

# Human Milk Oligosaccharides Improve All the Central Symptoms of Irritable Bowel Syndrome: A Multi-Center, Opel Label Trial

Olafur S. Palsson<sup>1</sup>

Anne Peery<sup>1</sup>, Dorthe Seitzberg<sup>2</sup>, Ingvild Dybdrodt Amundsen<sup>2</sup>, Bruce McConnell<sup>2</sup>, Magnus Simrén<sup>3</sup>

<sup>1</sup>Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, USA

<sup>2</sup>Glycom A/S, Hoersholm, Denmark

<sup>3</sup>Department of Internal Medicine and Clinical Nutrition, University of Gothenburg, Gothenburg, Sweden

IBS is one the most common disorders of the gastrointestinal (GI) tract.

It is characterized by recurrent abdominal pain accompanied by changes in bowel functioning -- diarrhea, constipation or a combination of both.

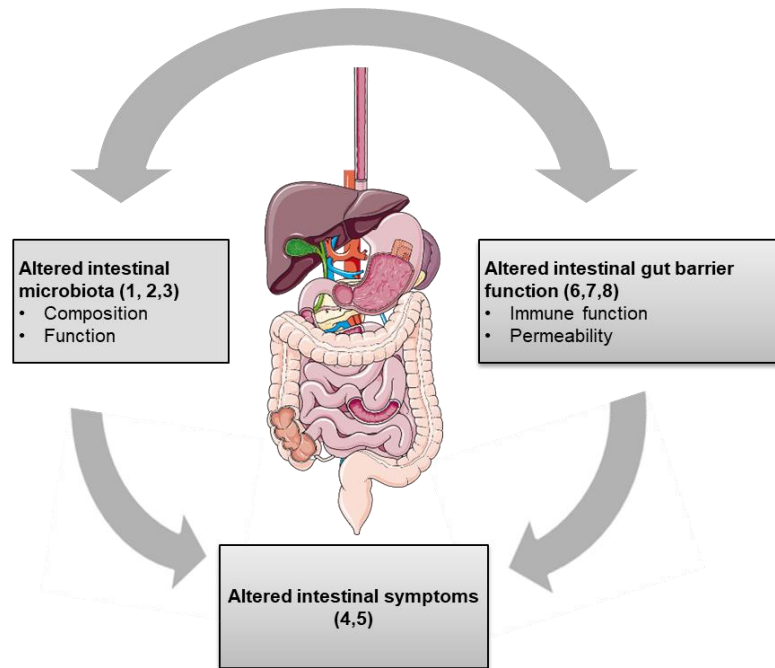
It is a chronic and troublesome disorder that is often challenging to treat successfully. Many patients continue to suffer for years from bothersome symptoms that interfere with their lives in spite of the best efforts of healthcare providers.

The causes of IBS are complex and inadequately understood. Several factors are thought to be involved in producing the symptoms, including:

- ❖ Increased pain sensitivity of the intestines
- ❖ Disturbance in gut motility
- ❖ Brain-gut dysregulation

Abnormal balance between the different families of gut bacteria (microbiota) appears to be a factor in IBS.

It is thought to contribute to bowel symptoms by driving inflammation and increasing the porousness (permeability) of the bowel wall, thereby increasing pain sensitivity and causing abnormal stool consistency



The challenge is to identify interventions that restore the normal bacterial balance.

Prior efforts have included **probiotics** (ingesting live bacteria), and **fecal microbiota transplantation**

# Human Milk Oligosaccharides (HMOs): A promising different approach to restore gut bacteria balance and gut barrier function

- ❖ A family of complex carbohydrates found in high concentration in human breast milk
- ❖ Stimulate the growth of beneficial bacteria

## HMOs in infants (via breastfeeding)<sup>1</sup>

- ❖ Primary determinants of the gut bacteria
- ❖ Help build healthy gut wall barrier and gut immune function
- ❖ Bind pathogens (viruses and harmful bacteria)

## HMOs in IBS<sup>2,3</sup>

- ❖ Specifically increase bifidobacteria abundance
- ❖ Increase concentration of metabolites essential for gut barrier functioning and immune modulation
- ❖ Do not induce significant gastrointestinal symptoms

