

**BDA
CONVERSATIONS**



A common and under treated complaint

The role of probiotics in constipation



Role of Probiotics in Constipation

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What we'll cover today

- Clinical burden of constipation
- Role of the gut microbiome
- Guidelines
- Probiotic mechanism and potential role
- NEW data from Symprove constipation study

Chronic constipation is a common, chronic, and often relapsing condition

- 14% global prevalence among adults (Suarez & Ford, 2011; Barberio et al., 2021)
- Encompasses primary (functional) and secondary causes (e.g., medications, metabolic, neurologic disorders)
- Pathophysiology is multifactorial: low fibre intake, dehydration, medication side effects, gut microbiota changes
- Clinical presentation: infrequent bowel movements (≤ 3 /week) , difficult evacuation (straining, incomplete evacuation, hard/lumpy stools), bloating and distension.
- Symptom heterogeneity reflects underlying pathophysiologic diversity (Lacy et al., 2016)
- Many patients experience persistent symptoms despite established treatment pathways, contributing to long-term disease burden
- Associated with increased healthcare utilization and economic costs (Peery et al., 2020)

Unmet clinical need in chronic constipation

- High rates of inadequate response to conventional therapies, with up to 40–50% of patients dissatisfied with laxatives (Rao et al., 2015)
- Ongoing symptoms significantly impair quality of life (QOL), including physical, psychological, and social domains
- Current management is largely symptom-focused, often not addressing underlying mechanisms (e.g., dysbiosis, neuromuscular dysfunction)
- Need for mechanism-based and individualized approaches targeting root causes of chronic constipation

Diet and lifestyle should be first line management

New BDA guidelines summarise evidence base for nutritional intervention for constipation

	Response	Stool output		Symptoms								Adverse events						Quality of life				
		Stool frequency	Stool consistency	Global	Straining (severity)	Straining (frequency)	Incomplete evacuation (severity)	Incomplete evacuation (frequency)	Manual maneuvers (frequency)	Anorectal obstruction (frequency)	Defecation pain (frequency)	Abdominal pain or discomfort (severity)	Abdominal pain (frequency)	Bloating (severity)	Bloating (frequency)	Flatulence (severity)	Flatulence (frequency)	Global	Physical	Psycho-social	Worries & concerns	Satisfaction
Fibre supplements																						
Overall fibre supps	✓	✓	✓	—	✓		—					—		—		✗						
Psyllium	✓	✓	✓		✓																	
Polydextrose	—	—	—	—	—													—	—	—	—	—
Mix of inulin+others	—	—																				
Galacto-oligosacch	—	—	—	—																		
Inulin-type fructans		—	✓													✗						
Pectin																						
Wheat bran																						
Probiotic supplements																						
Overall probiotics	✓	✓	—	✓	—	—	✓	—	—	—		—		—		✓		—	—	—	—	—
Multi-strain	—	—	✓	—								—		—		—		—	—	—	✓	✓
B. lactis	—	✓	—	—	—		—					—		—				—	—	—	—	—
Bacillus coagulans	—																					
Bacillus coagulans Unique IS2		—	—					—			✓		✓									
L. casei Shirota		—	—	—										—								
Synbiotic supplements																						
Overall synbiotics		—	—	—																		
Food supplements																						
Magnesium Oxide	✓	✓	✓	✓	✓		✓					✓		✓				✓	✓	✓	✓	✓
Senna	—	—																				
Kiwifruit supplement		—	—			—		✓	—				✓		—		—					
Foods and Drinks																						
Kiwifruits, whole	✓	✓	✓			✓																
Prunes, whole			✓		✓																	
Rye bread		✓		✗																		
Linseeds																						
High mineral water	✓	—		—								—										
Whole diets																						
High fibre diet																						
✓ Improvement (compared to placebo or positive control) ✓ No difference (compared to positive control) — No impact (compared to placebo) ✗ Wors																						

✓ Improvement (compared to placebo or positive control)
 ✓ No difference (compared to positive control)
 — No impact (compared to placebo)
 ✗ Wors

Disruption of the gut microbiome contributes to constipation

- Gut–brain axis (GBA): central regulator
 - Bidirectional signaling between gut microbiota, enteric nervous system, and CNS regulates motility, visceral sensitivity, and intestinal secretion
 - Microbial metabolites (e.g., short-chain fatty acids, bile acids, serotonin, methane) influence neuromuscular function and fluid balance
 - Evidence supports microbiota involvement in chronic constipation pathophysiology (Cryan et al., 2019; Vriesman et al., 2020).
- Movement (motility regulation)
 - Microbiota modulates colonic smooth muscle activity and transit via metabolic and neuroendocrine pathways
 - Reduced production of SCFAs and other metabolites leads to impaired enteric nervous system signalling and weakened peristaltic reflexes (Parthasarathy et al., 2016).
 - Dysbiosis is associated with reduced motility and stool frequency, supported by animal and human studies (De Palma et al., 2017).

Probiotic mechanism of action

Modulation of Gut Microbiota (Dysbiosis Correction)

- Chronic constipation is associated with altered microbial composition (↓ Bifidobacterium, Lactobacillus; ↑ methanogenic flora)
- Restore microbial balance, increasing beneficial taxa and reducing methane-producing organisms linked to slow transit

Enhanced Motility (Movement)

- Increase production of short-chain fatty acids (SCFAs) which stimulate gut smooth muscle activity and peristalsis
- Reduce methane production, associated with accelerated intestinal transit (Pimentel et al., 2006; Dimidi et al., 2017)

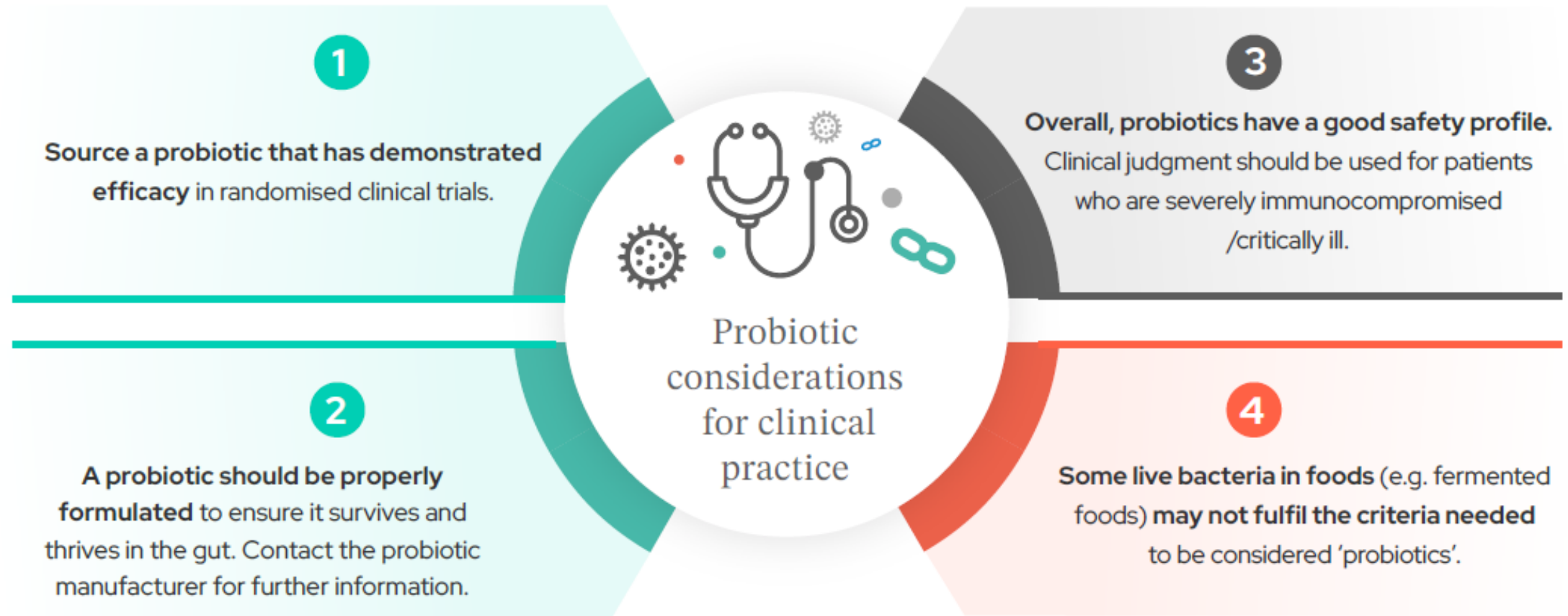
Gut–Brain Axis Modulation (Motility, Sensitivity, Secretion)

