MONASH University

Medicine, Nursing and Health Sciences

Extending knowledge of fermentable carbohydrates in health and gastrointestinal disorders

Dr Jaci Barrett, APD, RNutr
PhD, BSc(Biomed)(Hons), MND
Department of Gastroenterology, Central Clinical School, The Alfred

Themes to be covered

- **Basic concepts revisited**
  - **Functional gastrointestinal symptoms & fermentable carbohydrates**
    - **Definition**
    - **Breath testing and absorptive capacity**
    - **Mechanism**
- **Review of the evidence**
  - **2005-2010**
  - **New and emerging research**
- **Food composition**
- **Fermentable carbohydrates in health and disorders**

BASIC CONCEPTS REVISITED

Gastrointestinal Symptoms

- Abdominal pain, bloating, and altered bowel habits.
- Evident as functional symptoms in
  - Irritable bowel syndrome (IBS)
  - Inflammatory bowel disease (IBD)
  - Coeliac disease
- Until recently dietary management ineffective
- In 2005, previous research across the world was collated to form a group dietary carbohydrates that trigger gastrointestinal symptoms
  - Poorly absorbed, short chain carbohydrates

→ FODMAPs

Gibson & Shepherd, APT 2005

FODMAPs

Fermentable

Oligosaccharides

Disaccharides

Monosaccharides

And

Polyol**s**

Poor absorption of FODMAPs

- Can create gastrointestinal distress in those with functional gastrointestinal disorder, e.g. IBS
- Some FODMAPs are poorly absorbed in all of us
  - FODMAP malabsorption not the cause of symptoms
  - Fermented in everyone - prebiotic nature

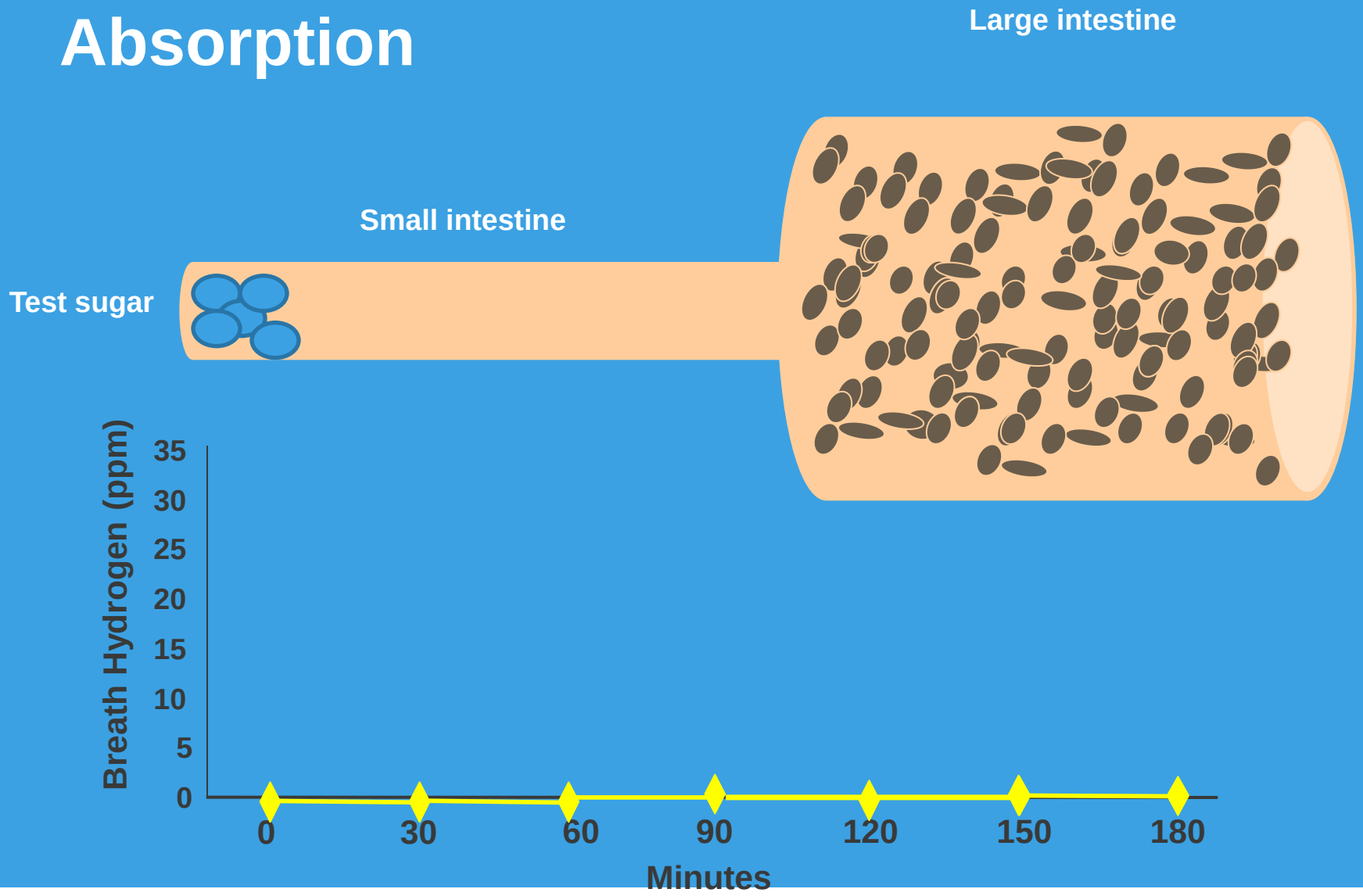
Poor absorption of FODMAPs

- Fructose
  - High capacity GLUT2 facilitated transport, requires glucose
  - Low capacity GLUT5 facultative transport across entire length of small intestine
    - Impaired in fructose malabsorption
- Lactose
  - Relies on adequate lactase enzyme to break down disaccharide
    - Lactase enzyme deficiency major cause of malabsorption
- Sugar polyols
  - Passive diffusion across entire length of small intestine
    - Malabsorption occurs and is dose dependent
- Fructo- and Galacto-Oligosaccharides
  - Malabsorption occurs in all of us

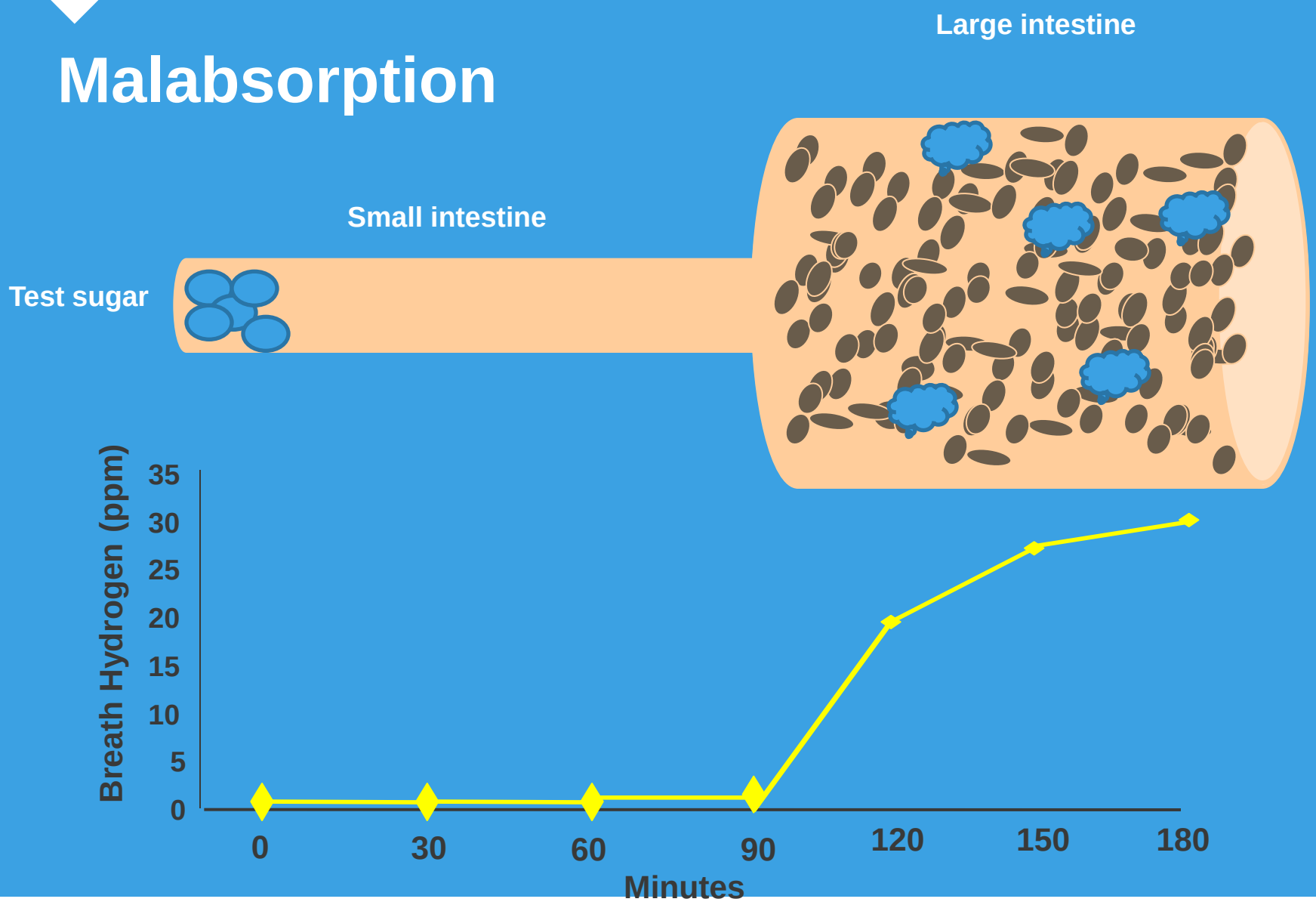
Breath Testing

- **Breath testing enables assessment of absorptive capacity of the small intestine for a tested carbohydrate**

