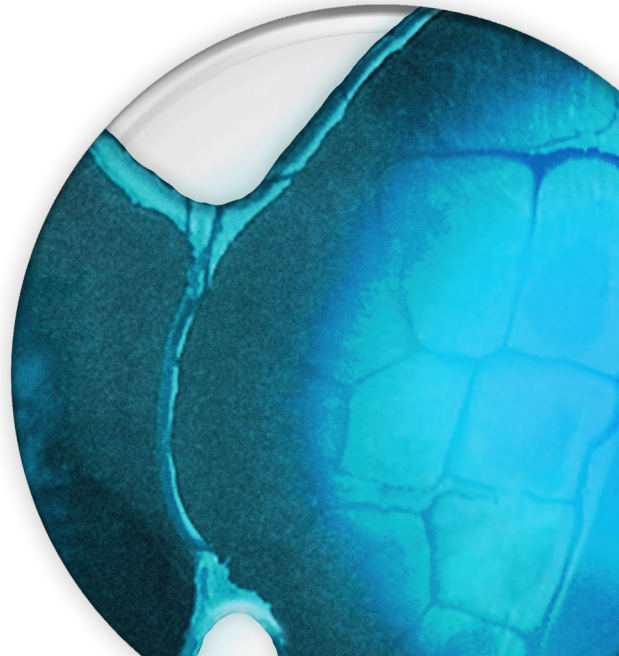
PrecisionBiotics®

Clinical Evidence Summary

Irritable Bowel Syndrome and a Dual Strain Probiotic



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Clinical Evidence Summary

Irritable Bowel Syndrome and a Dual Strain Probiotic

Irritable bowel syndrome (IBS) is a chronic disorder of gut-brain interaction, involving gastrointestinal and psychological symptoms. Clinical evidence has shown that a combination of the **35624**™ and **1714**™ probiotic strains, which have complementary modes of action, may be effective at helping to manage both the gastrointestinal and psychological symptoms of IBS and may improve quality of life[1-3].

Key Points:

- IBS is defined as a 'disorder of gut-brain interaction'[4]
- Psychological symptoms such as stress, anxiety and depression are common in IBS and may play a role in the development and exacerbation of the disease[5]
- The gut microbiota is a key regulator of the gut-brain axis6 and may contribute to the pathophysiology of IBS[4]. The profile of gut bacteria in people with IBS may differ from those without the disease[7].
- There is potential in combining two clinically studied *Bifidobacterium longum* probiotic strains with different but compatible mechanisms of action, to manage both gastrointestinal and psychological symptoms of IBS.
    - The **35624**™ strain: shown to significantly improve IBS symptoms in randomised placebo-controlled trials[8,9] and real-world studies[10-13]
    - The **1714**™ strain: shown to significantly improve stress coping and mental fatigue in healthy people in randomised placebo-controlled trials[14,15] and a real-world study[16]
- In women with IBS, the combination of the **35624**™ and **1714**™ strains was associated with significant improvements in[17]:
    - Gastrointestinal symptoms (only during supplementation period)
    - Depression scores
    - Anxiety scores
    - Quality of life
- Real-world studies have demonstrated similar benefits with a combination of the **35624**™ and **1714**™ strains found to be associated with significant improvements in[2,3]:
    - Gastrointestinal symptoms
    - Stress
    - Fatigue
    - Mood
    - Impact to daily life
- Whilst probiotics cannot always be successfully combined, the **35624**™ and **1714**™ strains have been selected for their compatibility, efficacy and complementary modes of action by PrecisionBiotics, who have over 20 years' experience of research and expertise in this field.

What is IBS?