- Probiotics influence enteric nervous system signaling and serotonin (5-HT) pathways, improving motility and secretion
- May reduce visceral hypersensitivity and discomfort via neuroimmune modulation (Cryan et al., 2019)

Anti-inflammatory & Barrier Effects

- Enhance intestinal barrier function and reduce low-grade inflammation, which may contribute to symptom persistence

How to choose a probiotic



NEW study: investigating role of probiotics in mild-to-moderate chronic constipation

Primary Objective

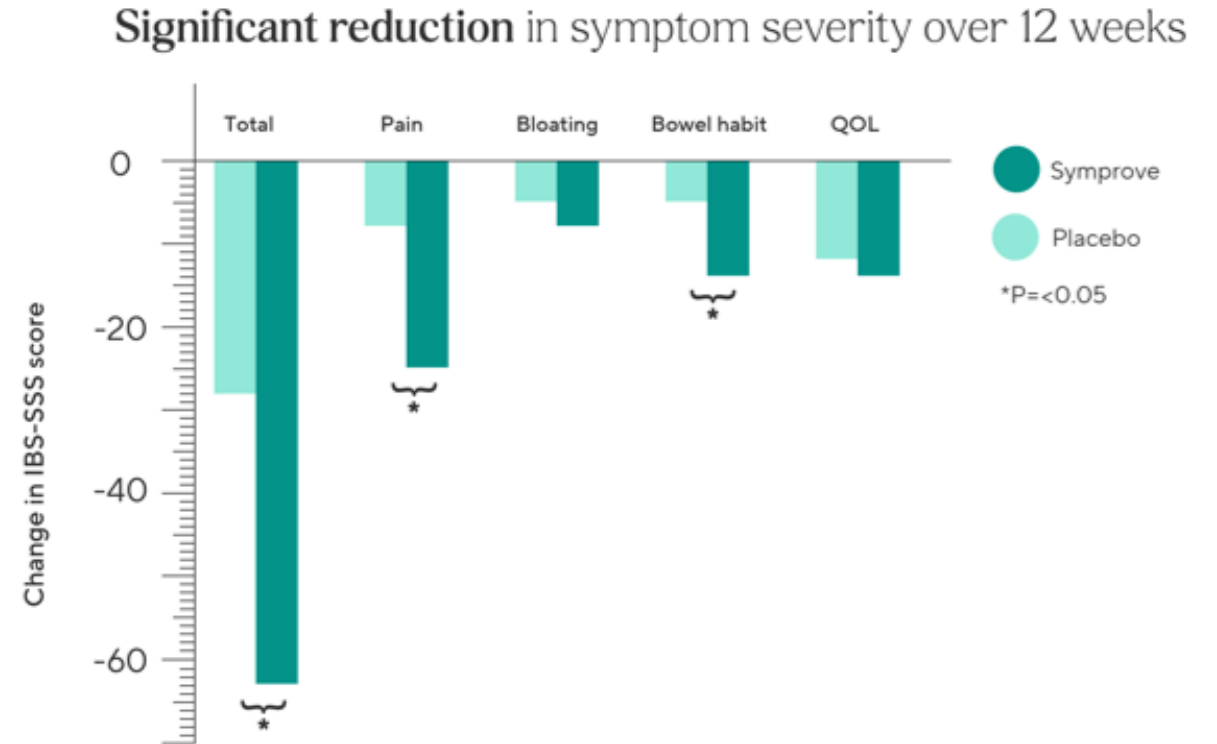
- Determine the effect of probiotic supplementation on constipation symptoms

Secondary Objectives

- Evaluate impact on constipation-related quality of life
- Examine effects on:
 - Gastrointestinal physiological function
 - Biomarkers associated with constipation

Why we chose Symprove for the study

- Proven in double-blind RCT in IBS, with significant improvement in bowel habit vs placebo
- Consistent effect seen across all subtypes of IBS, inc. IBS-C
- Hypothesis that Symprove's liquid format may drive changes throughout the whole GI tract



Study design

Single-arm study (n=20), 4 weeks of Symprove in people with self-reporting constipation in the general population

Outcomes:

- Symptoms of constipation (PAC-SYM, GSRS, gut diary)
- Constipation-related quality of life (PAQ-QoL)

Measurements:

- Breath testing (OMED device) – hydrogen and methane levels (produced by microbes). Methane assoc with constipation
- Gut capsule (ATMO) – measures whole and regional gut transit times

Status: data unpublished but submitted as an abstract to UEG and publication in development, targeting 2027

PATIENT ASSESSMENT OF CONSTIPATION

This questionnaire asks you about your constipation symptoms in the **past 2 weeks**. Answer each question according to your symptoms, as accurately as possible. There are no right or wrong answers.

For each symptom below, please indicate **how severe** your symptoms have been during the **past 2 weeks**. If you have not had the symptom during the past 2 weeks, tick 0. If the symptom seemed mild, tick 1. If the symptom seemed moderate, tick 2. If the symptom seemed severe, tick 3. If the symptom seemed very severe, tick 4. Please be sure to answer every question.

How severe have each of these symptoms been in the past 2 weeks?	Absent 0	Mild 1	Moderate 2	Severe 3	Very severe 4
1. discomfort in your stomach	☐	☐	☐	☐	☐
2. pain in your stomach	☐	☐	☐	☐	☐
3. bloating in your stomach	☐	☐	☐	☐	☐
4. stomach cramps	☐	☐	☐	☐	☐
5. painful bowel movements	☐	☐	☐	☐	☐
6. rectal burning during or after a bowel movement	☐	☐	☐	☐	☐
7. rectal bleeding or tearing during or after a bowel movement	☐	☐	☐	☐	☐
8. incomplete bowel movement, as though you didn't "finish"	☐	☐	☐	☐	☐
9. stools that were too hard	☐	☐	☐	☐	☐
10. stools that were too small	☐	☐	☐	☐	☐
11. straining or squeezing to try to pass stools	☐	☐	☐	☐	☐
12. feeling like you had to pass a stool but you couldn't (false alarm)	☐	☐	☐	☐	☐

12 Questions – 6 point Likert Scale

Clinically significant change >0.5
across domains

THE GASTROINTESTINAL SYMPTOM RATING SCALE (GSRS)

Please read this first:

This survey contains questions about how you have been feeling and what it has been like DURING THE PAST WEEK. Mark the choice that best applies to you and your situation with an “X” in the box.

