



Peter Gibson

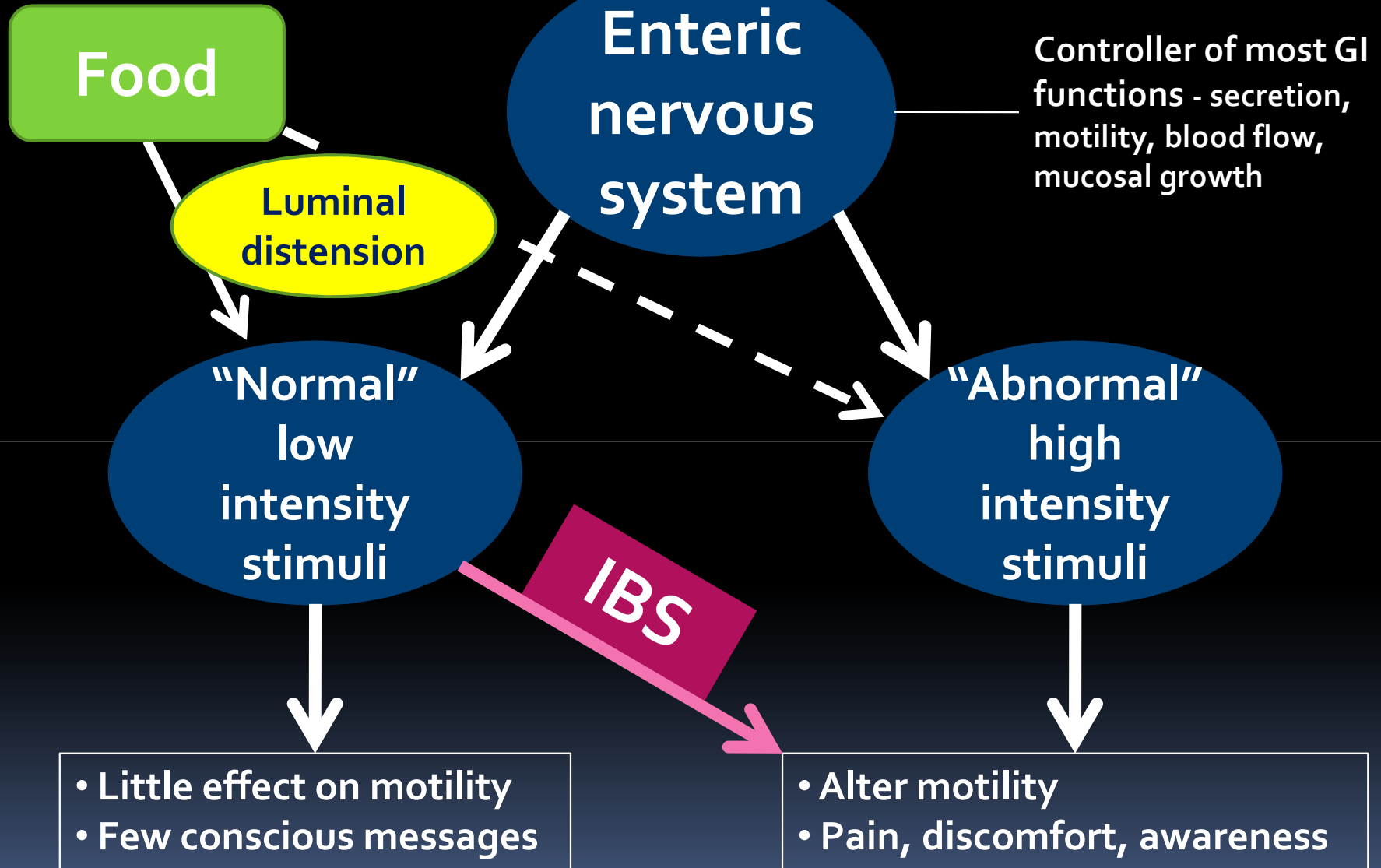
THE SCIENCE BEHIND FODMAPs

FODMAPS *Fermentable Oligo- Di- & Mono-* *saccharides And Polyols*

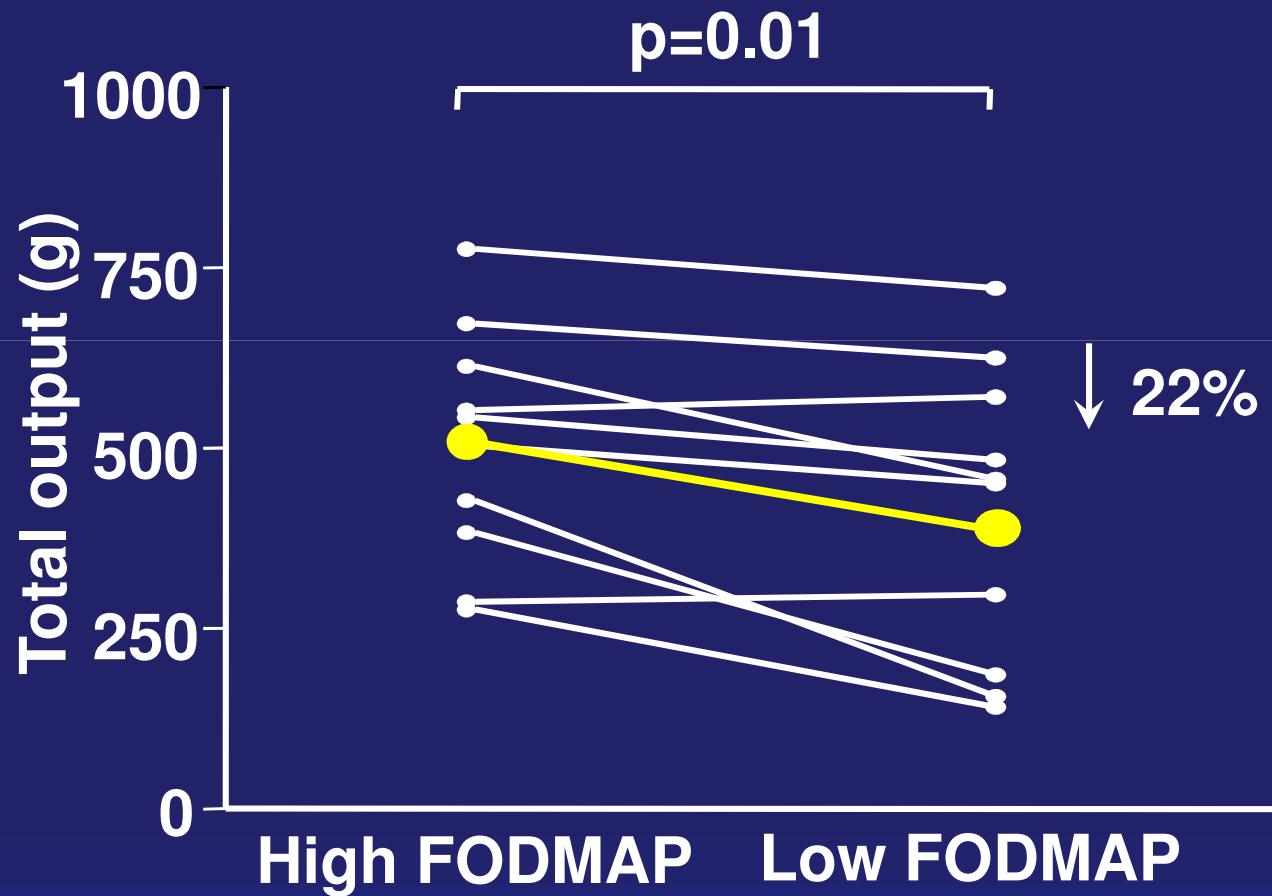
Theory: Act by distending the intestinal lumen via being:

- ***Osmotically active***
 - Small molecules
 - Trapped in the lumen → ↑ luminal water volume
 - Osmotic effect related to molecular size
 - fructose = ~0.5 lactose (lactulose) = ~0.25 FOS
- ***Rapidly fermented***
 - → gas → ↑ luminal volume

Core concept



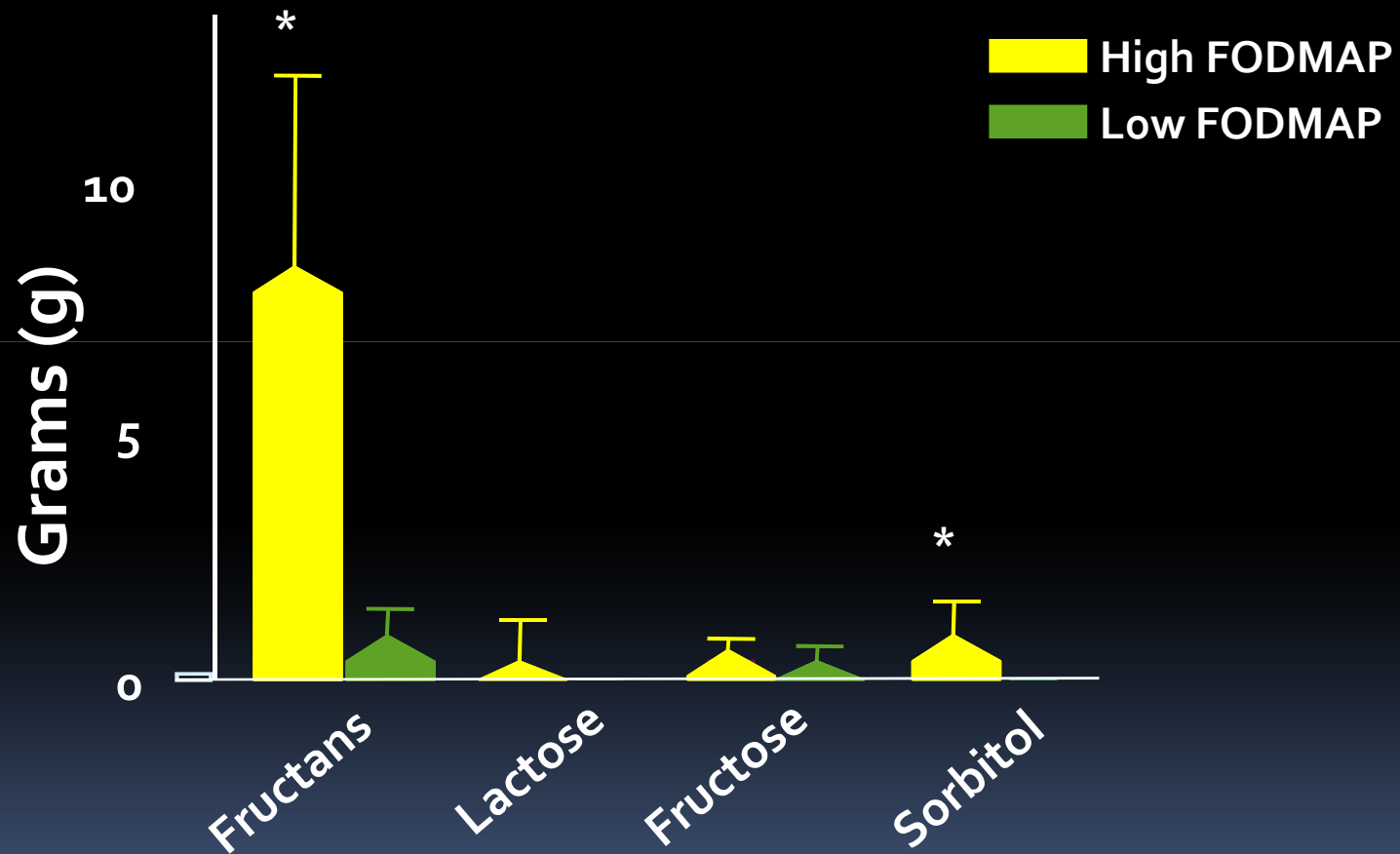
- 4-day randomised cross-over dietary study
- Diets differed in FODMAP content by ~10 g/day
- Daytime ileostomy output measured



