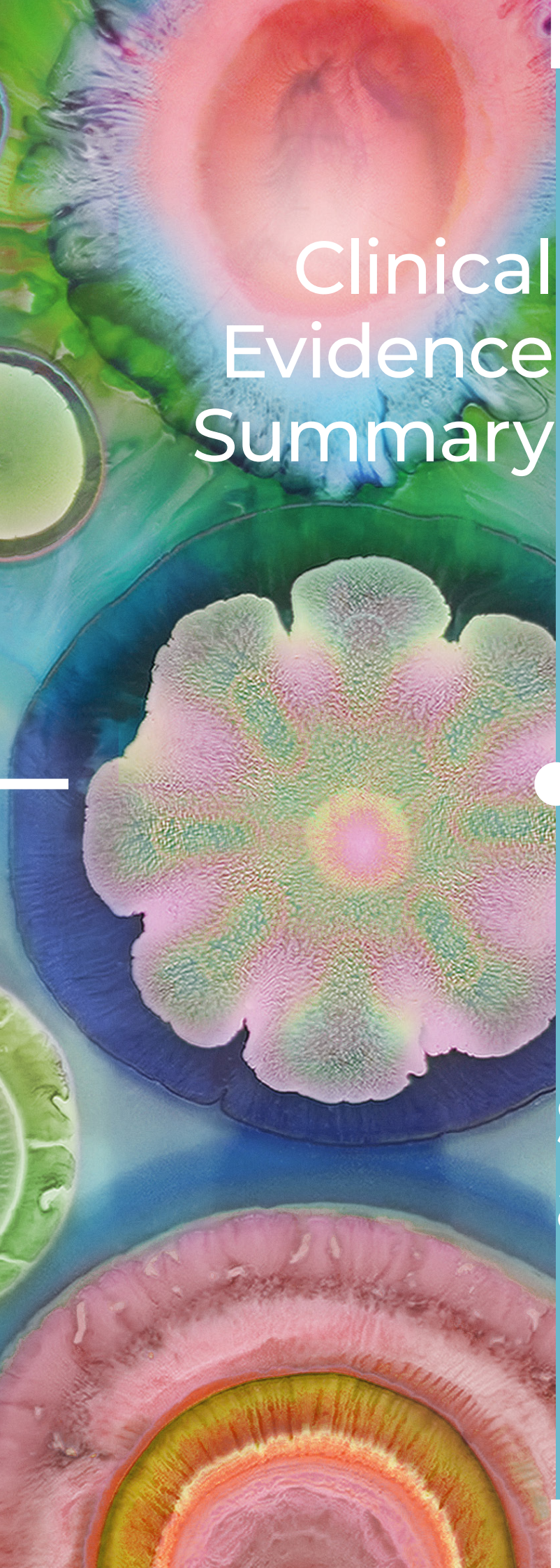

Precision Biotics

Clinical Evidence Summary

Irritable Bowel Syndrome and a Dual Strain Probiotic

CLINICAL EVIDENCE SUMMARY

Irritable Bowel Syndrome and a Dual Strain Probiotic

Irritable bowel syndrome (IBS) is a chronic disorder of gut-brain interactions, 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.

Scientific information. For healthcare professionals only

Key Points

- IBS is defined as a 'disorder of gut-brain interactions'[1]
- 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[2]
- The gut microbiota is a key regulator of the gut-brain axis[3] and may contribute to the pathophysiology of IBS[1]. The profile of gut bacteria in people with IBS may differ from those without the disease.[4]
- There is potential in combining two clinically studied *Bifidobacterium longum* probiotic strains with different but compatible mechanisms of activity, to manage both gastrointestinal and psychological symptoms of IBS.
  - The **35624**® strain: shown to significantly improve IBS symptoms in randomised placebo-controlled trials[5,6]
  - The **1714**® strain: shown to significantly improve stress coping and mental fatigue in healthy people in randomised placebo-controlled trials[7,8]
- In women with IBS, combination of the **35624**® and **1714**® strains was associated with significant improvements in[9]:
  - ✓ Gastrointestinal symptoms (only while supplementation was continued)
  - ✓ Depression scores
  - ✓ Anxiety scores
  - ✓ Quality of 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.

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What is IBS?