Absorption

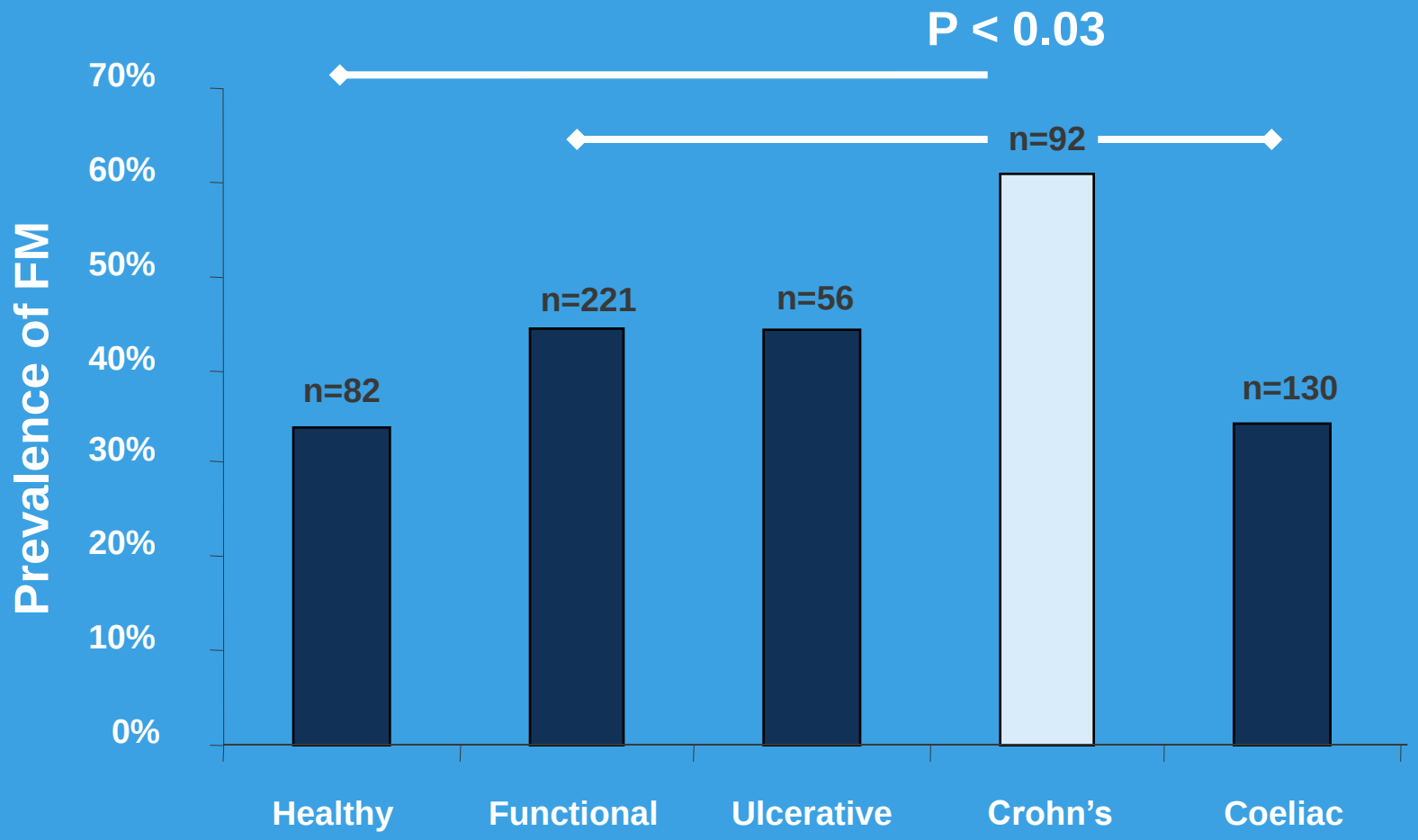

Large intestine
Small intestine
Test sugar
Breath Hydrogen (ppm)
35
30
25
20
15
10
5
0
0
30
60
90
120
150
180
Minutes

Malabsorption



Fructose

Barrett JS et al 2009, Aliment Pharmacol & Ther 30;165



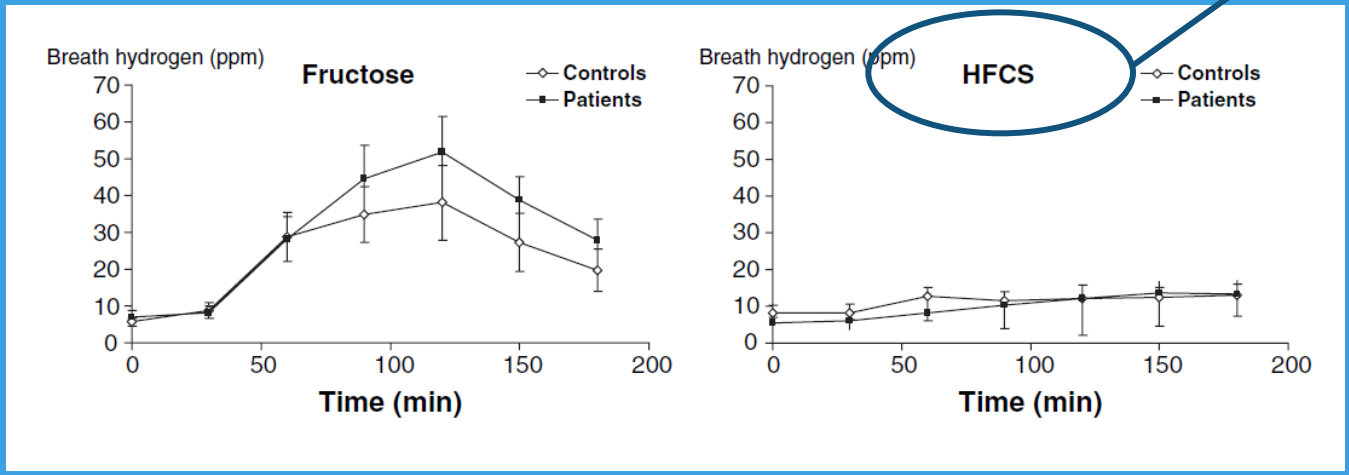
Fructose

Neurogastroenterol Motil (2008) **20,** 505–511 doi: 10.1111/j.1365-2982.2007.01074.x

Comparison of breath testing with fructose and high fructose corn syrups in health and IBS

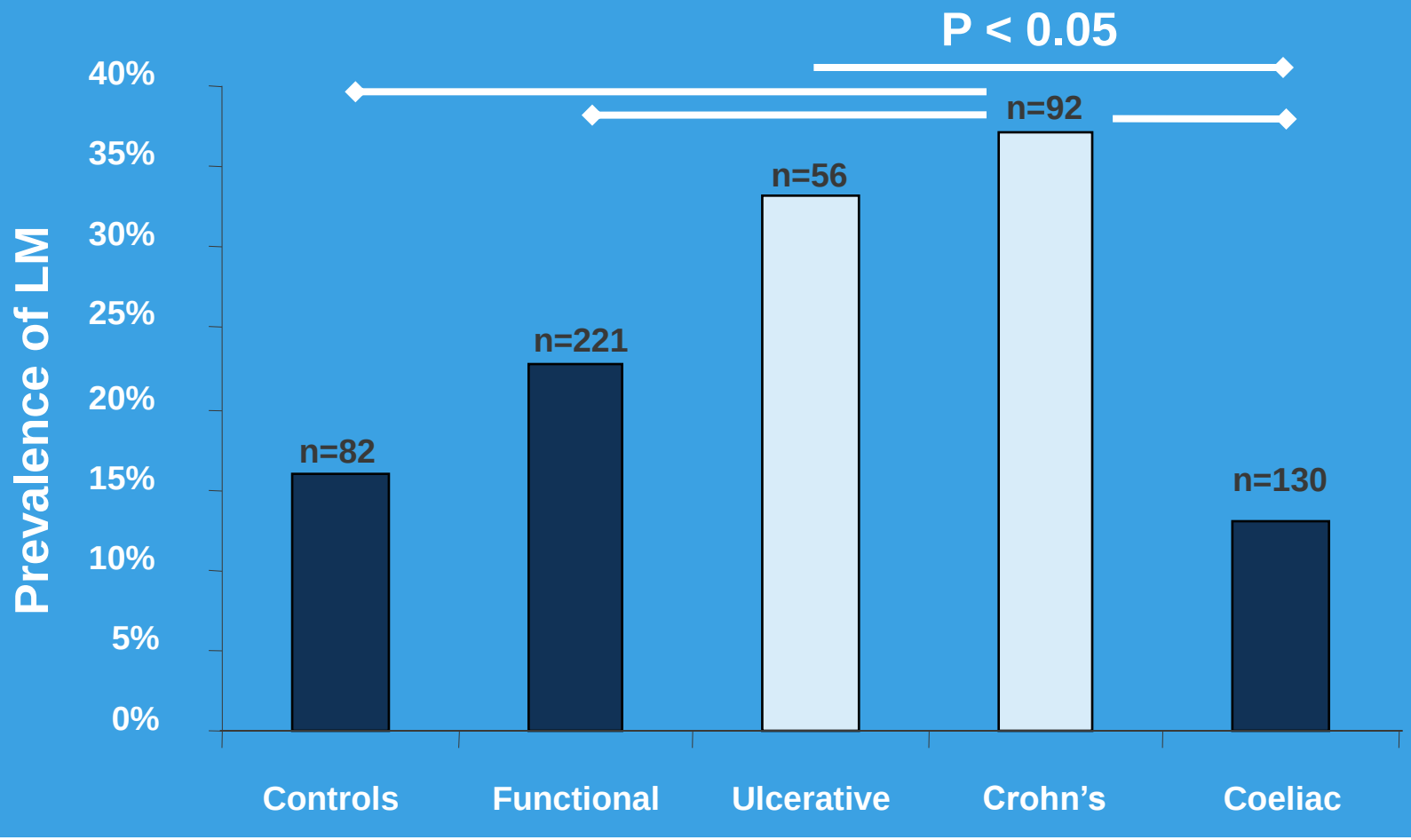
S. M. SKOOG, A. E. BHARUCHA & A. R. ZINSMEISTER