1. Have you been bothered by PAIN OR DISCOMFORT IN YOUR UPPER ABDOMEN OR THE PIT OF YOUR STOMACH during the past week?

- ☐ No discomfort at all
- ☐ Minor discomfort
- ☐ Mild discomfort
- ☐ Moderate discomfort
- ☐ Moderately severe discomfort
- ☐ Severe discomfort
- ☐ Very severe discomfort

15 Questions – 7 point Scale

Clinically significant change >0.5
across domains



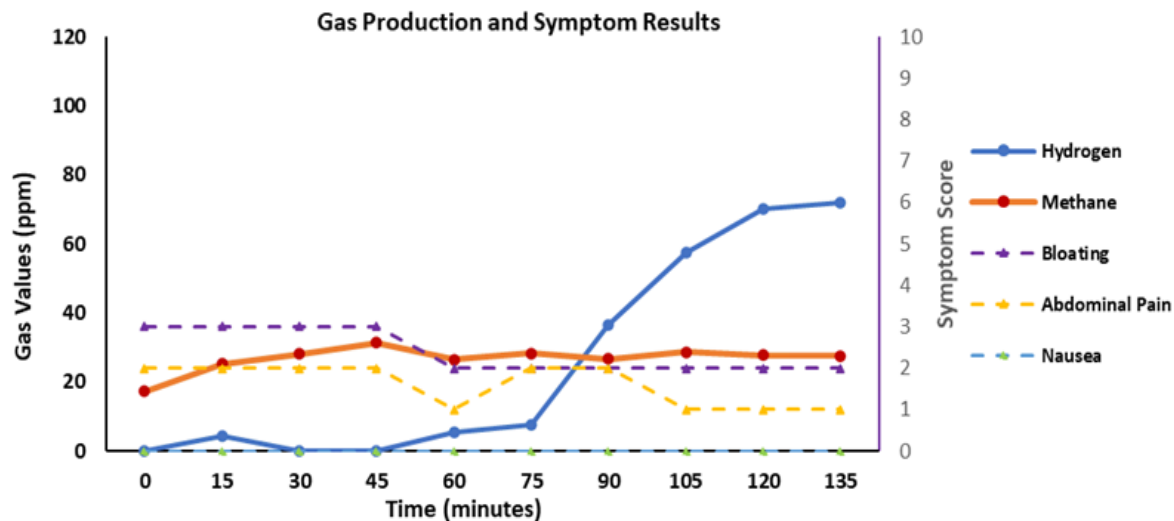
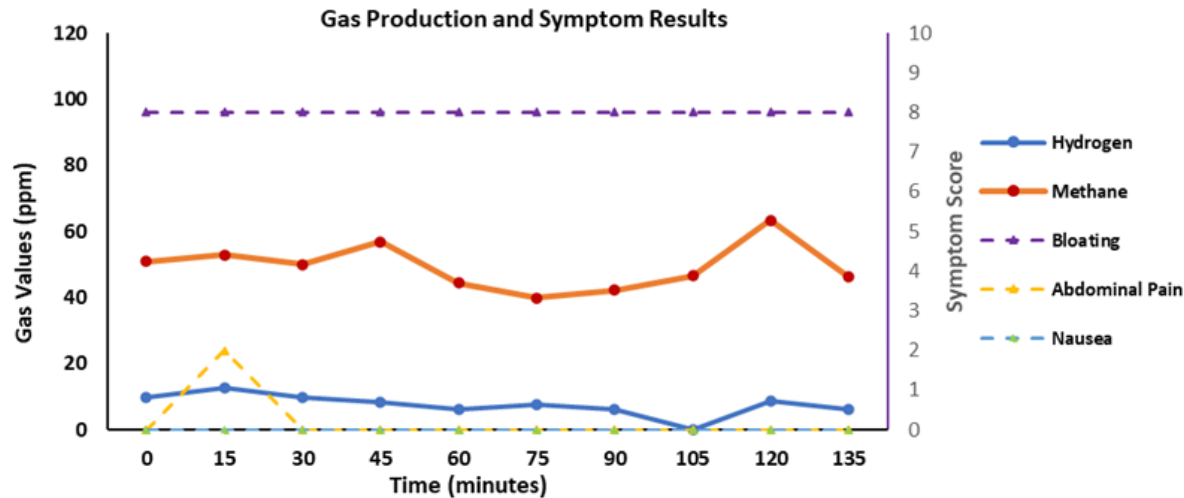
Hydrogen and Methane Breath testing - HMBT



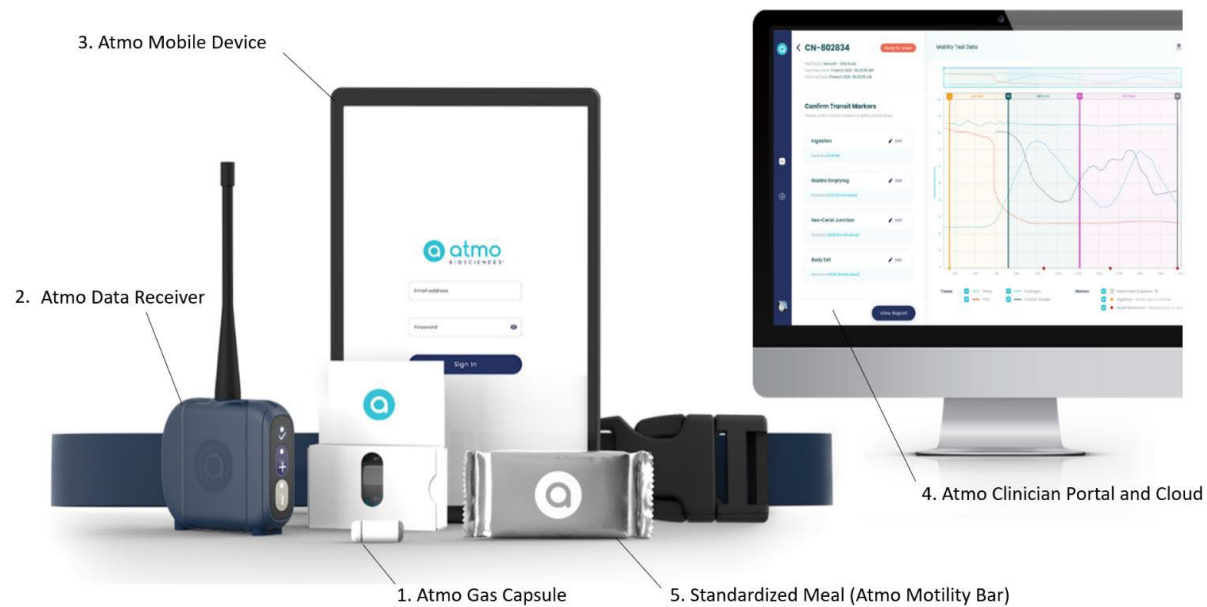
- Home test kit or in clinic
- A4 size box to fit through letterbox
- Compliant with national guidelines
- Lactulose or Glucose for SIBO

HMBT - Lactulose

- 24 hour white diet and morning fast
- Baseline sample then ingest 10g Lactulose
- Breath samples for next 2 hours
- SIBO+ Hydrogen rise of >10ppm within 60-mins or >20ppm within 90-minutes
- Methane + >10ppm at any point