IBS is a relapsing and long-term condition that affects the digestive system, with an estimated prevalence of one in ten people globally[18]. A diagnosis of IBS is made based on patient reported symptoms, in the absence of other detectable diseases[4,19,20]. The Rome IV Criteria defines IBS as recurrent abdominal pain occurring at least one day/week in the last three months on average*, associated with **two or more** of the following criteria:

1. Related to defecation
2. Associated with a change in frequency of stool
3. Associated with a change in form (appearance) of stool

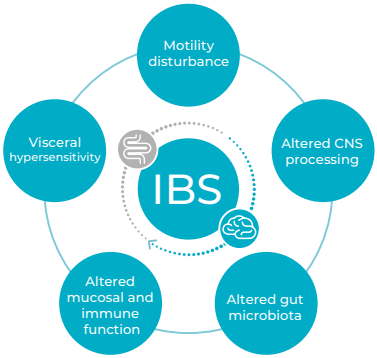
*For the last three months with symptom onset at least six months prior to diagnosis .

The Gut-Brain Axis

The pathophysiology of IBS is multifactorial. International experts recently redefined IBS as a 'disorder of gut-brain interactions' in light of the growing evidence for the role of psychosocial factors in its pathophysiology[4].

In addition to gastrointestinal symptoms, patients with IBS may have psychological comorbidities including stress, fatigue, anxiety and depression, which may play a role in the development of IBS and may be exacerbated as a consequence of its symptoms[5,21,22]. This bidirectional communication pathway between the gut and the brain is known as the **gut-brain axis**[23].

The gut-brain axis is a complex regulatory system involving the central nervous system, enteric nervous system (our 'second brain' which controls the function of our gastrointestinal tract), as well as the endocrine and immune systems[23,24].



CNS: central nervous system

The Microbiota-Gut-Brain Axis

The realisation that the gut microbiota is a key regulator of the gut brain axis prompted the proposal of a new term: the **microbiota gut-brain-axis**[24]. Whilst it is not yet clear whether it is a cause or consequence of IBS, the composition of gut bacteria of people with IBS may differ from that of people without the disease[7]. The gut microbiota has been proposed as a therapeutic target in the management of IBS[25,26].

Probiotics in IBS Management

Numerous international clinical guidelines recognise the potential benefits of certain probiotics as a treatment strategy for managing the symptoms of IBS[19,20,27,28]. As the effects of probiotics are strain specific, it is important to choose a probiotic with clinical evidence of efficacy in IBS[20].

A combination of probiotic strains with different but complementary modes of action may be considered to address both the gastrointestinal and brain-associated mechanisms of IBS. However, mixing bacterial strains together can affect their individual properties and efficacy. For multi-strain probiotic formulations, it is important to assess the compatibility of the strains to ensure they have a synergistic rather than an antagonistic effect[29]. Clinical evidence for any multi-strain formulation should come from clinical trials of the combination and not simply be extrapolated from studies of individual strains[30].

A Dual Strain Approach

In line with the recently updated IBS definition and based on clinical evidence, a new probiotic formulation has been developed that combines two compatible *Bifidobacterium longum* strains with complementary modes of action relevant for IBS, with the aim of managing both gastrointestinal and psychological symptoms.

The **35624**™ strain

- Randomised, placebo-controlled trials demonstrated this strain to be effective in managing symptoms of IBS[8,9]
- Real-world evidence has shown the **35624**™ strain significantly improves symptoms of IBS and quality of life[10-13,31,32]

The **1714**™ strain

- Placebo-controlled trials demonstrated that this strain was associated with significant improvements in stress coping and mental fatigue[14,15]
- A real-world study has shown the **1714**™ strain significantly improved feelings of stress, anxiousness, tiredness/fatigue and overall wellbeing[16]

Mechanism of Action

The dual strain combination of **35624**™ and **1714**™ strains targets the gut-brain axis through the compatible modes of action of these strains. While both strains are genetically very similar, they each have strain-specific features. For example, each strain produces a unique exopolysaccharide (EPS) which contributes to the anti-inflammatory and immunoregulatory activity of each strain[33-35].

Bifidobacterium longum **35624**™ engages with dendritic cells within the gastrointestinal tract, downregulating proinflammatory immune responses and upregulating anti-inflammatory immune responses to help reduce signs of inflammation in the gut, thereby alleviating GI symptoms of IBS[33,34,36,37].

Bifidobacterium longum **1714**™ produces tryptophan and has anti-inflammatory and immunoregulatory activity that directs tryptophan metabolism towards a neuroprotective pathway, increasing neuroprotective tryptophan metabolites in the gut[35].

