicans*
- Reduction in antibiotic resistance in the re-growth microbiota

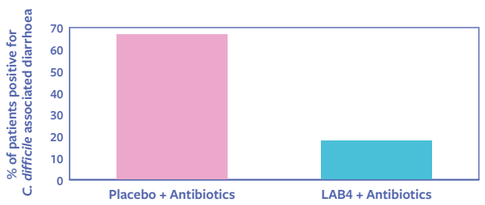
Reduction in *C. difficile*

This randomised, double-blind, placebo-controlled study was designed to assess whether supplementing with Lab4 Probiotics while taking antibiotics can help prevent *C. difficile* diarrhoea. The study was conducted by Cambridge University/Addenbrooke's Hospital in the UK.



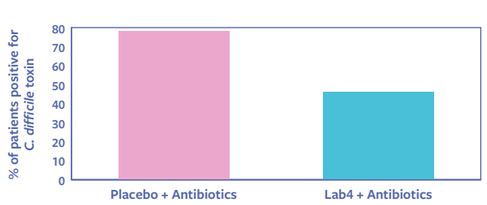
Results

Incidence of *C. difficile* associated diarrhoea



- Participants taking Lab4 Probiotics experienced a lower incidence of *C. difficile* diarrhoea compared to those taking the placebo.

Presence of *Clostridium difficile* toxin



- This effect was due to a reduction in the presence of the *C. difficile* toxin in the Lab4 group.

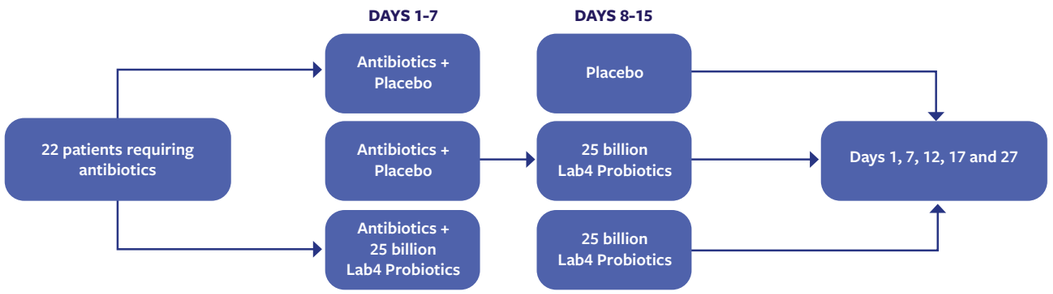
Conclusion

Supplementation with Lab4 Probiotics may reduce the incidence of the *C. difficile* toxin and associated diarrhoea in hospitalised patients.

Scan for more info

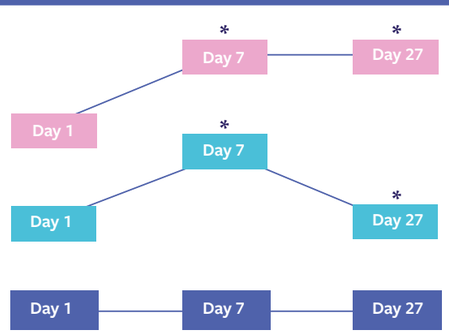
Reduction in Opportunistic Pathogens

This randomised, double-blind, placebo-controlled study investigated the effect of Lab4 Probiotics on preventing the overgrowth of pathogenic microorganisms following antibiotic therapy. The study was conducted by Cambridge University/Addenbrooke's Hospital in the UK.



Results

Effect of antibiotics and Lab4 on opportunistic facultative anaerobes



Antibiotic / Placebo
Antibiotic followed by Lab4
Antibiotic with and followed by Lab4

The numbers of opportunistic facultative anaerobes (enterobacteria, staphylococci and enterococci):

- Significantly increased in patients receiving antibiotics and placebo at the end of antibiotic treatment (*P<0.05) and remained increased post antibiotic therapy (*P<0.05).
- Significantly increased in patients receiving antibiotics and placebo at the end of antibiotic treatment (*P<0.05), but decreased significantly following the introduction of Lab4 Probiotics supplementation post antibiotic therapy (*P<0.05).
- Remained stable in patients who received antibiotics and Lab4 Probiotics at the same time throughout the study period.