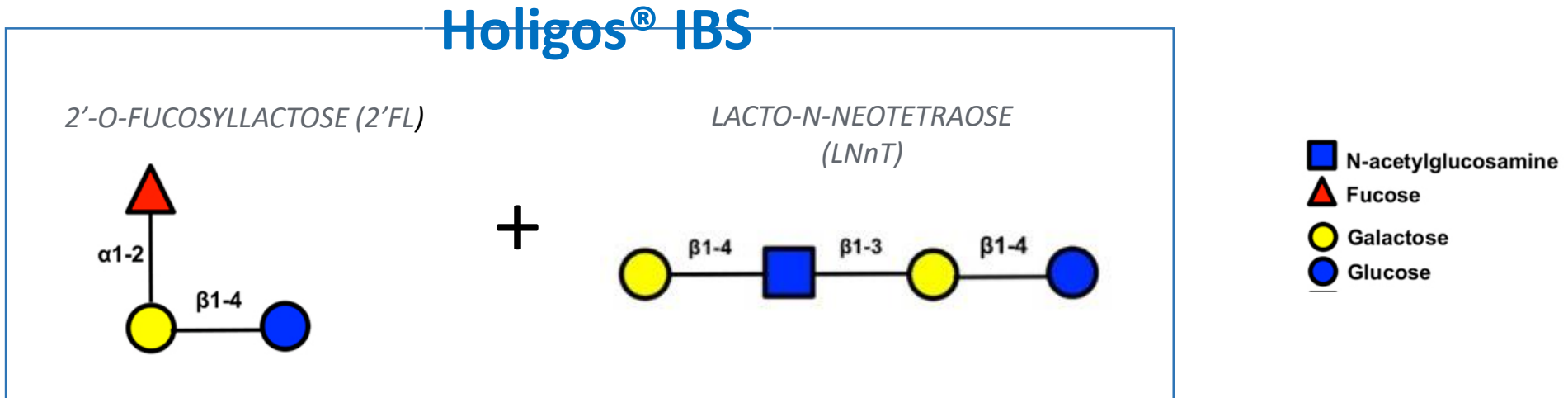
1. Bode, *Glycobiology* 2012; 22(9); p. 1147-62

2. Iribarren et al, abstract DDW 2019; 3. Vignæs et al, abstract The 11<sup>th</sup> Vahouny Fiber Symposium

In our study we tested a combination of two HMOs.

This unique HMO blend, brand-named **Holigos<sup>®</sup> IBS**, is a medical food that has been reviewed and given a "generally recognized as safe" ("GRAS") designation by the FDA in the U.S. It has recently been made available on the U.S. market.

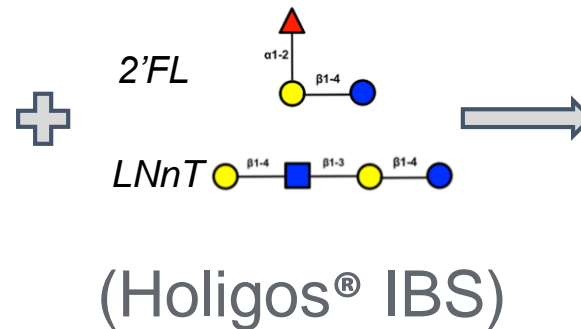
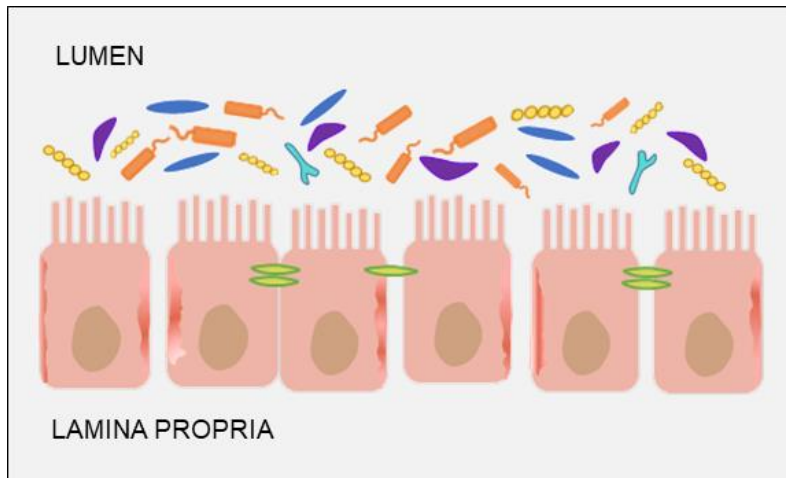
The two HMOs in **Holigos<sup>®</sup> IBS** are identical to HMOs in mother's milk, but are not extracted from milk but manufactured by Glycom A/S in Denmark.