Together, this dual strain combination supports the protection of the gastrointestinal tract whilst also helping to reduce physical gut symptoms. Improvement in gut symptoms has been shown to correlate with normalisation of the cortisol awakening response (a marker of associated stress), thereby helping to improve overall quality of life[1].

Clinical Evidence

In women with moderate or severe IBS (n=33), eight weeks of supplementation with the combination of the **35624**™ and **1714**™ probiotic strains resulted in the following improvements (compared to baseline)[1]:

Significant improvement of IBS gastrointestinal symptoms (p<0.0001) including[1]:

- 82% of patients experienced a clinically meaningful decrease in IBS Symptom Severity Score (IBS-SSS; defined as a decrease of ≥50 points) (Figure 1)
- Overall IBS-SSS reduced by 45% on average, including improvements in:
  - Abdominal pain severity (p<0.0001*)
  - Abdominal pain frequency (p<0.0001*)
  - Abdominal distension severity (p<0.0001*)
  - Bowel habit satisfaction (p<0.01*)

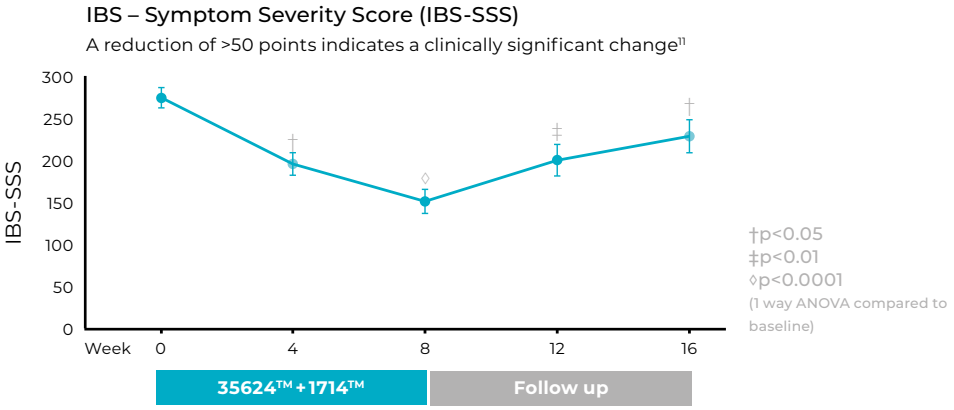


Figure 1: IBS – Symptom Severity Score (IBS-SSS)1

Significant improvements in psychological symptoms including1:

- Depression scores and anxiety scores, measured via the Hospital Anxiety and Depression Scale ($p<0.05$; Figures 2a and 2b)
- Sleep quality ($p<0.05$)
- IBS-SSS quality of life domain ($p<0.0001$*)

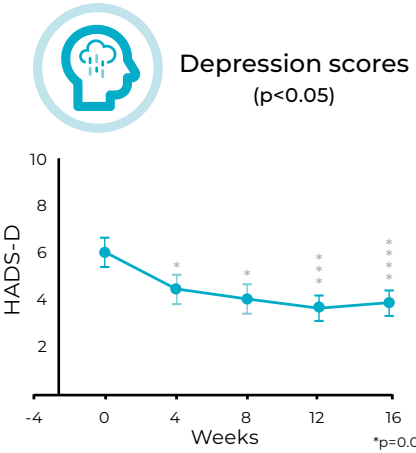
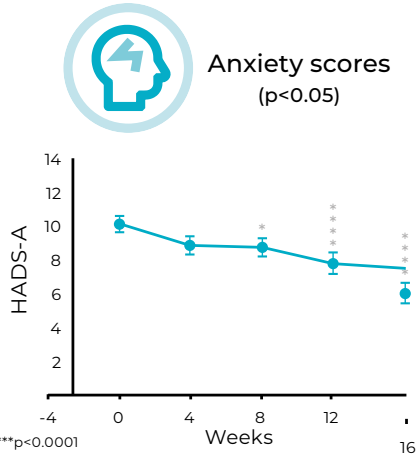