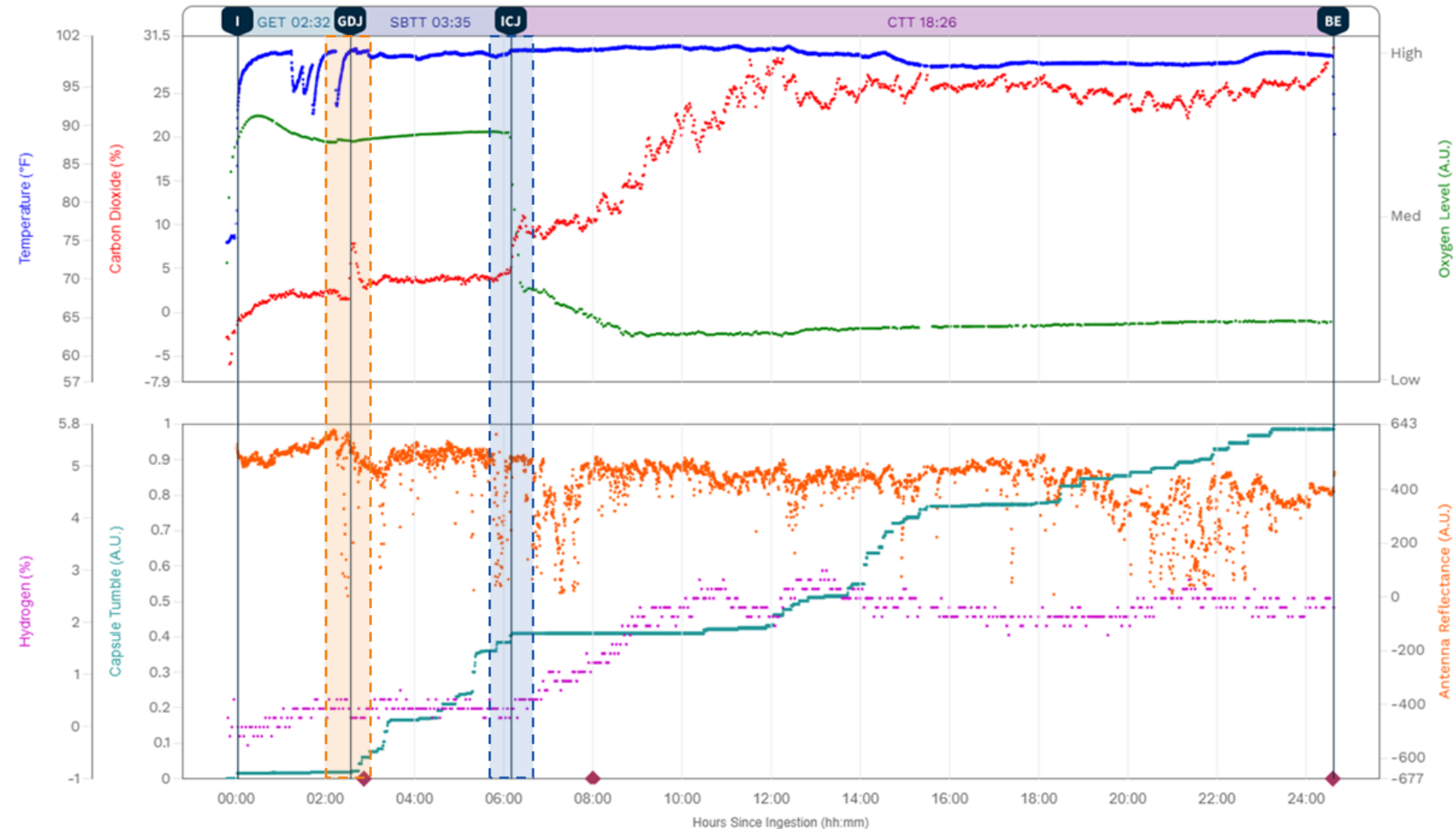


Measuring motility: ATMO Gas sensing capsule

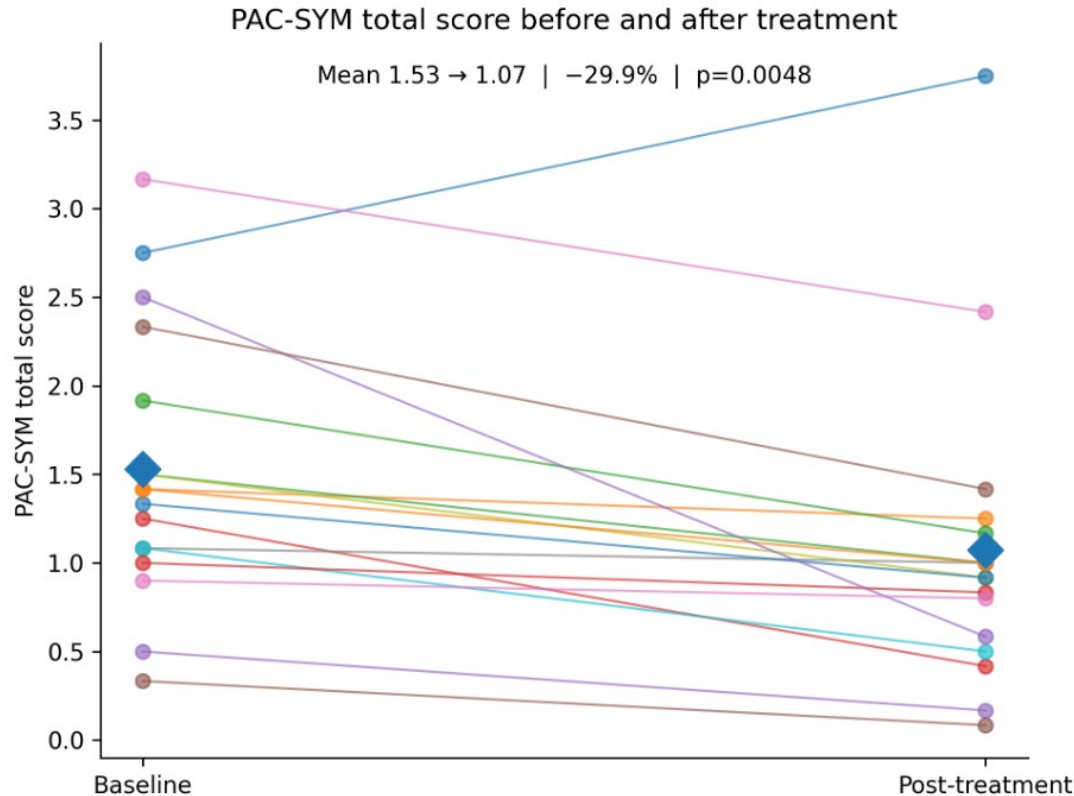


The Atmo Gas Capsule

The Atmo Gas Capsule is an FDA-cleared wireless motility capsule that senses gases and other modalities to detect GI landmarks and allow measurement of transit metrics.



Study results – PAC-SYM



- PAC-SYM (n=17):

- Mean changes

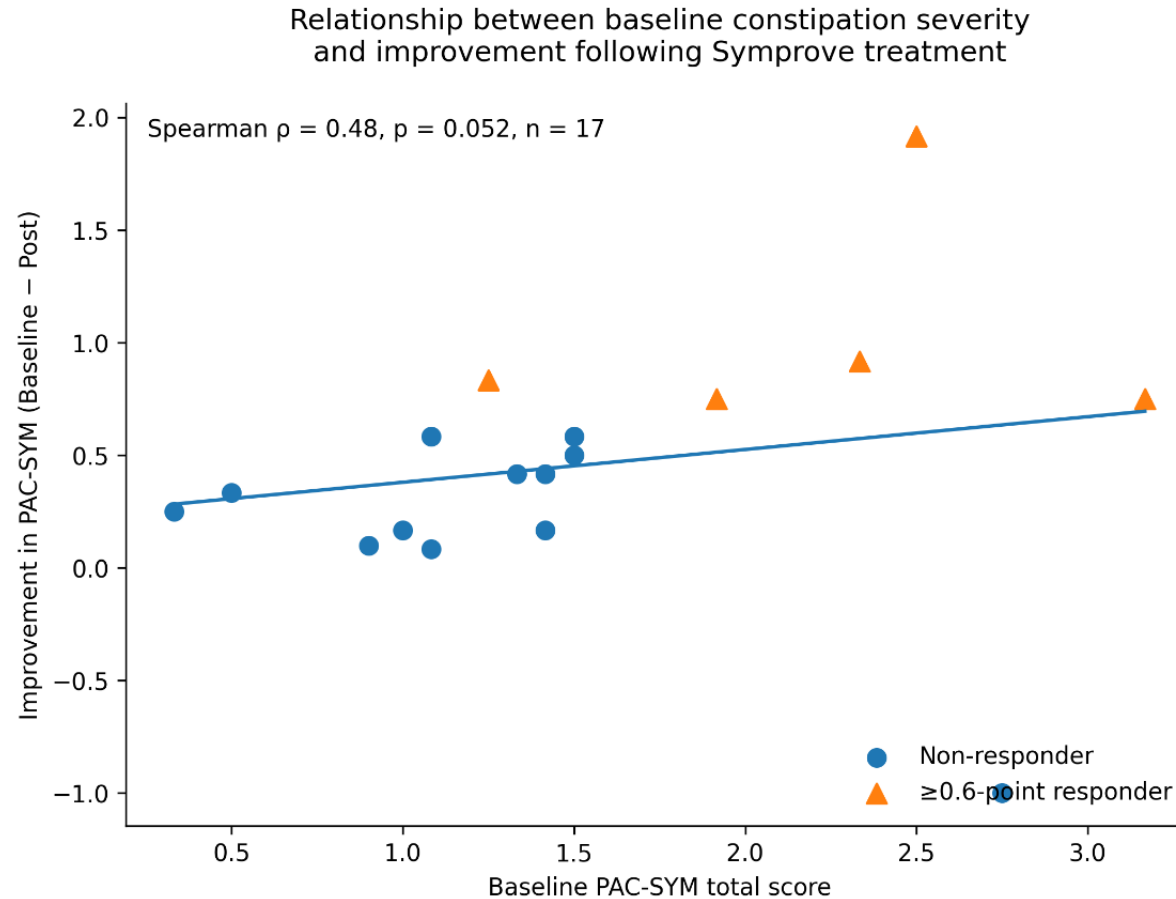
- Total score: 1.53 → 1.07 (p=0.0048)
- Stool domain: 1.99 → 1.52 (p=0.025)
- Abdominal domain: 1.53 → 1.07 (p=0.038)