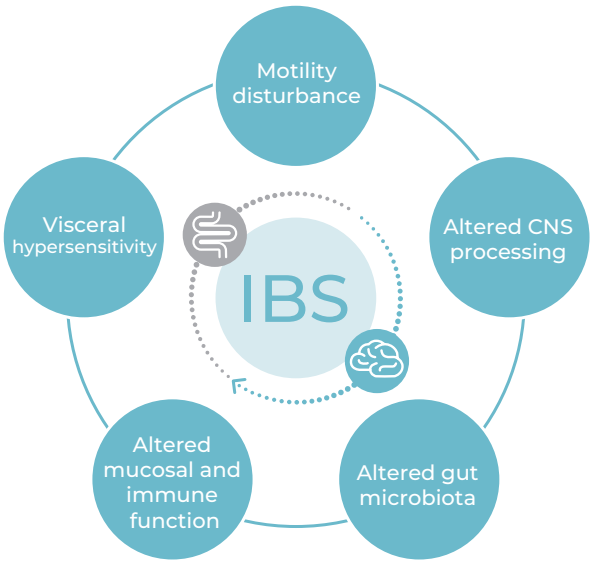
IBS is a chronic condition, characterised by the presence of abdominal pain or discomfort, which may be associated with bowel movement and/or a change in bowel habit (constipation, diarrhoea or both). Symptoms sometimes overlap with other gastrointestinal conditions, which should be ruled out for diagnosis of the disease[1,10].

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[1].

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 be exacerbated as a consequence of its symptoms[2,11,12]. This bidirectional communication pathway between the gut and the brain is known as the **gut-brain axis**[13].

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[13,14].



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**[14]. 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[4]. The gut microbiota has been proposed as a therapeutic target in the management of IBS[15,16].

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[17-19]. As the effects of probiotics are strain specific, it is important to choose a probiotic with clinical evidence of efficacy in IBS.

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[20]. 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.

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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 showed this strain to be siginficantly effective in managing symptoms of IBS.[5,6]
- Real world data showed the **35624**® strain significantly improved IBS severity and quality of life[21]
- The **1714**® strain - randomised, placebo-controlled trials showed that this strain was associated with significant improvements in stress coping and mental fatigue[7,8]

The clinical evidence for the combination of **35624**® and **1714**® strains is summarised below.

Clinical Benefits of The Dual Strain Approach in IBS[9]

In women with moderate or severe IBS, supplementation with the combination of the **35624**® and **1714**® probiotic strains resulted in:

- **Significant improvement of IBS symptoms**
- 82% of patients experienced a clinically significant improvement in IBS Symptom Severity Score (defined as a change of ≥50 points) (Figure)
- Overall IBS Symptom Severity 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 ($p<0.01$)
- IBS symptom severity gradually increased when supplementation with the two strains was stopped.
- **Significant improvements in psychological symptoms including:**
  - Depression scores ($p<0.05$)
  - Anxiety scores ($p<0.05$)
  - Sleep quality ($p<0.05$)
  - Quality of life ($p<0.0001$)

Improvements in the cortisol (stress hormone) response were also observed during the combined probiotic supplementation, supporting the above findings through a biological marker of the stress response. These results highlight the link between the stress response and gastrointestinal symptoms in people with IBS.

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Overview of Study Methods[9]

The results described above were from a study investigating the efficacy of the combination of the **35624**® and **1714**® probotic strains. This was a single-arm clinical trial of 40 women with IBS 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)[22].

Participants consumed one capsule per day of the **35624**® and **1714**® probiotic strains, at 1 x 10^9 (one billion) colony forming units combined, for eight weeks, followed by an eight-week follow up period without any probiotic supplementation.

TIMELINE

Validated tools were used to measure self-reported outcomes including the IBS Symptom Severity Score[23] and the Hospital Anxiety and Depression Scale[22] and the Pittsburgh Sleep Quality Index[24]. To assess the stress response, salivary cortisol levels were measured. Outcomes were measured at baseline and at weeks 4, 8, 12 and 16.

Results from a subset of women with moderate or severe IBS (n=33) are presented above, which demonstrated clinical benefits associated with supplementation with the combination of the **35624**® and **1714**® strains, even in subjects with more severe IBS symptoms.

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

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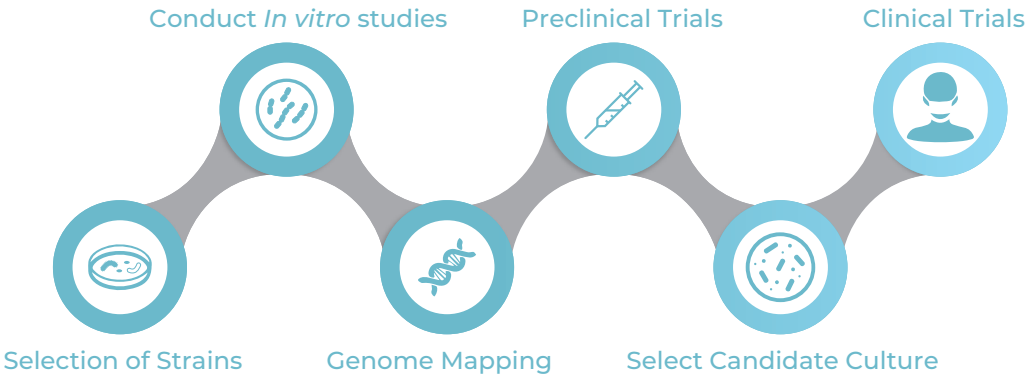
The Precise Approach to Probiotic Development

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.

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