Figure 2a: Depression scores



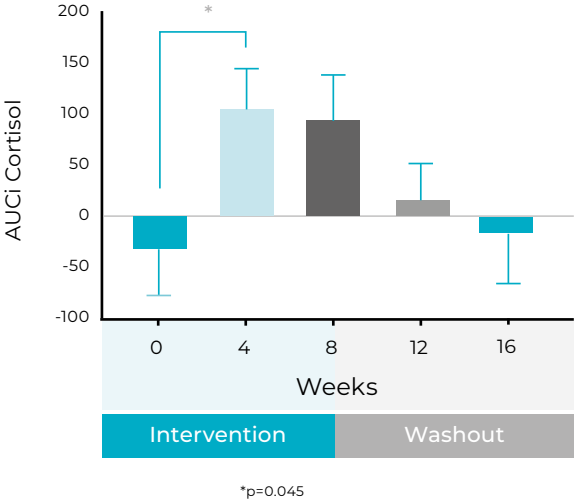
*p=0.05; ***p<0.01; ****p<0.0001

Figure 2b: Anxiety scores

HADS-D: Hospital Depression and Anxiety Scale - depression subscale
HADS-A: Hospital Anxiety and Depression Scale - anxiety subscale

*one-way ANOVA compared to baseline

- Significant improvements in the cortisol awakening response (CAR) at week 4 compared to baseline ($p<0.05$, Figure 3)
- Significant improvements in circulating tumour necrosis factor alpha (TNF-α, an inflammatory biomarker) at week 12 compared to baseline ($p<0.01$)



Prior to intervention, participants with moderate or severe IBS had a blunted CAR compared to non-IBS controls. Levels of cortisol (stress hormone) at the time of awakening were significantly higher in participants with IBS (compared to control participants who did not have IBS), but there was no expected rise within 30 minutes after awakening. Treatment with **35624**™ and **1714**™ strains normalised CAR in participants with moderate or severe IBS.

Figure 3: Salivary CAR, increase in saliva cortisol within 60 minutes after awakening, represented as the area under the curve with respect to the increase (AUCi)1

- The improvements in the cortisol awakening response were found to correlate with improvements in gastrointestinal symptoms, suggesting that the stress response may be a major driver of IBS symptoms.
- The improvements in TNF-α were found to be a significant driver of the decreases in depression scores, suggesting that a reduction in inflammation may help to alleviate psychological symptoms in individuals with IBS.
- The observed improvements in IBS symptom severity, depression and anxiety scores and cortisol awakening response occurred during the supplementation period and were not maintained after discontinuation of the dual strain probiotic supplement.

Real-World Evidence

Similar improvements were observed in real-world studies that explored the effects of this combination of the **35624**™ and **1714**™ probiotic strains in individuals with IBS[2,3]. Benefits included:

- Significant improvements in the frequency and/ or severity of gastrointestinal symptoms after intervention, compared to baseline (Figures 4a and 4b)[2]

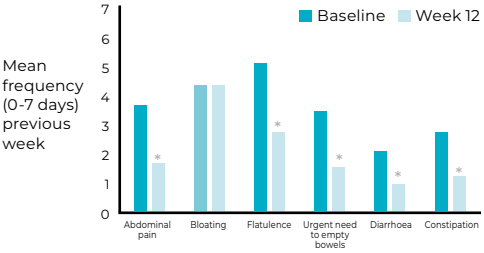


Figure 4a. Frequency of gastrointestinal symptoms

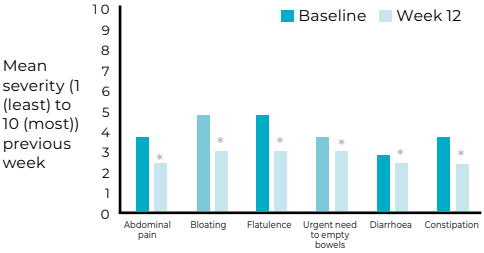


Figure 4b. Severity of gastrointestinal symptoms

- Significant improvements to the frequency and severity of psychological symptoms after intervention, compared to baseline (Figures 5a and 5b)[2]