- Response rate:

- 16/17 (94%) had improvement in total PAC-SYM score
- 5/17 (29%) hit the threshold for clinically meaningful improvement.

Significant improvement overall and within stool and abdominal symptom domains

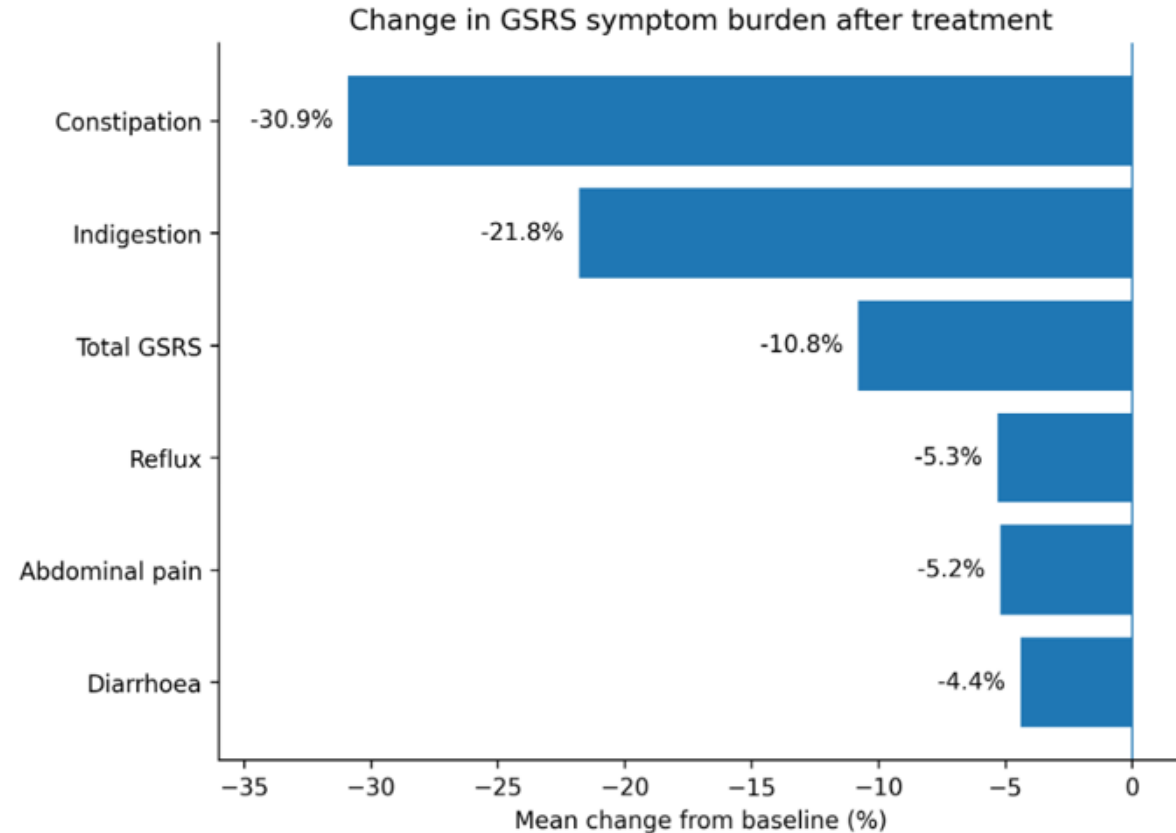
Study results – PAC-SYM



Moderate positive correlation seen between baseline constipation severity and treatment response

Study results – GSRS

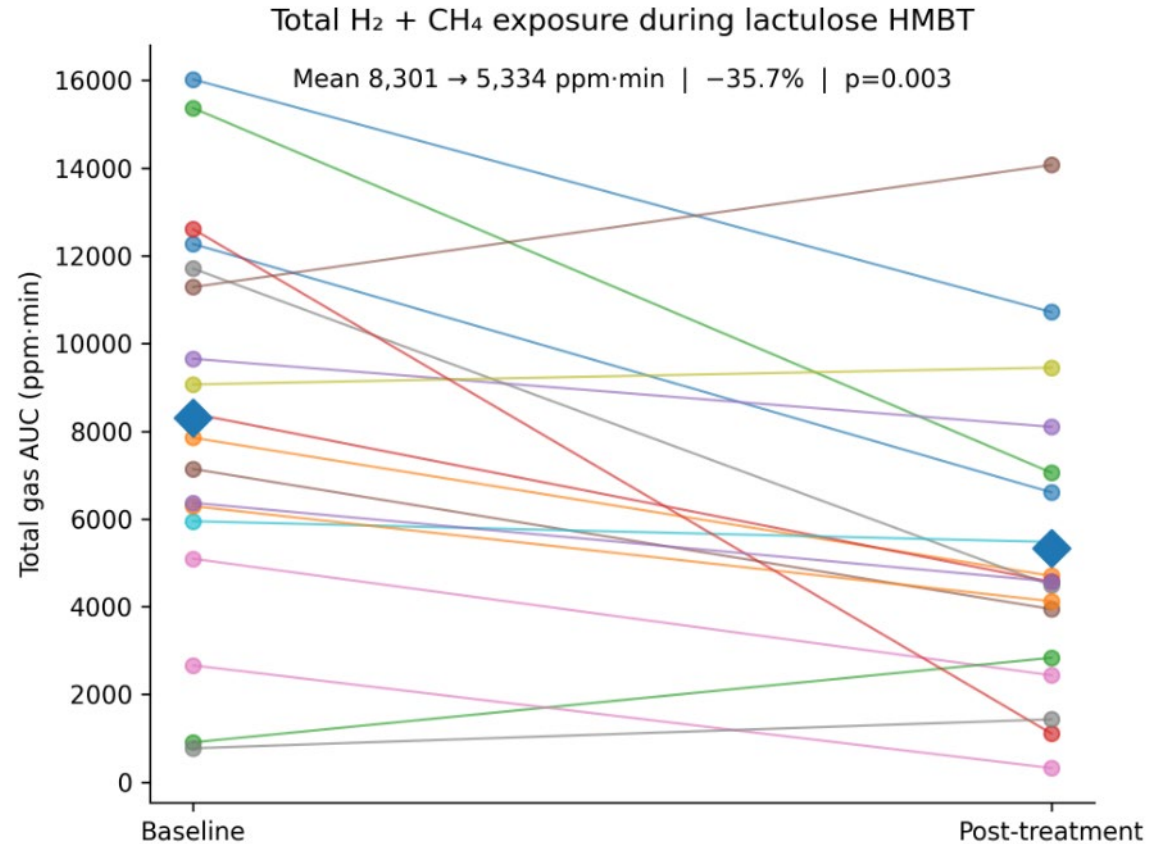
- GSRS (n=19):
 - Constipation domain:
4.32 → 2.98 (p<0.001)
 - Total score:
38.89 → 34.68 (p=0.036)
 - Indigestion domain:
3.01 → 2.36 (p=0.002)