Barrett et al APT 2010

Wilcoxon signed rank test

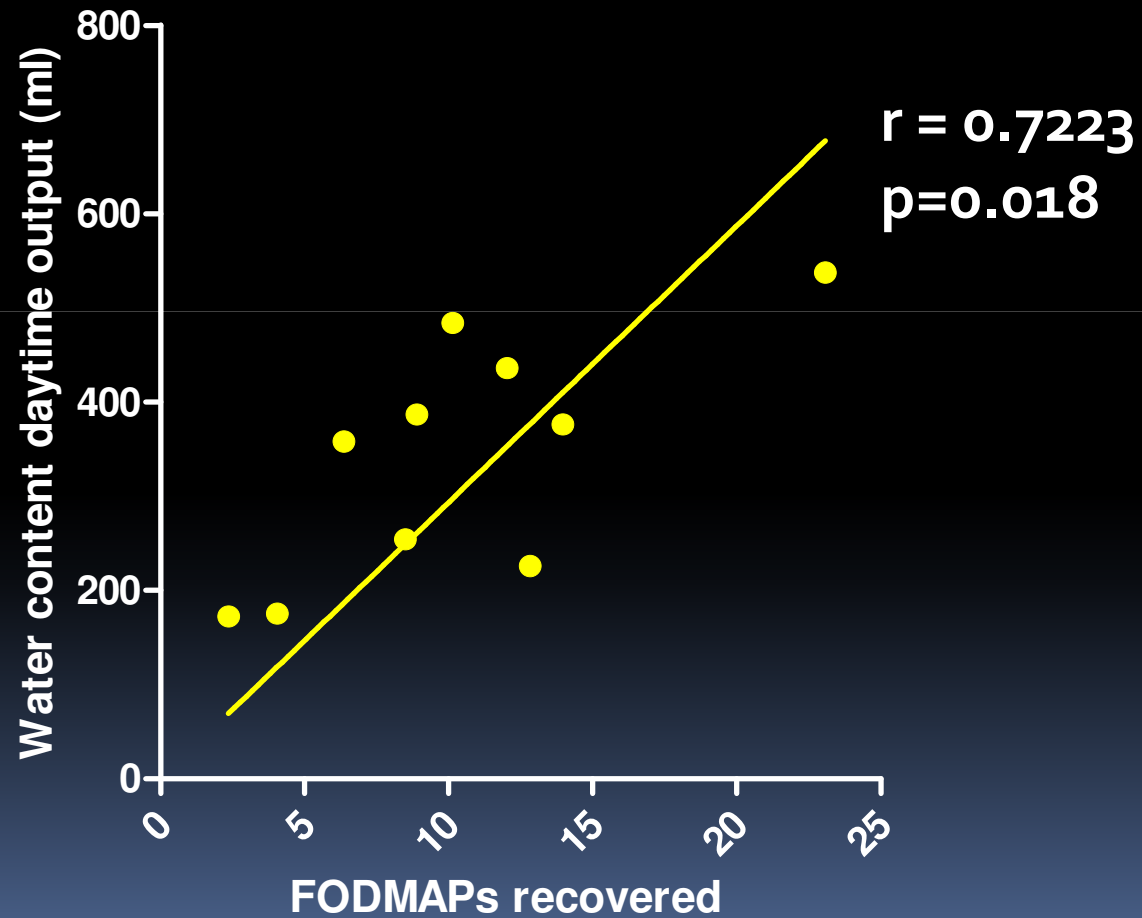
FODMAP recovery



Barrett et al APT 2010

* $p < 0.05$ Wilcoxon signed rank test

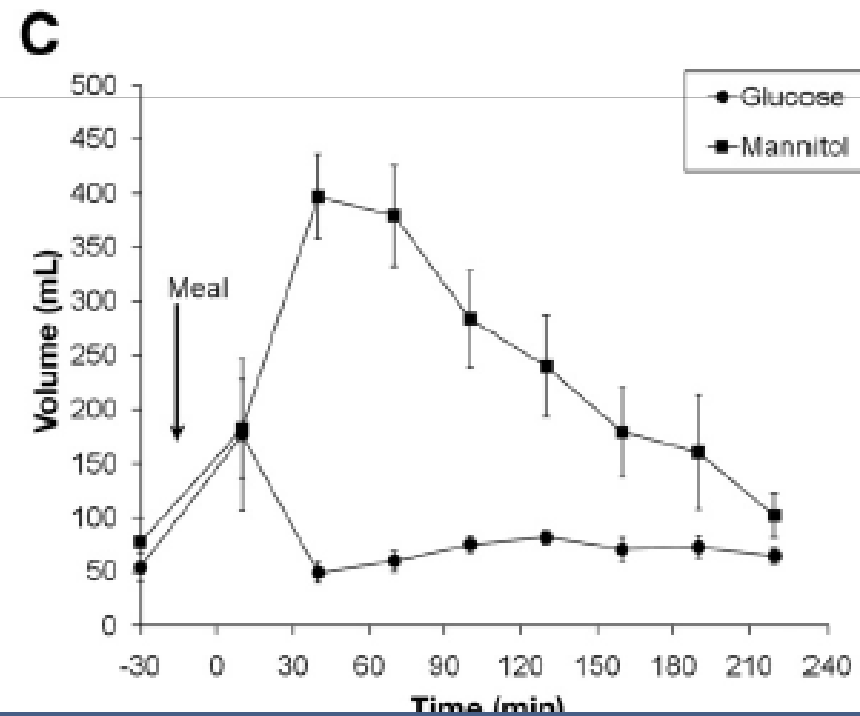
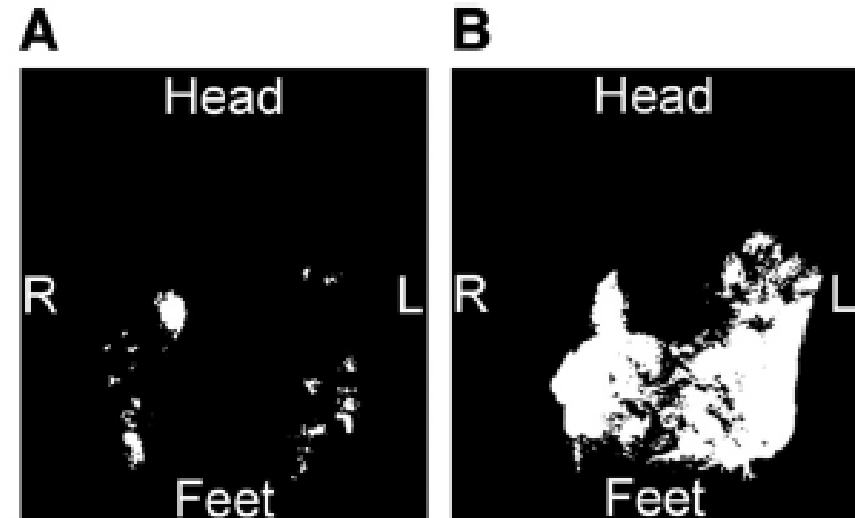
Correlation of water and FODMAP recovery



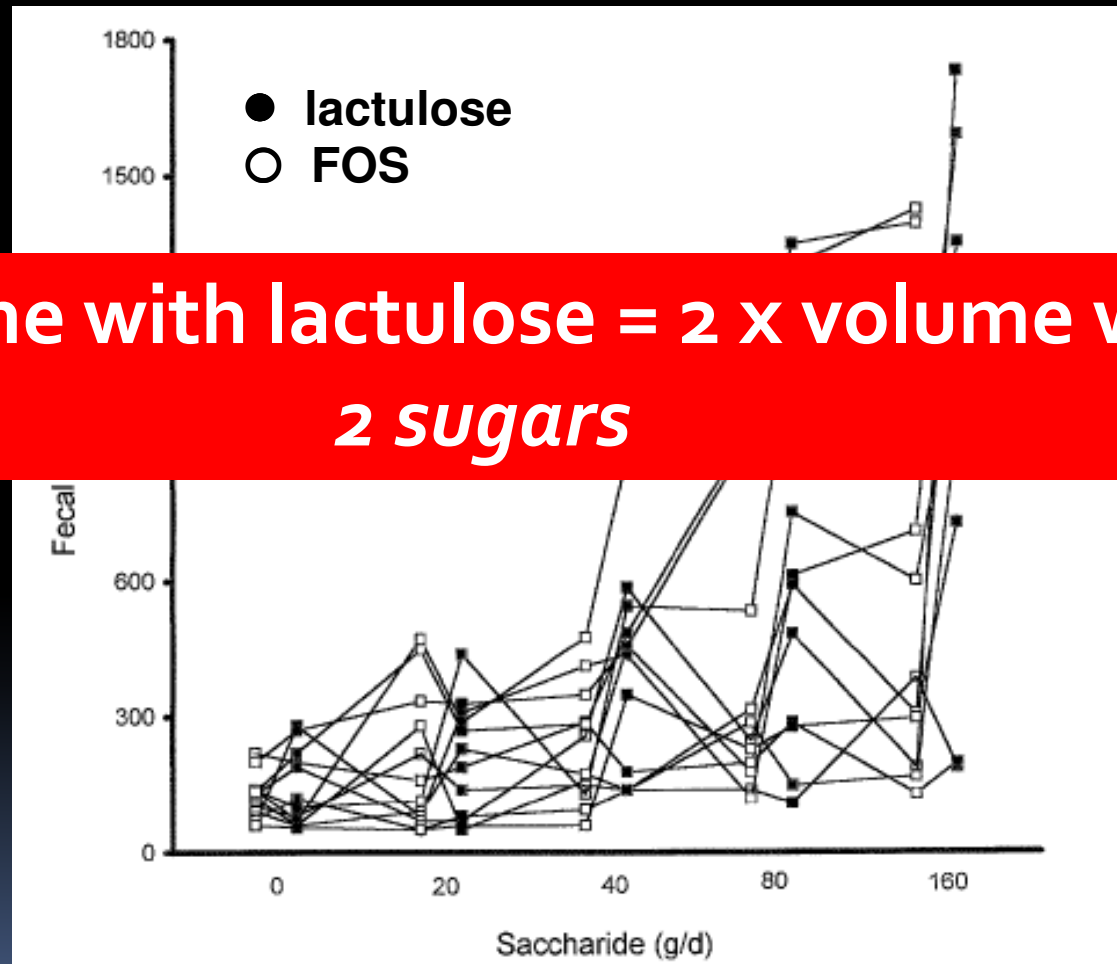
Barrett et al APT 2010

Spearman's correlation

Liquid volume in small intestinal lumen: *mannitol vs glucose*



↑ **colonic water: Dose-dependence of effect on faecal volume in response to Lactulose/FOS**