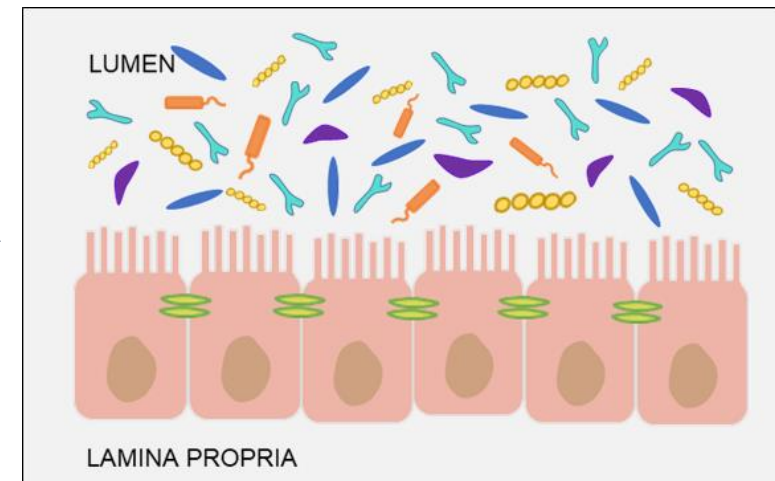
# Aim of the study

To assess the potential for a blend of two HMOs to support normal stool consistency and improve other bowel symptoms and the quality of life of patients with IBS.