Improvement in total GSRS reduction was driven by reduction in constipation and indigestion symptoms – the predominant symptoms at baseline

Study results – HMBT data

- Hydrogen (n=18):
 - AUC: 4945ppm.min → 3317ppm.min (p=0.063)
 - Peak: 72.5ppm → 52ppm (p=0.092)
- Methane (n=18):
 - AUC: 3355ppm.min → 2216ppm.min (p=0.049)
- Total combined gas (n=18)
 - AUC: 8301ppm.min → 5334ppm.min (p=0.003)



Decrease in hydrogen and methane AUC. Total gas AUC reduction was significant from baseline to end of study

Study results – HMBT data

- SIBO & IMO status:
 - 11 participant SIBO +ve at baseline
 - 5 of these became SIBO –ve at End of study
 - 7 Participant SIBO –ve at baseline
 - 2 SIBO –ve participants became SIBO +ve
 - 7 Participants were IMO +ve at baseline
 - All 7 remained +ve at End of study
 - 11 Participant IMO –ve at baseline remained –ve at end of study

Alteration in SIBO status seen in 7 participants. Methane status was stable in all participants

Study results ATMO Capsule

- Transit times (n=17):
 - Small bowel: 5.24h → 4.49h (p=0.066)
 - 12/17 (71%) of participant had a reduction in Small bowel transit
 - Colonic and whole gut transit unchanged
 - 40% of constipated patients at a tertiary-care level have delayed transit so incidence will be less in this population. Most probiotics and 'laxative foods' have very little to no effect on transit in this population

More data to come...

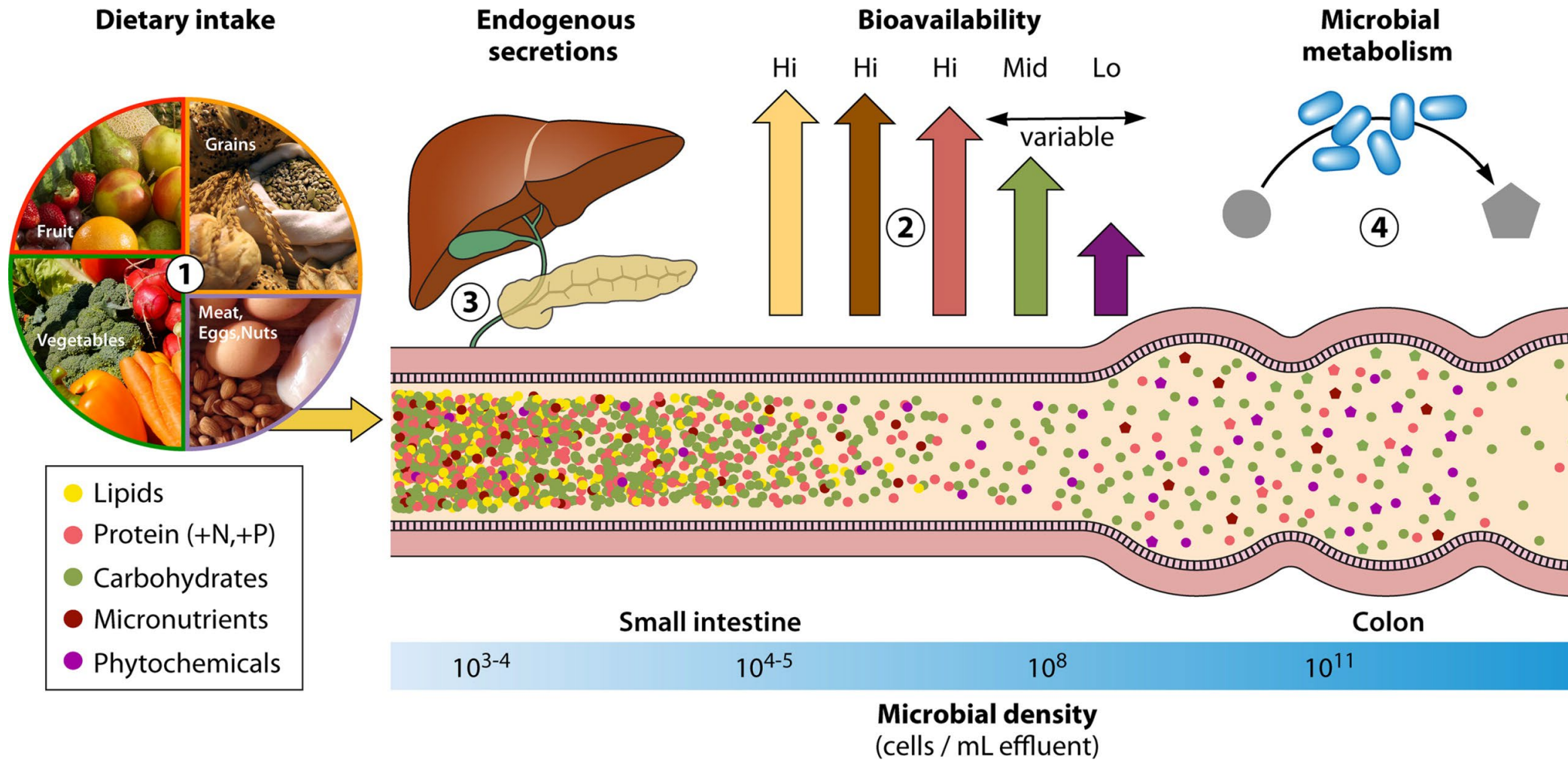
- Bowel diary assessment
- In-depth analysis of symptom scores
- In-depth analysis of breath testing
- In-depth analysis of ATMO capsule

Targeting an abstract of the full cohort at UEG and publication by end of the year

Small bowel as a therapeutic target for probiotics?

