UNIVERSITY OF GOTHENBURG

Gruppo Italiano per lo Studio della Motilità dell'Apparato Digerente

Role of Intestinal Microbiome in Gastrointestinal diseases

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Dept of Internal Medicine, Institute of Medicine

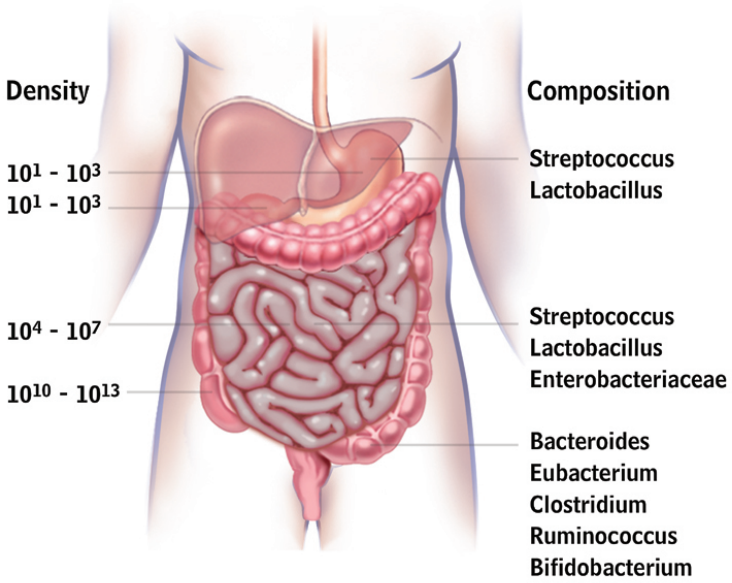
Sahlgrenska Academy

University of Gothenburg

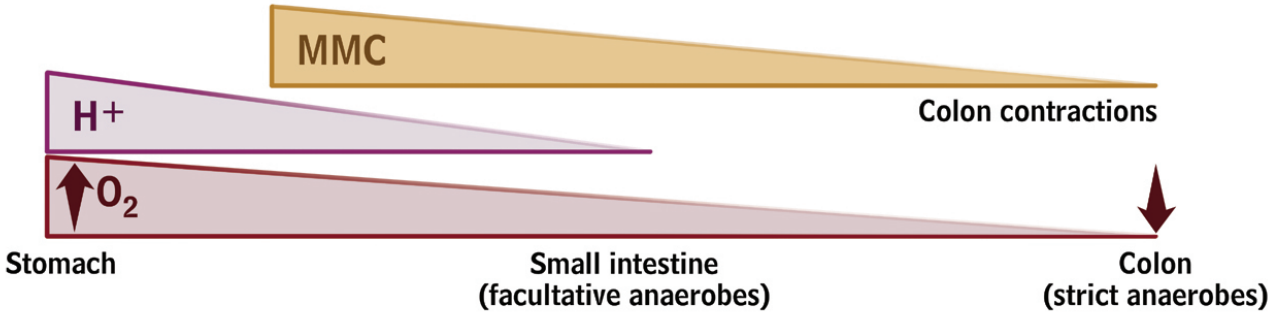
Gothenburg, Sweden

The Sahlgrenska Academy

Intrinsic and extrinsic factors affecting gut microbiota distribution and composition

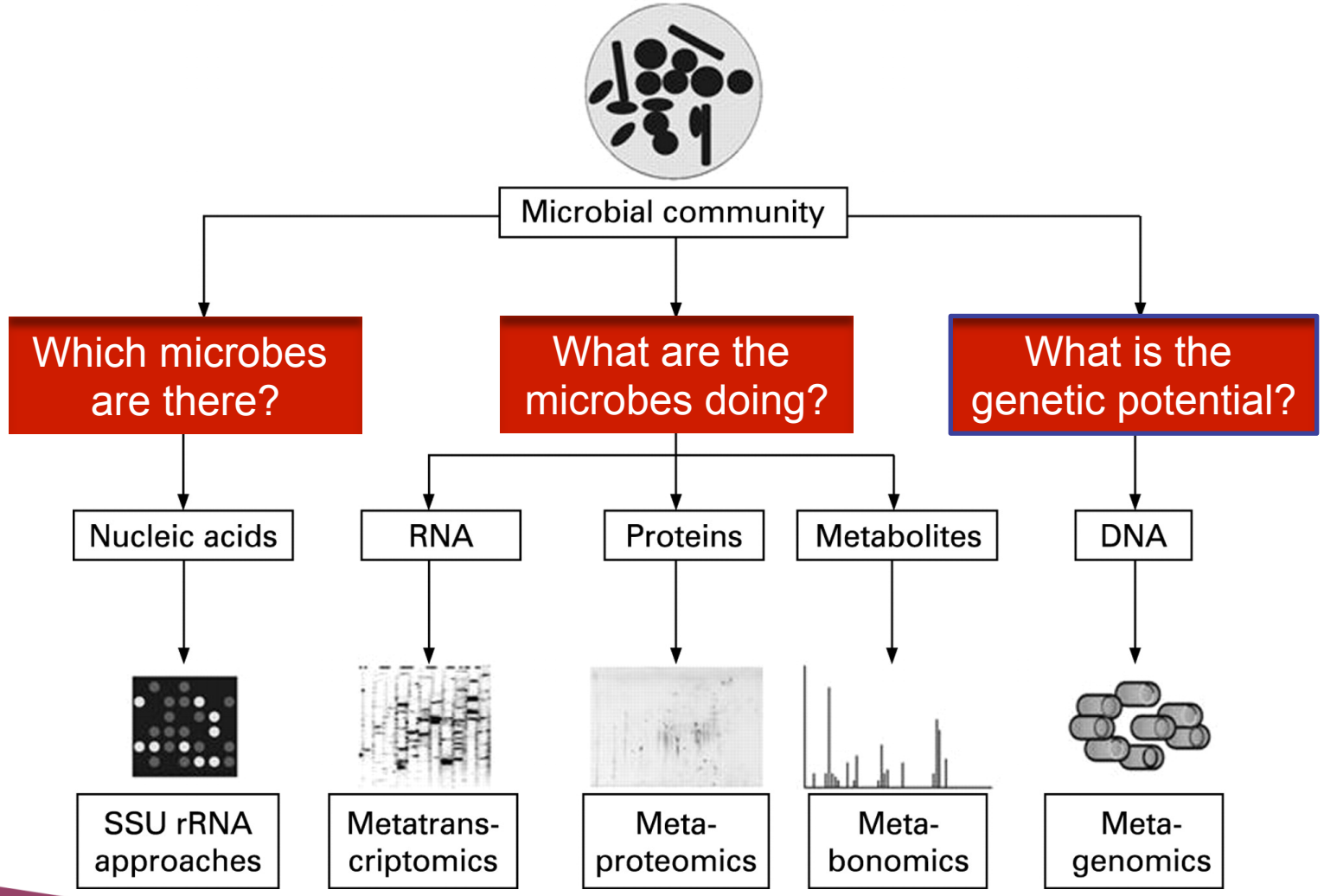


Intrinsic factors	Extrinsic factors
Gastric acid	Diet, Pre and probiotics
O_2	PPIs, H2 blockers
Motility	Antibiotics
Mucus	Prokinetics
GI secretions	Laxatives
Antimicrobial peptides	Opioids
Immunity (sIgA)	NSAIDs



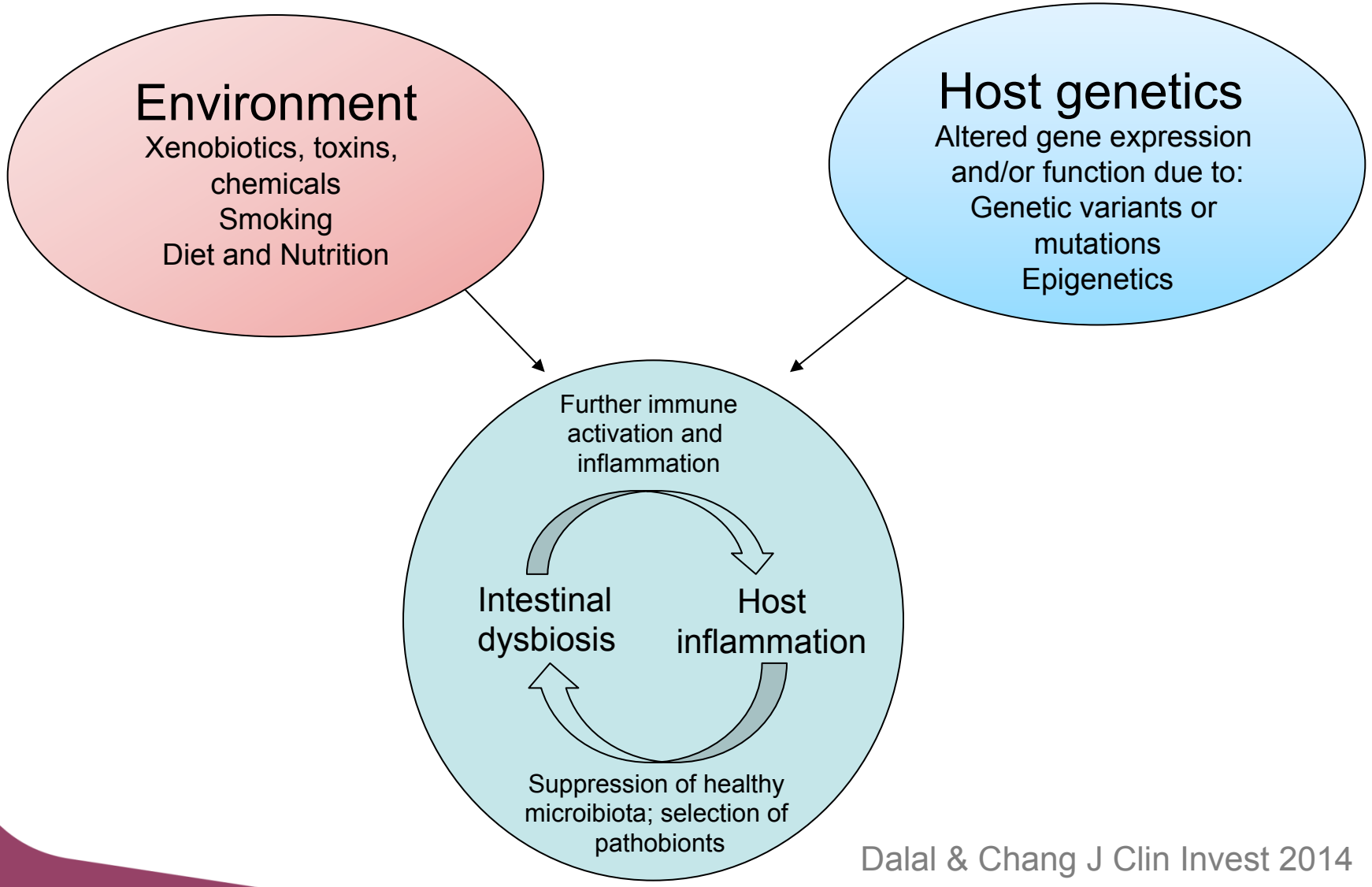
Rome Foundation Working Team - Intestinal microbiota in FBD.
Simren et al Gut 2013