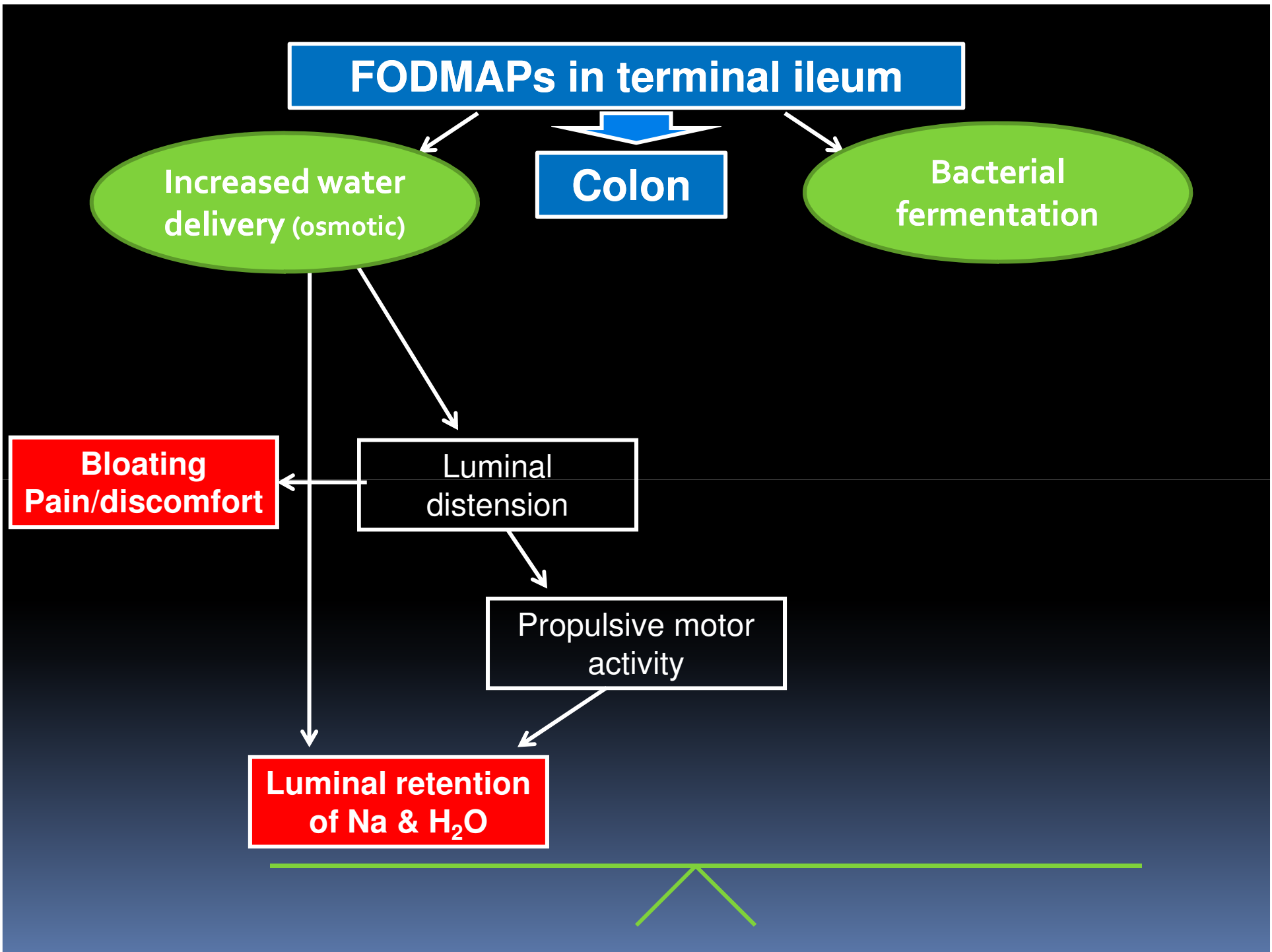


Volume with lactulose = 2 x volume with FOS

2 sugars

4 sugars

Clausen et al DDS 1998



FODMAPs are rapidly fermentable

- *In vitro* - fecal slurries:

- Rapid fermentation of FODMAPs

- Lactulose = fructose = lactose = FOS > sorbitol > GOS

Clausen et al Dig Dis Sci 1998

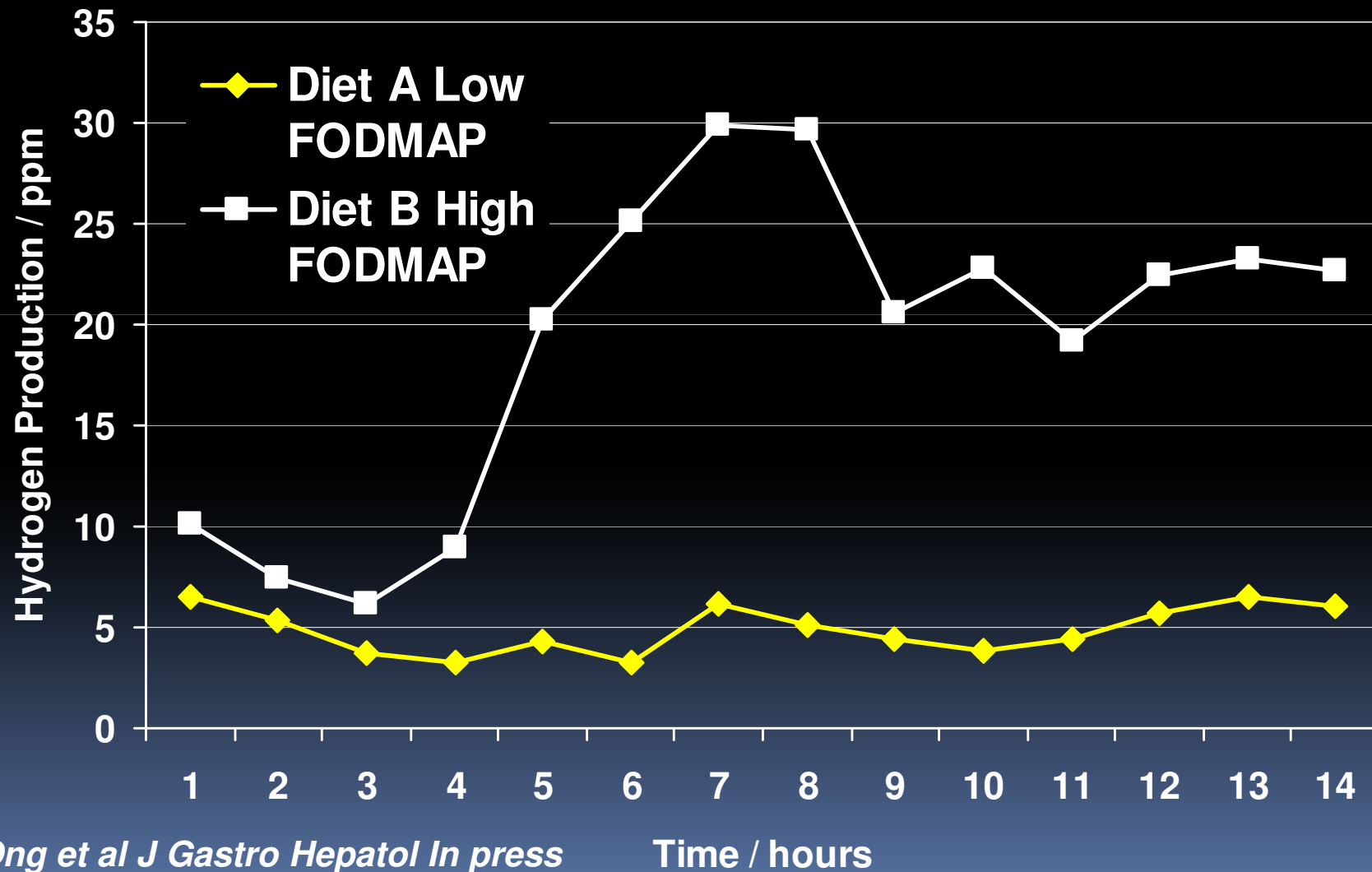
- Fermentability of carbohydrates dependent upon chain length

- e.g., *in vivo* - breath hydrogen production:

- 4.7 ppm/h.....Resistant starch
 - 19.1 ppm/h.....Inulin
 - 26.6 ppm/h.....Lactulose

Brighenti et al Ital J Gastro 1995

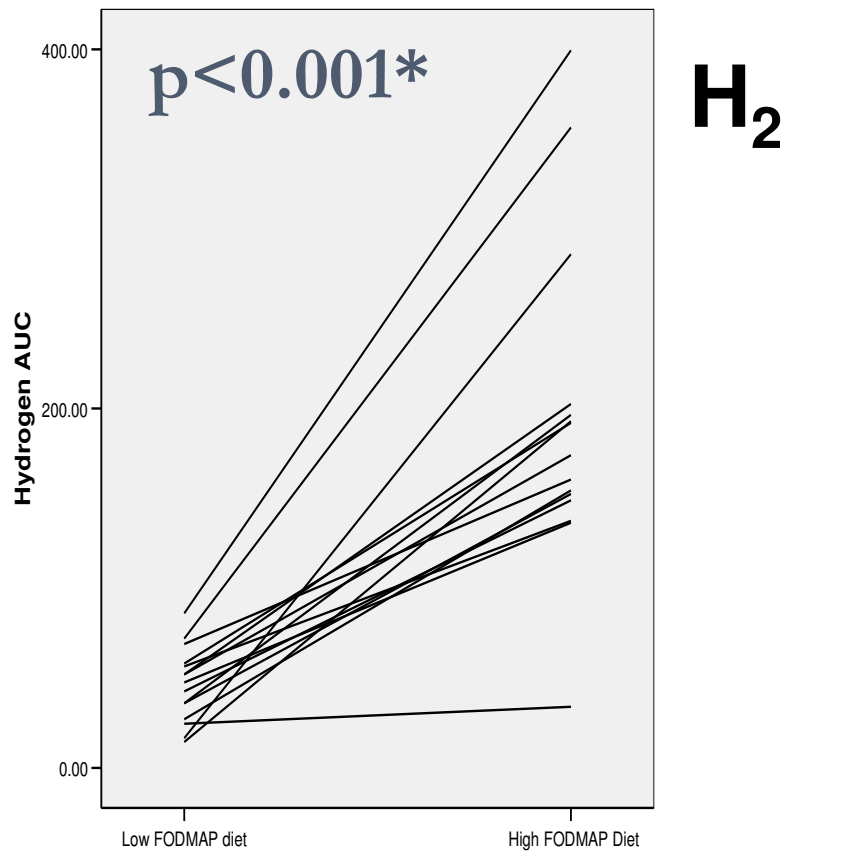
Typical effect of FODMAP intake on hydrogen production during the day