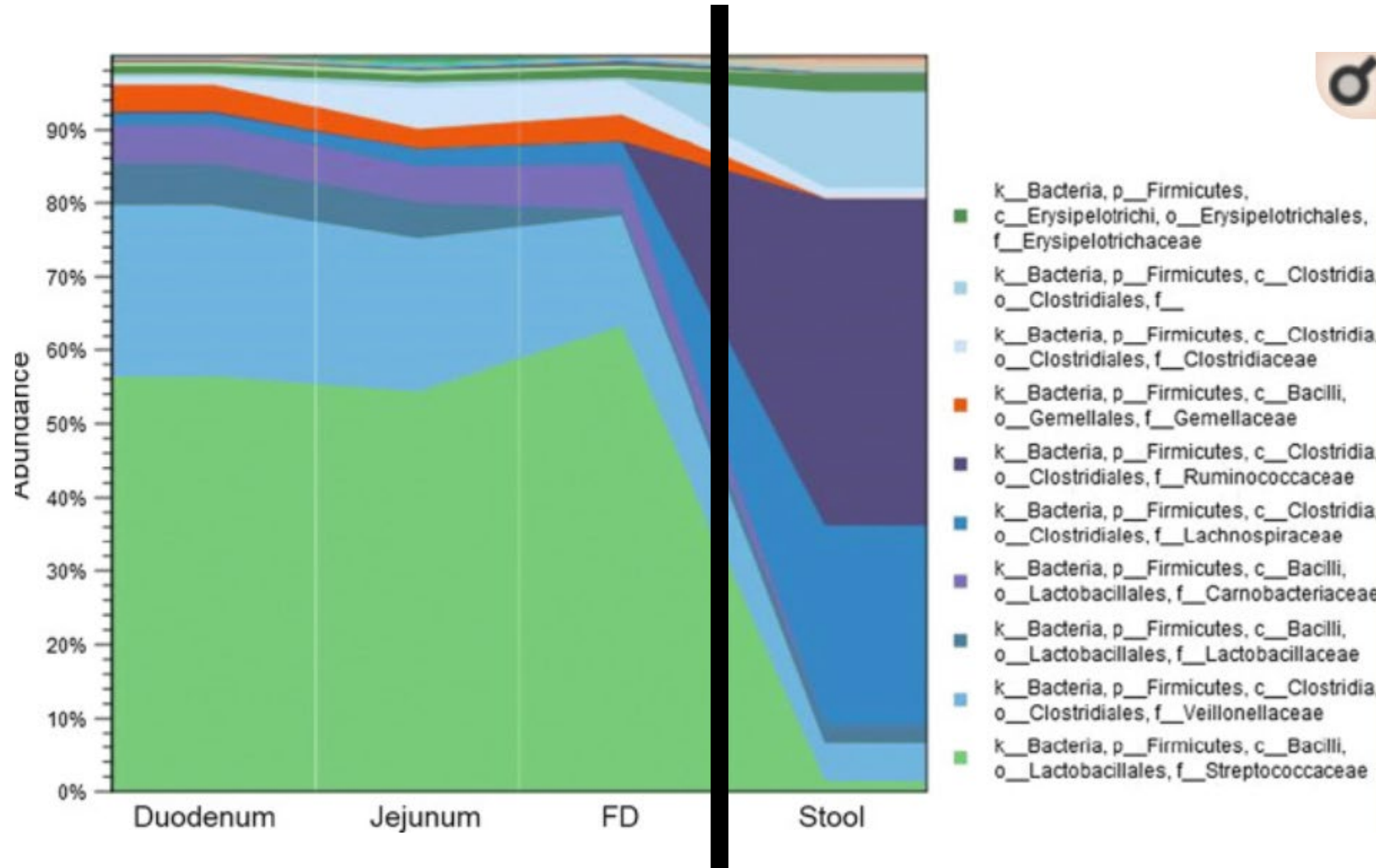
- Small bowel has large surface area and rich vagal innervation to allow significant interaction of probiotics and their metabolites.
- Abundance of microbes within small bowel much lower than colon which may allow more significant effect.
- Small bowel transit related to fluid absorption so more rapid transit allows more fluid into the colon to help with stool formation and motility.
- Reduction of gas production within the small bowel and colon as by products of fermentation can reduce bloating and distension symptoms
- Reduction of methane (which slows small bowel transit) as well as activation of vagal pathways may explain effect on transit.

Digestion and fermentation



Symprove = 1.47×10^8 cfu per ml (based on 10 billion cfu in 70ml dose)

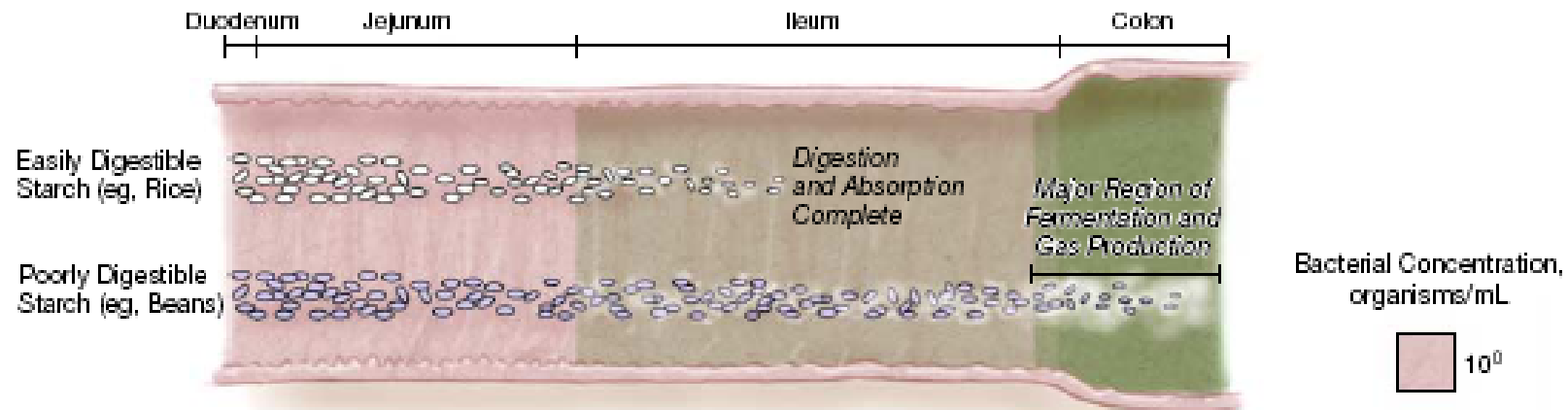
Small bowel as a target for probiotic therapy in constipation



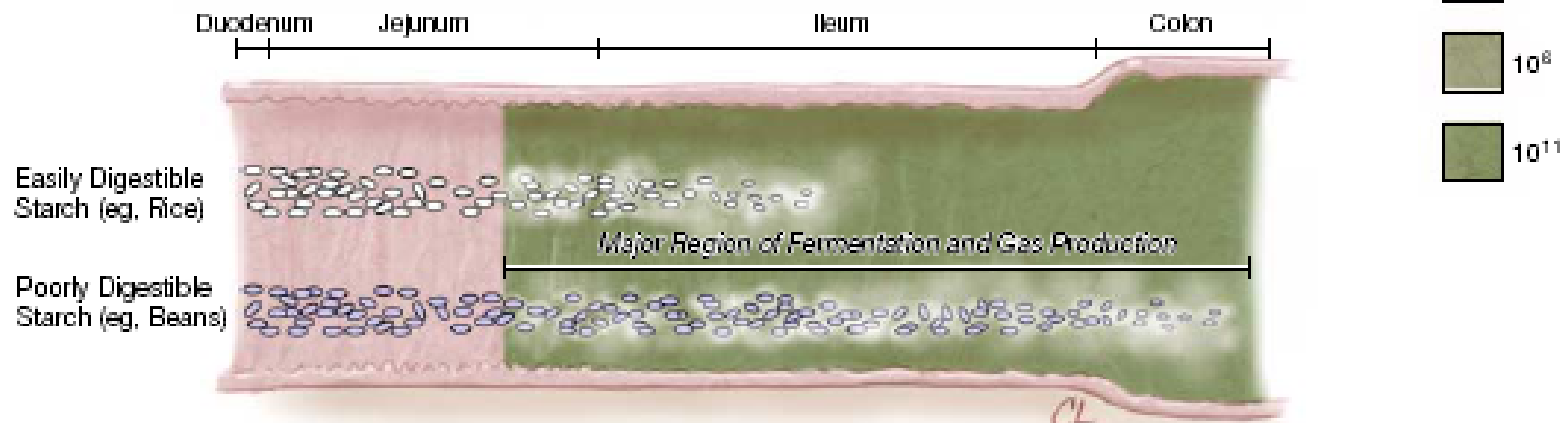
Small bowel
microbiome very
different to stool
microbiome

Small Intestinal Bacterial Overgrowth (SIBO)