G:F 11:9



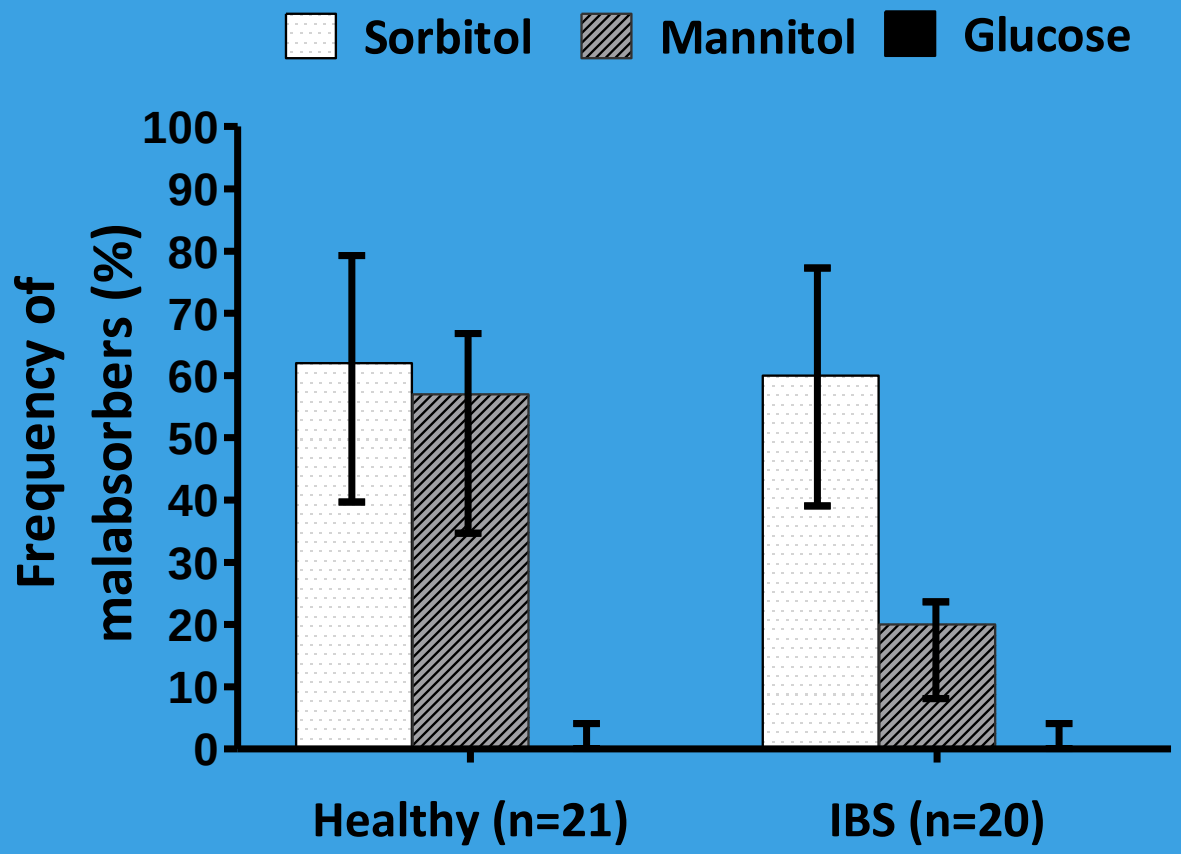
Lactose

Barrett JS et al 2009, Aliment Pharmacol & Ther 30;165



Polyols

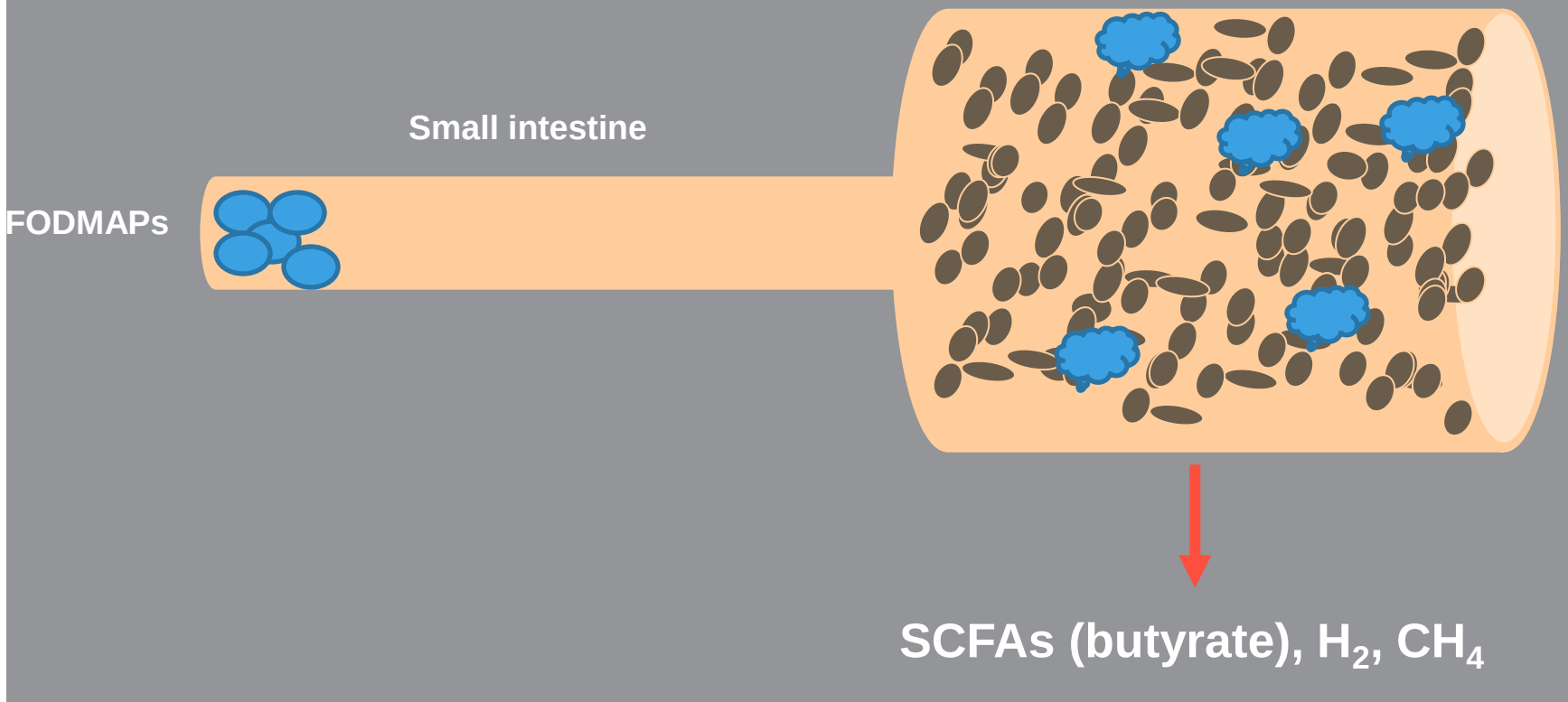
Yao CK et al 2012, submitted to *Am J Clin Nutr*



Oligosaccharides

- Multiple studies have demonstrated fructans and GOS pass through the small bowel without degradation
- We have no human enzymes to cleave the bonds
- They are a source of fermentation in all of us
- Described as prebiotics

Activity in health



Beneficial effects

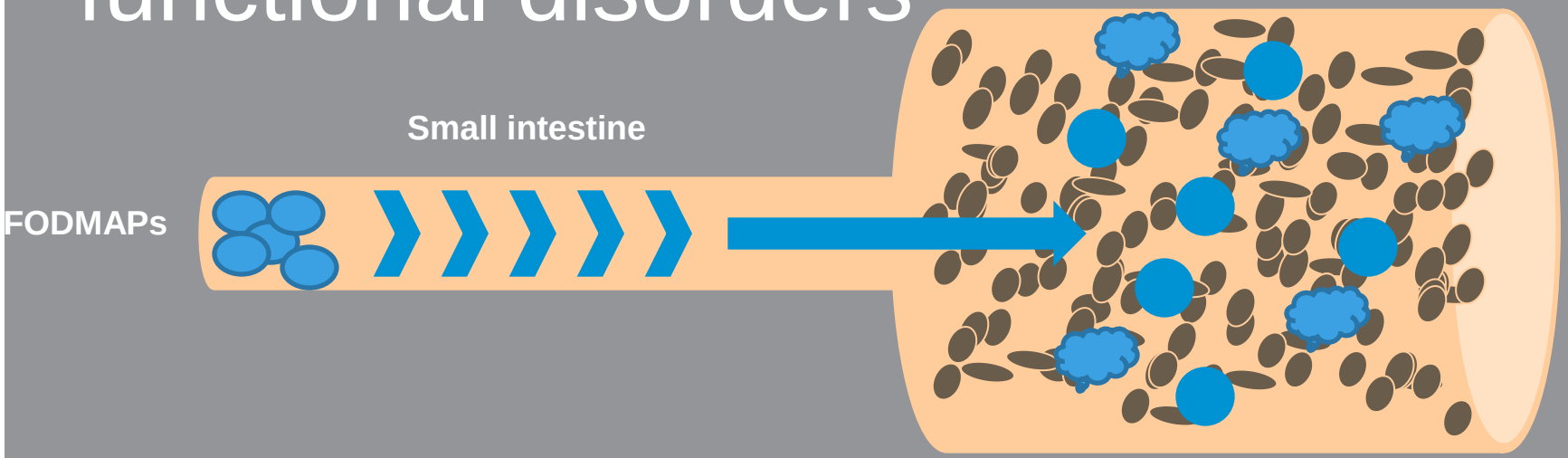
- **FOS, inulin and GOS**
  - **Increase number of bifidobacteria**
  - **Decrease number of *E.coli, Bacteroides* spp. and *Clostridium* spp.**

Roberfroid et al J Nutr 1998, Gibson et al Gastroenterol 1995, Holma et al J Gastroenterol 2002