Studying microbiota composition and function



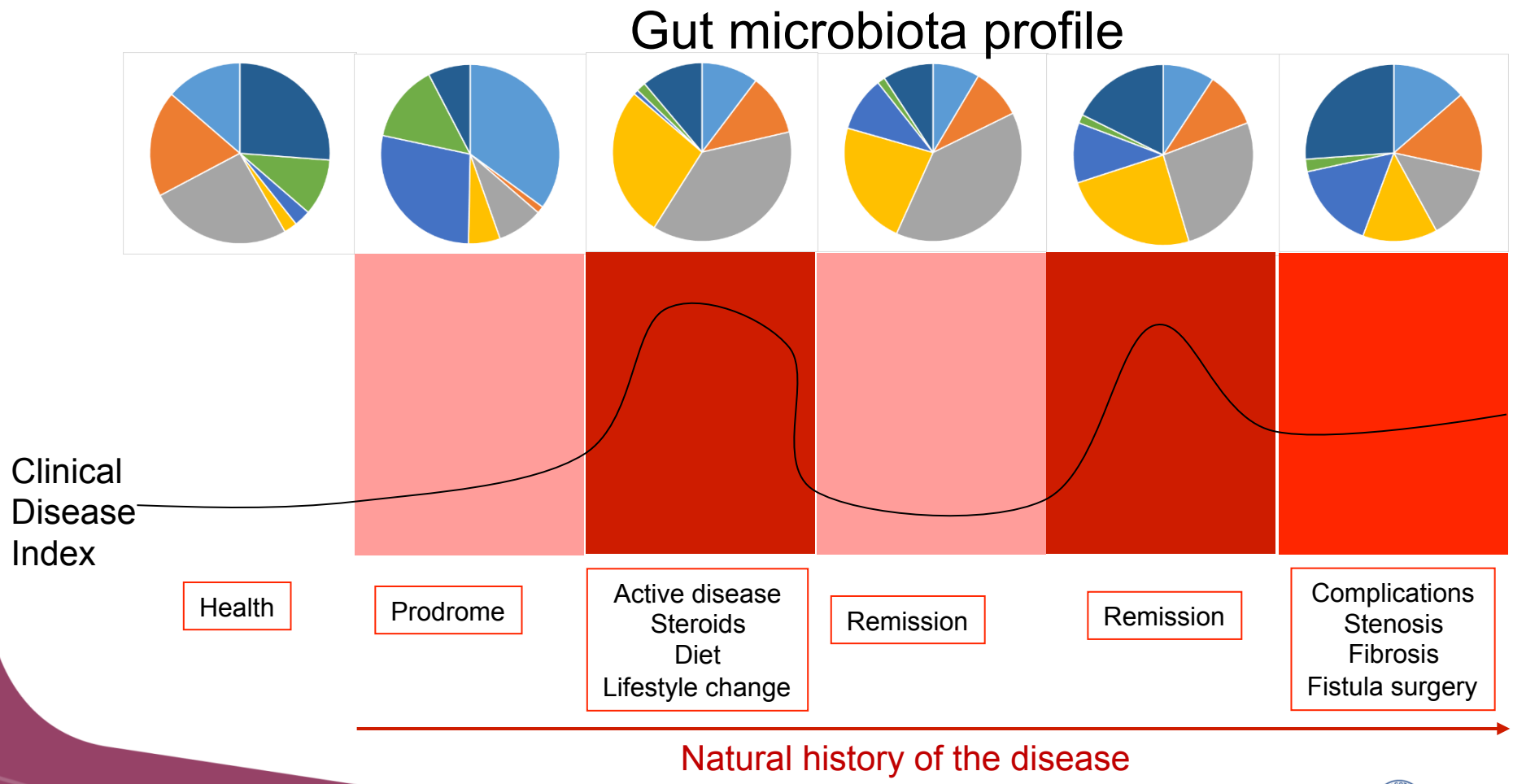
Zoetendal E G et al Gut 2008

Inflammatory Bowel Diseases



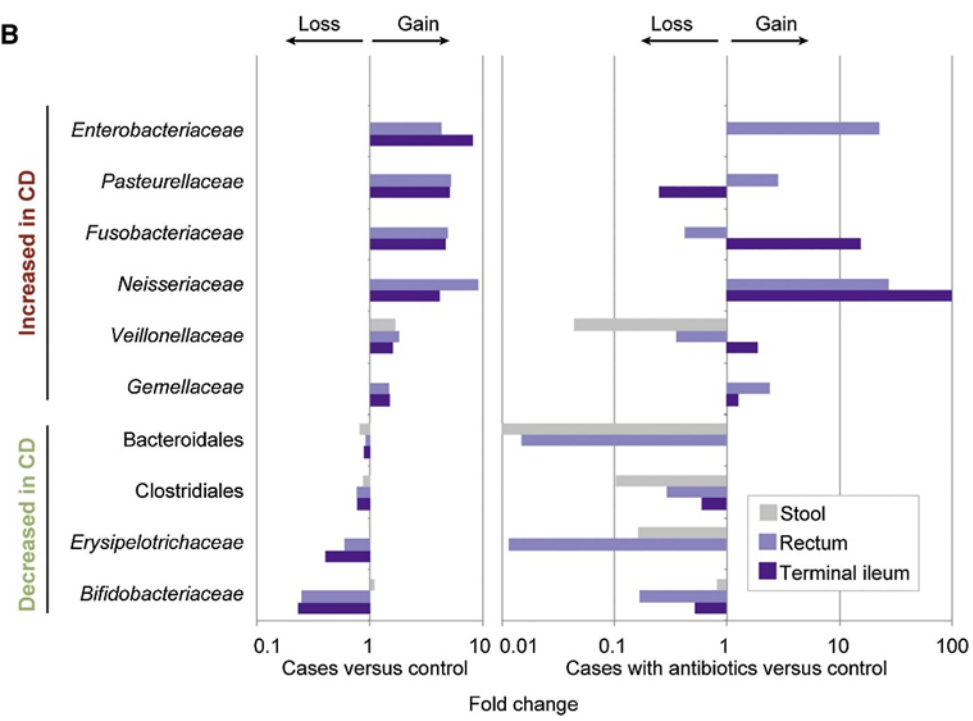
Dalal & Chang J Clin Invest 2014

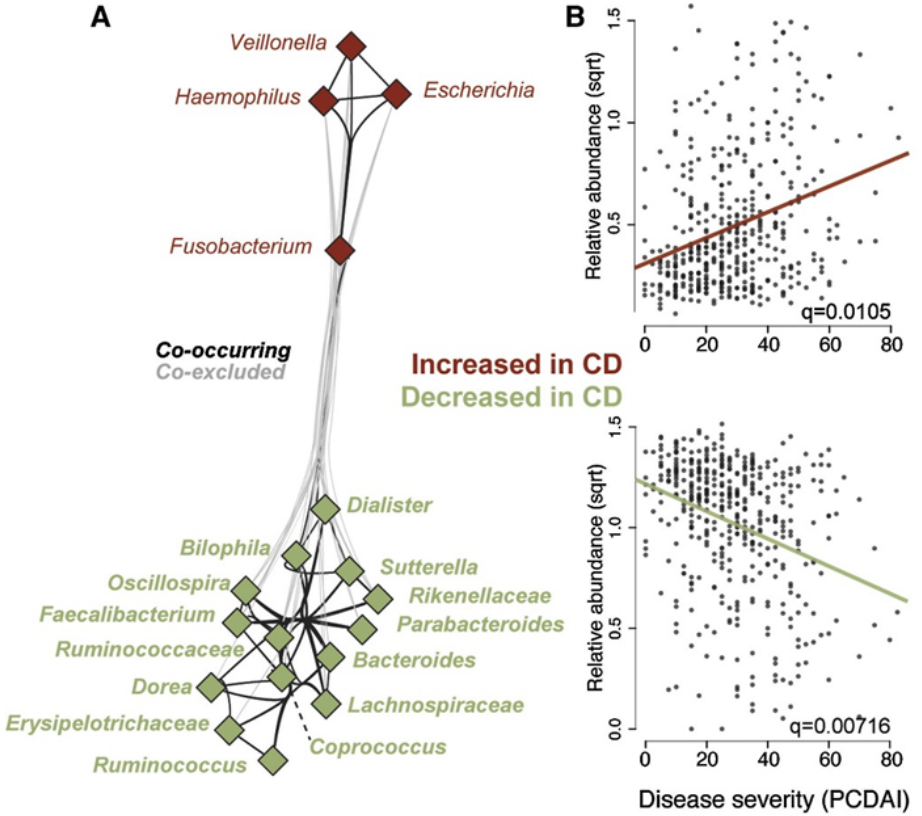
IBD – chronic, progressive diseases
Gut microbiota changes



Dalal & Chang J Clin Invest 2014

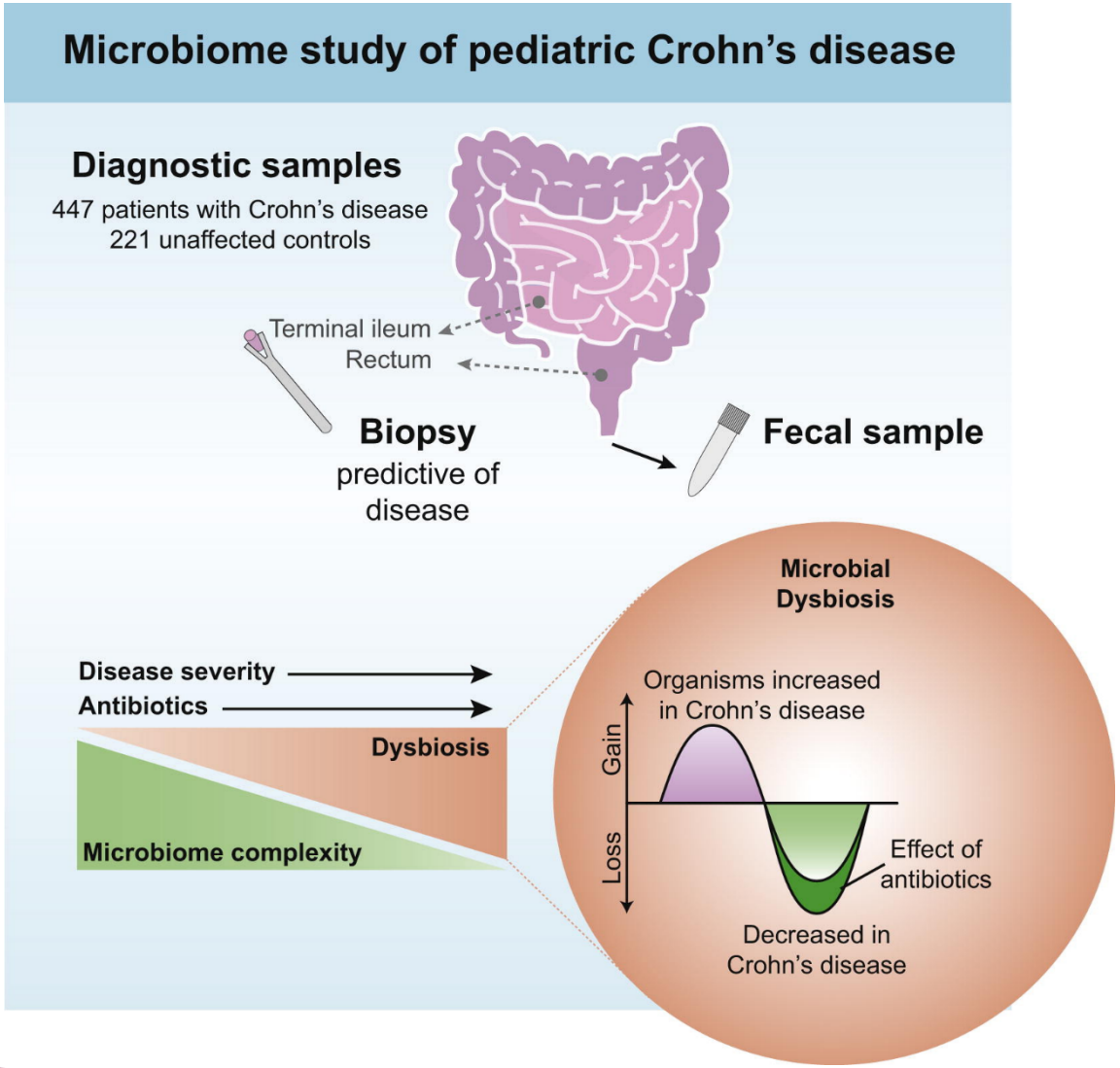
The Treatment-Naive Microbiome in New-Onset Crohn's Disease





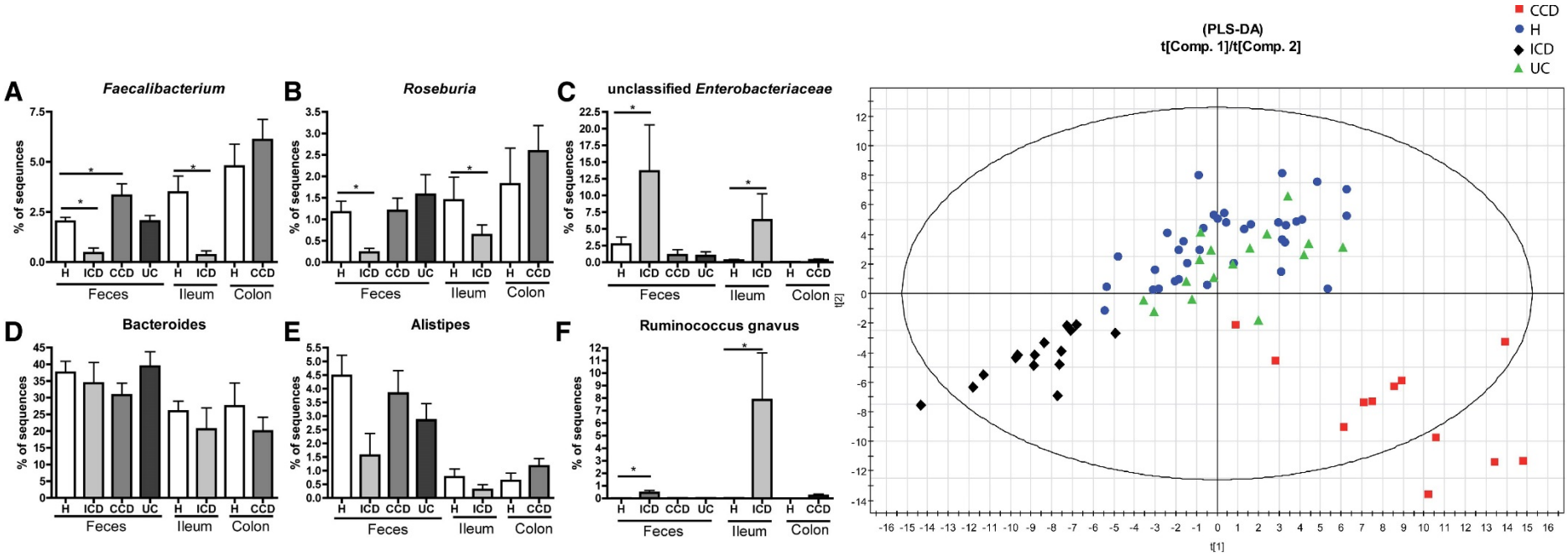
Gevers et al Cell Host Microbe 2014

The Treatment-Naive Microbiome in New-Onset Crohn's Disease



Gevers et al Cell Host Microbe 2014

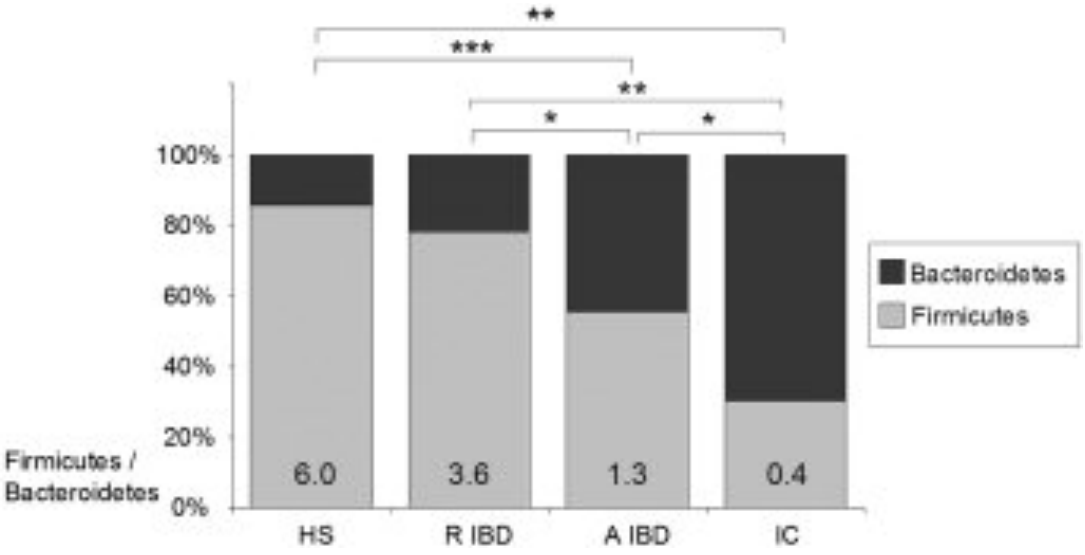
IBD: Discrimination of disease phenotype based on microbial composition