**IBS GUT**  
ALTERED  
GUT MICROBIOTA

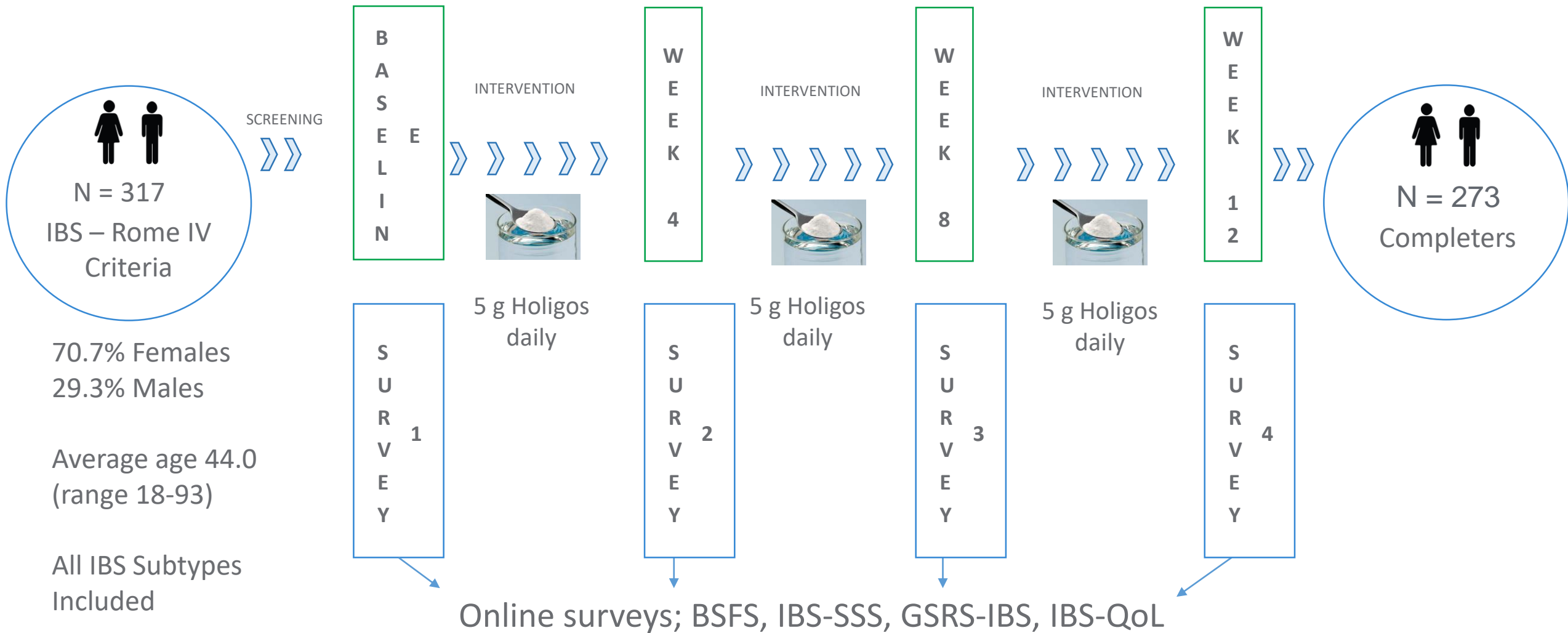


**HEALTHY GUT**  
IMPROVED  