- **Produce butyrate**
  - **May protect against DNA damage in colon cancer**

Reddy BS Carcinogenesis 1997

Activity in functional disorders



↑ water delivery

↑ gas production

Luminal distension

Altered motility

Pain, bloating, distension, wind, constipation +/-

EVIDENCE
2005 - 2010

Efficacy of the low FODMAP diet

- Induce symptoms with acute challenge

Multiple studies

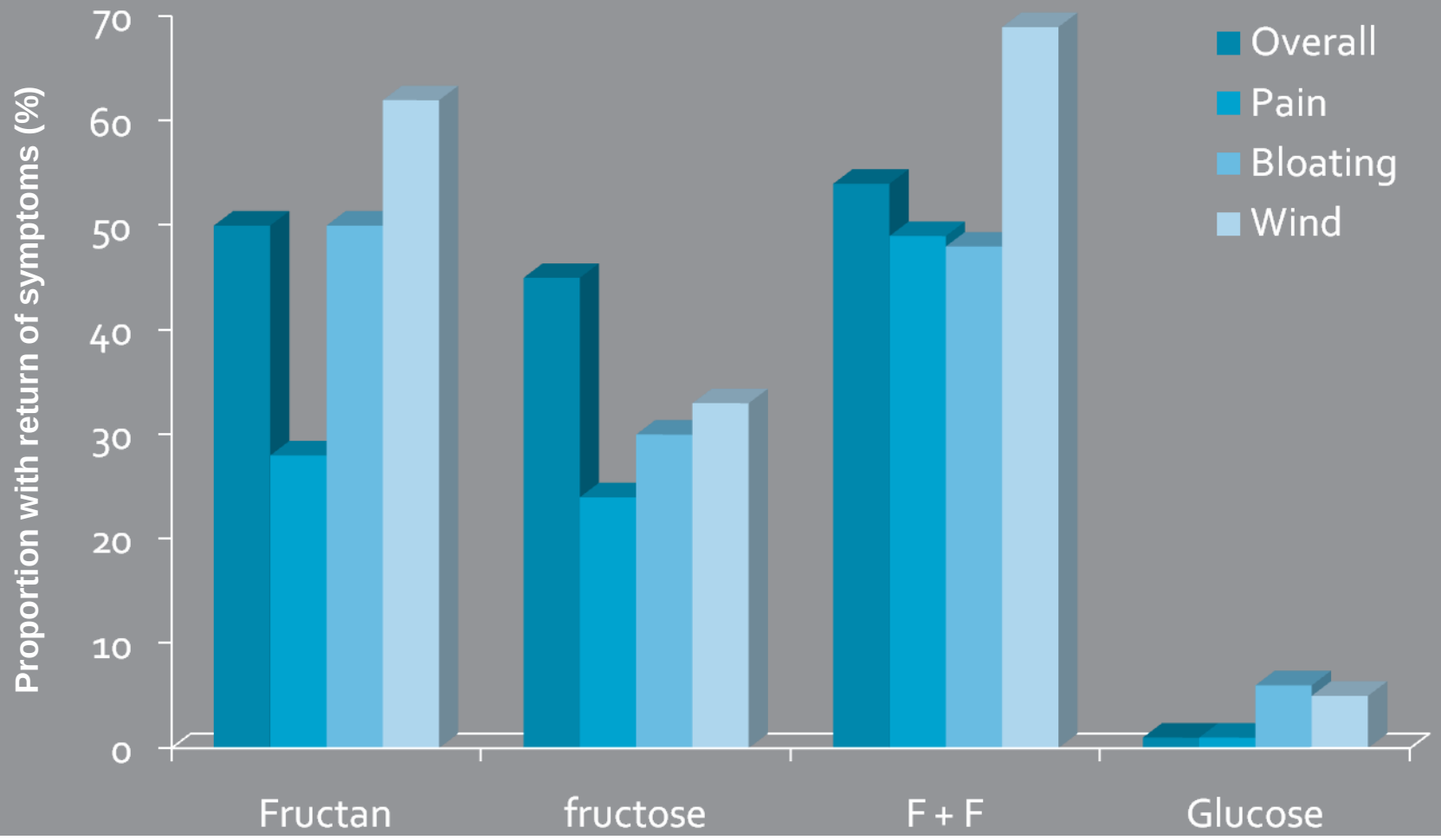
- Dietary restriction of FODMAPs provides considerable relief from all symptoms in 74% of IBS patients

Shepherd et al JADA 2006

- Fructose and fructans induce symptoms in randomised placebo-controlled rechallenge experiments

Shepherd et al CGH 2008

Rechallenge experiments



Efficacy of the low FODMAP diet

- Induce symptoms with acute challenge

Multiple studies

- Dietary restriction of FODMAPs provides considerable relief from all symptoms in 74% of IBS patients

Shepherd et al JADA 2006

- Fructose and fructans induce symptoms in randomised placebo-controlled rechallenge experiments

Shepherd et al CGH 2008

- Low FODMAP diet provides relief of functional gastrointestinal symptoms in 70% of IBD patients