Ong et al J Gastro Hepatol In press

Time / hours

AUC breath gas production over 12 h in 15 healthy volunteers

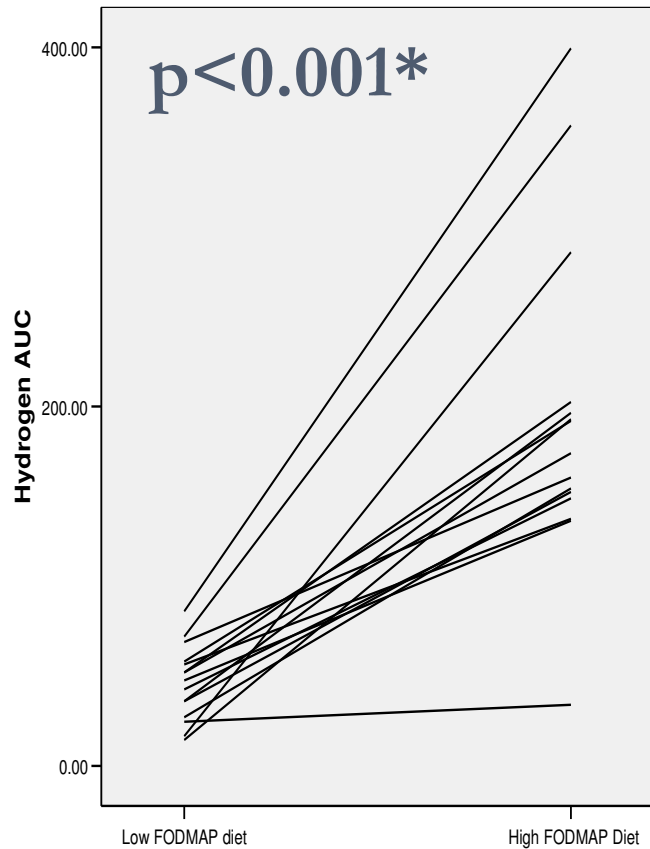


Low

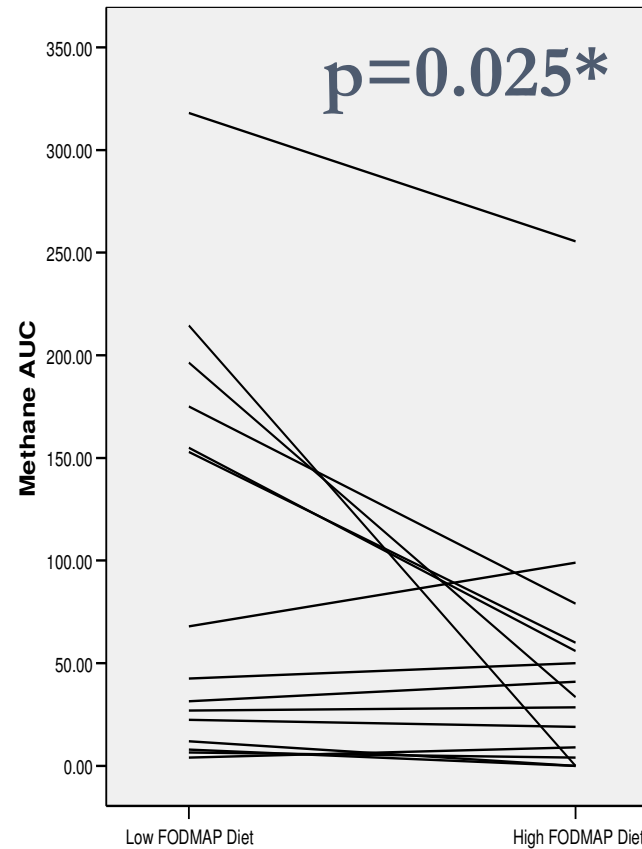
High

FODMAP content of diet

AUC breath gas production over 12 h in 15 healthy volunteers



H₂



CH₄

Low

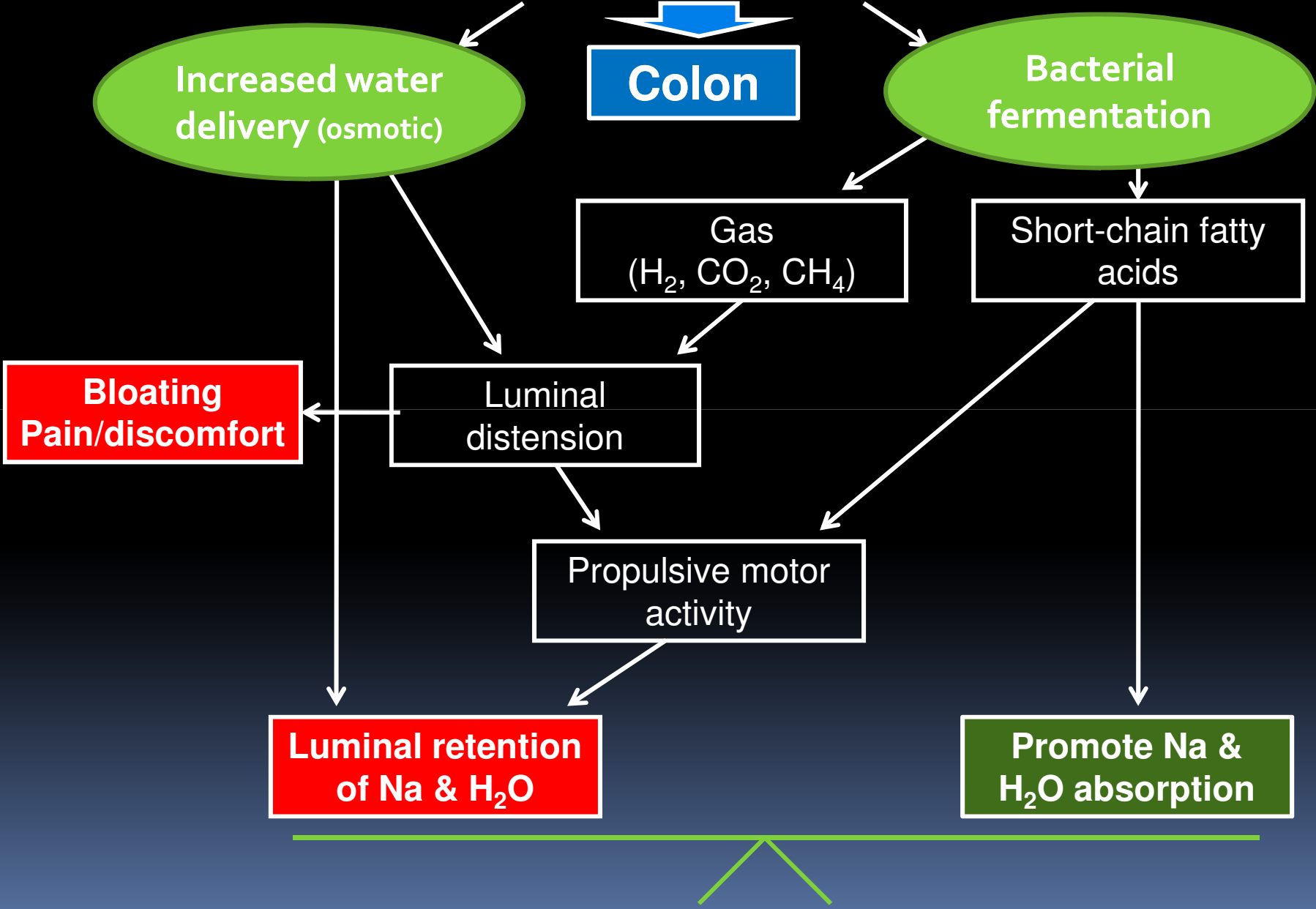
High

Low

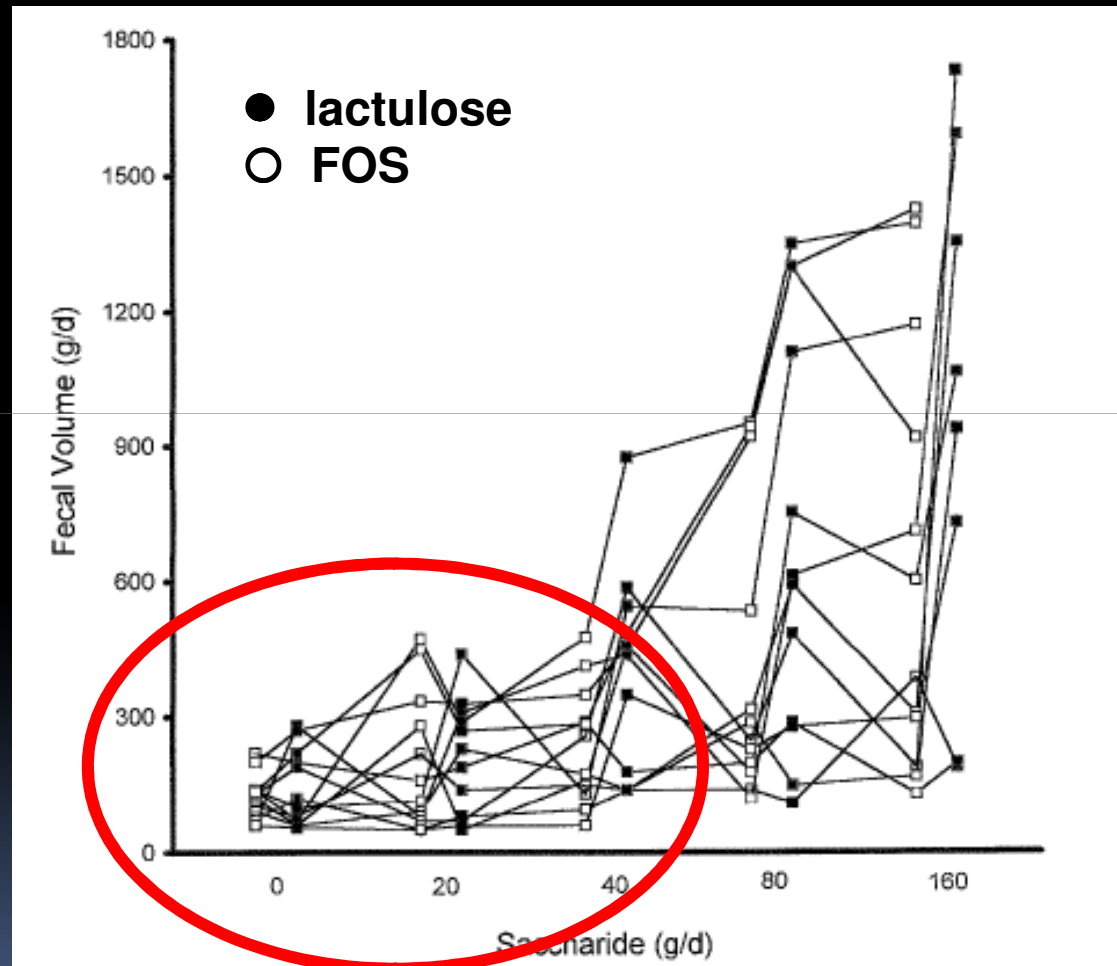
High

FODMAP content of diet

FODMAPs in terminal ileum

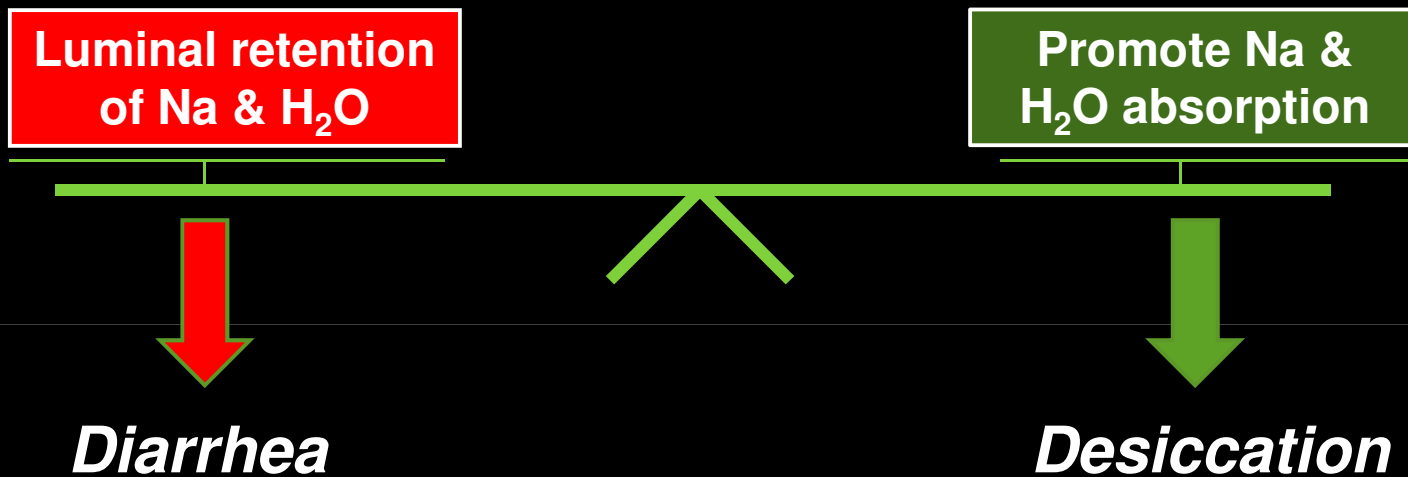


Dose-dependence of effect on fecal volume in response to lactulose/FOS



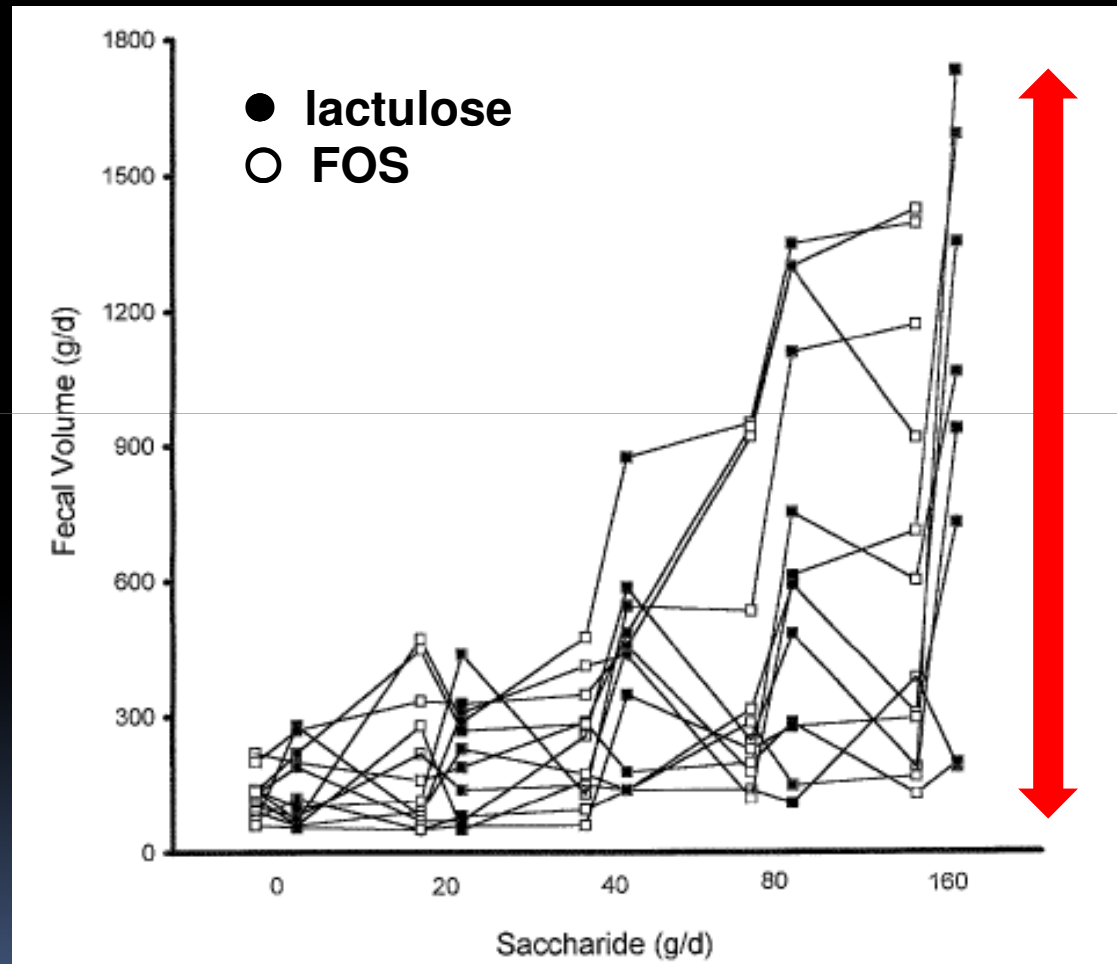
Clausen et al DDS 1998