GUT MICROBIOTA

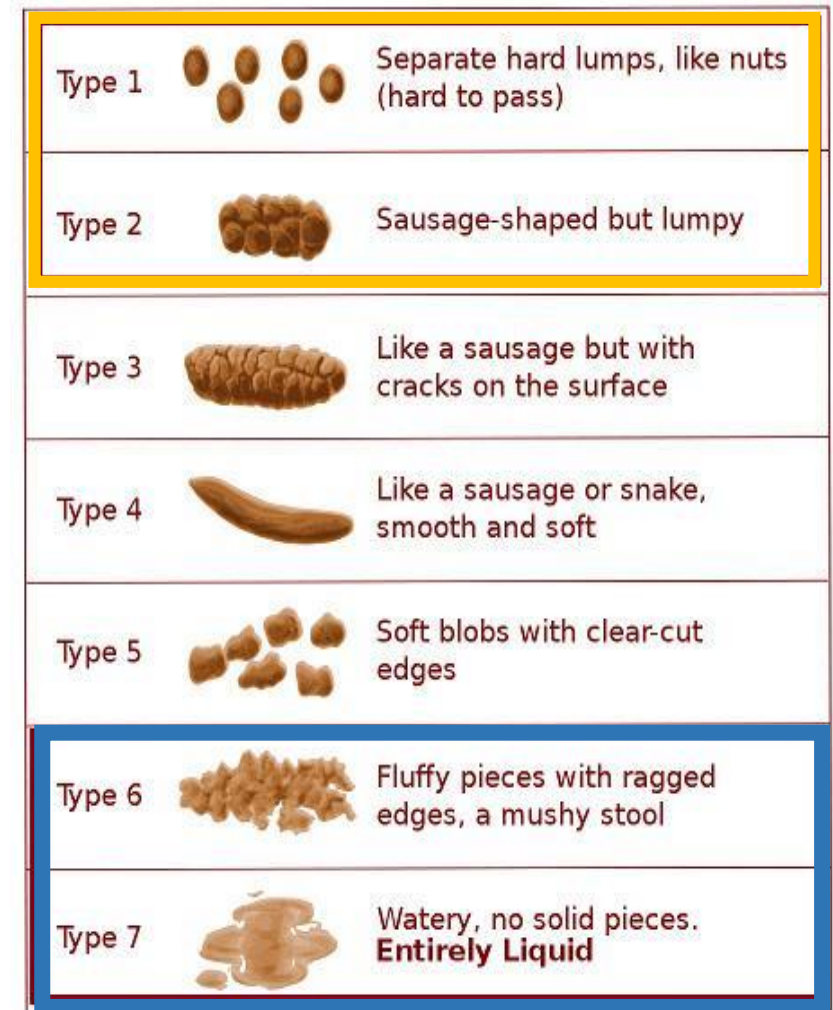
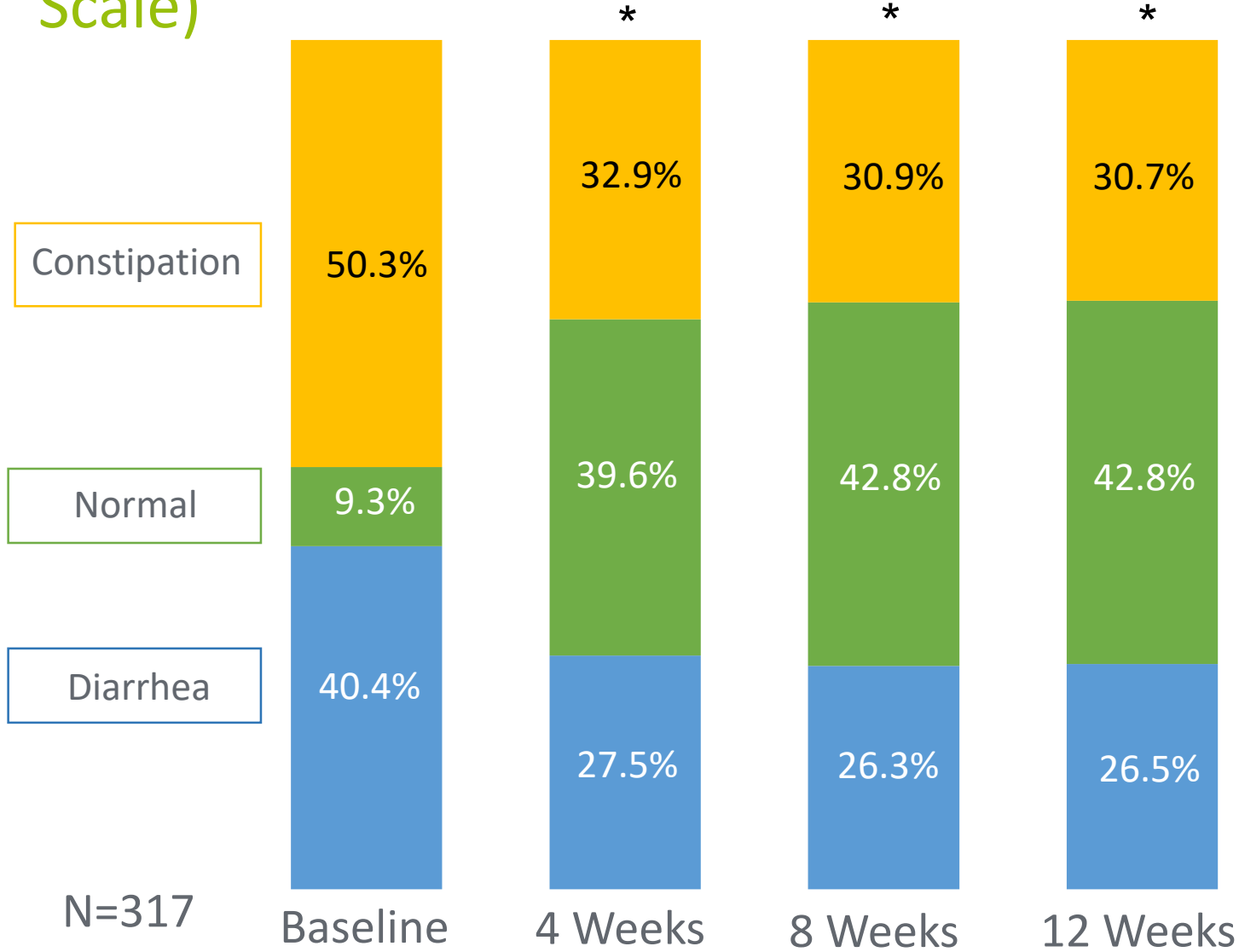