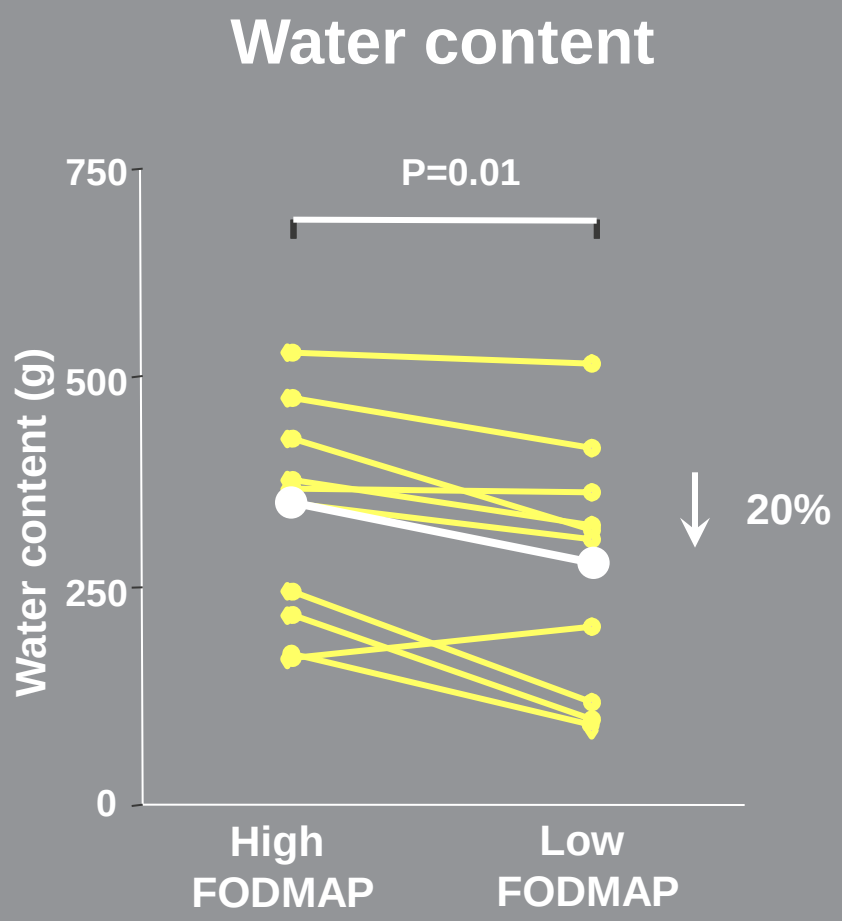
Gearry et al JCC 2008

FODMAP activity

- Low FODMAP diet reduces liquid effluent content in ileostomates

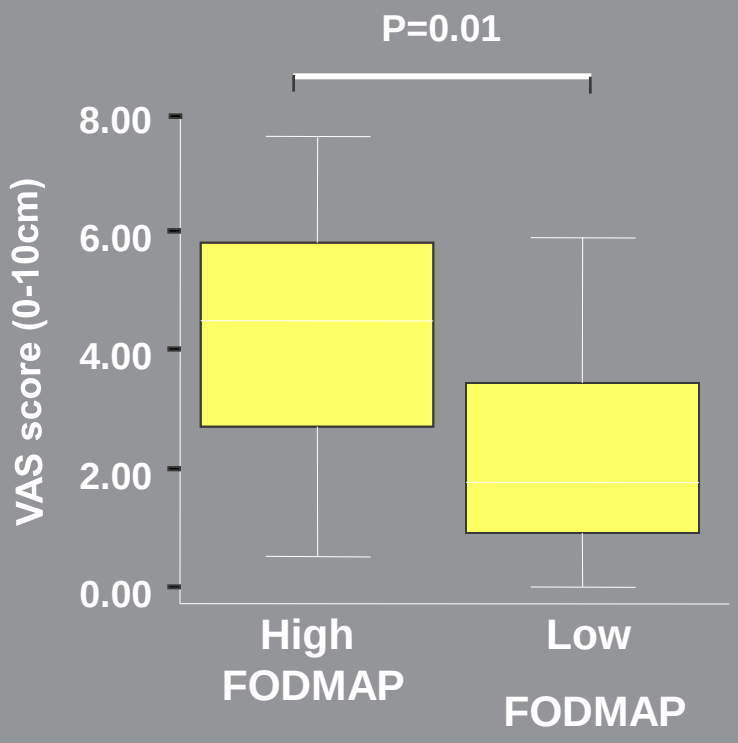
Barrett et al APT 2010

Daytime Effluent Composition

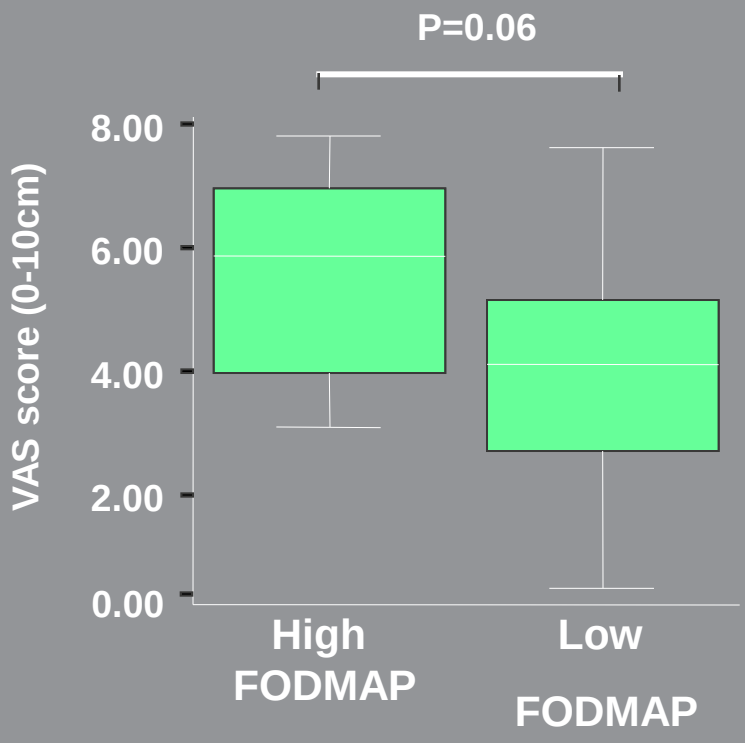


Perceptions

Effluent consistency



Effluent volume



FODMAP activity

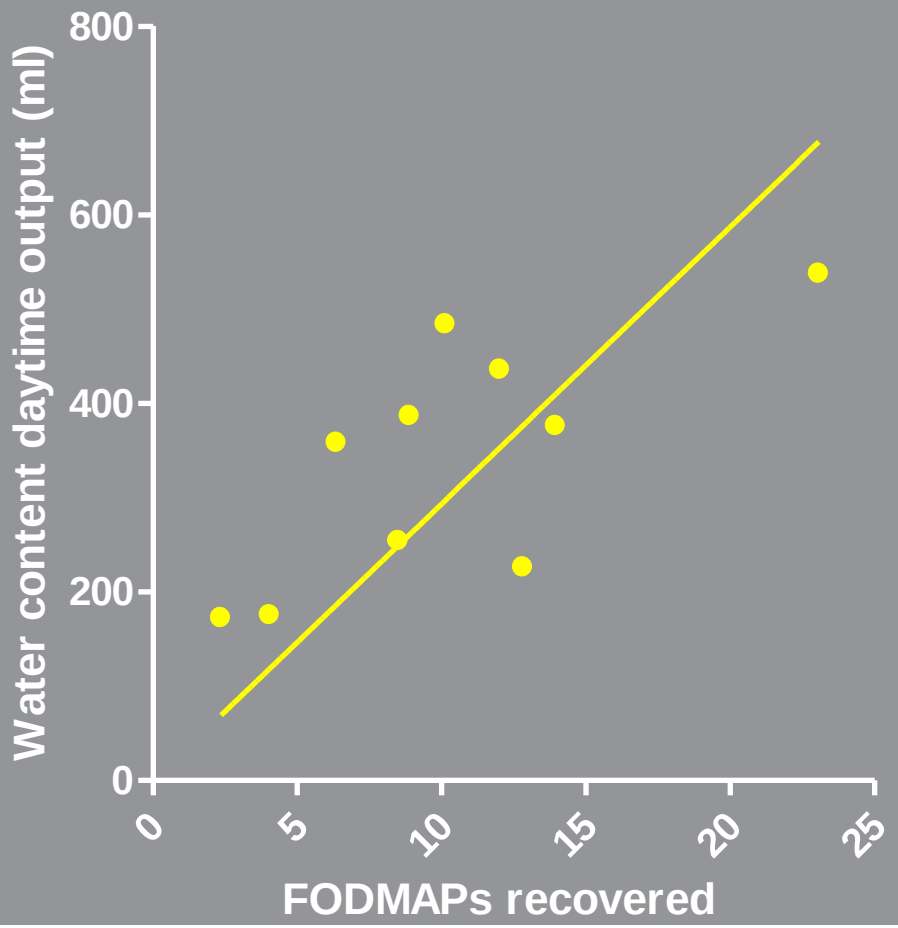
- Low FODMAP diet reduces liquid effluent content in ileostomates

  Barrett et al APT 2010

- Malabsorption of FODMAPs correlates with delivery of water through the small bowel

  Barrett et al APT 2010

Correlation of water and FODMAP recovery



r = 0.7223
p=0.018

Spearman's correlation

FODMAP activity

- Low FODMAP diet reduces liquid effluent content in ileostomates

  Barrett et al APT 2010

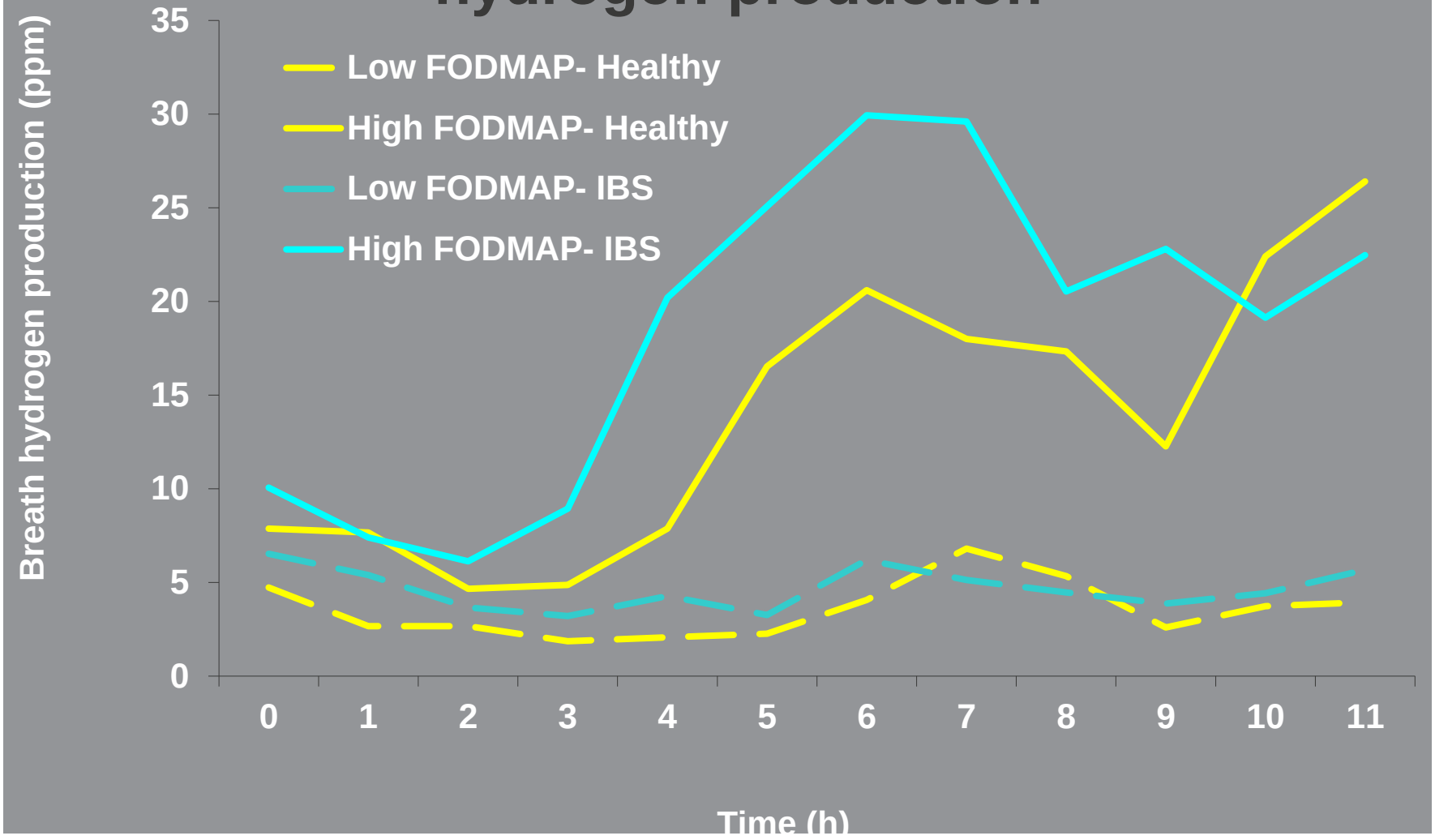
- Malabsorption of FODMAPs correlates with delivery of water through the small bowel

  Barrett et al APT 2010

- FODMAP ingestion increases breath hydrogen production, with levels accumulating over the day

  Ong et al JGH 2010

Influence of FODMAP intake on breath hydrogen production



FODMAP activity

- Low FODMAP diet reduces liquid effluent content in ileostomates

  Barrett et al APT 2010

- Malabsorption of FODMAPs correlates with delivery of water through the small bowel

  Barrett et al APT 2010

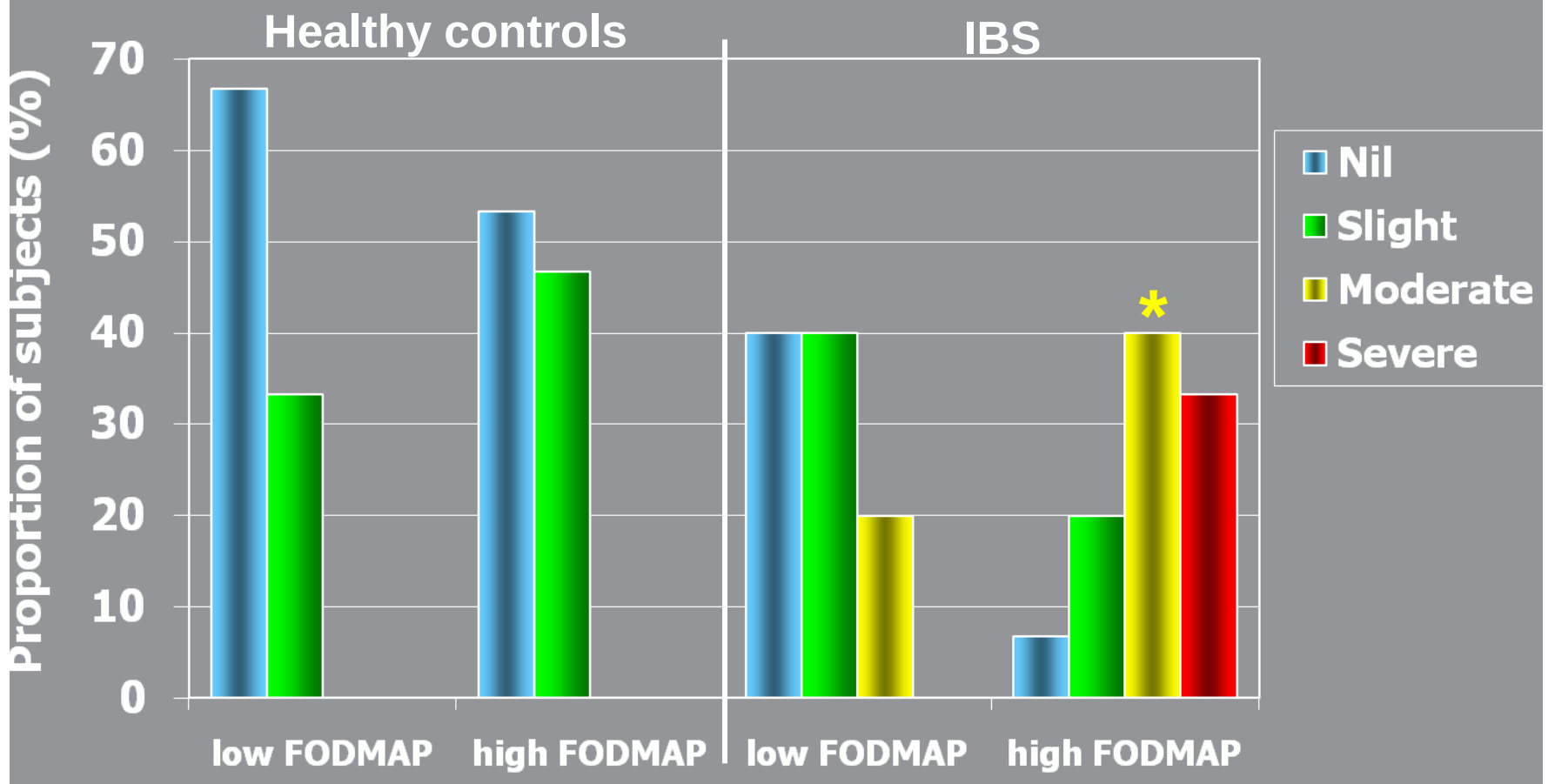
- FODMAP ingestion increases breath hydrogen production, with levels accumulating over the day

  Ong et al JGH 2010

- Although breath hydrogen levels in healthy and IBS volunteers are similar, gastrointestinal symptoms in IBS are severe following FODMAP ingestion