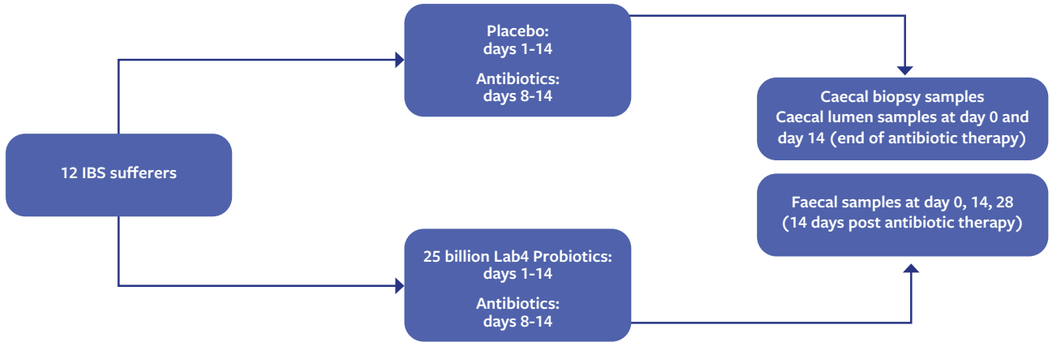
Conclusion

When Lab4 was given immediately after the antibiotic course, it helped rectify the overgrowth of opportunistic pathogens (enterobacteria, staphylococci and enterococci). However, even more importantly, when Lab4 was given at the same time as the antibiotic course, it prevented any overgrowth of these opportunistic pathogens. This finding contributed to the now prevailing guidance of administering probiotics alongside antibiotics, rather than waiting until after the course is completed.

Scan for more info

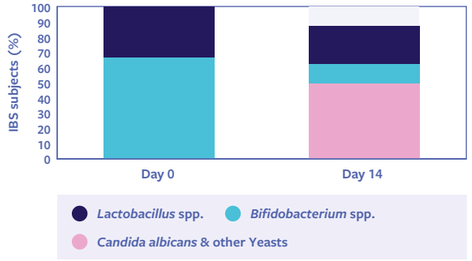
Reduction in *Candida albicans* and other yeasts

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



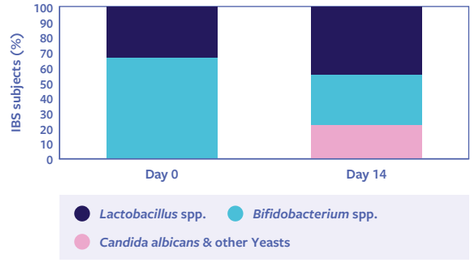
Results

PLACEBO + ANTIBIOTICS *Caecal Biopsy*



- 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.

Lab4 + ANTIBIOTICS *Caecal Biopsy*



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

Conclusion

In this unique, small, and invasive study, supplementation with Lab4 Probiotics alongside antibiotic therapy reduced the levels of *C. albicans* and other intestinal yeasts associated with the caecal epithelium.