Improved  
Symptoms  
and  
Wellbeing

# A Multi-Center, Open Label, Single Arm Trial Conducted at 17 clinical sites across the U.S.



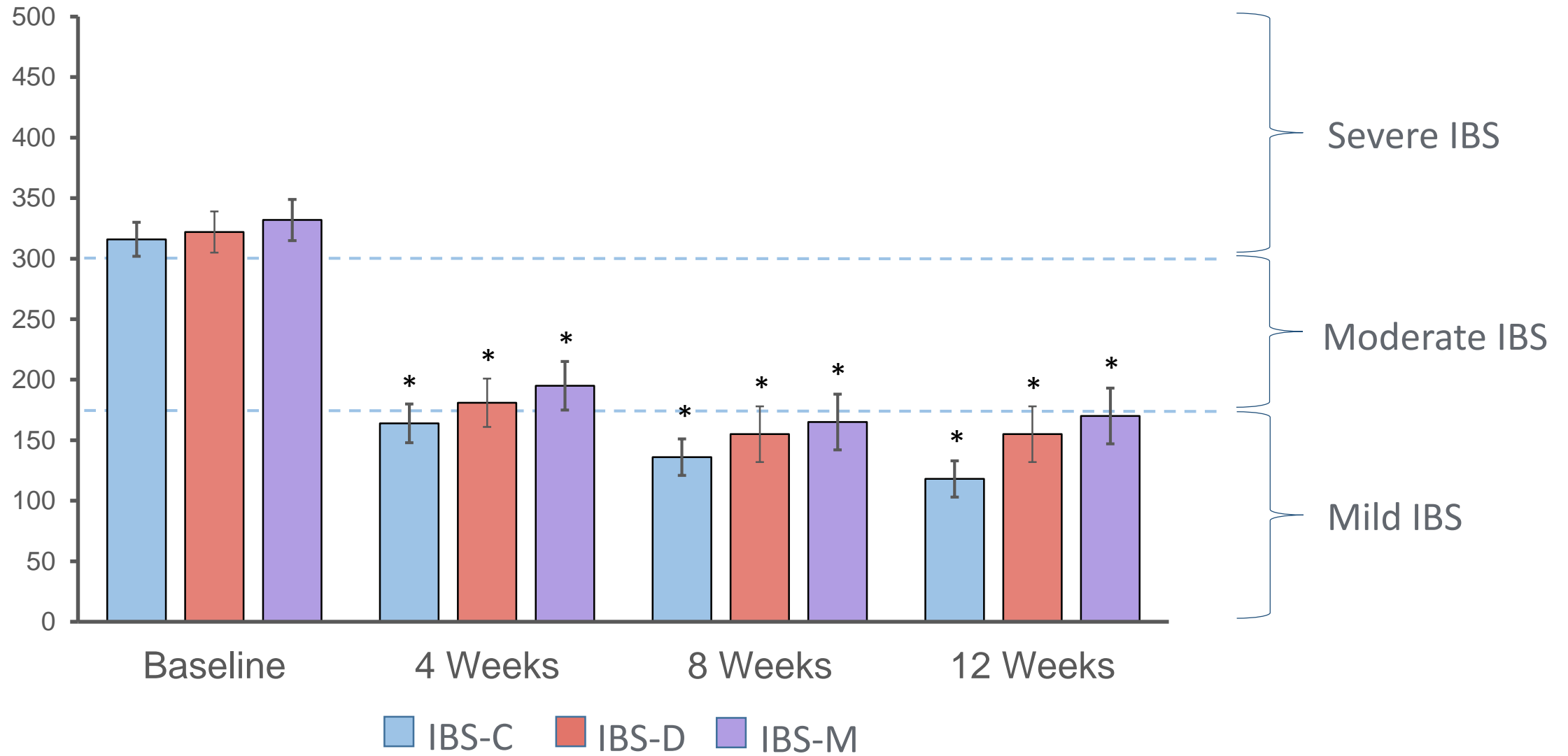
# Change in Total % of Abnormal Consistency Stools (Bristol Stool Form Scale)