Opposing forces of FODMAP disposal in colon



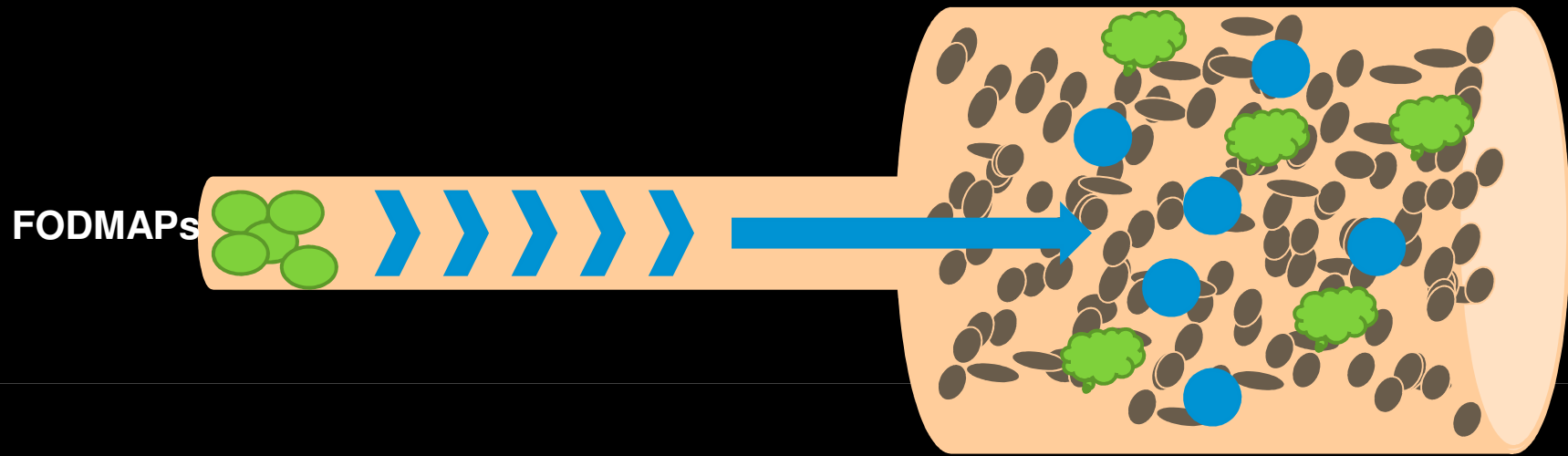
- *Dose of FODMAPs*
- *Efficiency of fructose & lactose absorption*
 - *Efficiency of fermentation*
- *Motility responses to distension/butyrate*
 - *Epithelial function/dysfunction*

Wide individual variation of fecal volume in response to lactulose/FOS



Clausen et al DDS 1998

Mode of action of FODMAPs



↑ water delivery

↑ gas production

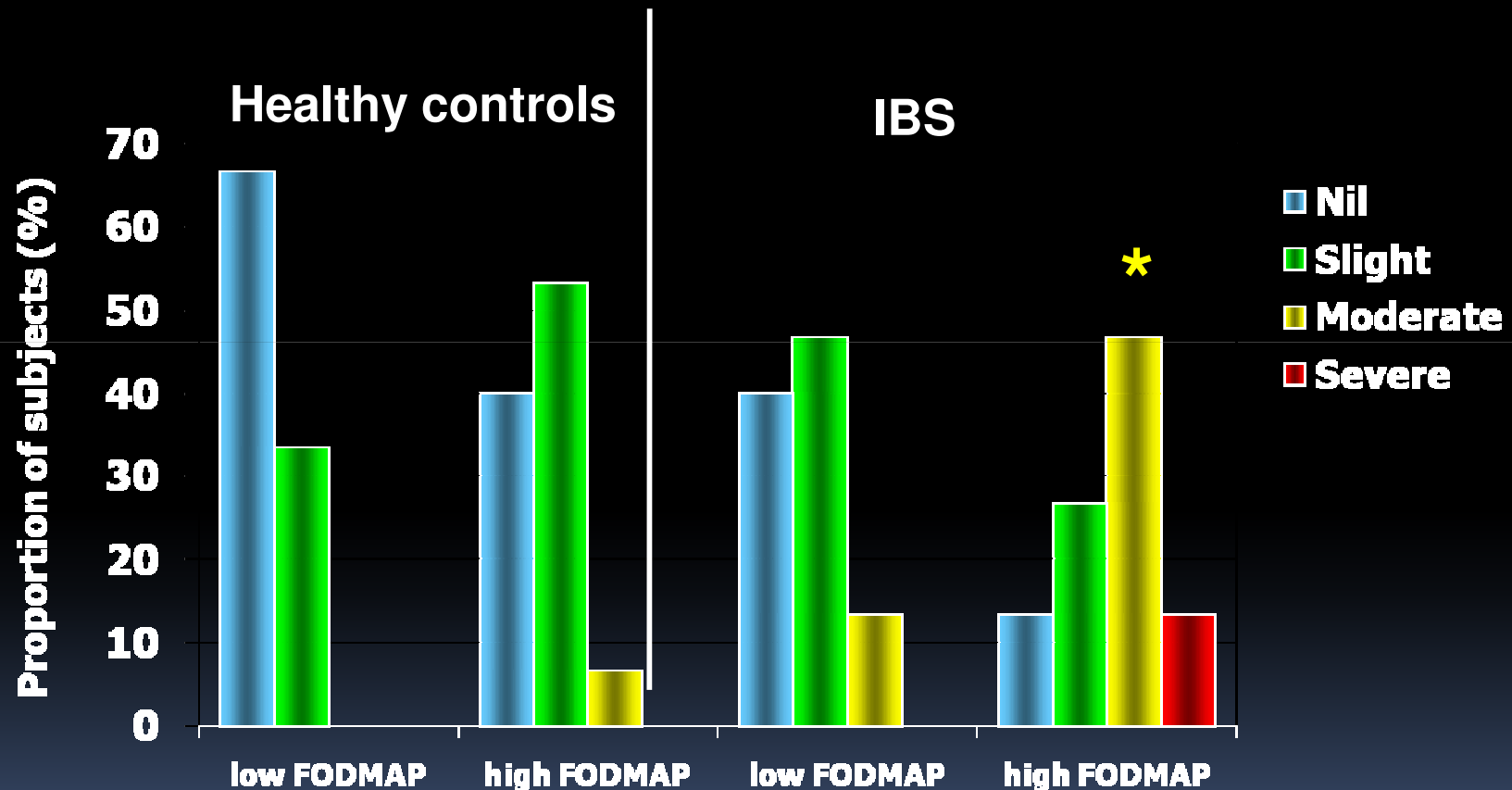


Luminal distension
Altered motility



Pain, bloating, distension,
constipation &/or diarrhoea

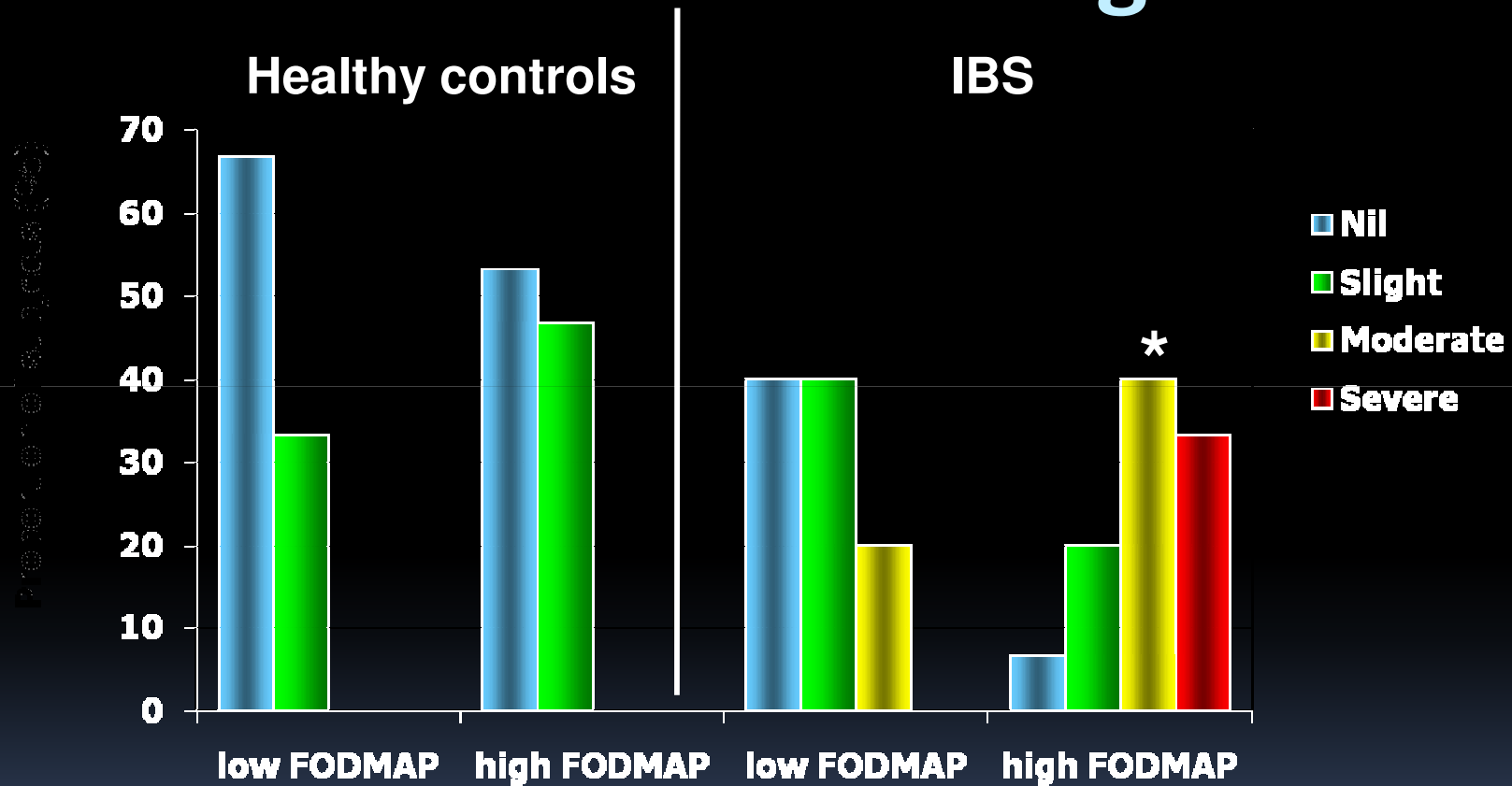
2 days' (blinded) high FODMAP diet induces abdominal pain