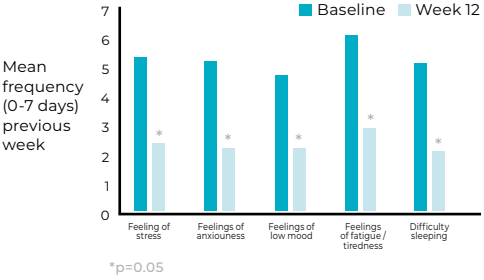


Figure 5a. Frequency of psychological symptoms

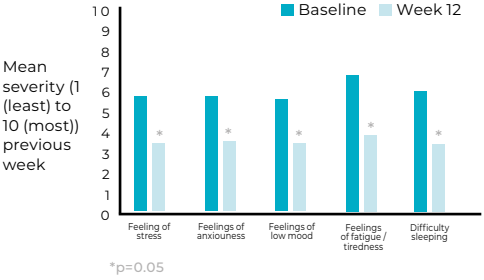


Figure 5b. Severity of psychological symptoms

Overview of Study Methods[9]

The efficacy of a combination of *Bifidobacterium longum* strains **35624**™ and **1714**™ has been assessed in one clinical trial and two real-world evidence studies.

Groeger et al 2023: To evaluate the efficacy of *Bifidobacterium longum* 35624™ and 1714™ in combination in female IBS patients with mild to moderate anxiety and/or depression[1]

Single-arm clinical trial of 40 women diagnosed with IBS according to Rome III criteria, and mild to moderate anxiety and/or depression using the Hospital Anxiety and Depression scale (HADS) (HADS-A or HADS-D scores ranging from 8-14)[38]. Participants received a daily capsule containing both the **35624**™ and **1714**™ probiotic strains at a combined level of 1 x 10^9 (one billion) colony forming units (CFU) for eight weeks, followed by an eight-week follow up period without any probiotic supplementation. Symptoms were assessed using the IBS severity scoring system, HADS and the Pittsburgh Sleep Quality Index. To assess the stress response, salivary cortisol levels were measured. Outcomes were measured at baseline and at weeks 4, 8, 12 and 16.

Kinnear et al 2022: Real-world evidence evaluating *Bifidobacterium longum* 35624™ and 1714™ in combination, in people with IBS[3]

Real-world experience study of 63 adults with IBS. Participants were referred to the programme by UK registered dietitians, and received a daily probiotic containing both *Bifidobacterium longum* **35624**™ and **1714**™ at a combined level of 1x10^9 CFU for four weeks. IBS symptoms were recorded on a 10-point Likert scale in online surveys at baseline and Week 4.

Kinnear et al 2023: The effect of dual *Bifidobacterium longum* 35624™ and 1714™ on physical and psychological symptoms in adults with IBS in real world settings[2]

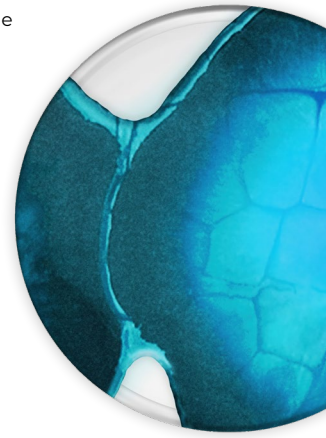
Real-world experience study of 133 adults diagnosed with IBS according to latest Rome IV criteria, and at least one psychosocial comorbidity. Participants receive a daily probiotic containing both *Bifidobacterium longum* **35624**™ and **1714**™ at a combined level of 1x10^9 CFU for 12 weeks. Participants rated the severity and frequency of their GI and psychosocial symptoms over the previous week by Likert scales in online surveys at baseline and week 12.