\*Significantly reduced total % of abnormal stools (diarrhea + constipation) compared to baseline at  $p < 0.0001$

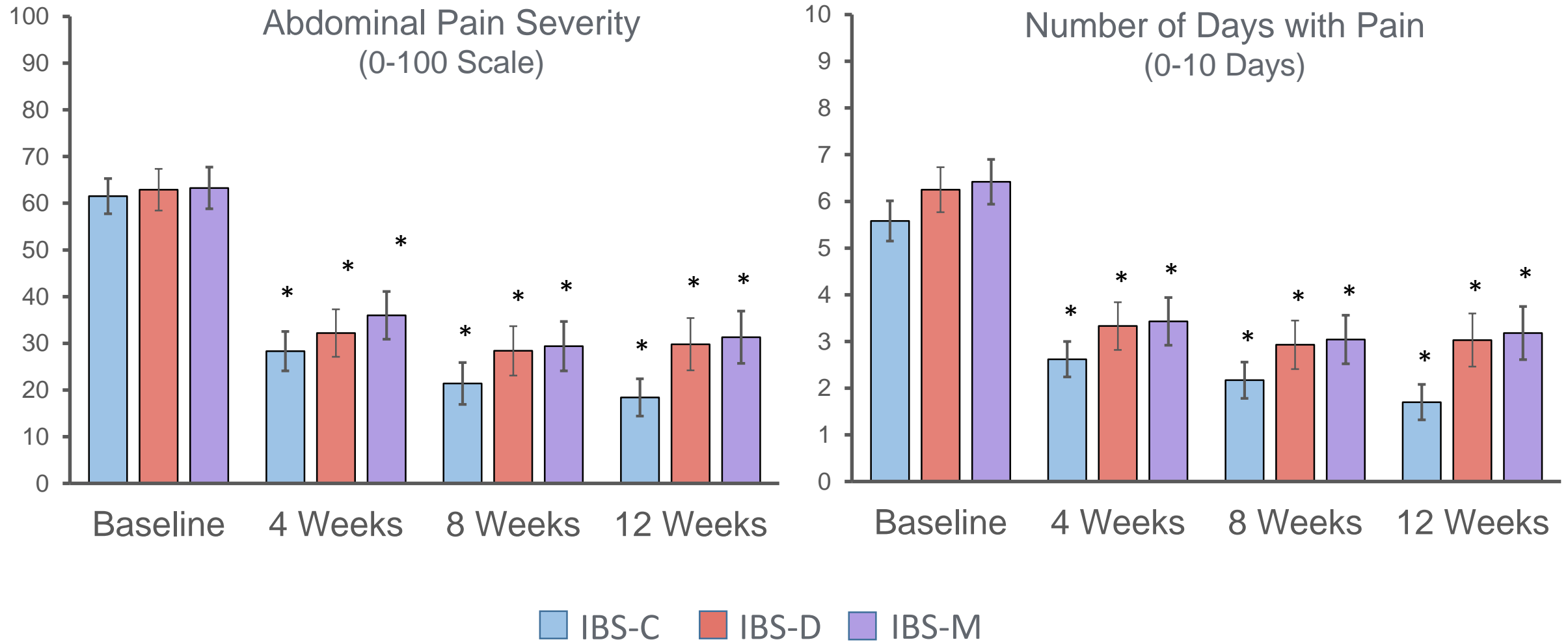


# Changes in Overall IBS Severity Score (IBS-SSS, 0-500 scale)



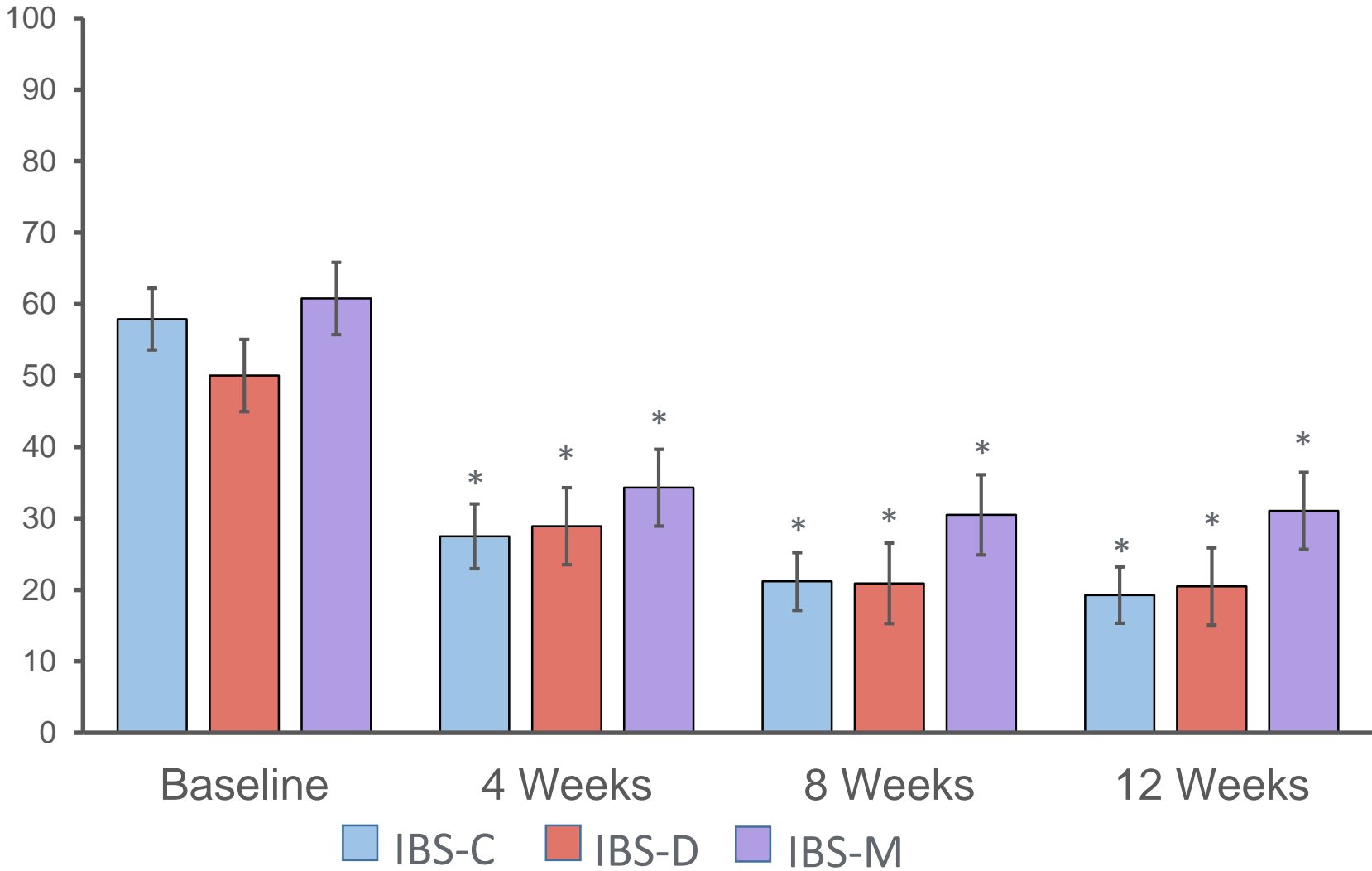
\*significantly different from baseline at  $p < 0.0001$ . Error bars: 95% CI.