Ong et al JGH 2010

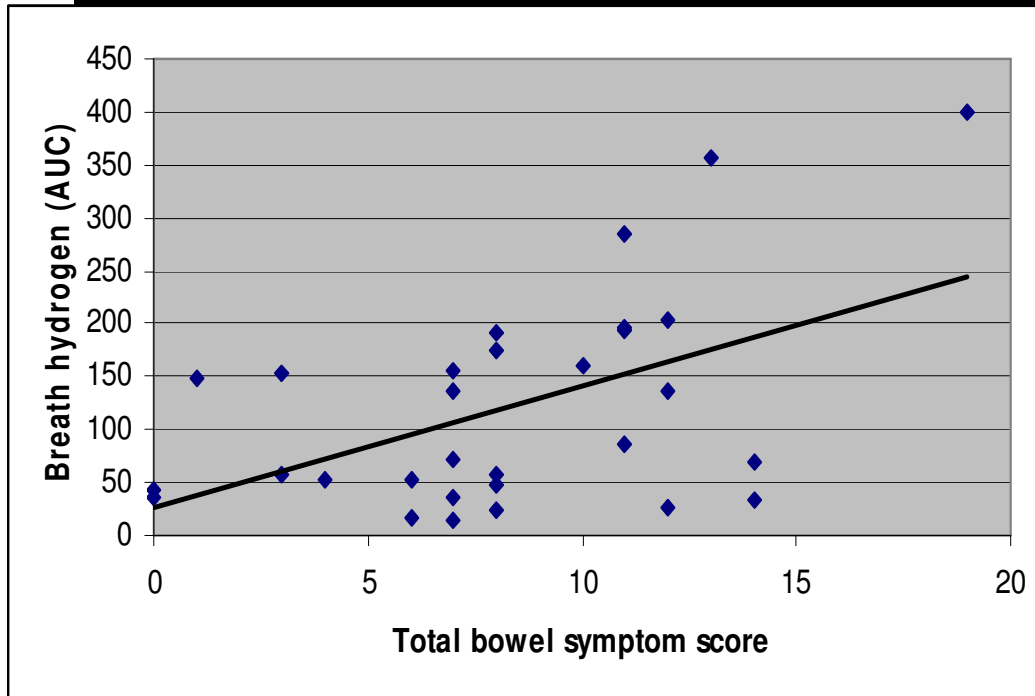
* $p < 0.05$ Mann-Whitney U & Wilcoxon signed ranks tests

2 days' (blinded) high FODMAP diet induces bloating



Ong et al JGH 2010

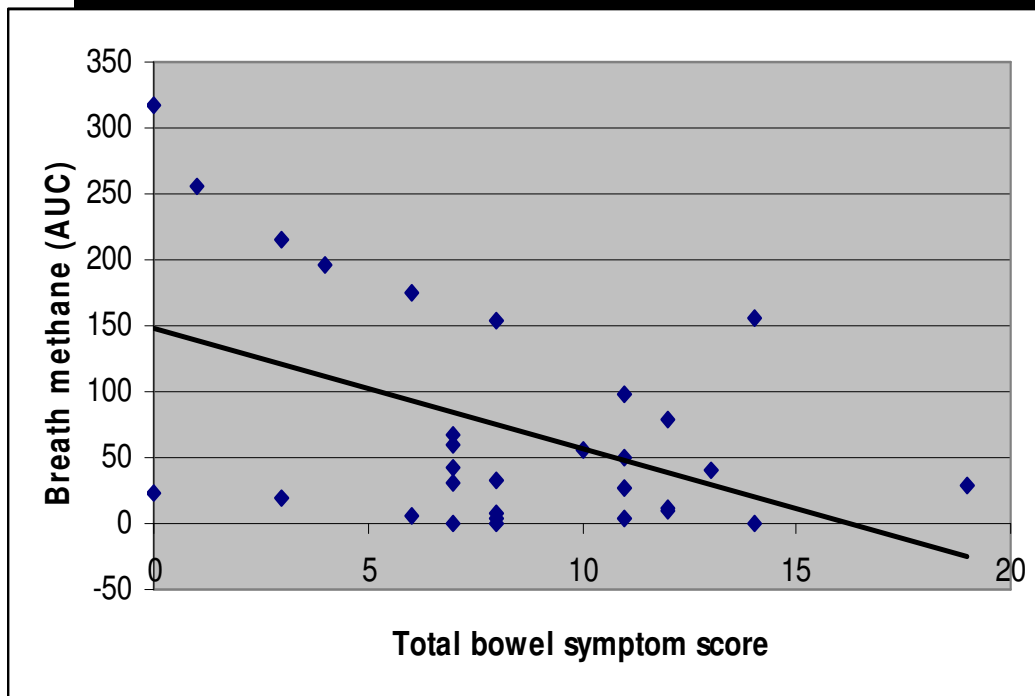
* $p < 0.05$ Mann-Whitney U & Wilcoxon signed ranks tests



**Breath hydrogen vs
total symptom score**

$r=0.467$

$p=0.012$



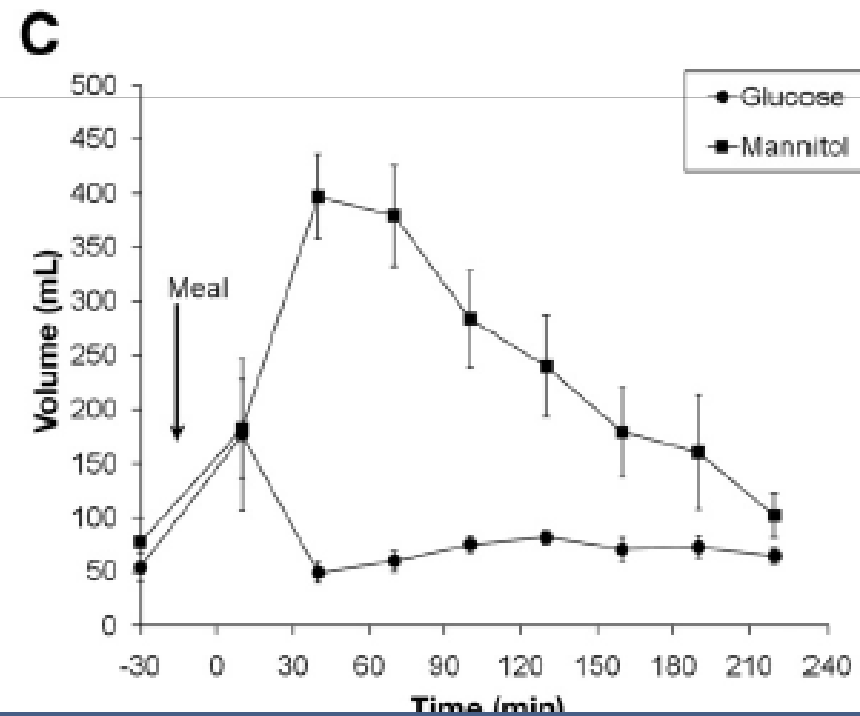
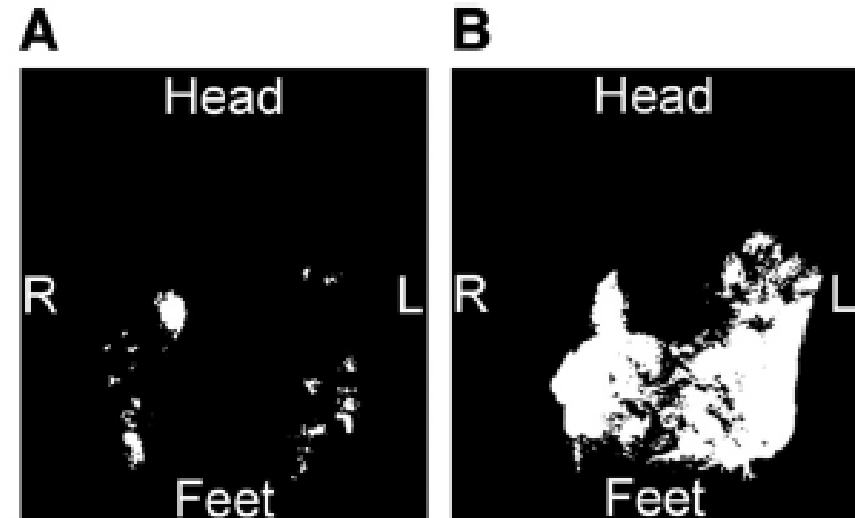
**Breath methane vs
total symptom score**

$r=-0.434$

$p=0.021$

Ong et al JGH 2010

Liquid volume in small intestinal lumen: *mannitol vs glucose*



Is benefit of low FODMAP diet only a placebo effect? – ‘rechallenge’

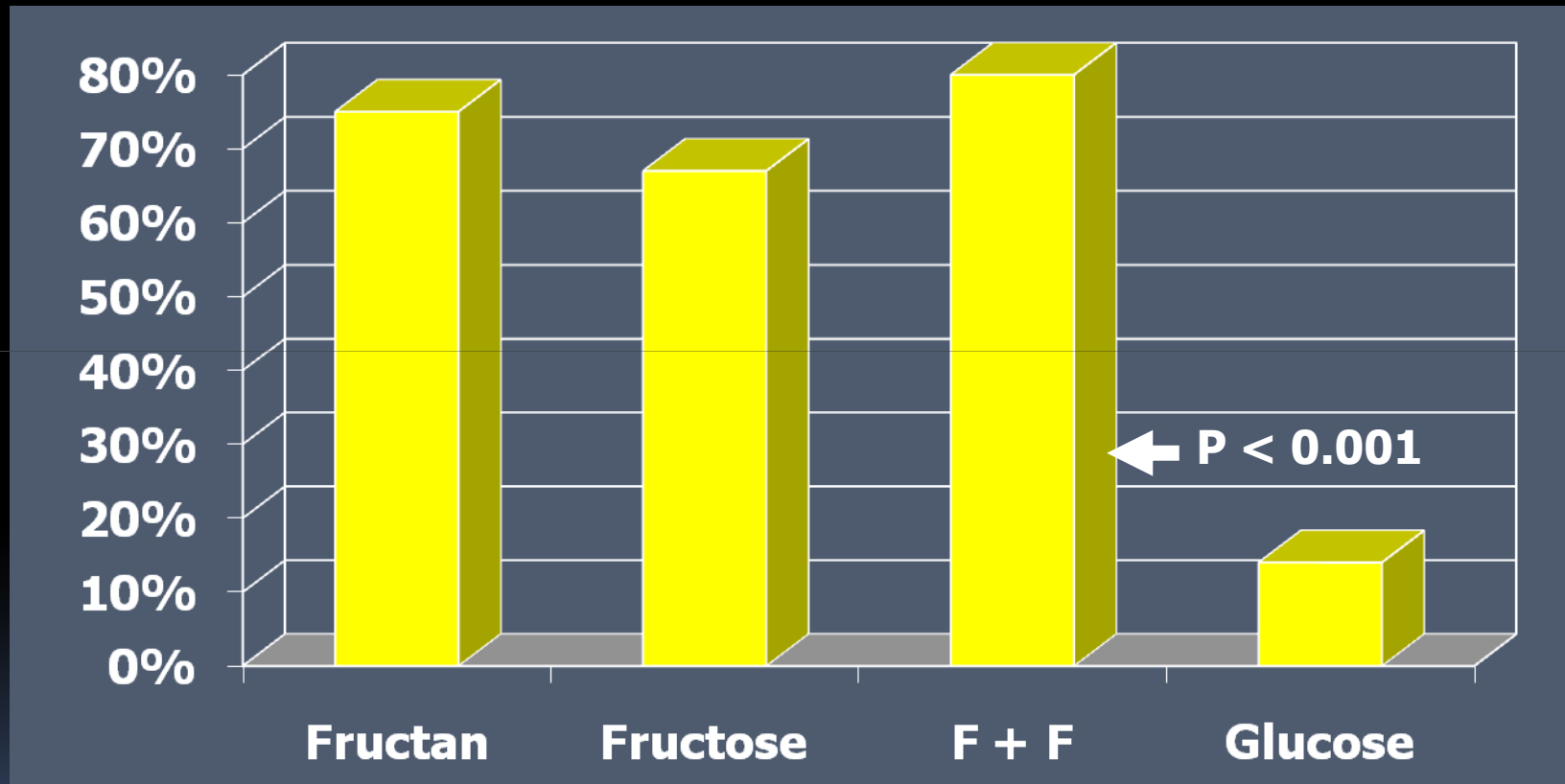
Randomised placebo-controlled 4-arm cross-over trial of reintroduction of fructose/fructans