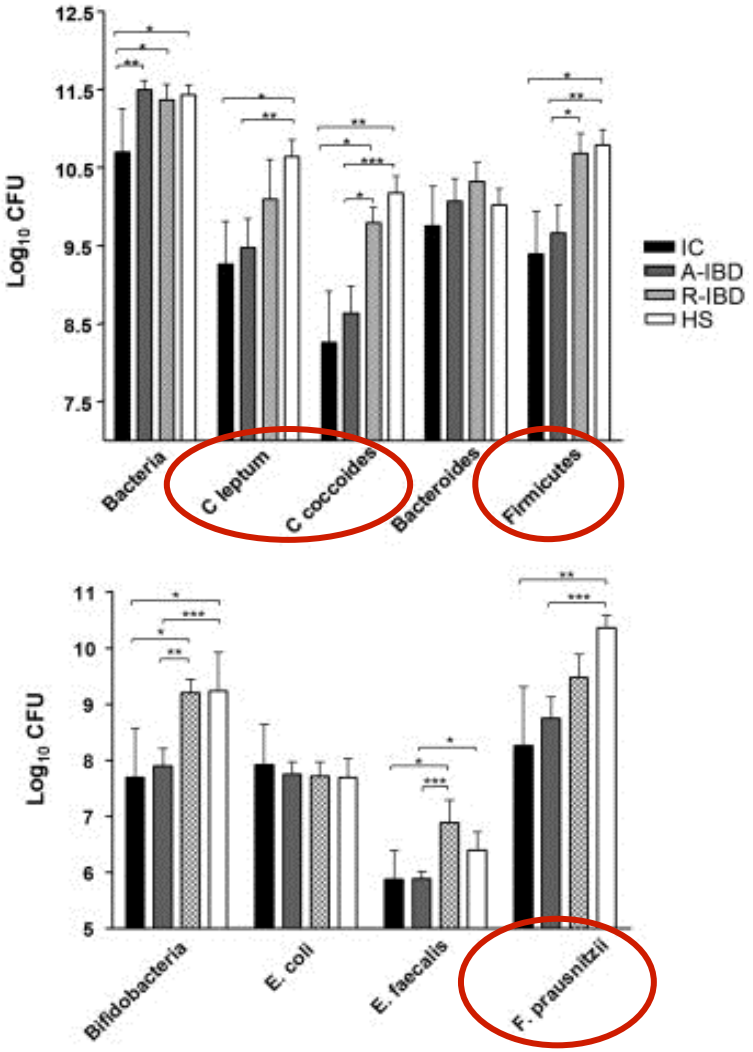


Willing et al Gastroenterology 2010

Low counts of Faecalibacterium prausnitzii in IBD

Firmicutes/Bacteroidetes ratio

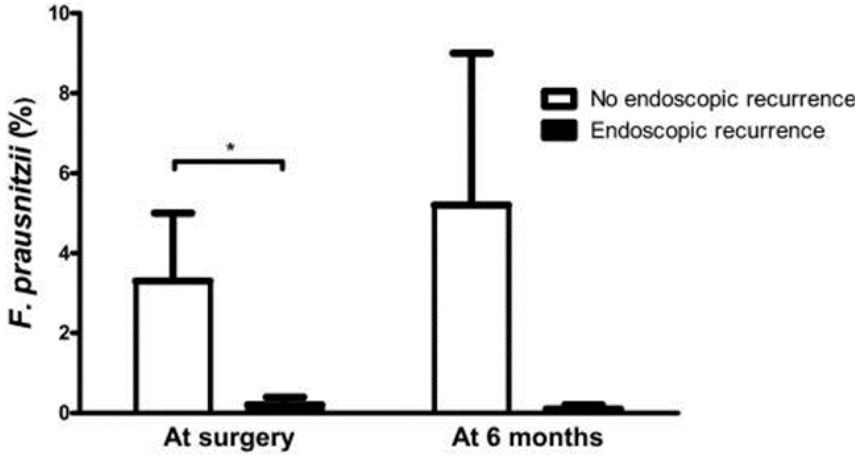




Sokol et al IBD 2009

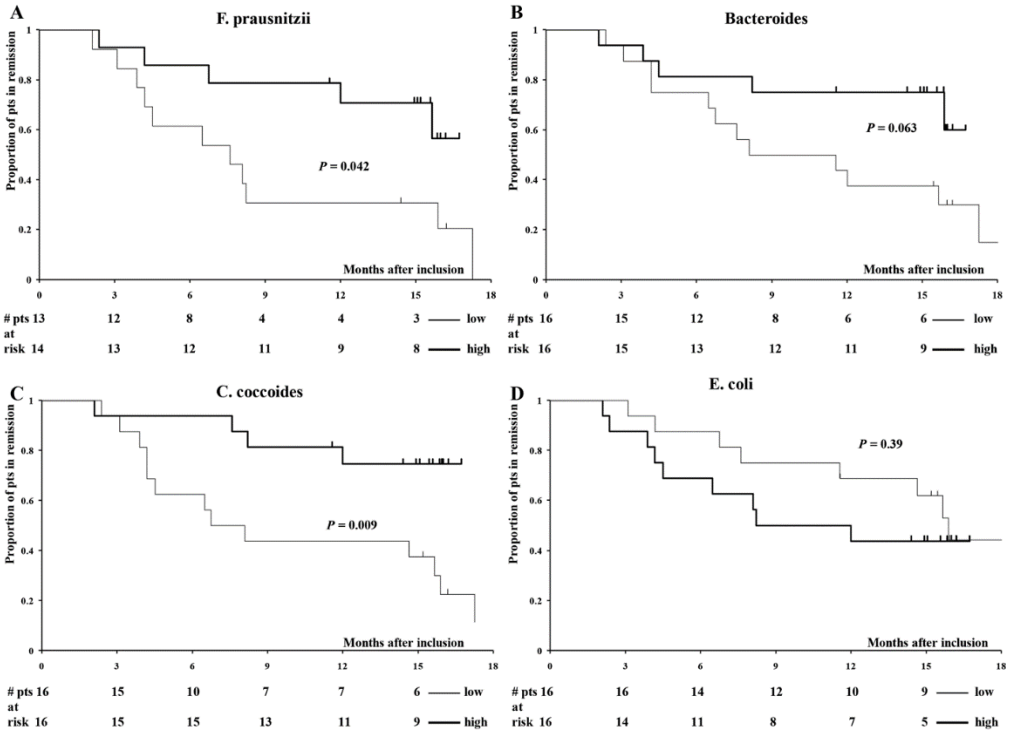
Gut microbiota – prognosis in IBD

Relapse after surgery



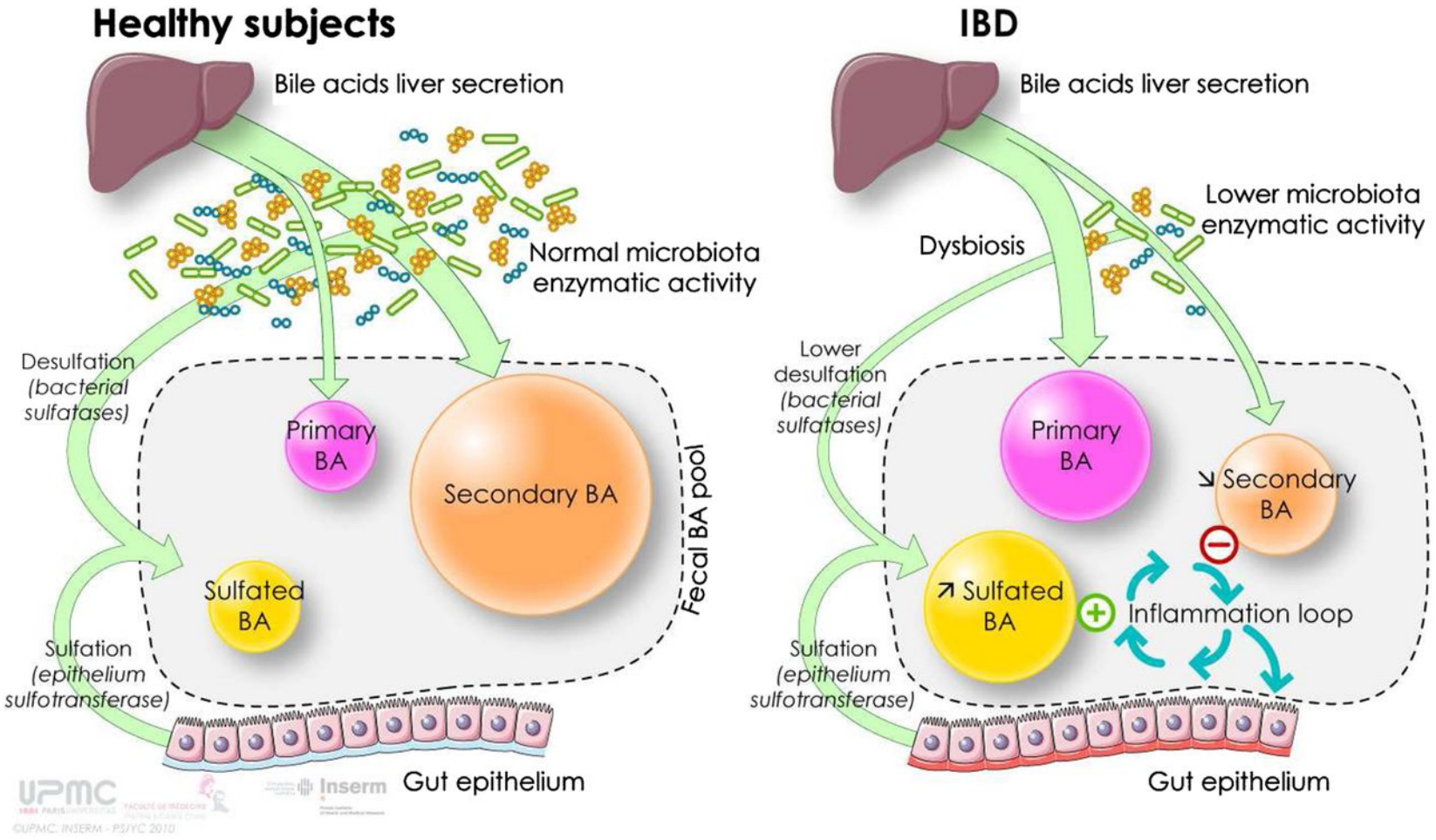
Sokol et al Proc Natl Acad Sci U S A 2008

Relapse after anti-TNF treatment



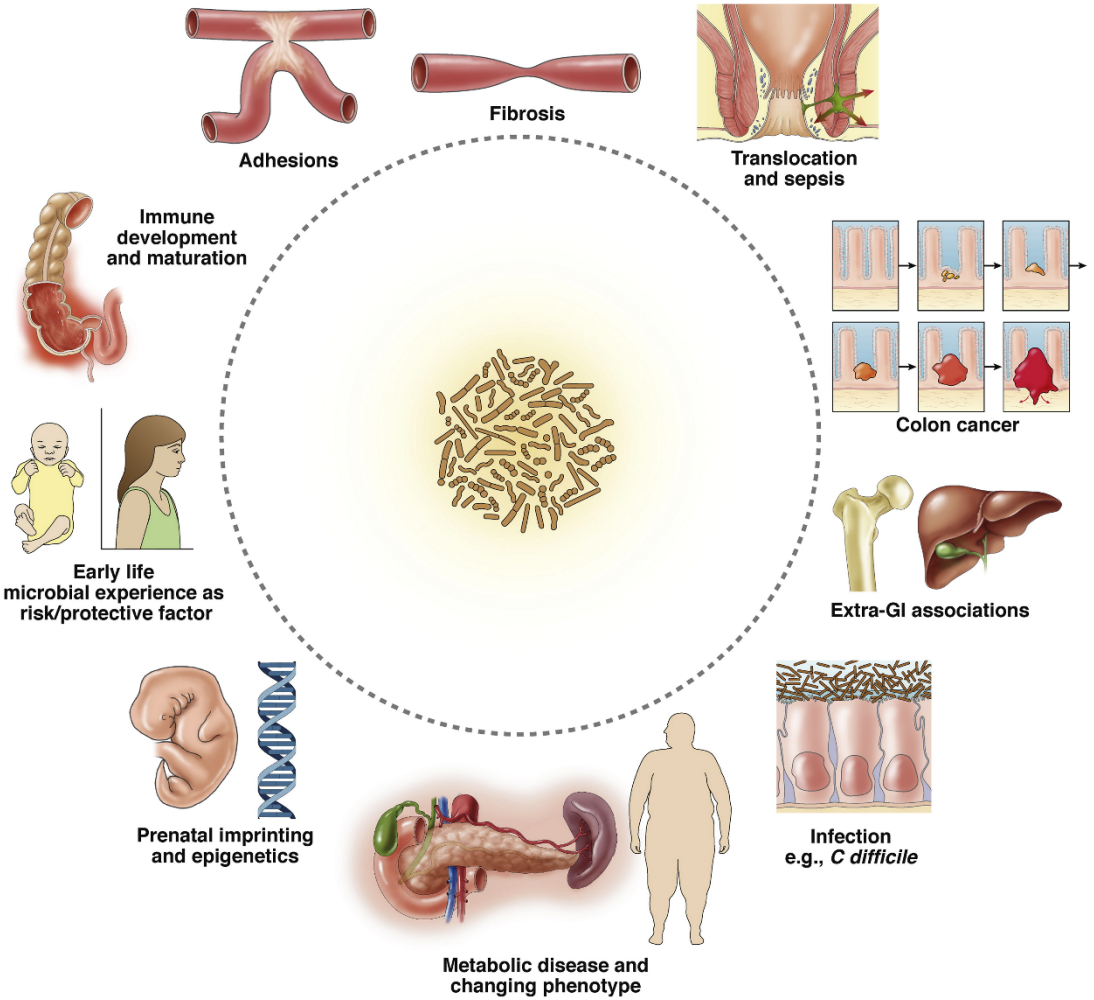
Rajca et al IBD 2014

Luminal bile acid dysmetabolism in inflammatory bowel diseases.



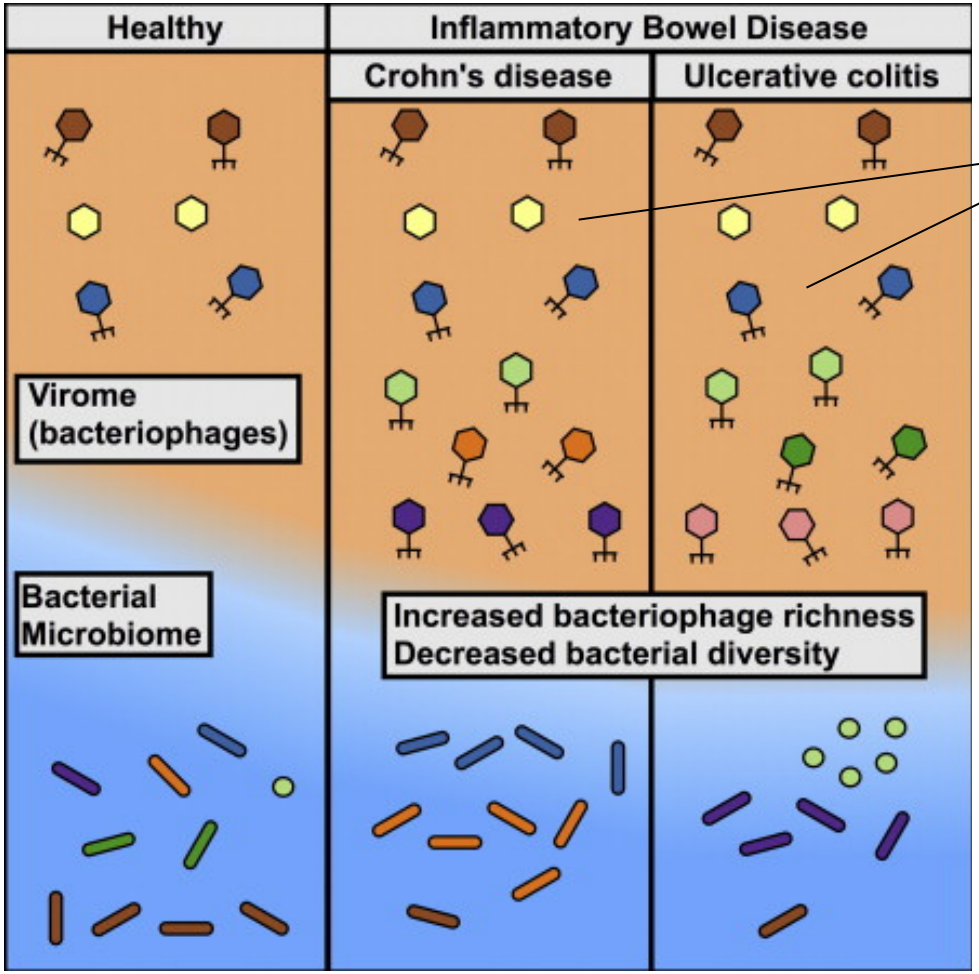
Duboc et al. Gut 2013

Effects of alterations in the microbiota on the development of IBD



Shanahan & Quigley Gastroenterology 2014

Disease-Specific Alterations in the Enteric Virome in Inflammatory Bowel Disease

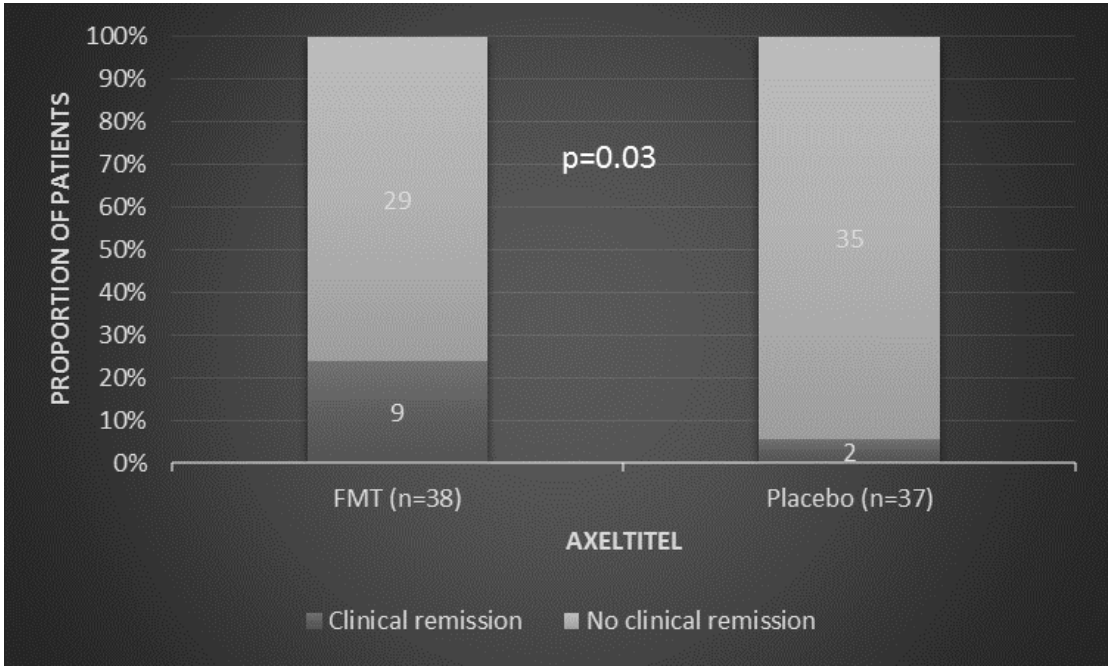


…expansion of the Caudovirales bacteriophages

"The enteric virome is abnormal in multiple cohorts of inflammatory bowel disease patients, exhibiting disease-specific features that are not explained by changes in bacterial diversity and richness."