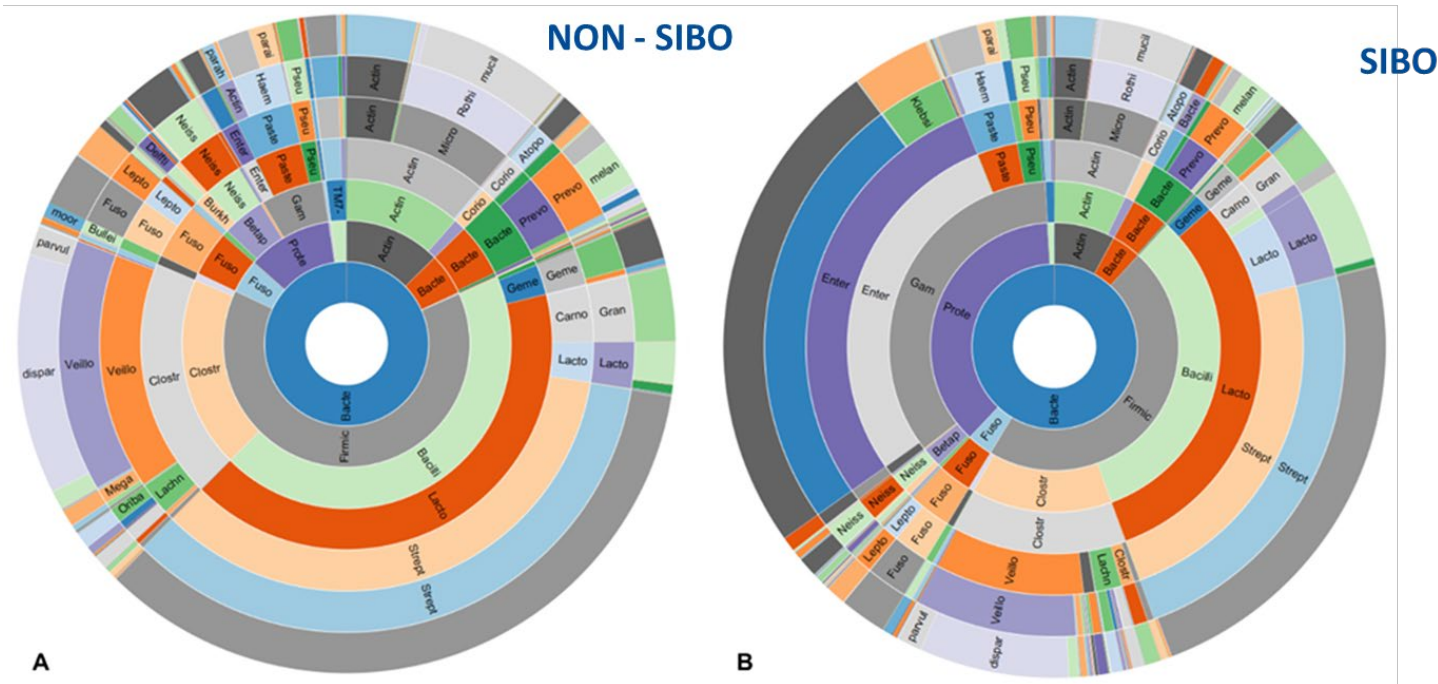
A Normal Distribution of Intestinal Bacterial Flora



B Small Intestinal Bacterial Overgrowth



Sequencing SIBO



1. Increase in proteobacteria

■ E. Coli

■ Klebsiella

2. Reduction in firmicutes

Phylum	Non-SIBO (N = 98)	SIBO (N = 42)	Non-SIBO vs. SIBO		
	Relative abundance (%)	Relative abundance (%)	Fold Change	P-value*	FDR P-value**
Firmicutes	64	47	-1.36	0.0007	0.4
Actinobacteria	13	8	-1.59	0.0004	0.36
Proteobacteria	11	37	3.19	<0.0001	2.21E-14
Fusobacteria	4	3	-1.34	0.0062	0.9
Bacteroidetes	6	4	-1.43	0.05	0.9
TM7	2	1	-2.3	0.0004	0.14

Significant changes (P-value<0.05 and FDR P-value<0.05) are indicated in bold.

*—Mann-Whitney test;

**—Wald-test.

Adapted from Leite et al. PLOS One. 2020

Constipation Is Related to Small Bowel Disturbance Rather Than Colonic Enlargement in Acquired Chagasic Megacolon

Mauro Bafutto^{a, b}, Alejandro Ostermayer Luquetti^b, Salustiano Gabriel Neto^{b, c},
Felix Andre Sanches Penhavel^{b, c}, Enio Chaves Oliveira^{b, c, d}

Bafutto et al

Gastroenterol Res. 2017;10(4):213-217

Table 2. Results of Orocecal Transit Time in Clinical Groups

Groups	Subgroups	n	Mean (SD)	95% CI	OCTT (min)	
					< 120, n (%)	> 120, n (%)
Non-constipated ^a	N ^b	9	87.0 (47.9)	52.8 - 121.2	8 (88.89)	1 (11.11)
	ChN ^b	20	109.0 (54.6)	83.5 - 134.5	13 (65.0)	7 (35.0)
	ChMc ^b	16	110.0 (63.8)	76.0 - 144.0	10 (66.67)	6 (33.33)
Constipated ^a	CN ^c	38	119.8 (55.4)	102.5 - 137.0	19 (50.0)	19 (50.0)
	CCh ^c	14	93.3 (50.5)	65.4 - 121.3	5 (35.72)	9 (64.28)
	CChMc ^c	18	172.6 (47.4) ^d	149.8 - 195.5	1 (5.56)	17 (94.44)
Total		115	119.0 (58.8)	108.5 - 129.6	56	59

SD: standard deviation; CI: confidence interval; OCTT: orocecal transit time. ^aP < 0.000; ^bP = 0.345; ^cP = 0.005; ^dP = 0.001 (Kruskal-Wallis test).

Irritable bowel syndrome: relationship of disorders in the transit of a single solid meal to symptom patterns

P A CANN, N W READ, C BROWN,
N HOBSON, AND C D HOLDSWORTH

From the Clinical Research Unit, Royal Hallamshire Hospital, Sheffield

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Cann, Read, Brown, Hobson, and Holdsworth

Table 3 *Transit measurements and stool data in normal volunteers and patients with irritable bowel syndrome*

			<i>Irritable bowel syndrome</i>			
			<i>Control</i>	<i>Diarrhoea</i>	<i>Constipation</i>	<i>Pain/distension</i>
Gastric emptying (t½; h)	F	1.6±0.1	1.6±0.1	1.8±0.2	1.4±0.2	
	M	1.3±0.1	1.3±0.2			
Small bowel transit time (h)		4.2±0.2	3.3±0.3*‡§	5.4±0.3*†	5.4±0.4*†	
Whole gut transit time (50% markers; h)		53±4	35±5*‡§	87±13*†	61±4†	
Daily stool weight (g)	F	112±12	128±25‡	61±17*†	86±12	
	M	166±20	230±24*			
Daily stool frequency			2.3±0.2‡§	0.9±0.2†§	1.5±0.2†‡	
Percent unformed stools			75‡§	18†§	48†‡	

Results are expressed as mean ± SEM, and p values are calculated using Student's *t* test for all data except percent unformed stools, which are expressed as means with p values calculated from the Wilcoxon's rank sum test (see Methods).

* Significantly different (*p*<0.05) from corresponding control group; †diarrhoea group; ‡constipated group; §pain/distension group.

Summary

- Chronic constipation continues to be an issue for patients and clinicians, with multifactorial pathophysiology including gut microbiome changes
- Diet and lifestyle approach should always be first line, with the new BDA guidelines summarised evidence per nutritional intervention
- Potential role for probiotics but remember not all probiotics are created equal they need to survive stomach passage.
- New study shows Symprove was associated with improved constipation symptoms, with reduced hydrogen and methane production, effect on SIBO and shortening of small bowel transit time suggesting effects on proximal gut motility and fermentation.
- Could be due to direct effects of motility and fluid absorption – reduced gas production helps bloating and distension.

Thank you

Supported by
Symprove