25 patients with IBS (12 IBS-D)

- 23-60 y; 4 men
- Fructose malabsorption (breath test)
- Durable response to low FODMAP diet (at least 3 months)
- Well controlled symptoms

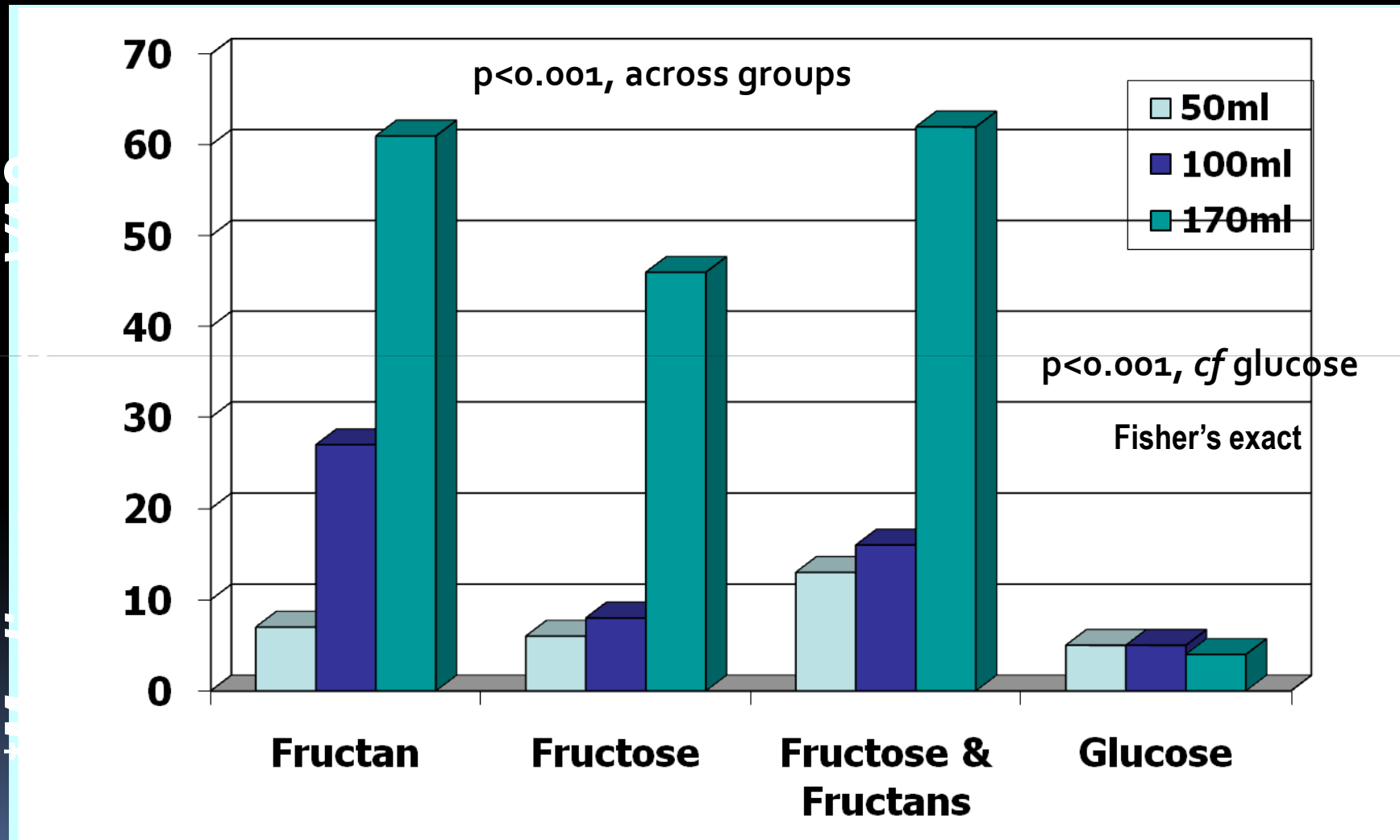
Shepherd et al, Clin Gast Hep 2008

1° end-point
% symptoms not adequately controlled



Shepherd et al Clin Gastro Hepatol 2008

Median overall symptom score



Rechallenge RCT

- Improvement with low FODMAP diet was not a placebo effect
- Involved not just fructose but fructans
- Fructose & fructans have additive effects = supporting the FODMAP concept

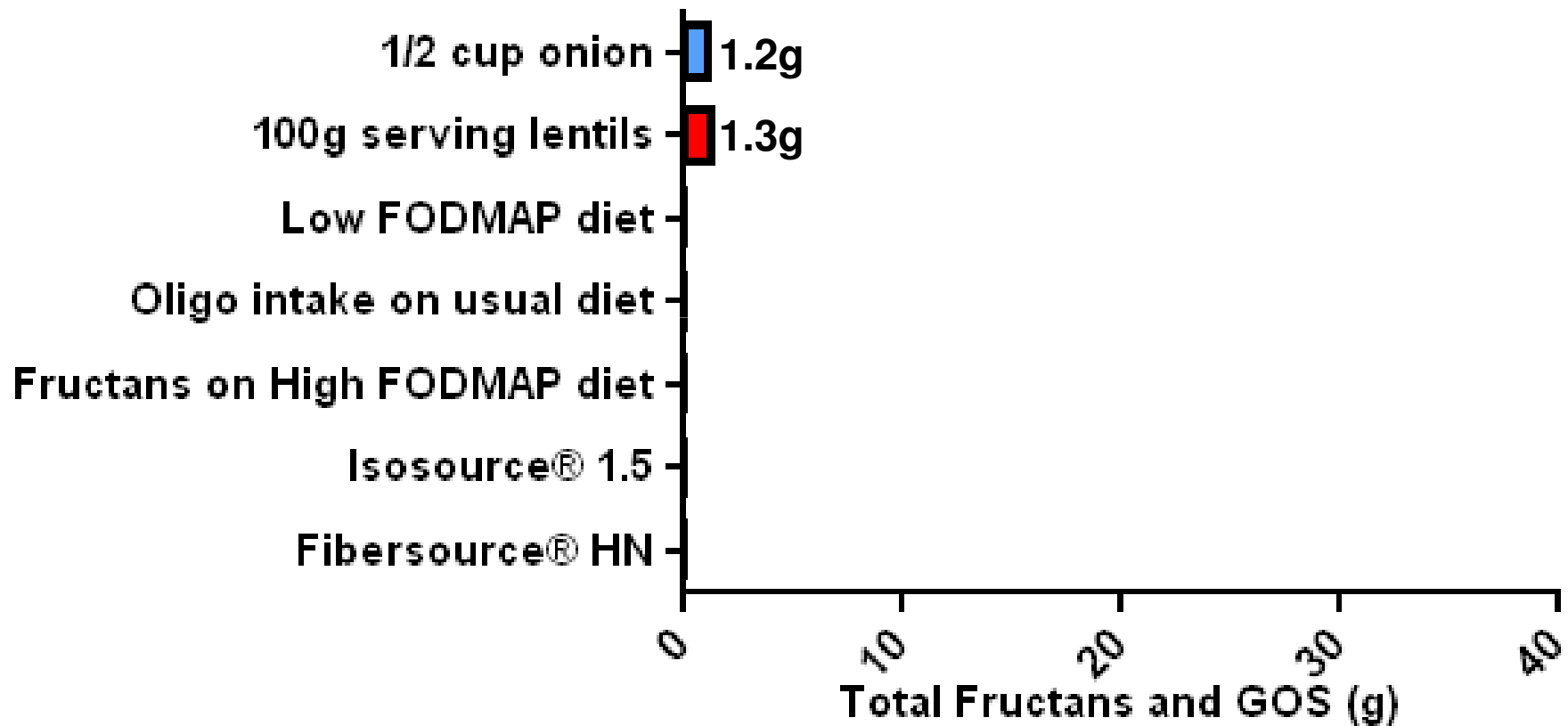
FODMAP content of food

- By combination of enzymatic and HPLC techniques, content of wide variety of Australian foods now known

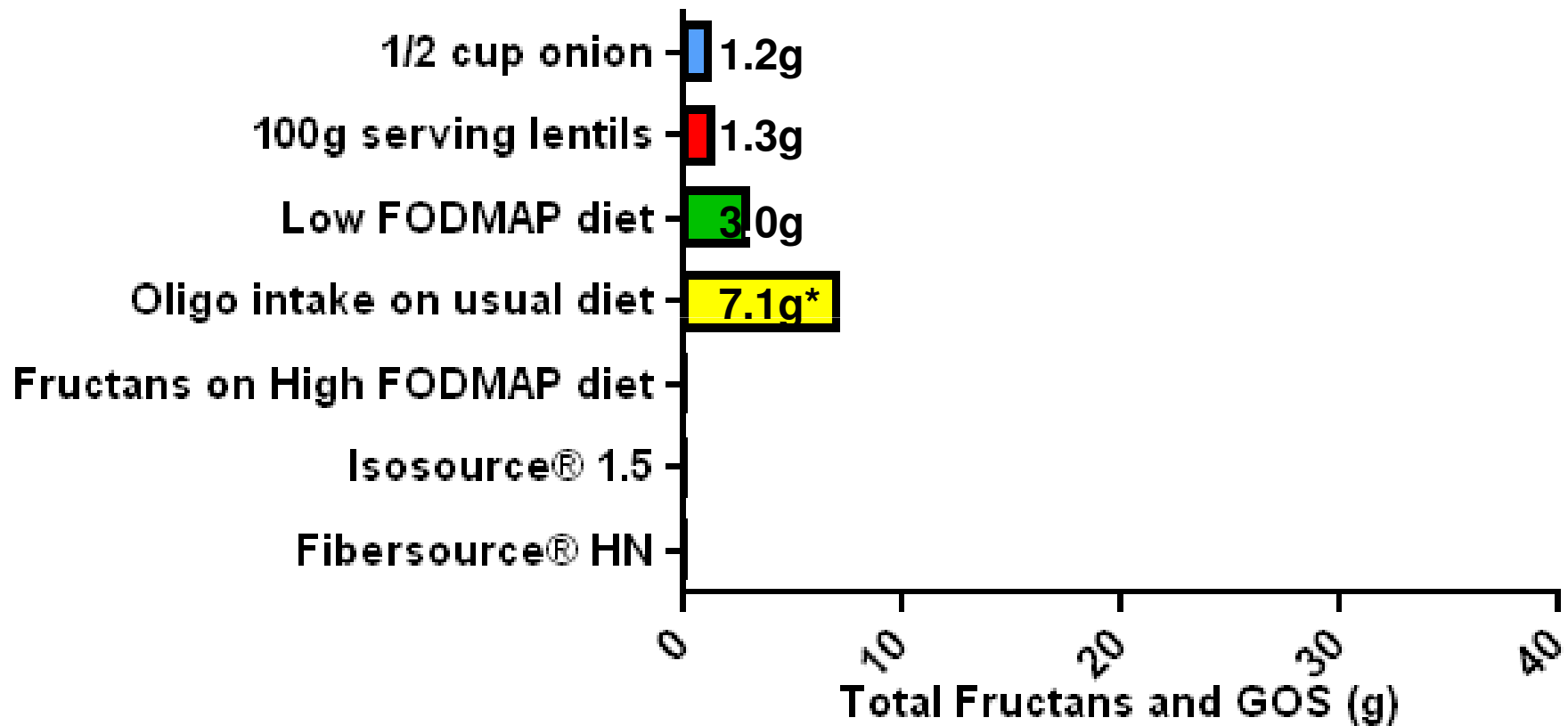
Muir et al JAFC 2007 & 2009; Biesierkierski et al JHND 2011

- Tables of 'safe' and 'unsafe' foods continuing to be updated → *beware old lists on the internet!*