  Ong et al JGH 2010

Effect of high FODMAP intake on abdominal bloating



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

NEW AND EMERGING RESEARCH

UK Study

- **35 patients with IBS**
  - **randomised to the low FODMAP diet or habitual diet for 4 weeks**
  - **symptoms and stool output were recorded for seven days at baseline and follow-up**
  - **stool sample was collected and analysed for major bacterial groups**

UK Study

- **Symptoms improved in**
  - **60% on low FODMAP diet vs 23% control diet**
  - **Low FODMAP diet group reported lower stool frequency compared with controls (mean 9.3 vs 14.2 stools per week, P=0.025)**
  - **Lower concentrations (7.4 (0.7) vs 8.2 (0.6) $\log_{10}$ cells/g, P=0.001) and proportions (1.2% (2.1) vs 5.5% (4.9), P=0.002) of bifidobacteria in the low FODMAP diet group**

- **Conclusion: The low FODMAP diet improves symptoms but reduces luminal bifidobacteria, a genera that may be important in IBS**

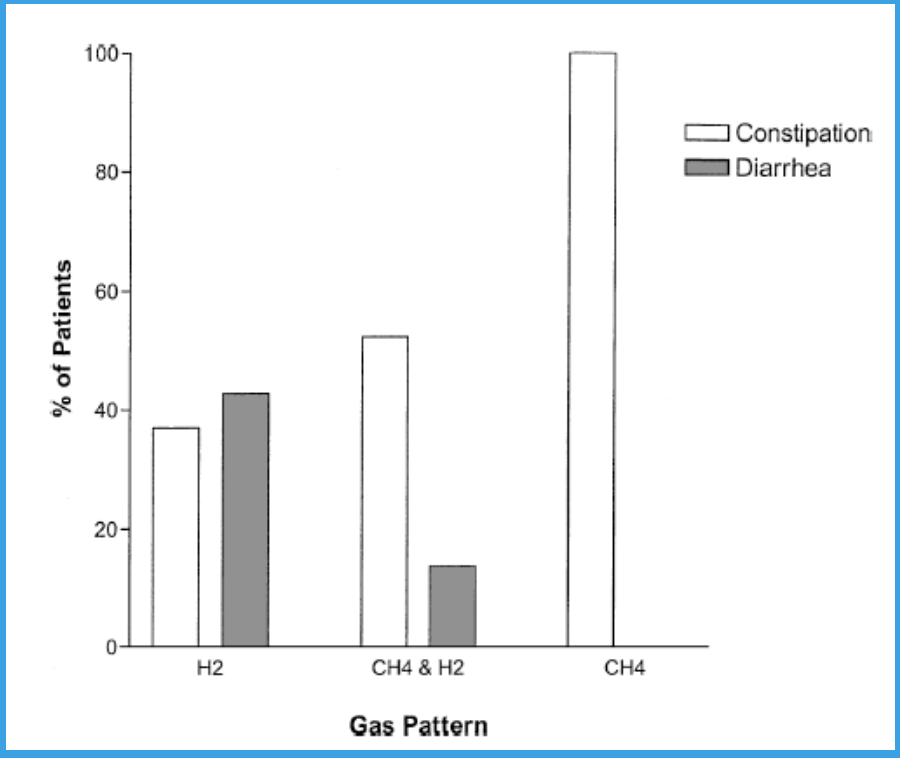
Implications

- **Reduction in bifidobacteria on low FODMAP diet may mean**
  1. **Nothing**
     - **Dietary modifications frequently alter microbiota, but even if the diet is continued, microbiota has been seen to return to normal after 3 months**
  2. **FODMAP restriction has a negative impact on microbiota**

Methane and constipation

- Production of hydrogen or methane depends on the type of microflora in the gut
- Evidence to suggest that methane production is linked to constipation-predominant conditions
- Suggested that methane slows transit

Methane Production During Lactulose Breath Test Is Associated with Gastrointestinal Disease Presentation



The Degree of Breath Methane Production in IBS Correlates With the Severity of Constipation

Soumya Chatterjee, M.B.B.S., Sandy Park, B.A., Kimberly Low, B.A., Yuthana Kong, M.P.H., and Mark Pimentel, M.D., F.R.C.P.(C)

Cedars-Sinai Medical Center, Burns and Allen Research Institute, Los Angeles, California

(Am J Gastroenterol 2007;102:837–841)

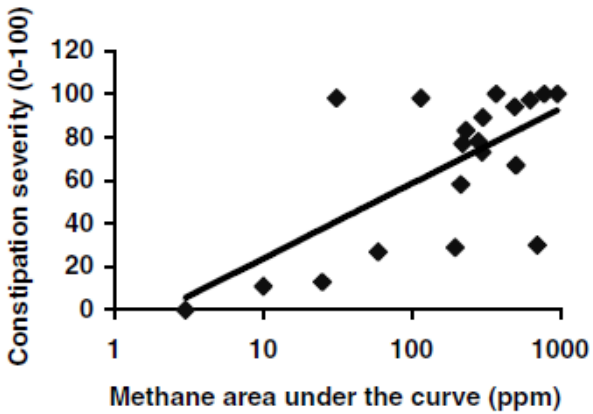


Figure 1. Correlation between degree of methane production (area under the curve) and subjective constipation severity. r = 0.60, $P <$ 0.01. The constipation is determined by VAS from 0 to 100 mm with 100 being most severe.

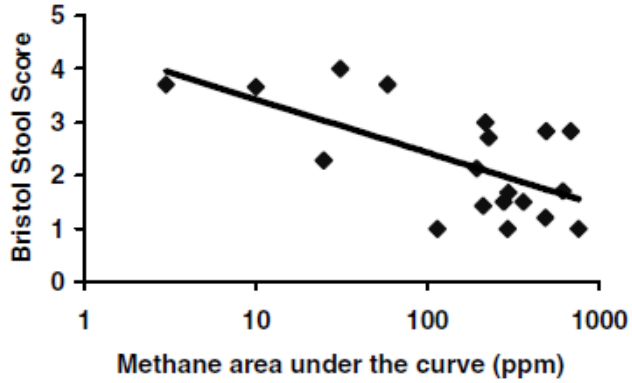


Figure 3. The correlation between the amount of methane on LBT (area under the curve) and Bristol Stool Score. r = −0.58, $P < 0.01$. This graph includes only 19 patients since one patient had no bowel movements the entire week to provide a score.

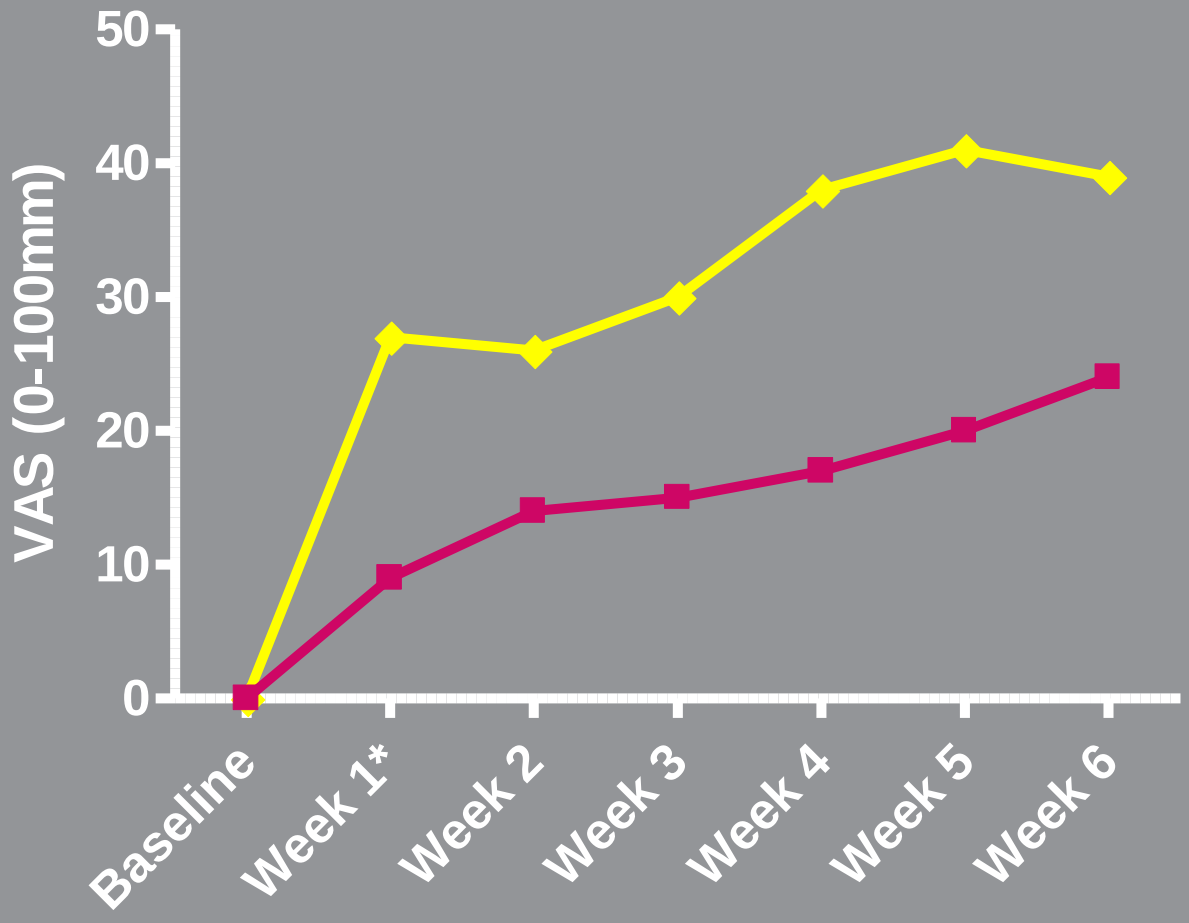
Implications

- IF
  - Methane production is a contributor to slow transit constipation
  - AND, FODMAP production reduces fermentation gases
    - Provides evidence for use of the FODMAP diet for constipation predominant disorders of the bowel

Non-coeliac gluten intolerance

- Many people assume gluten intolerance is major cause of symptoms in those without coeliac disease
  - Pushed by alternative health practitioners and gluten free product manufacturers
- Never formally researched
- Jess Biesiekierski undertook
  - Double-blind, randomised, placebo-controlled challenge pilot trial in those with self-diagnosed gluten intolerance, with no coeliac disease