Norman et al Cell 2015

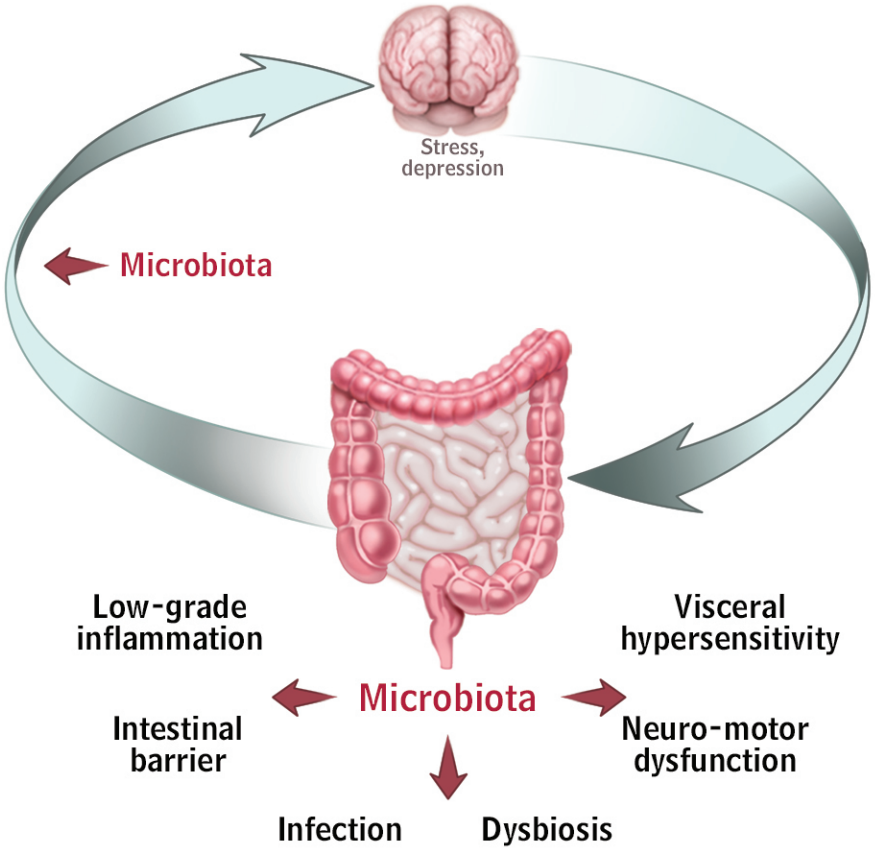
Fecal microbial transplantation in Ulcerative Colitis



- Response donor dependent
- Secondary endpoints not met
- No differences in adverse events
- Short duration of IBD – better response

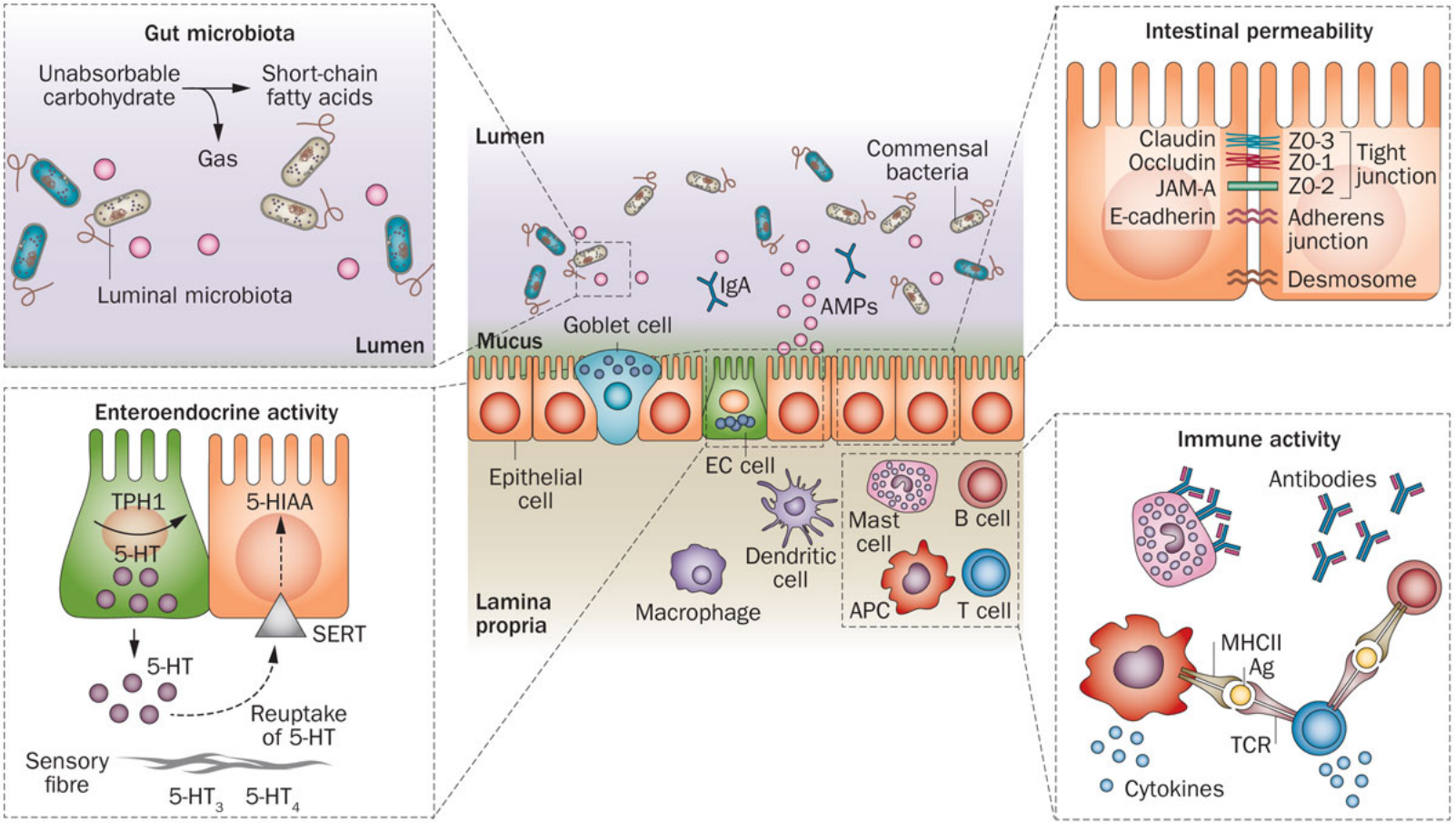
Moayyedi et al Gastroenterology 2015

Integrated conceptual framework of the pathophysiology of IBS.



Rome Foundation Working Team - Intestinal microbiota in FBD.
Simren et al Gut 2013

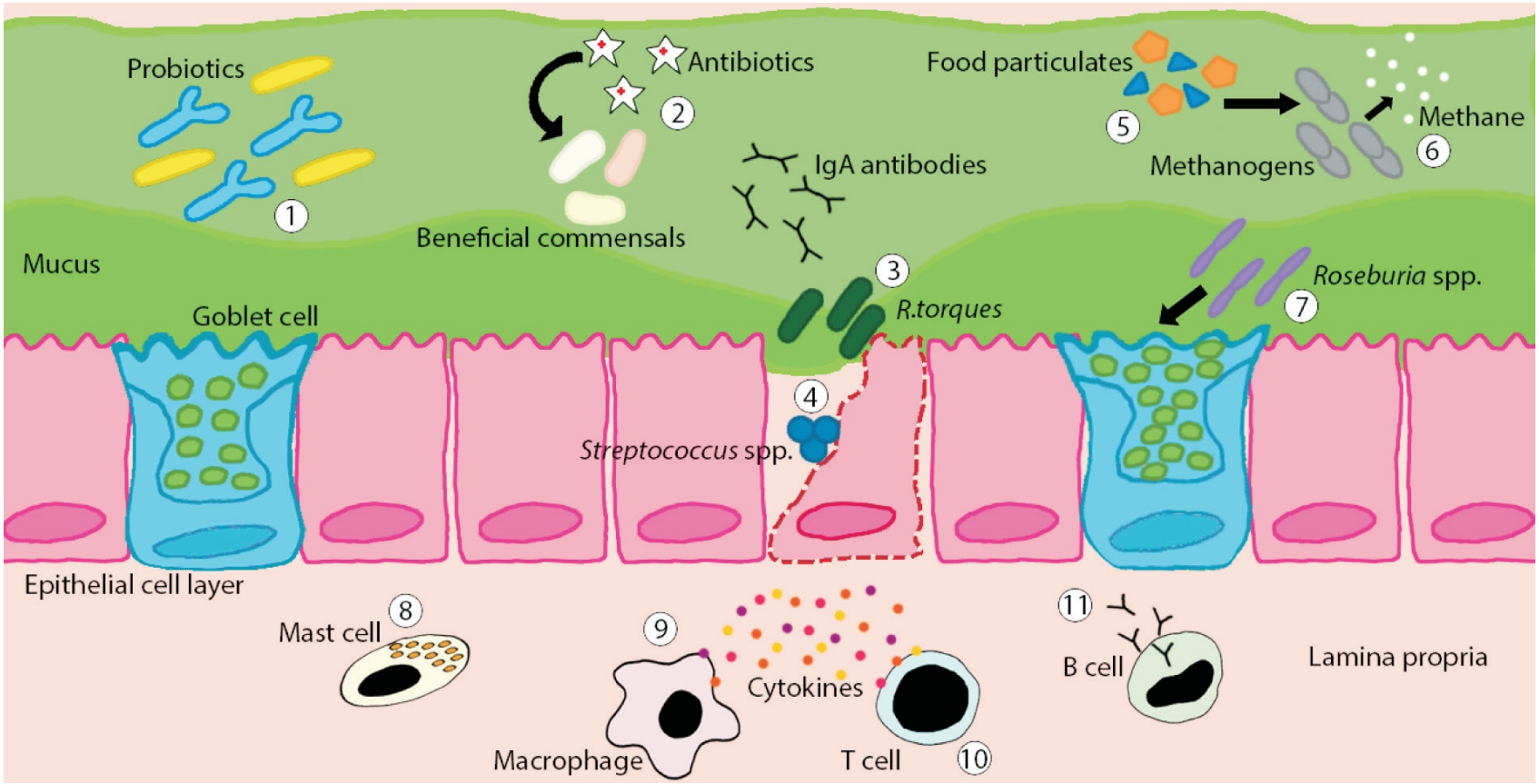
Peripheral factors involved in the pathophysiology of IBS



Nature Reviews | Gastroenterology & Hepatology

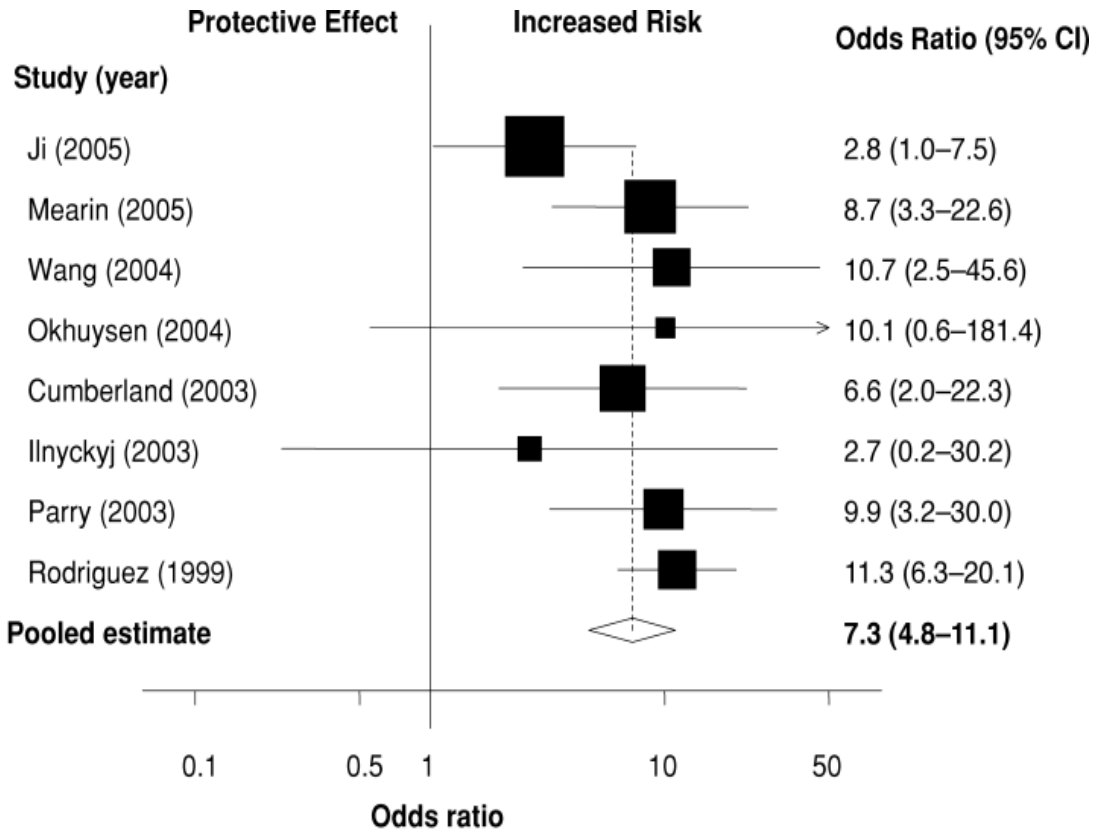
Öhman, Törnblom & Simrén Nat Rev Gastroenterol Hepatol 2015