Further Information: Clinical Evidence for Individual Strains

For further information relating to the clinical evidence for the individual **35624**® and **1714**® strains, refer to:

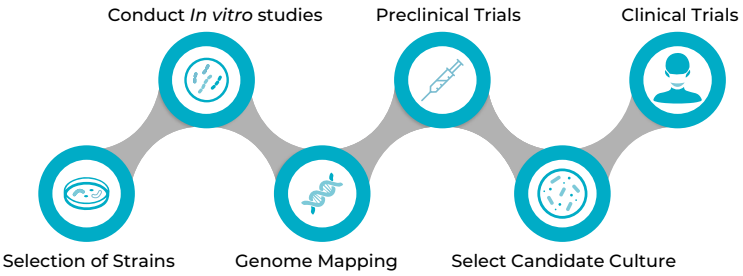
Gut Health & The **35624**® Strain – available at **precisionbiotics.science/resources**

Stress & The **1714**® Strain – available at **precisionbiotics.science/resources**



The Precise Approach to Probiotic Development

For over twenty years, PrecisionBiotics has discovered and developed unique probiotic strains in partnership with scientists and clinical experts from a world-leading centre of research into the microbiome and gut-brain axis - the APC Microbiome Institute, University College Cork, Ireland. This follows a robust process to develop targeted probiotics:



The result has been the development of safe, effective, evidence-based probiotic supplements with strains selected for their specific action for specific conditions.

Summary

In addition to gastrointestinal symptoms, psychological symptoms such as stress, anxiety and depression are common in IBS and may play a role in the development and exacerbation of the disease. In recognition of the role of psychological factors, IBS is now recognised as a disorder of the gut-brain axis.

A dual strain probiotic combining *Bifidobacterium longum* strains **35624**™ and **1714**™ was developed to target the gut-brain axis for the management of both gastrointestinal and psychosocial symptoms of IBS. Clinical and real-world studies have demonstrated that supplementation with this dual strain probiotic helps to significantly reduce both gastrointestinal and psychological symptoms of IBS[1-3].