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

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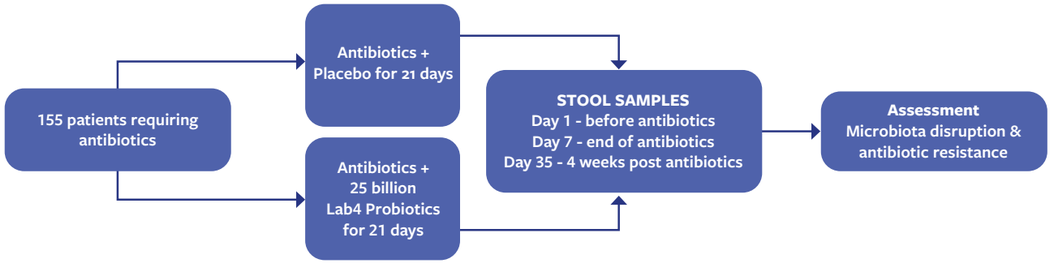
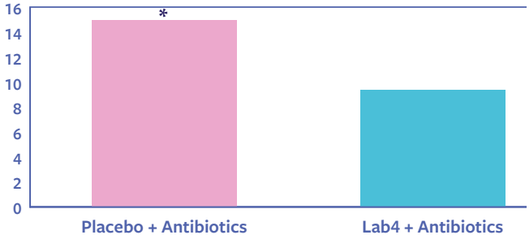
Reduction in levels of antibiotic resistance within the re-growth microbiota

This randomised, double-blind, placebo-controlled study investigated the impact of Lab4 Probiotics on antibiotic resistance in the re-growth gut microbial population following antibiotic therapy. The study was conducted by Cambridge University/Addenbrooke's Hospital in the UK.



Results

Development of enterococcal amoxicillin resistance in initially sensitive patients 4 weeks post antibiotic therapy



- In the placebo group, the number of patients harbouring antibiotic-resistant enterococci increased significantly following antibiotic therapy (*P= 0.012).
- In the Lab4 group, no significant change was observed post antibiotic therapy.

Conclusion

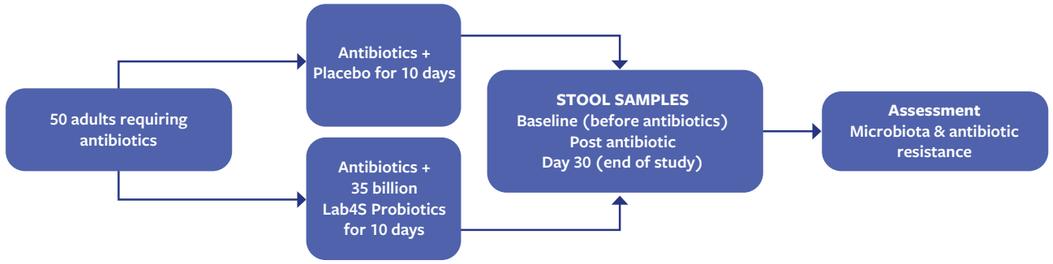
Lab4 Probiotics supplementation can reduce the level of antibiotic resistance in the re-growth microbiota following antibiotic use. This important finding showed that probiotic use may serve as a proactive intervention to help reduce the progression of antibiotic resistance.

Scan for more info

The Evidence for Lab4 plus *S. boulardii* (Lab4S)

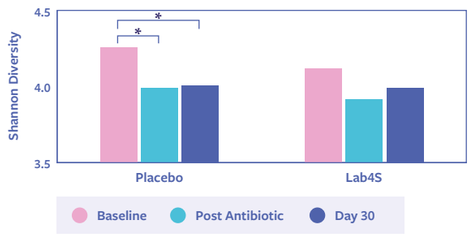
Lab4S Probiotics, when given alongside antibiotics, showed the following benefits compared to placebo:
- Protection of gut microbiota diversity
- Reduction in undesirable and potentially opportunistic pathogenic bacteria and an increase in beneficial bacteria
- Reduction in levels of antibiotic resistance in the re-growth microbiota

This randomised, double-blind, placebo-controlled study investigated the effect of Lab4S Probiotics alongside antibiotic therapy on gut microbiota composition and antibiotic resistance.