Gut Microbiota as Potential Orchestrators of Irritable Bowel Syndrome



Bennet, Öhman & Simrén Gut and Liver 2015

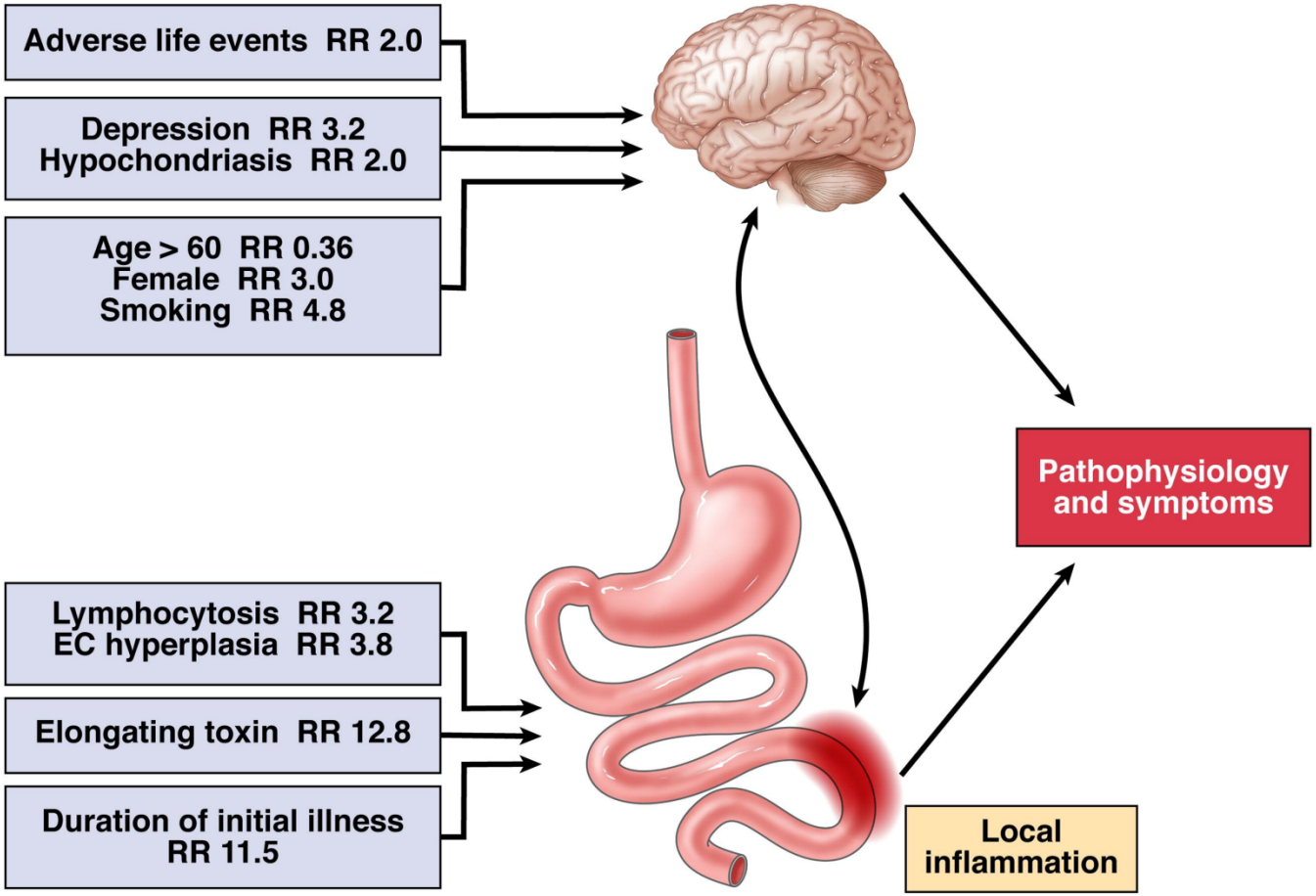
Postinfectious IBS – A meta-analysis



* size of boxes denotes inverse-variance weight of each study

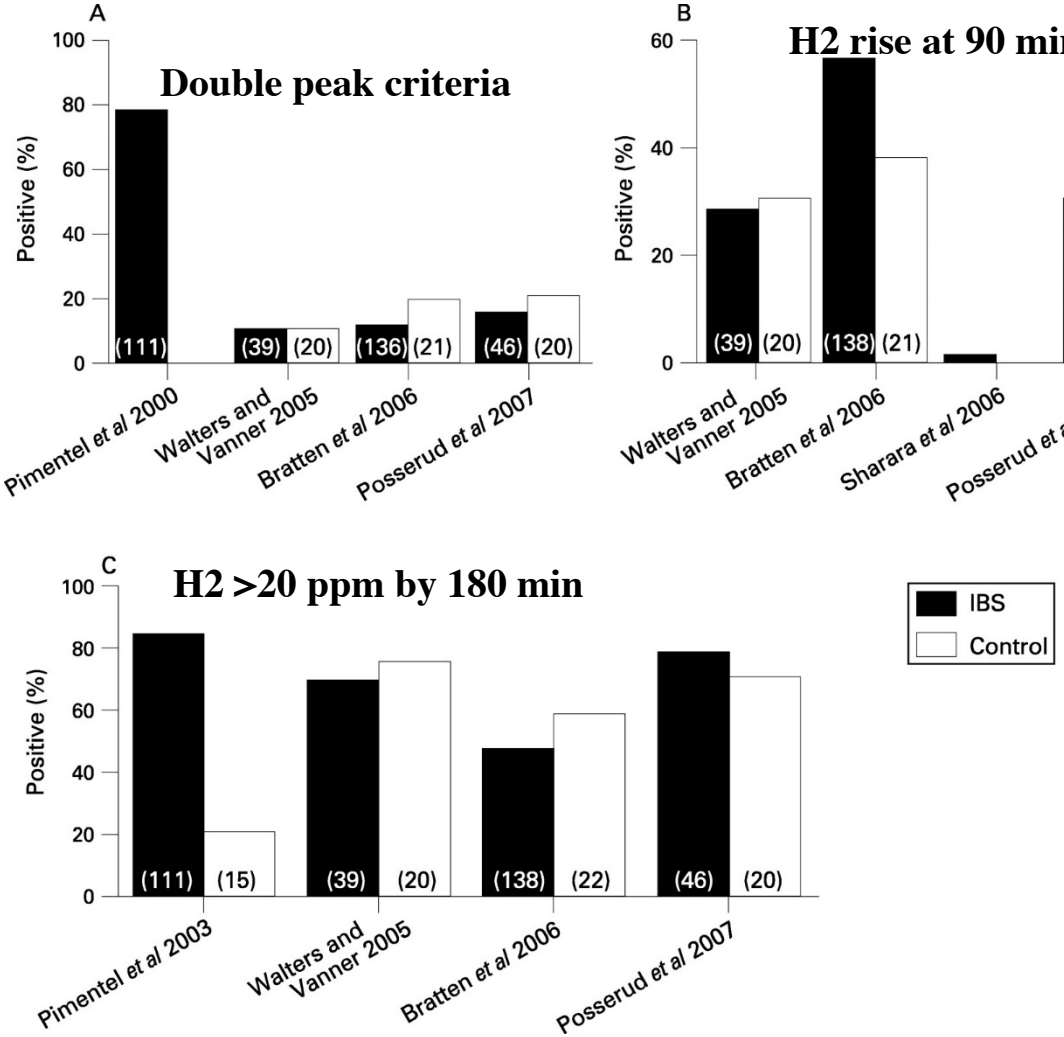
Halvorsen et al Am J Gastroenterol 2006

Risk factors for post-infectious IBS: Highlighting neuroimmune interactions



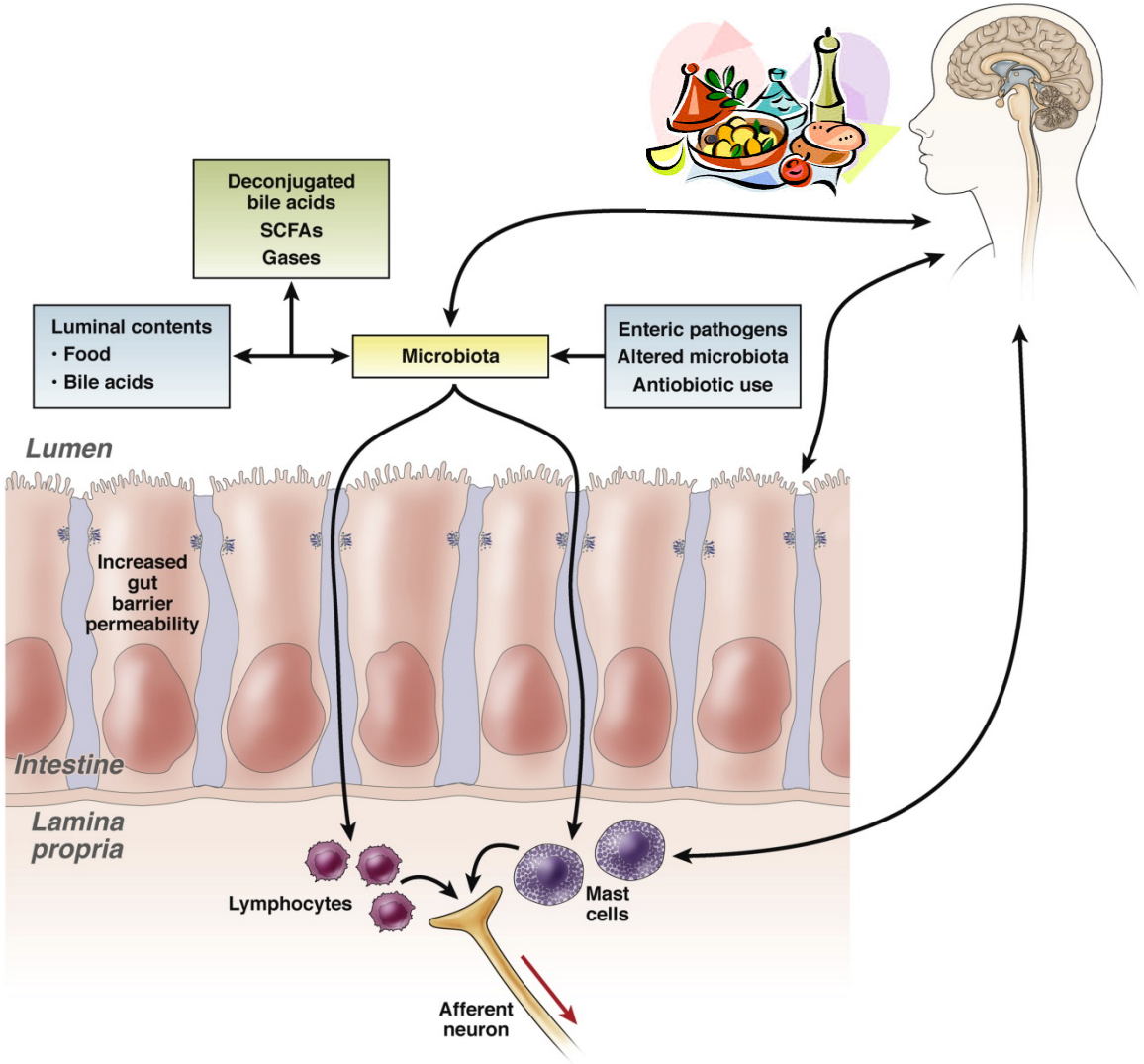
Spiller & Garsed. Gut 2009

SIBO - Irritable Bowel Syndrome
Lactulose Hydrogen Breath Test



Vanner Gut 2008

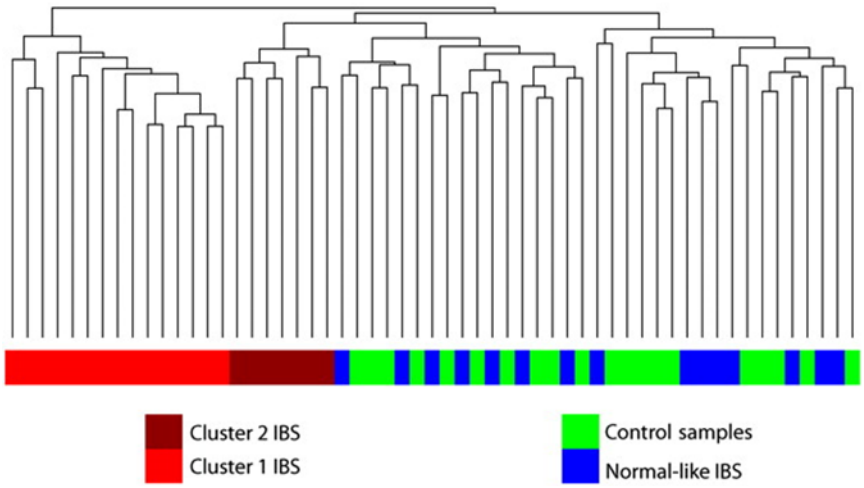
Gut microbiota - IBS



Shanahan & Quigley Gastroenterology 2014

Gut microbiota: IBS vs. healthy controls

57 Swedish subjects
37 IBS + 20 healthy



22 IBS with IBS-type signatures

15 IBS with healthy-like microbiota

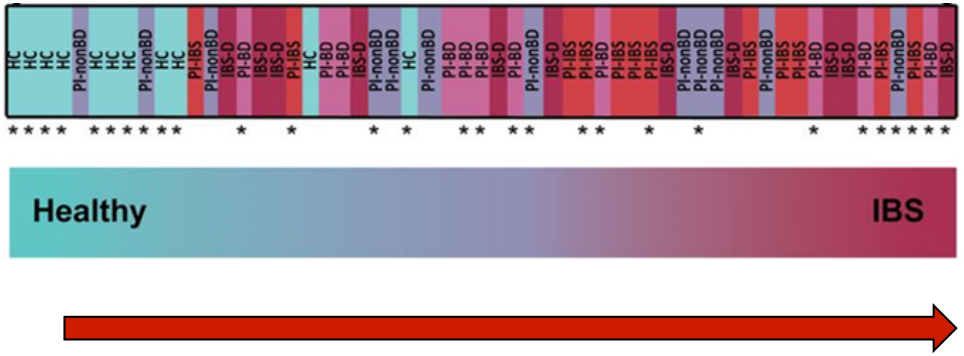
ORIGINAL ARTICLE

An irritable bowel syndrome subtype defined by species-specific alterations in faecal microbiota

Ian B Jeffery,[1] Paul W O'Toole,[1,2] Lena Öhman,[3] Marcus J Claesson,[1,2] Jennifer Deane,[1,2] Eamonn M M Quigley,[2] Magnus Simrén[3]

Gut 2012;61:997-1006

57 UK subjects – PI-IBS
46 PI-IBS / BD / non-BD & IBS-D + 11 healthy



Gradient of IBS-signature bacteria - also including some healthy subjects

ORIGINAL ARTICLE

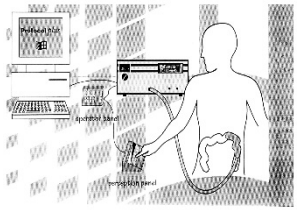
Faecal microbiota composition and host–microbe cross-talk following gastroenteritis and in postinfectious irritable bowel syndrome

Jonna Jalanka-Tuovinen,[1] Jarkko Salojärvi,[1] Anne Salonen,[2] Outi Immonen,[1] Klara Garsed,[3] Fiona M Kelly,[4] Abed Zaitoun,[3] Airi Palva,[1] Robin C Spiller,[3] Willem M de Vos[1,2,5]