Oligosaccharide content

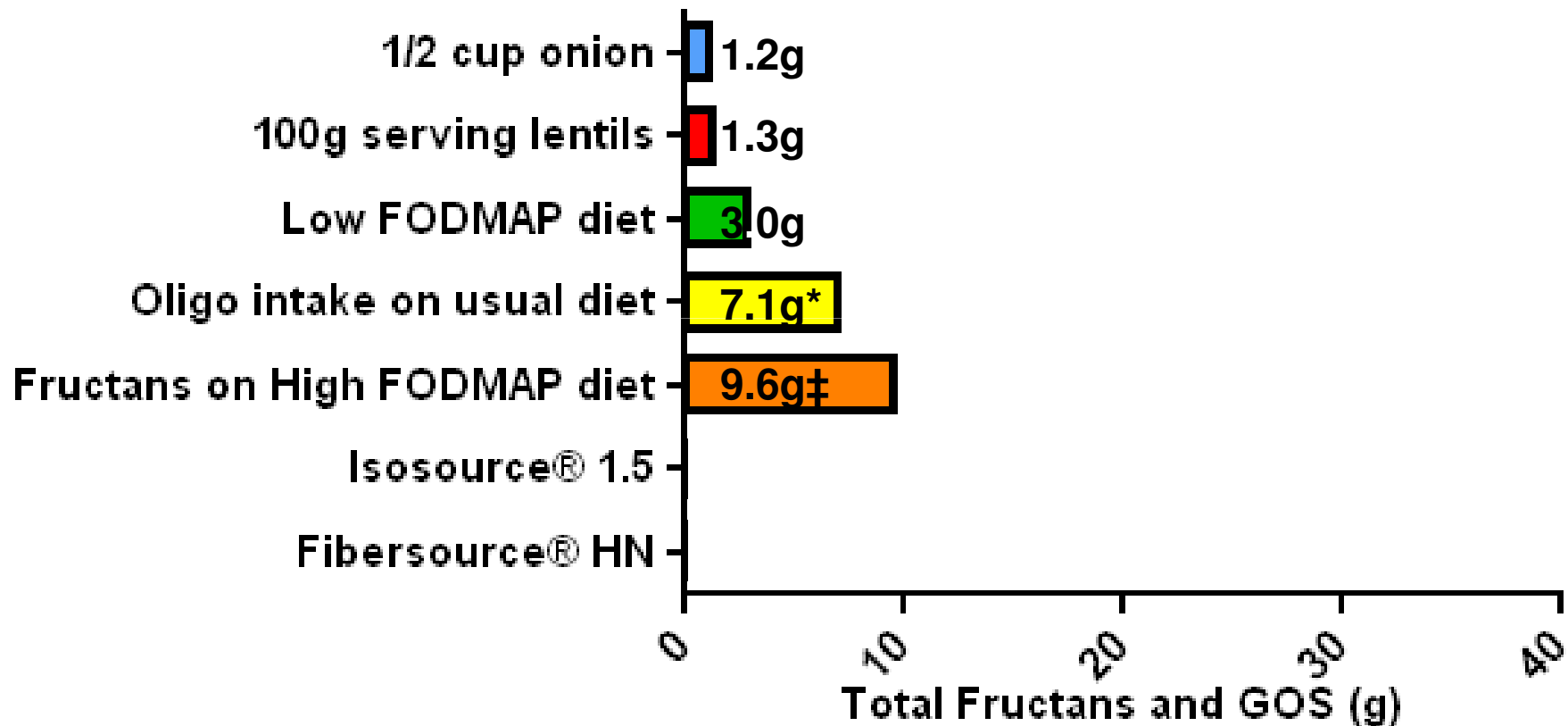


Oligosaccharide content



* Barrett FFQ, data unpublished, upper range of daily oligosaccharide intake

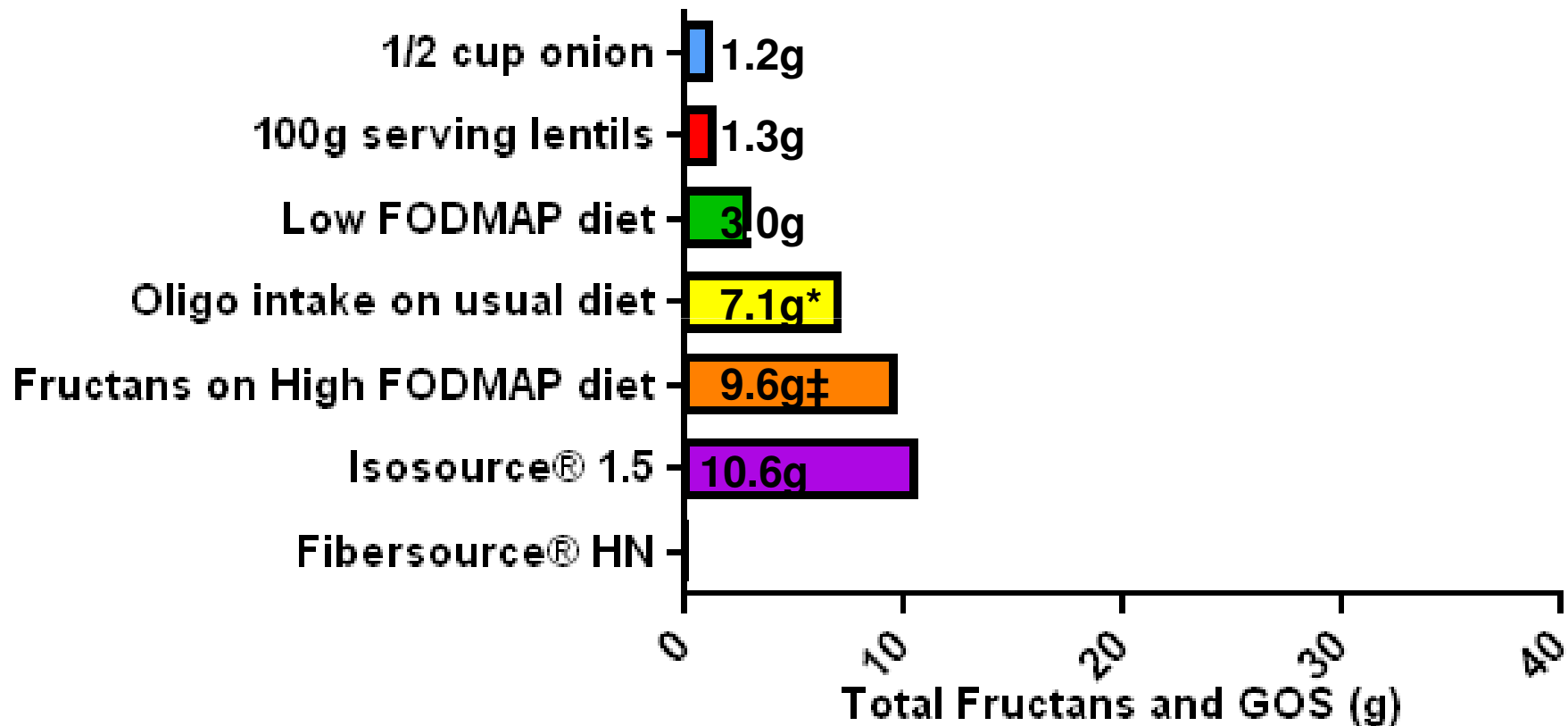
Oligosaccharide content



* Barrett FFQ, data unpublished, upper range of daily oligosaccharide intake

‡ Barrett et al. *Aliment Pharmacol Ther* 2010

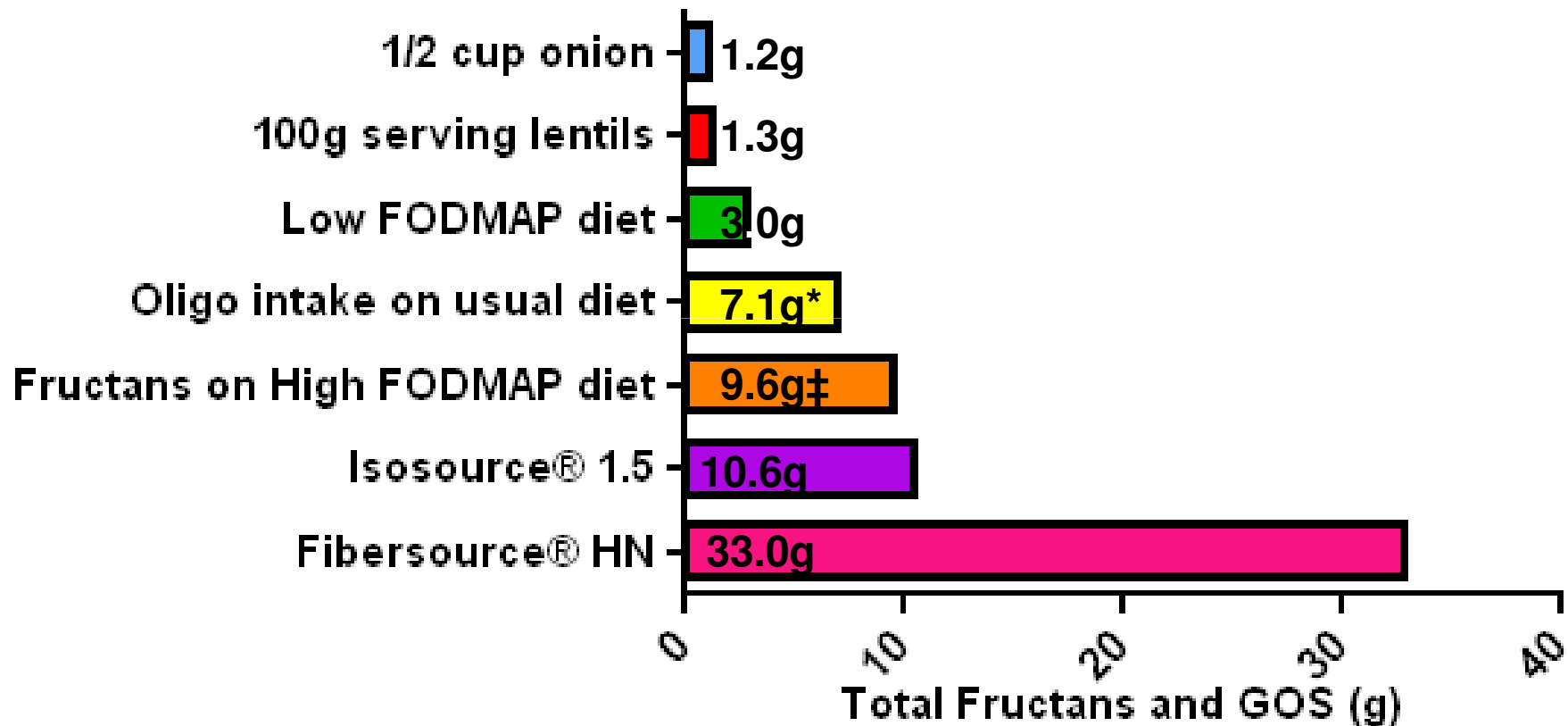
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Do IBS patients consume more FODMAPs than non-IBS?

- Not known, but now have a validated Food Frequency Questionnaire ('Monash CNAQ')

Barrett & Gibson JADA 2011

- Fructose & lactose malabsorption occurs at similar frequency in IBS as for healthy population

Barrett et al APT 2010

Unanswered questions

- Long-term safety
 - Nutritional adequacy of the diet
 - Effect on microbiota (reduction of natural prebiotics)
 - Effect on colorectal carcinogenesis
- Effect on physiology of the bowel
 - e.g., does it change visceral hypersensitivity?
- Mechanism of action in
 - Induction of fatigue *Ong et al JGH 2010*
 - Increasing gastro-oesophageal reflux *Piche et al GE 2003*

The science behind FODMAPs

- FODMAPs distend the intestinal lumen
 - Retain water via osmotic effects
 - Induce increased gas production → favours higher volume H₂ vs methane
- FODMAPs induce symptoms when present in food most likely via luminal distension with water and gas
- Many questions still to be answered

- Senior Dietitians
 - Sue Shepherd
 - Jane Muir
 - Jaci Barrett
- Dietitians/PhD students
 - Emma Halmos
 - Jessica Biesierkierski
 - CK Yao
- Scientists
 - Nia Rosella
 - Rosemary Rose
 - Kelly Liels

- Gastroenterology Fellows
 - Richard Garry
 - Peter Irving
 - Sally James
 - Debbie Nathan
 - Melissa Haines
 - Evan Newnham
 - Catherine Croagh
 - Daniel van Langenberg
- Honours students
 - Derrick Ong
 - Shayleen Mitchell