References

1. Groeger D, Murphy EF, Tan HTT, Larsen IS, O'Neill I, Quigley EMM. Interactions between symptoms and psychological status in irritable bowel syndrome: An exploratory study of the impact of a probiotic combination. *Neurogastroenterol Motil.* 2023 Jan;35(1):e14477.
2. Kinnear F, Sanders K, Sorensen K, *et al.* The effect of dual *Bifidobacterium longum* probiotic strains 35624 and 1714 on physical and psychosocial symptoms in adults with irritable bowel syndrome in real-world settings. *United European Gastroenterology Journal.* 2023;11:1170-1171.
3. Kinnear F, Sorensen K, Power N, *et al.* A dual strain *Bifidobacterium longum* probiotic is associated with improvements in gastrointestinal and psychosocial symptoms in people with irritable bowel syndrome- a real-world experience programme. *United European Gastroenterology Journal.* 2022;10:862.
4. Schmulson MJ and Drossman DA. What Is New in Rome IV. *Journal of Neurogastroenterology and Motility.* 2017;23(2):151-163.
5. International Foundation for Functional Gastrointestinal Disorders. Psychological Factors and IBS. [Online] Available: https://aboutibs.org/what-is-ibs/psychological-factors-and-ibs/ (Accessed 07.10.2024).
6. Mukhtar K, Nawaz H and Abid S. Functional gastrointestinal disorders and gut-brain axis: What does the future hold? *World Journal of Gastroenterology.* 2019;25(5):552-566.
7. Jeffery IB, O'Toole PW, Öhman L, *et al.* An irritable bowel syndrome subtype defined by species-specific alterations in faecal microbiota. *Gut*. 2012;61(7):997-1006.
8. O'Mahony L, McCarthy J, Kelly P, *et al. Lactobacillus* and *Bifidobacterium* in irritable bowel syndrome: symptom responses and relationship to cytokine profiles. *Gastroenterology.* 2005;128(3):541-551.
9. Whorwell PJ, Altringer L, Morel J, *et al.* Efficacy of an encapsulated probiotic *Bifidobacterium infantis* 35624 in women with irritable bowel syndrome. *American Journal of Gastroenterology.* 2006;101(7):1581-1590.
10. Sabaté JM and Iglicki F. Effect of Bifidobacterium longum 35624 on disease severity and quality of life in patients with irritable bowel syndrome. *World Journal of Gastroenterology.* 2022;28(7):732-744.
11. Arriaza Peso E, Araméndiz, Araujo R, *et al.* Efficacy of *Bifidobacterium longum* subsp. *longum* 35624® treatment in the symptomatic improvement of irritable bowel syndrome. *El Médico, Sanidad y Ediciónes*. 2022.
12. Lenoir M, Wienke J, Fardao-Beyler F, *et al.* An 8-Week Course of *Bifidobacterium longum* 35624® Is Associated with a Reduction in the Symptoms of Irritable Bowel Syndrome. *Probiotics and Antimicrobial Proteins*. 2023.
13. Kinnear F, O'Donovan D, Sorensen K, *et al.* Real world experiences of *Bifidobacterium longum* 35624® as part of the long-term management of irritable bowel syndrome symptoms. *Neurogastroenterology & Motility.* 2023;35:e14655.
14. Allen AP, Hutch W, Borre YE, *et al. Bifidobacterium longum* 1714 as a translational psychobiotic: modulation of stress, electrophysiology and neurocognition in healthy volunteers. *Translational Psychiatry.* 2016;6(11):e939.
15. Wang H, Braun C, Murphy EF, *et al. Bifidobacterium longum* 1714™ Strain Modulates Brain Activity of Healthy Volunteers During Social Stress. *American Journal of Gastroenterology.* 2019;114(7):1152-1162.
16. Sorensen K, Kupuseravic J, Curristin M, *et al.* Experiences of sleep, stress and wellbeing during 10 weeks of probiotic supplementation – a real-world study in hybrid workers. *Agro Food Industry Hi-Tech*. 2024;35(1).
17. Groeger D, Murphy EF, Tan HTT, *et al.* Interactions between symptoms and psychological status in irritable bowel syndrome. An exploratory study of the impact of a probiotic combination. *Neurogastroenterology & Motility.* 2022;35:e14477.
18. Black CJ and Ford AC. Global burden of irritable bowel syndrome: trends, predictions and risk factors. *Nature Reviews Gastroenterology and Hepatology.* 2020;17(8):473-486.
19. Quigley EM, Fried M, Gwee KA, *et al.* World Gastroenterology Organisation Global Guidelines Irritable Bowel Syndrome: A Global Perspective Update September 2015. *Journal of Clinical Gastroenterology.* 2016;50(9):704-713.
20. Guarner F, Sanders M, Szajewska, H, *et al.* World Gastroenterology Organisation Global Guidelines - Probiotics and prebiotics. [Online] Available: https://www.worldgastroenterology.org/UserFiles/file/guidelines/probiotics-and-prebiotics-english-2023.pdf (Accessed 10.07.2024).
21. Fond G, Loundou A, Hamdani N, *et al.* Anxiety and depression comorbidities in irritable bowel syndrome (IBS): a systematic review and meta-analysis. *European Archives of Psychiatry and Clinical Neuroscience.* 2014;264(8):651-660.
22. Qin HY, Cheng CW, Tang XD, *et al.* Impact of psychological stress on irritable bowel syndrome. *World Journal of Gastroenterology.* 2014;20(39):14126-14131.
23. Ancona A, Petito C, Lavarone I, *et al.* The gut-brain axis in irritable bowel syndrome and inflammatory bowel disease. *Digestive and Liver Disease.* 2021;53(3):298-305.
24. Cryan JF, O'Riordan KJ, Cowan CSM, *et al.* The Microbiota-Gut-Brain Axis. *Physiology Reviews.* 2019;99(4):1877-2013.
25. Enck P, Aziz Q, Barbara G, *et al.* Irritable bowel syndrome. *Nature Reviews Disease Primers.* 2016;2:16014.
26. Quigley EMM. The Gut-Brain Axis and the Microbiome: Clues to Pathophysiology and Opportunities for Novel Management Strategies in Irritable Bowel Syndrome (IBS). *Journal of Clinical Medicine.* 2018;7(1).
27. Vasant DH, Paine PA, Black CJ, *et al.* British Society of Gastroenterology guidelines on the management of irritable bowel syndrome. *Gut*. 2021;70(7):1214-1240.
28. Moayyedi P, Andrews CN, MacQueen G, *et al.* Canadian Association of Gastroenterology Clinical Practice Guideline for the Management of Irritable Bowel Syndrome (IBS). *The Journal of the Canadian Association of Gastroenterology.* 2019;2(1):6-29.
29. Timmerman HM, Koning CJ, Mulder L, *et al.* Monostrain, multistrain and multispecies probiotics--A comparison of functionality and efficacy. *International Journal of Food Microbiology.* 2004;96(3):219-233.
30. Quigley EMM. Clinical Trials of Probiotics in Patients With Irritable Bowel Syndrome: Some Points to Consider. *Journal of Neurogastroenterol and Motility.* 2022;28(2):204-211.
31. Emmanuel A, Martin L and Passananti V. Efficacy of *Bifidobacterium longum* 35624 in IBS patient's refractory to a low FODMAP diet. *The Mexican Association of Gastroenterology National Gastro Week.* 2019; Conference proceeding.
32. Solovyeva O, Nekrasova A, Topalova I, *et al.* Long-term probiotic administration for irritable bowel syndrome: a legal need. *Terapevticheskii Arkhiv.* 2023;95(8):7.
33. Schiavi E, Gleinser M, Molloy E, *et al.* The Surface-Associated Exopolysaccharide of Bifidobacterium longum 35624 Plays an Essential Role in Dampening Host Proinflammatory Responses and Repressing Local TH17 Responses. *Applied and Environmental Microbiology.* 2016;82(24):7185-7196.
34. Schiavi E, Plattner S, Rodriguez-Perez N, *et al.* Exopolysaccharide from *Bifidobacterium longum* subsp. *longum* 35624 modulates murine allergic airway responses. *Beneficial Microbes.* 2018;9(5):761-773.
35. Groeger, D *et al.* Data on file - Manuscript submitted. 2024.
36. Konieczna P, Groeger D, Ziegler M, *et al. Bifidobacterium infantis* 35624 administration induces Foxp3 T regulatory cells in human peripheral blood: potential role for myeloid and plasmacytoid dendritic cells. *Gut*. 2012;61(3):354-366.
37. Giron F and Quigley EMM. Pharmabiotic Manipulation of the Microbiota in Gastrointestinal Disorders: A Clinical Perspective. *Journal of Neurogastroenterology and Motility.* 2018;24(3):355-366.
38. Zigmond AS and Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica.* 1983;67(6):361-370.
39. Francis CY, Morris J and Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. *Alimentary Pharmacology & Therapeutics*. 1997;11(2):395-402.
40. Buysse DJ, Reynolds CF, Monk TH, *et al.* The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research*. 1989;28(2):193-213.