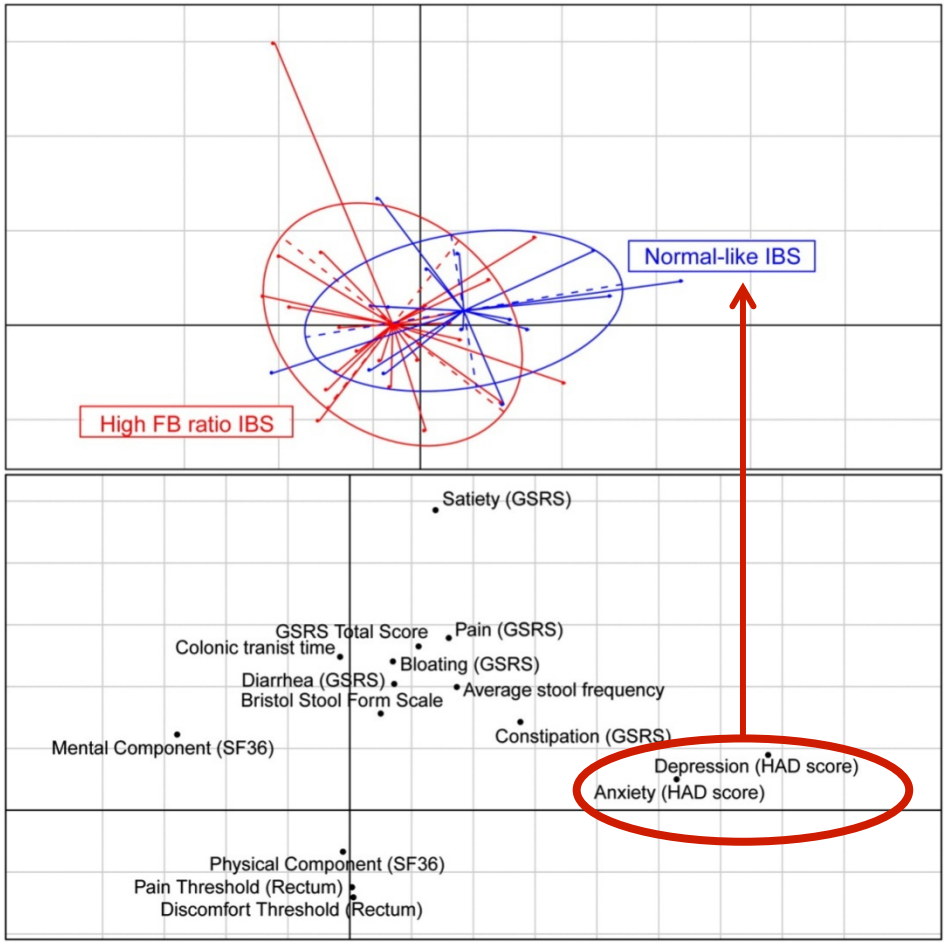
Gut 2014;63:1737-45

An Irritable Bowel Syndrome subtype defined by species-specific alterations in fecal microbiota

Microbial composition and clinical data

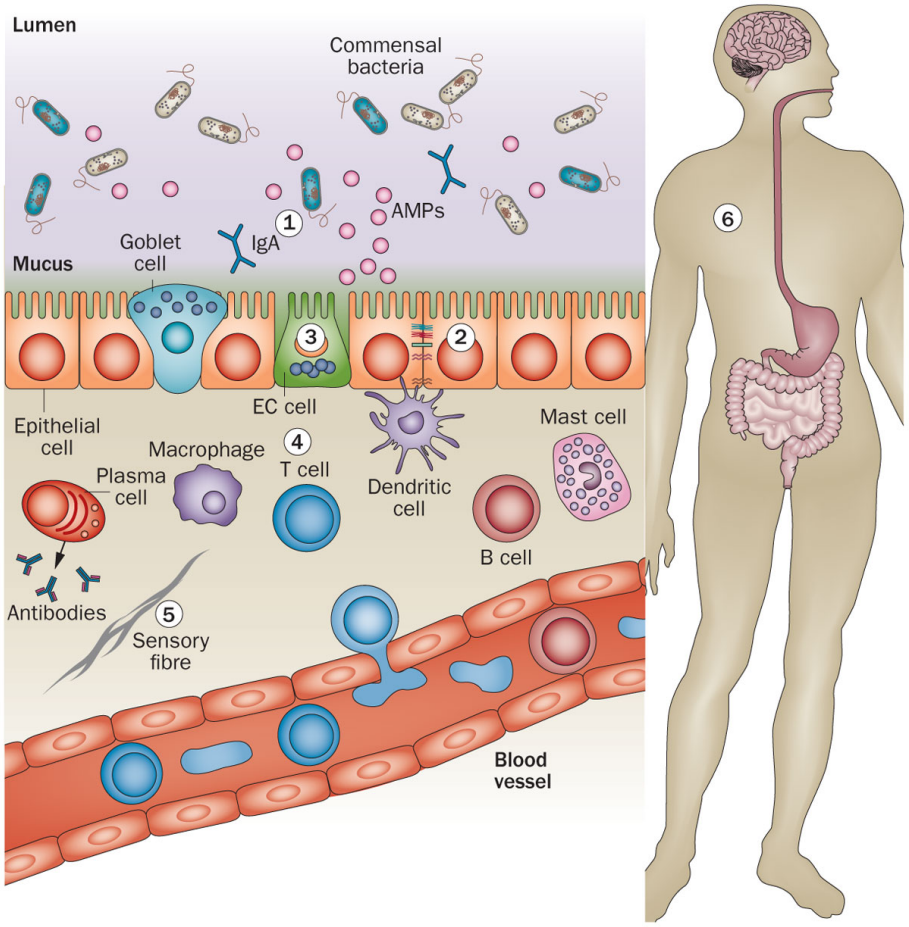


Clinical variables and IBS subtypes.



Jeffery et al Gut 2012

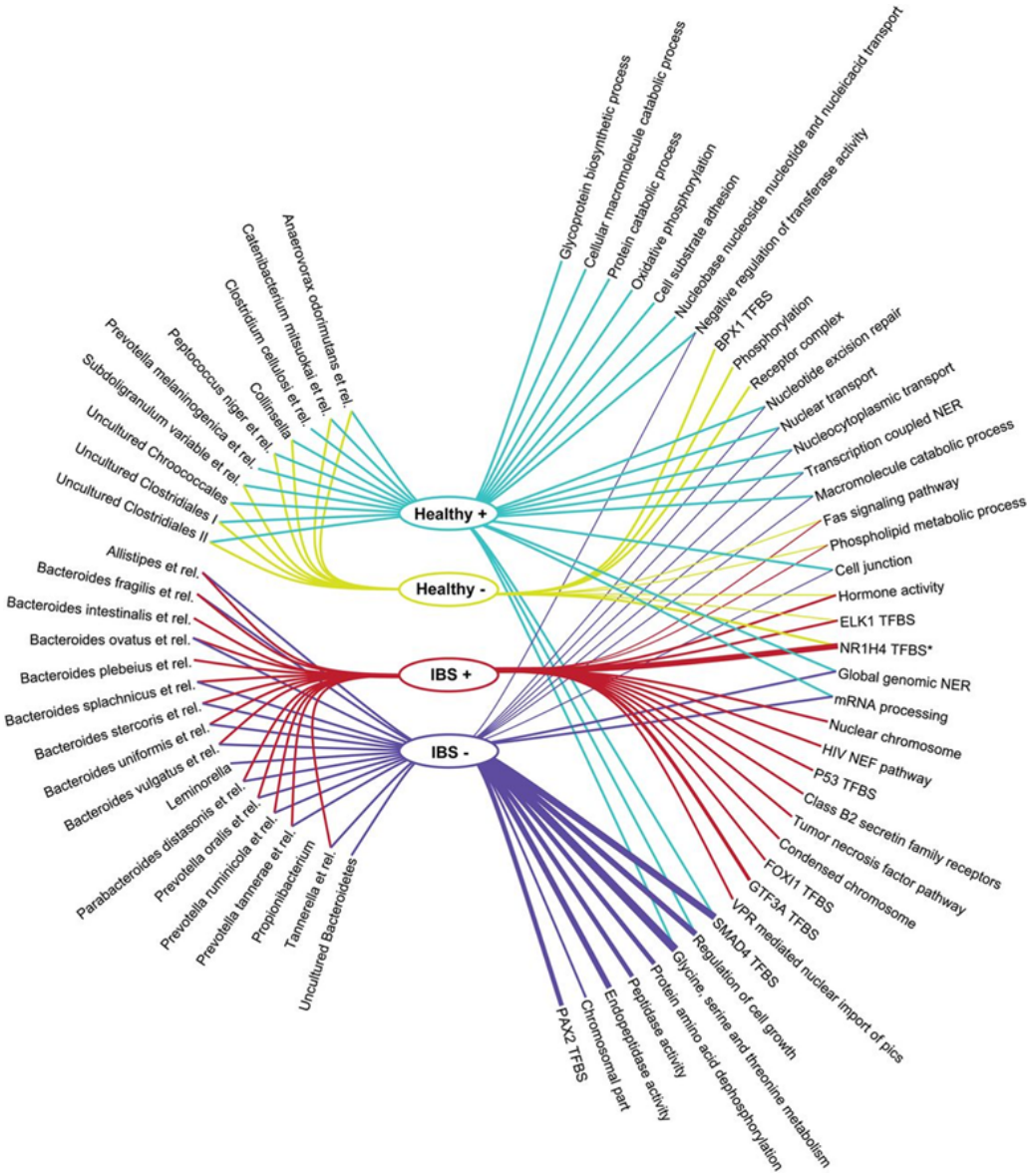
Different structural abnormalities can interact with each other and contribute to the generation of symptoms in IBS



Nature Reviews | Gastroenterology & Hepatology

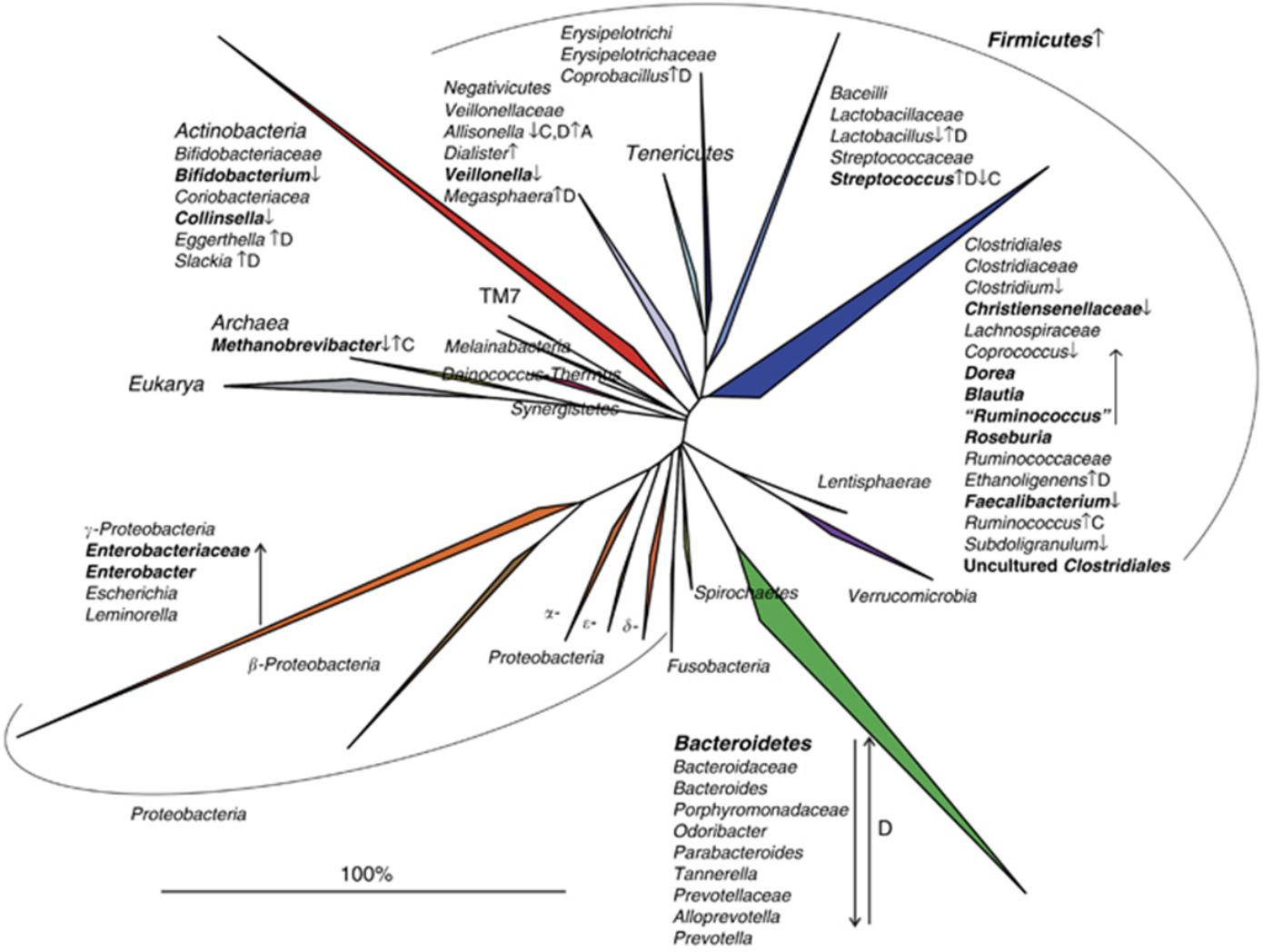
Öhman, Törnblom & Simrén Nat Rev Gastroenterol Hepatol 2015