Change in overall symptoms



VAS score: 100=worst 0=none

*p=0.047; Independent Samples t-test

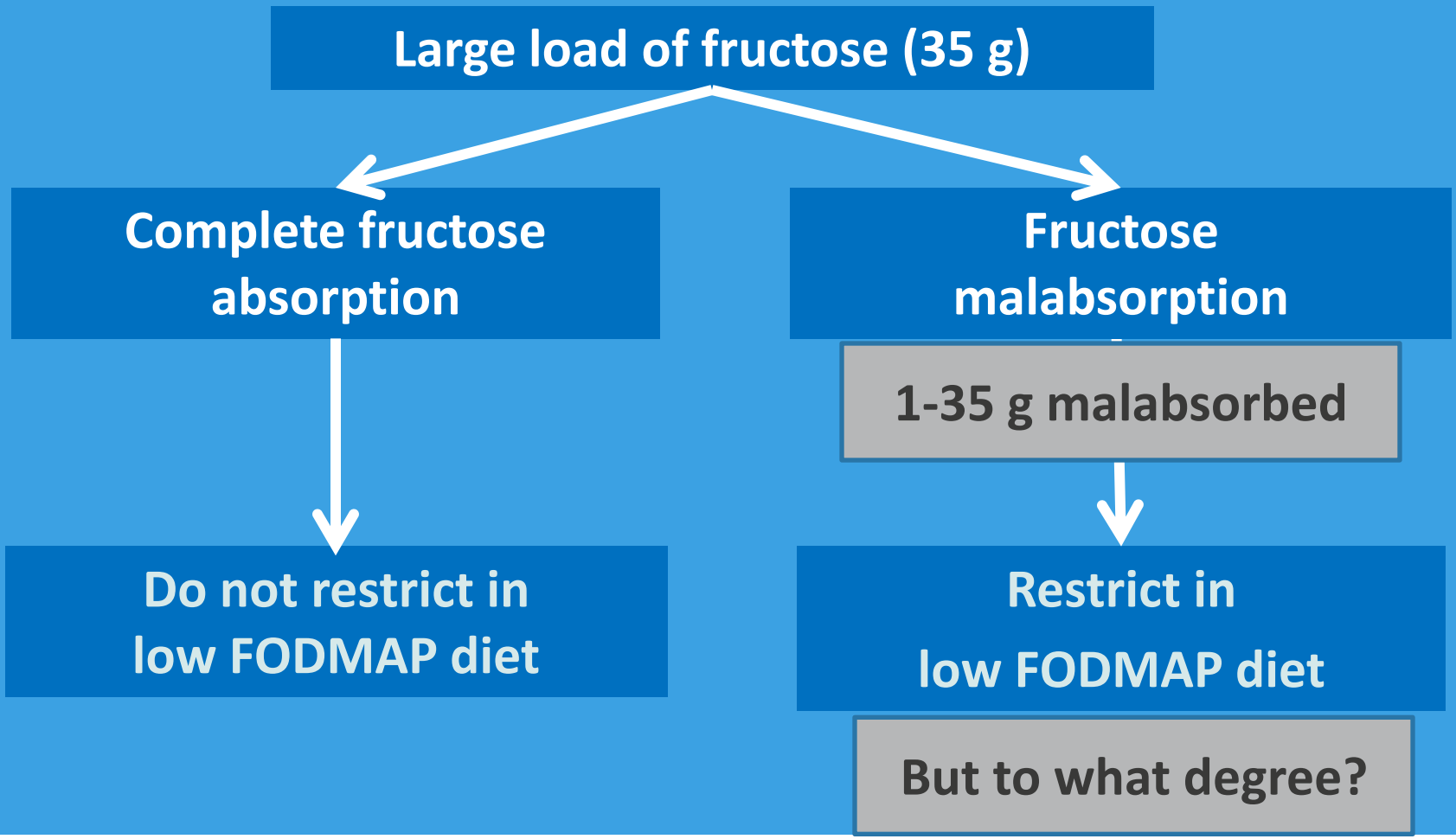
Non-coeliac gluten intolerance

- Follow up PhD studies failed to confirm these findings
  - Subjects were enrolled if they stated their symptoms controlled completely on gluten free diet
  - BUT, study involved further restricting their diet with reduction of FODMAP intake
    - Major improvement in symptoms seen, despite previously stating symptom free

- This suggests that perhaps FODMAPs are more of a problem for these patients all along, and benefit seen from a gluten free diet, may be caused by the concurrent reduction in FODMAPs

Semi-quantitative breath test analysis

Interpreting hydrogen breath testing

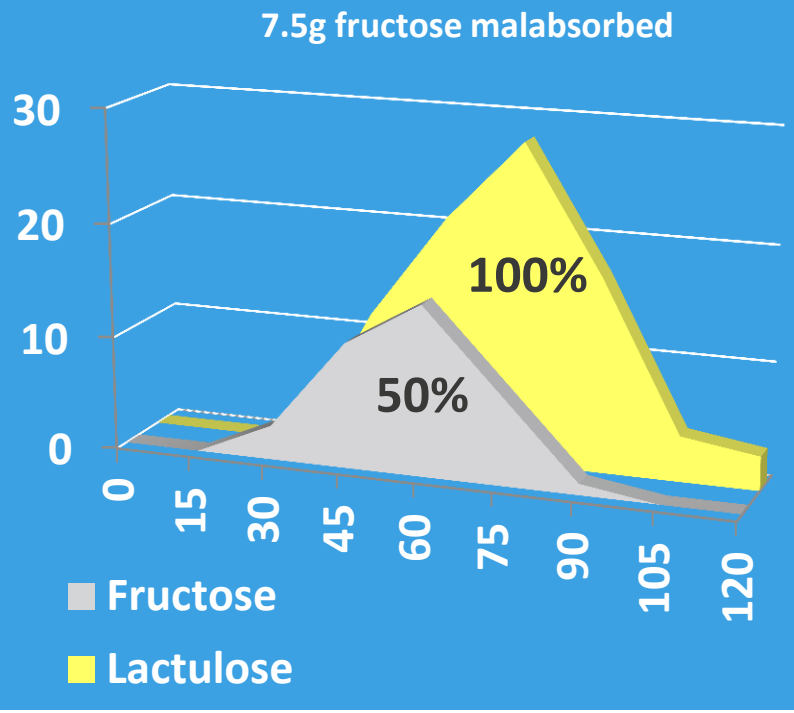


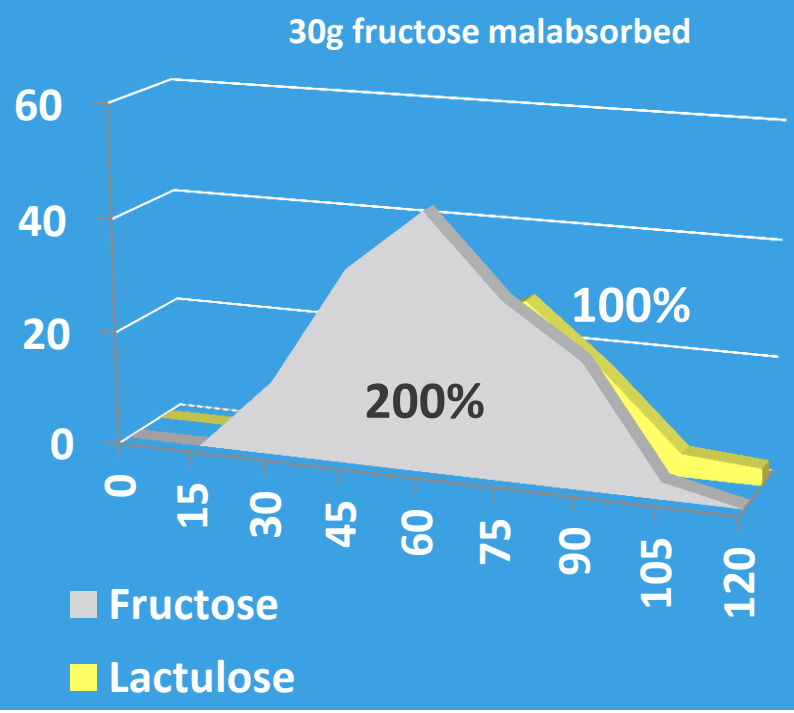
Semi-quantitative methodology

Fructose malabsorbed =

(Fructose AUC/Lactulose AUC) x 15 g

assuming 100% of lactulose is malabsorbed





Semi-quantitative methodology

- **Malabsorption categorised as:**
  - ***Nil* (<10%)**
  - ***Small degree* (10-30%)**
  - ***Convincing* (>30%)**

Implications

- Semi-quantitative reporting of breath hydrogen tests
  - is simple
  - could be utilised for lactose and sorbitol
- As a dietitian, this may allow a more lenient approach to dietary restrictions for symptom management
  - Important nutritionally – maintain intake of moderate lactose-containing dairy products, moderate fructose/sorbitol fruits and vegetables
  - A controlled trial is needed to confirm this