# Changes in Abdominal Pain Severity and Frequency (IBS-SSS)



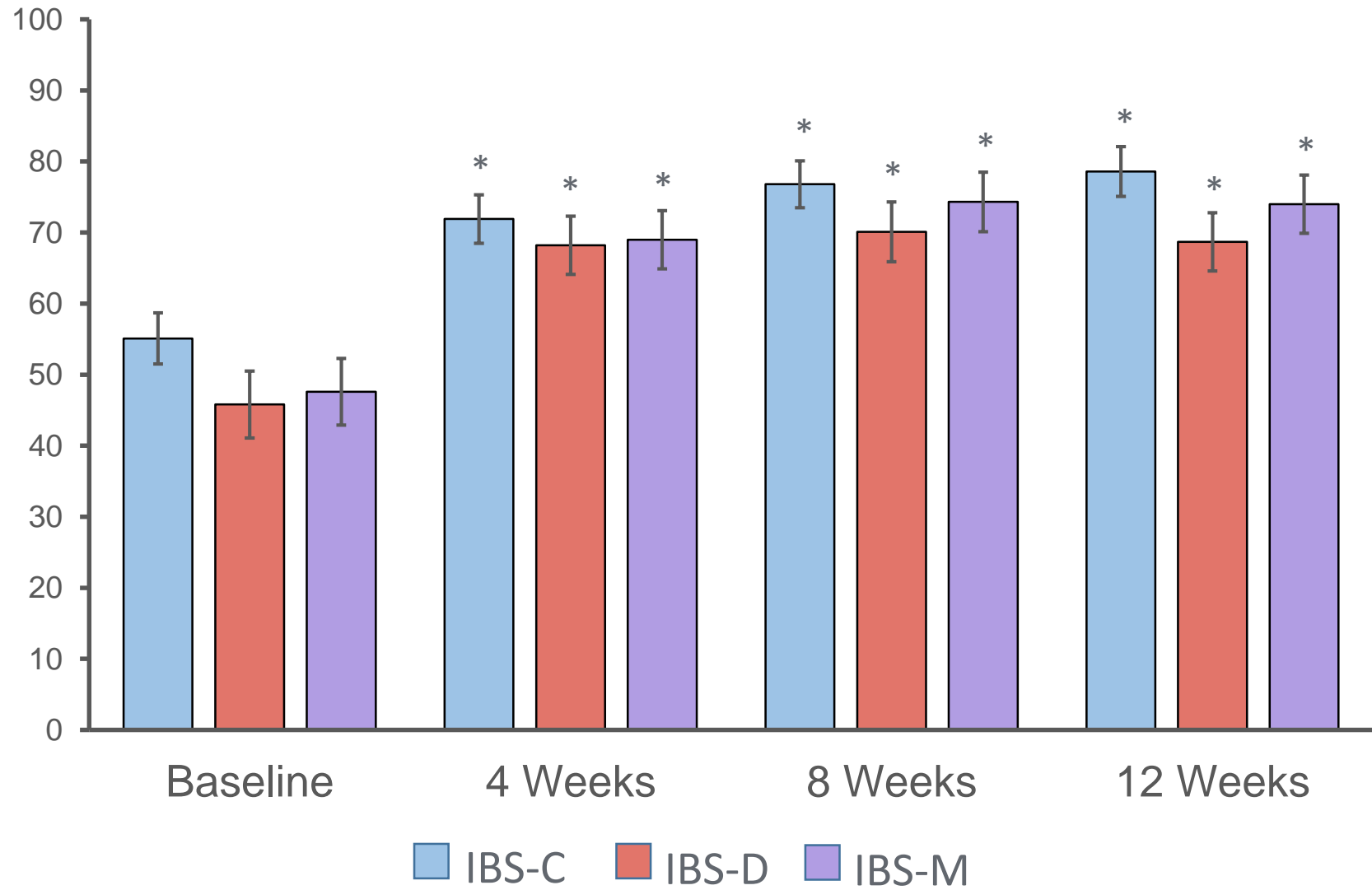
\*significantly different from baseline at  $p < 0.0001$ . Error bars: 95% CI.

# Changes in Bloating Severity (IBS-SSS, 0-100 Scale)



\*significantly different from baseline at p<0.0001. Error bars: 95% CI.

# Changes in Health Related Quality of Life (IBS-QoL, 0-100 scale)



\*significantly different from baseline at p<0.0001. Error bars: 95% CI.

# Product tolerability and side effects

Response	Survey		
	(4 weeks)	(8 weeks)	(12 weeks)
Well tolerable	60.0%	53.2%	57.2%
Tolerable	38.3%	45.3%	39.2%
Poorly tolerable	1.7%	1.4%	3.7%

- ❖ 15% of patients reported adverse events during the trial
- ❖ The most common side effects related to the product
  - ❖ Gas, bloating, abdominal pain, diarrhoea and urgency; generally mild (80%)
- ❖ 8 patients (2.5%) discontinued the study due to side effects

# Conclusions

- ❖ Daily supplementation with **Holigos<sup>®</sup> IBS** (a blend of 2'FL and LNnT HMOs) can provide nutritional support for individuals with IBS of all subtypes that:
  - ❖ reduces abnormal stool consistency (improves both diarrhoea and constipation)
  - ❖ reduces abdominal pain and bloating
  - ❖ improves overall severity of IBS symptoms
  - ❖ improves health-related quality of life