Host-microbial interactions in IBS



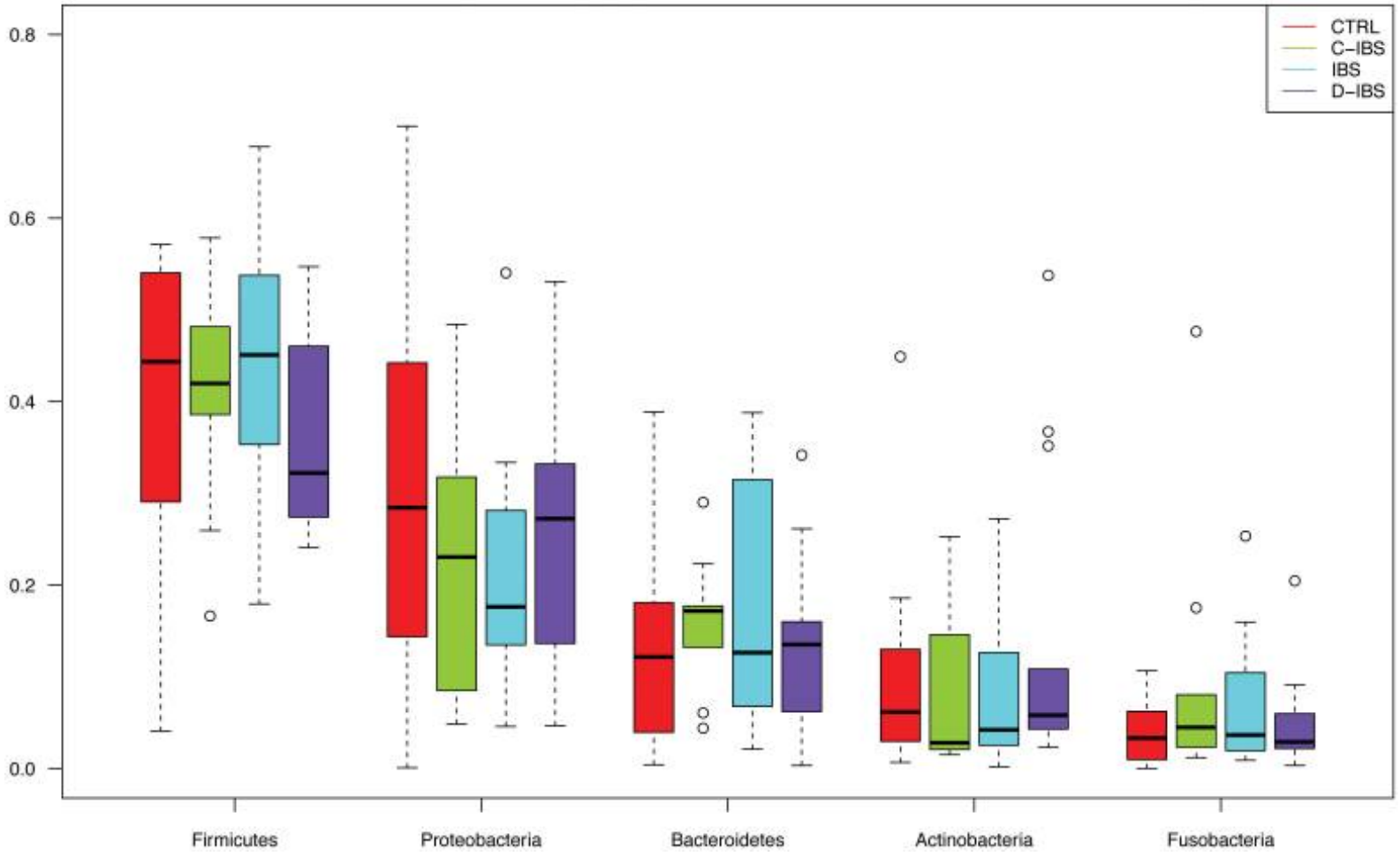
Jalanka-Tuovinen et al Gut 2014

Gut microbiota: IBS vs. Controls



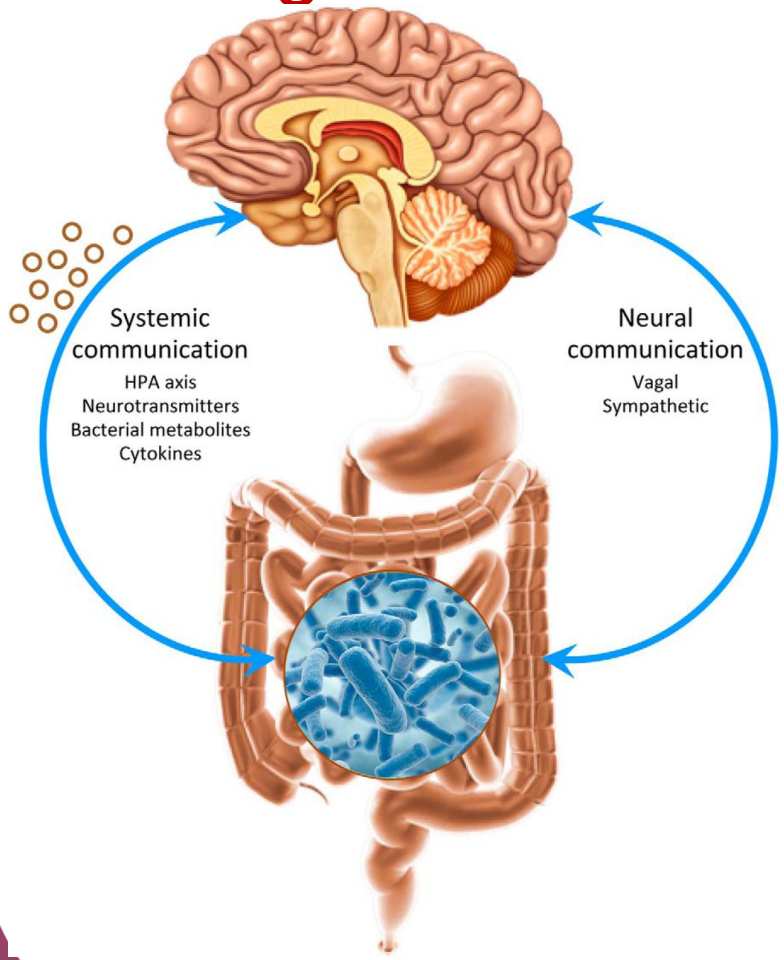
Rajilic-Stojanovic et al Am J Gastroenterol 2015

Small bowel bacteria - IBS

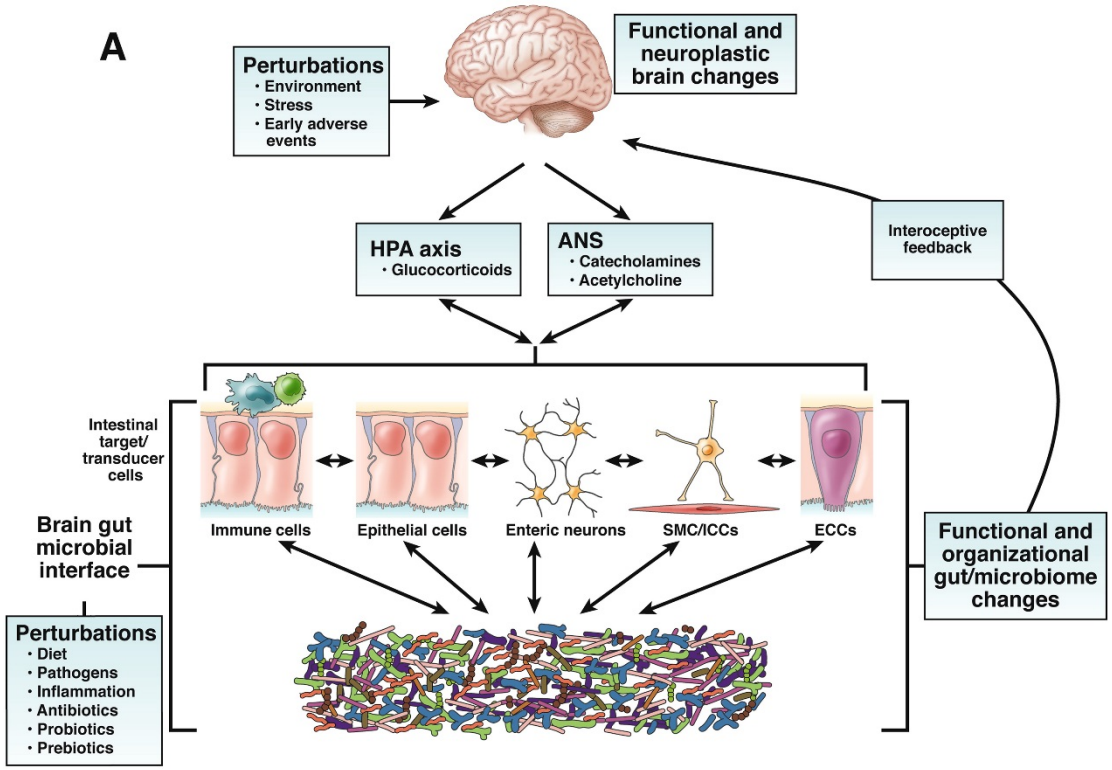


Dlugosz et al Sci Rep 2015

Bidirectional communication channels between the gut microbiome, the gut, and the brain.

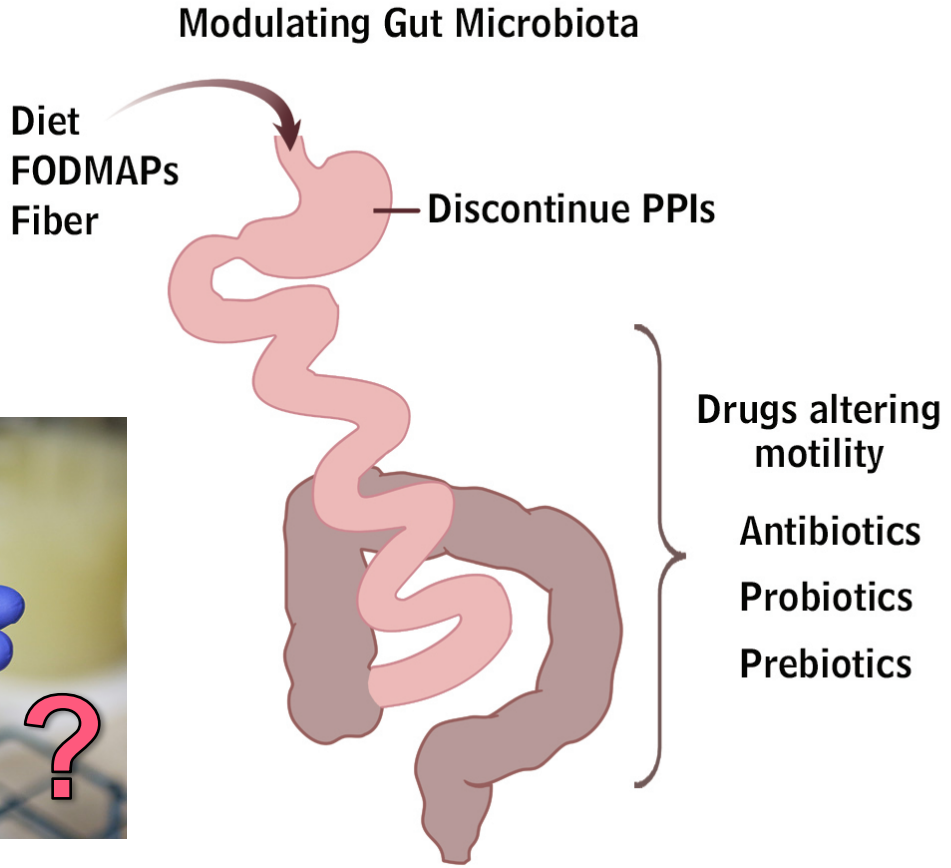


Mayer EA et al J Neurosci 2014



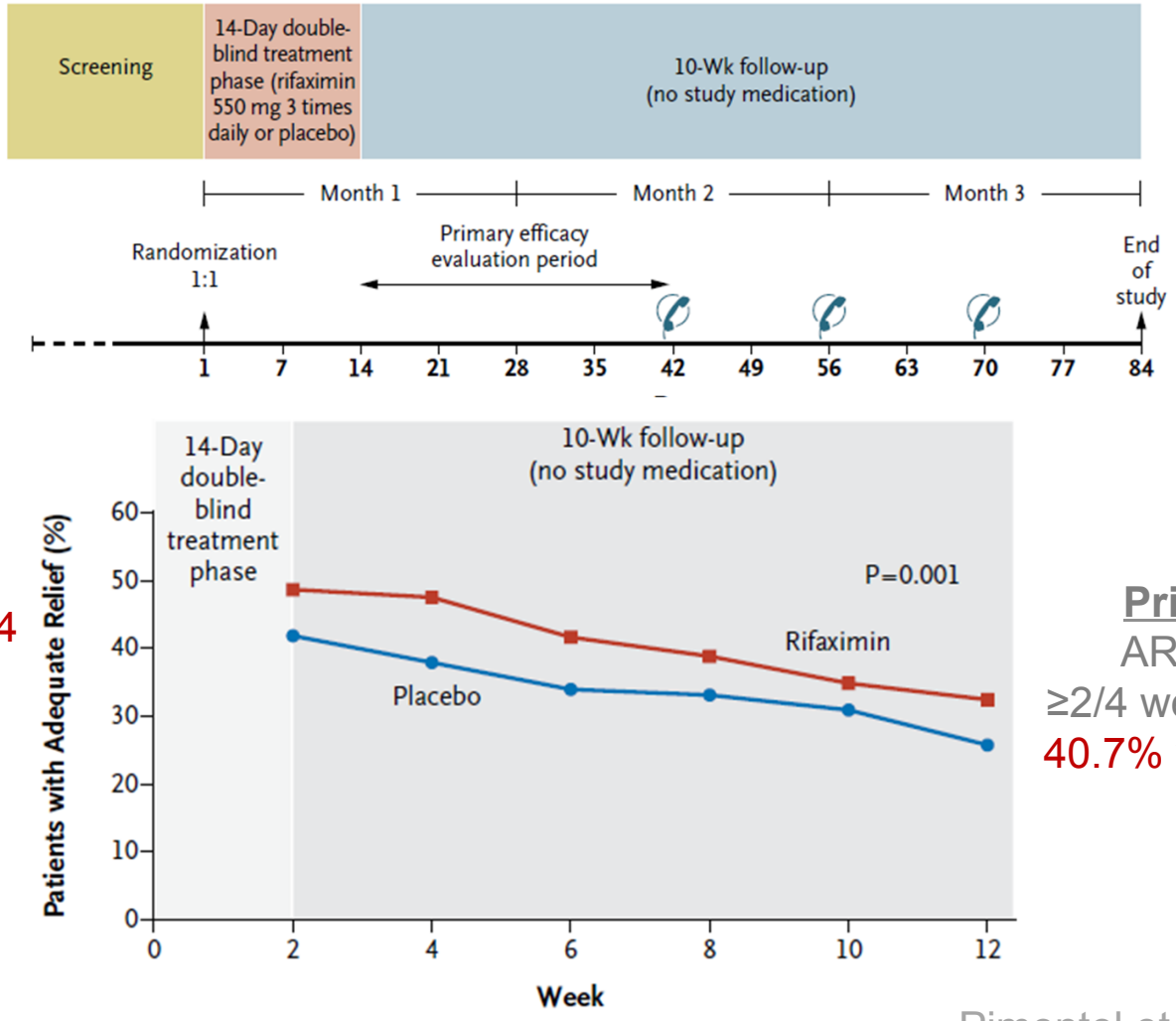
Mayer EA et al Gastroenterology 2014

Different ways to modulate gut microbiota.



Rome Foundation Working Team - Intestinal microbiota in FBD.
Simren et al 2013

Rifaximin – IBS
TARGET 1 & 2

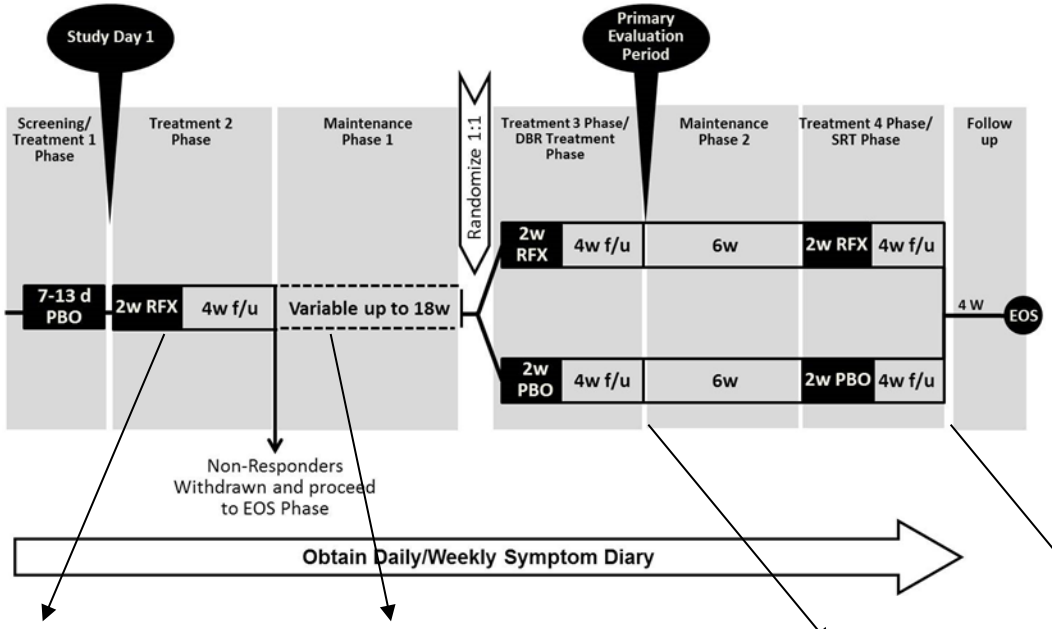


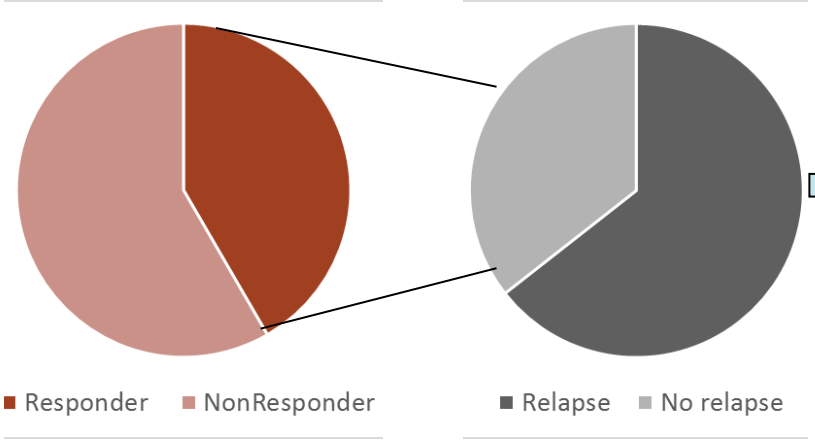
Rifaximin, n=624
Placebo, n=624

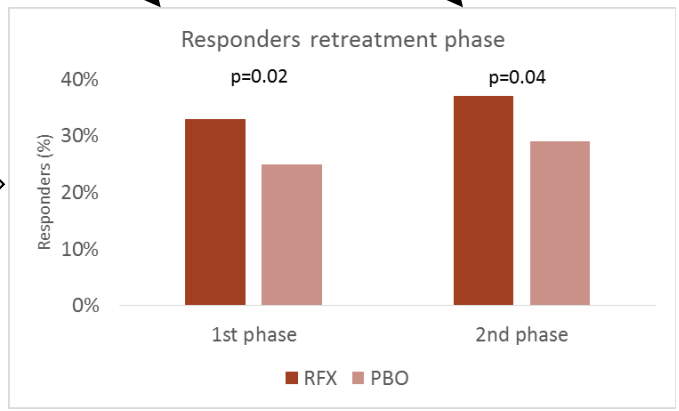
Primary endpoint:
AR of global IBS sx
≥2/4 weeks after treatment:
40.7% vs. 31.7%; p<0.0001