Enteral feeding associated diarrhoea

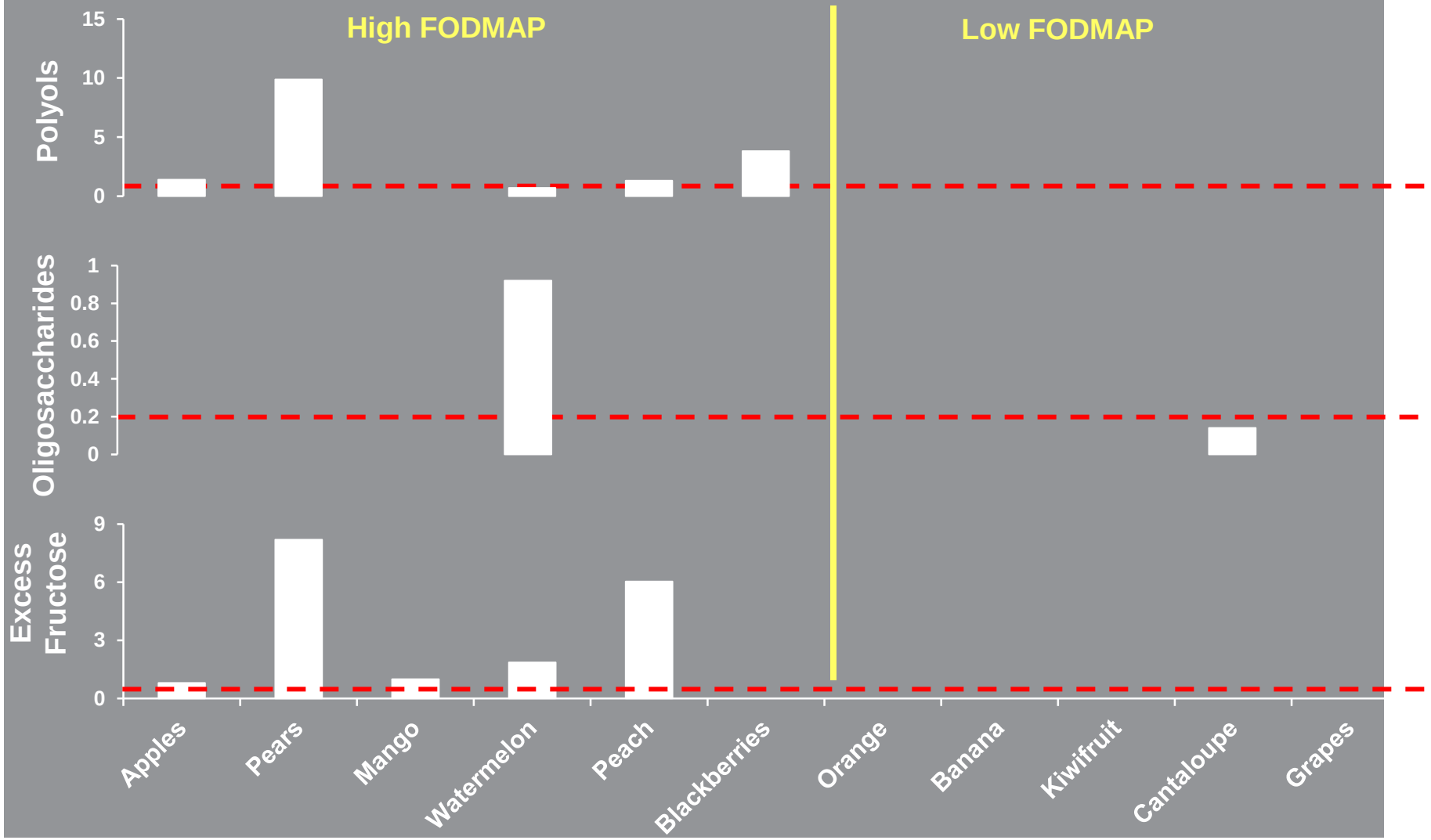
Emma Halmos' PhD work has demonstrated a possible link between

FOOD COMPOSITION

Food composition

- Quantifying FODMAPs in food is a time-consuming process
  - Takes 4-6 weeks
  - Expensive laboratory testing
- Many foods have more than one FODMAP carbohydrate
- 'Cut-off' levels based 'clinical experience', are now backed up with research evidence
  - Excess fructose (0.2 g/serve)
  - Oligosaccharides (GOS + fructans)(0.2 g/serve or 0.35g/serve for grains and cereals)
  - Sugar polyols (0.5 g/serve)

Fruits (g/serve)



Food composition

- Food lists have changed over the years
  - New foods being tested
  - Alteration to “cut-off” levels as we learn more about individual tolerance

- The internet is therefore a disaster in terms of reliability for FODMAP information
  - Garlic and rye are on old safe lists when they are in fact rich sources of FODMAPs
  - Green beans and cantaloupe are completely safe, but have appeared on high FODMAP food lists in the past

Monash University Low FODMAP Diet

- To ensure people understand where to get the most up-to-date information, our research department has now termed the diet

The Monash University Low FODMAP Diet

- All our future publications will label the diet as such so that we can separate ourselves from incorrect information on the public domain
- Our Monash University Low FODMAP Diet Booklets will continue to be produced and updated annually. This is the best way for health professionals to stay up to date with changes to food lists
- Our department has moved to The Alfred, Monash University, Central Clinical School, and therefore our website has changed to

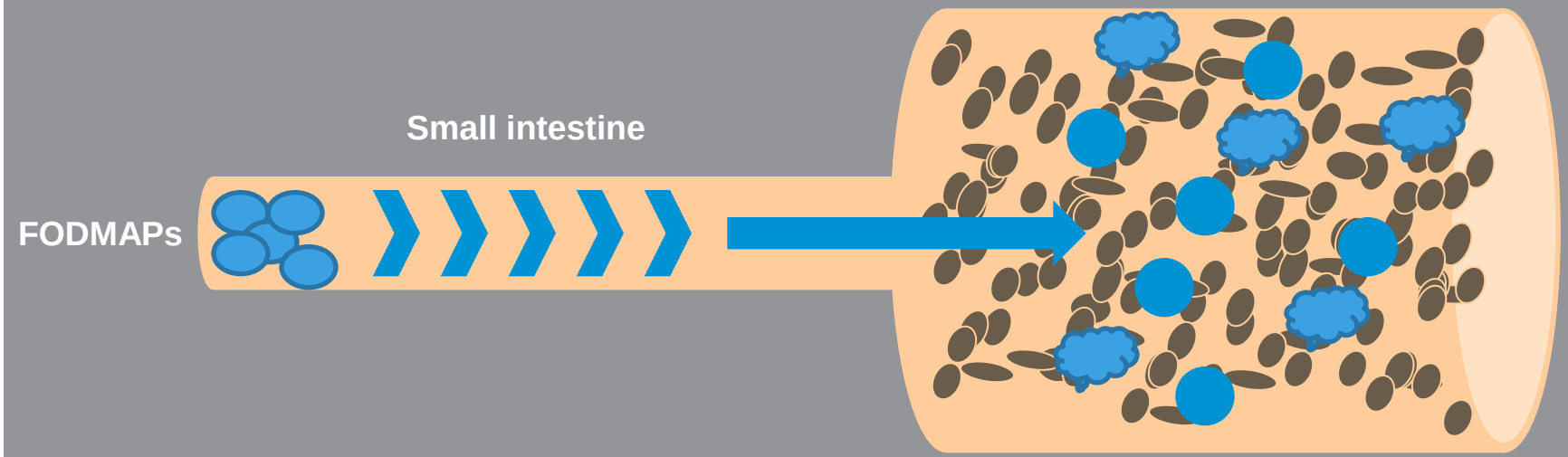
http://www.med.monash.edu/cecs/gastro/index.html

FODMAPS IN HEALTH AND GASTROINTESTINAL DISORDERS

FODMAPs in health and gastrointestinal disorders

- FODMAPs can be poorly absorbed in both healthy and IBS sufferers
- So what differs between healthy and IBS sufferers that causes symptoms?
- IBS Pathophysiology
  - Altered microflora
  - Hypersensitivity to luminal distension
  - Motility disorders

Diarrhoea-predominant IBS



↑ water delivery

↑ gas production

Luminal distension

Altered motility

Pain, bloating, distension, wind, *diarrhoea*

Constipation-predominant IBS

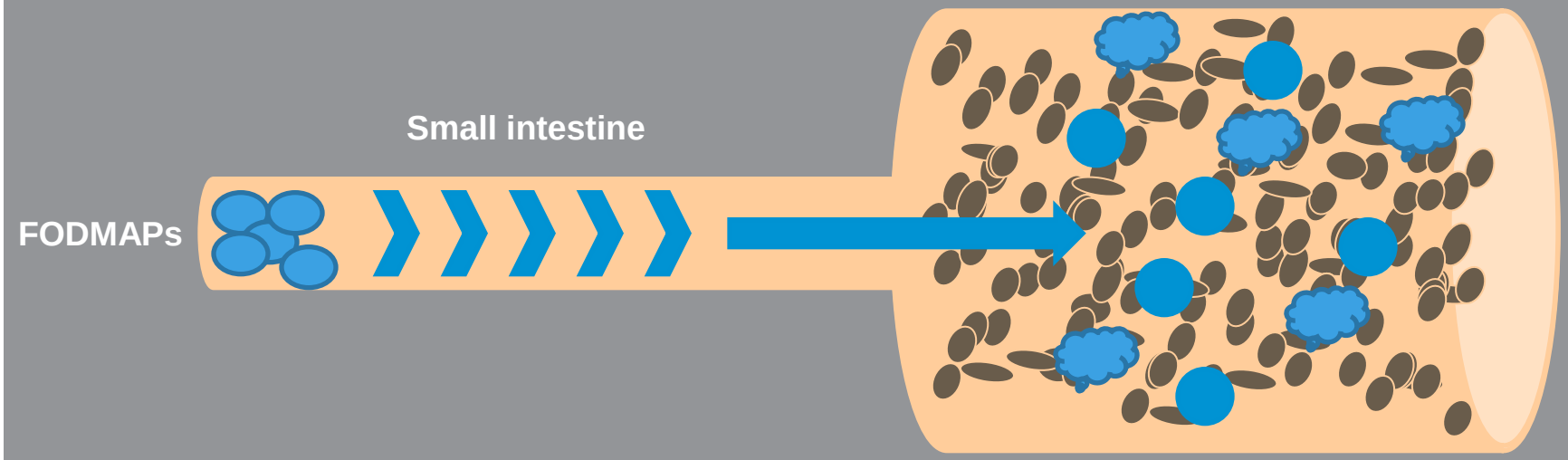
↑ gas (CH_4) production

Luminal distension

Altered motility

Pain, bloating, distension, wind, *constipation*

Healthy subjects



↑ water delivery

↑ gas production

→ Natural laxation, SCFA production, wind

SUMMARY

Summary

➔**FODMAPs, ingested as part of a meal**

- **increase delivery of water and fermentable substrate to the proximal colon**
  - **Laxative effect that may be problematic in those with diarrhoea**
- **are fermented by intestinal microflora resulting in gas production across the day**
  - **Contributes to other IBS symptoms, bloating, wind, abdominal pain and constipation**

Summary

- **Fructose and/or FODMAP malabsorption are not disorders**
  - **Fructans and GOS are malabsorbed in all of us**
  - **Fructose is malabsorbed in 33% of healthy individuals**
  - **~50-60% prevalence of sorbitol and mannitol malabsorption in healthy individuals**

- **Malabsorption of FODMAP carbohydrates has beneficial effects on gut health**

Summary

- In the setting of a functional gut disorder, these beneficial effects may be overshadowed by the contribution to symptoms made by these carbohydrates due to
  - Altered gut flora
  - SIBO
  - Hypersensitivity
- A low FODMAP diet should be encouraged as a trial to manage IBS symptoms
- Individuals with IBS on a low FODMAP diet need only comply as strictly as their symptoms require (or they are happy with)
- Reintroduction of FODMAPs should be encouraged to the level of tolerance in all patients, due to the potential benefits of FODMAPs, i.e. SCFA production

Summary

- The research to date provides physiological explanation for why a low FODMAP diet improves functional gut symptoms
- Also suggests broad application of the diet
  - Functional symptoms in IBS, IBD and Coeliac disease
  - High ileostomy output
  - Enteral feeding intolerance
  - Toddler's diarrhoea

- Health professionals should look for the phrase

"Monash University Low FODMAP Diet"