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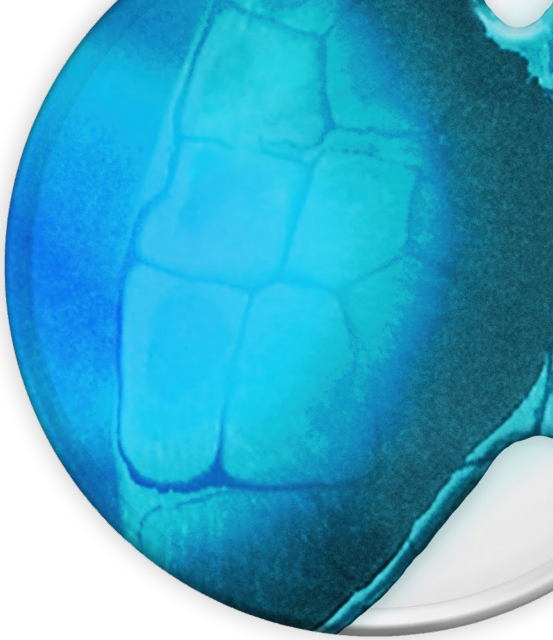

Break through the burden of IBS with a dual strain approach.

Learn how supplementation with *Bifidobacterium longum* **35624**® and **1714**® could benefit your patients with IBS by visiting our CPD Learning Hub at

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PrecisionBiotics®

Science in every strain

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