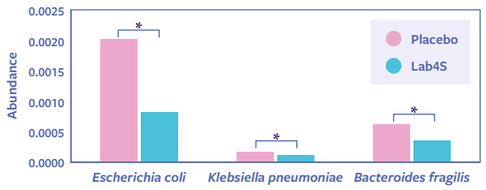
Results

Protection of bacterial diversity



- There was a significant decrease in alpha diversity (the number of different bacterial species and the abundance of each species) post antibiotic treatment in the placebo group (*P=0.0320), that remained consistent until the end of the study (*P=0.0014).
- The alpha diversity remained stable in the Lab4S Probiotics group throughout the study, suggesting a protective effect.

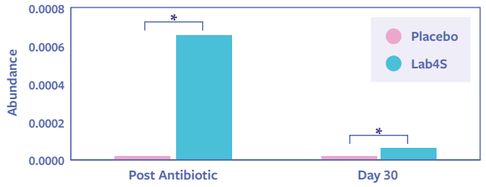
Reduction in undesirable bacteria



- Lab4S Probiotics significantly limited the overgrowth of undesirable bacteria in the re-growth population.
- In the placebo group, a significant increase in the numbers of *E. coli* (*P<0.0001), *Klebsiella pneumoniae* (*P=0.0084) and *Bacteroides* fragilis (*P=0.021) was observed at Day 30 compared to the Lab4S group.

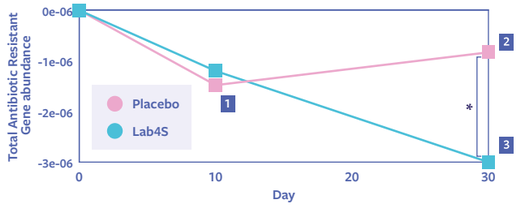
Results

Increase in beneficial species



- Lab4S Probiotics helped preserve beneficial bacteria during and after antibiotic treatment.
- A significant reduction in *Lactobacillus acidophilus* numbers was observed in the placebo group in response to antibiotic treatment (*P<0.0001) and remained reduced at Day 30 (*P=0.0017).

Reduction in Antibiotic Resistance



- Both groups show a reduction in total antibiotic-resistant gene abundance, likely due to the overall reduction in bacterial population caused by the antibiotic treatment.
- In the placebo group, antibiotic-resistant bacteria 'survive' the antibiotic course and become a larger proportion of the re-growth microbial population.
- In the Lab4S group, colonisation and growth of the probiotic population not only prevent the overgrowth of antibiotic-resistant bacteria but also appear to outcompete them, leading to a further reduction in their abundance.

Conclusion

Lab4S may help reduce antibiotic-associated disturbances by preserving microbial diversity.

This is a second demonstration of the ability of Lab4 to reduce levels of antibiotic resistance when taken alongside antibiotics. As possibly the only proactive intervention to show this effect - given that most strategies focus on reducing antibiotic use - this may be considered a significant finding and a potential new tool in tackling the global health challenge of antibiotic resistance.

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A multitude of benefits

- Lab4 Probiotics has shown simultaneous benefits on digestive health, immune function, athletic performance, gut-brain axis, and alongside antibiotic use
- Lab4S Probiotics is a unique combination of the Lab4 bacterial consortium and the yeast, *S. boulardii*, a completely non-pathogenic saprophytic yeast that is unaffected by antibiotics. This combination has shown benefits in helping prevent the overgrowth of undesirable bacteria and other yeasts.
- 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.

Complementing the microbiota during antibiotic use

When taken alongside antibiotics (ideally at least two hours away the antibiotic dose), these probiotic organisms are able to complement the normal intestinal microbiota and mitigate the damaging and depleting effect of the antibiotic. Repeated supplementation throughout the course of antibiotic treatment maintains this effect.

High dose

The recommended daily dose of Lab4S provides 25 billion CFU Lab4 and 10 billion CFU *S. boulardii* – both at levels shown to be clinically effective. 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.

*In powder and capsule products produced and packed appropriately

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 **info@lab4probiotics.co.uk** or on **01639 825100**
www.lab4probiotics.co.uk

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