Pimentel et al NEJM 2011

TARGET 3: Rifaximin – IBS - retreatment

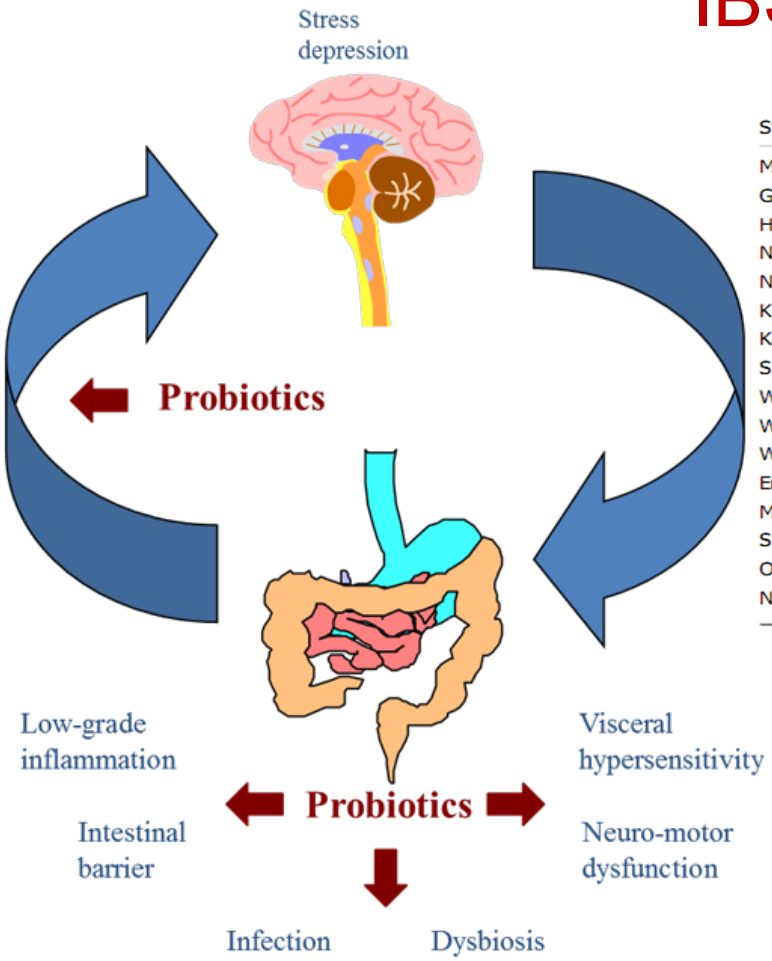




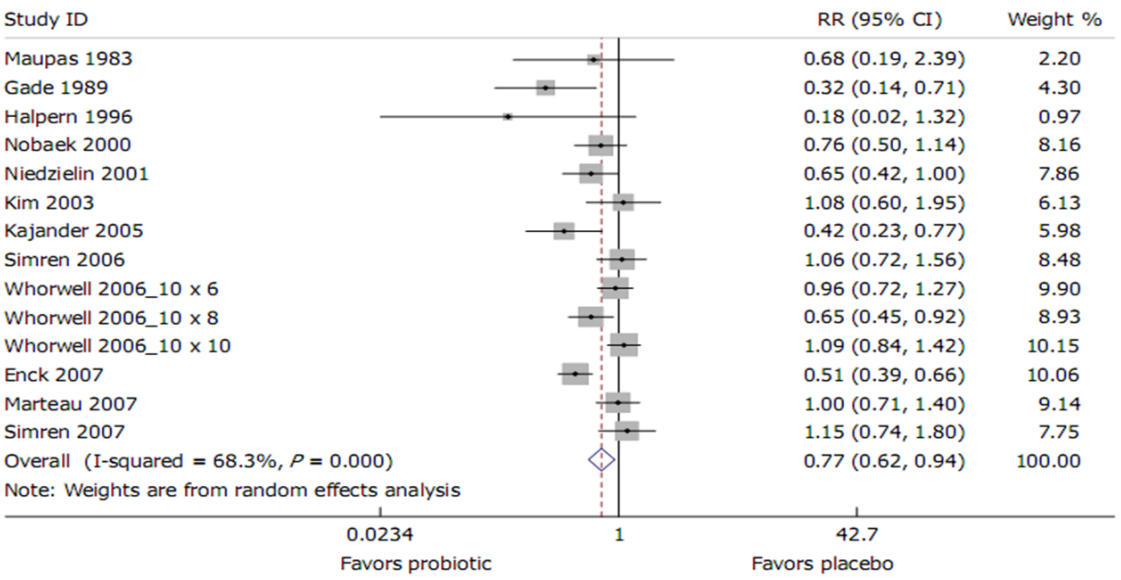


Lembo et al ACG 2014

IBS - Probiotics



Simrén et al Gut 2013

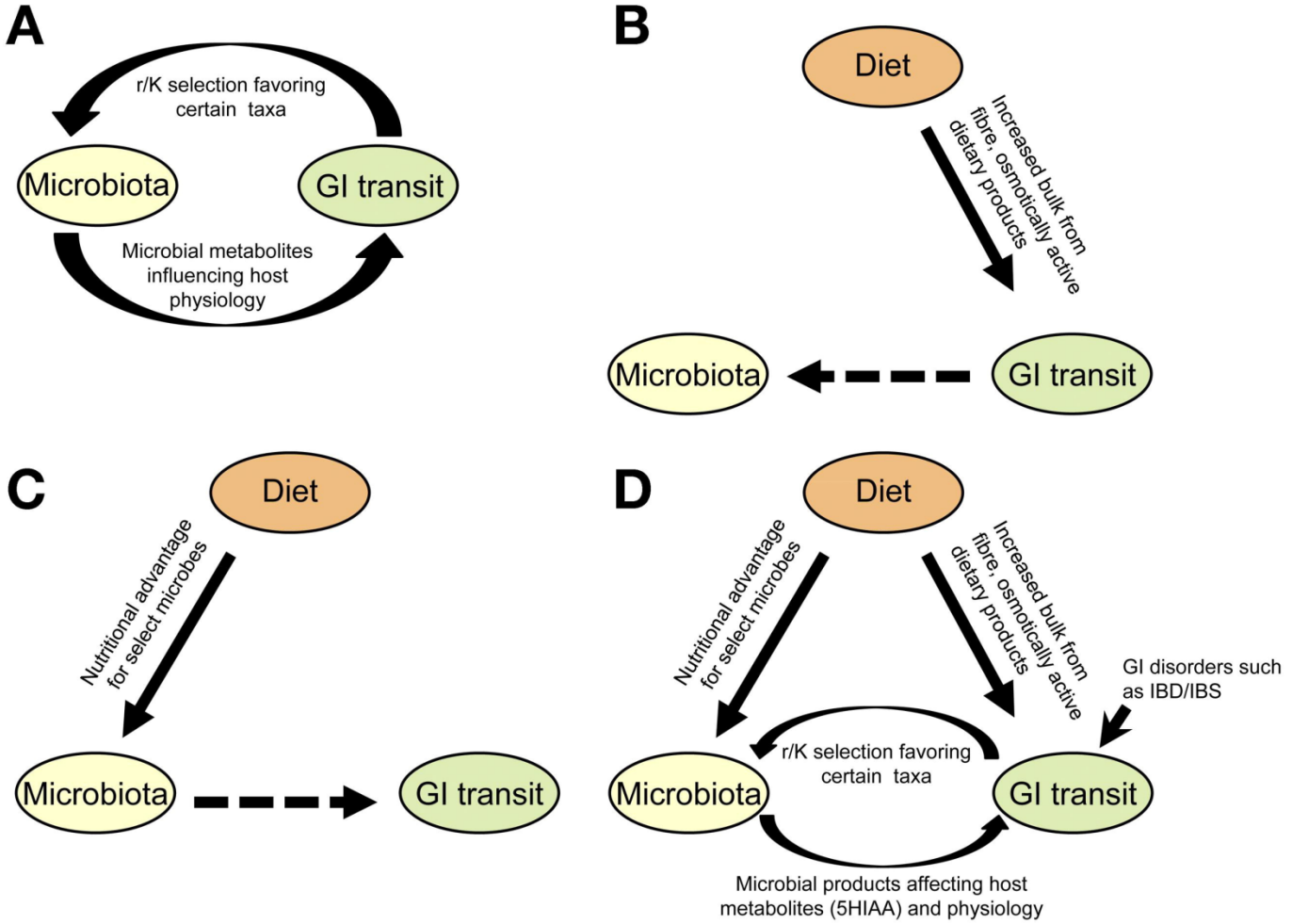


McFarland et al WJG 2008

- *"Probiotics are effective treatments for IBS…"*
- *"…which individual species and strains are the most beneficial remains unclear…."*
- *…a NNT of 7 and significant improvements in terms of global symptom, abdominal pain, bloating, and flatulence score…"*

Ford et al Am J Gastroenterol 2014

Interplay between diet, the gut microbiota, and GI transit

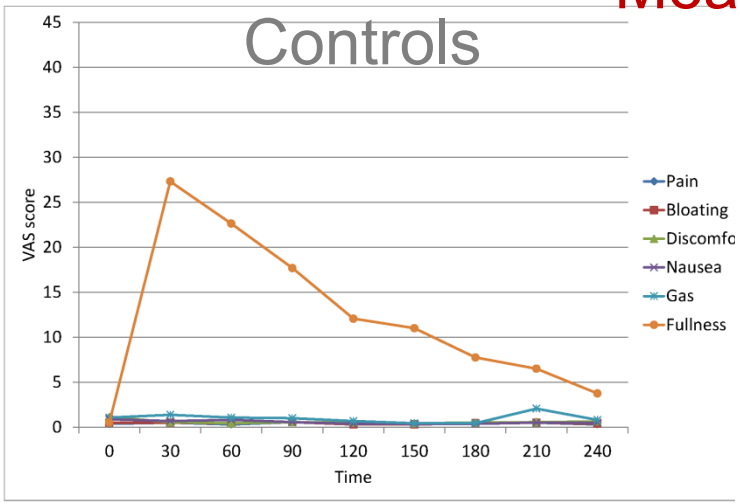


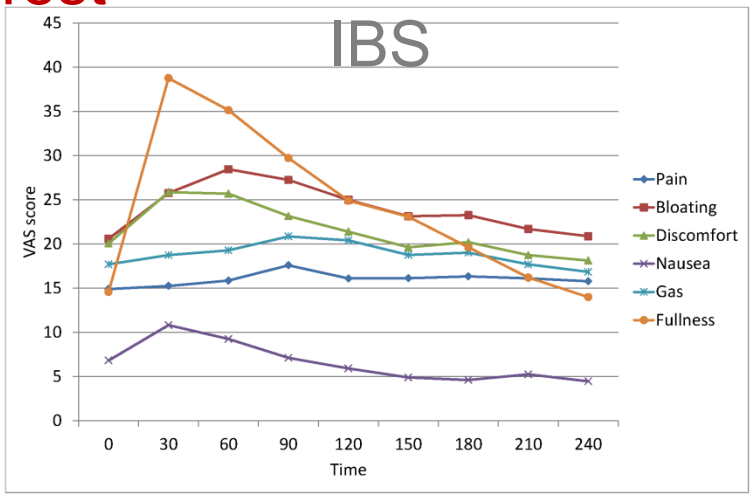
Kashyap et al Gastroenterology 2013

Food and IBS

- 62% - ”adverse reactions to one or more foods” (Dainese et al Am J Gastroenterol 1999)
- 64% -”symptoms aggravated by food” (Svedlund et al Scand J Gastroenterol 1985)
- 63% - ”meal related symptoms” (Simrén et al Digestion 2001)
- 70% - ”symptoms related to food intake” ; 62% ”limited or excluded food items from the diet” (Monsbakken et al Eur J Clin Nutr 2006)

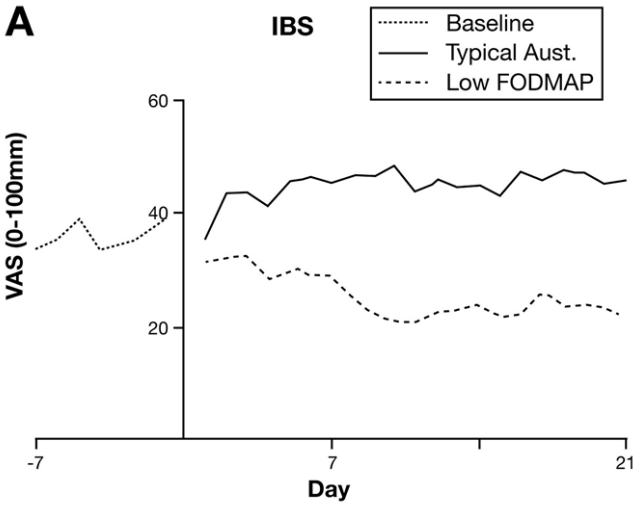
Meal Test

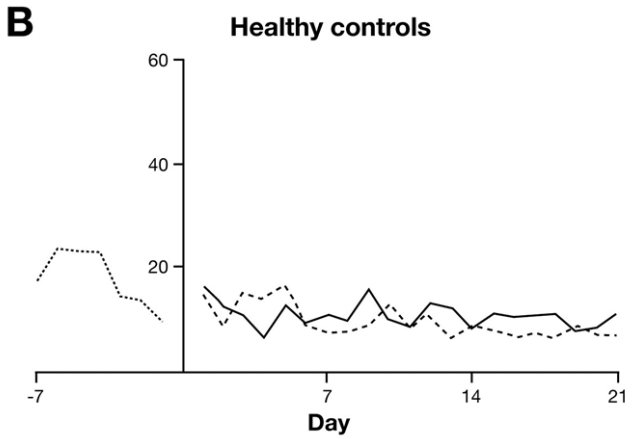




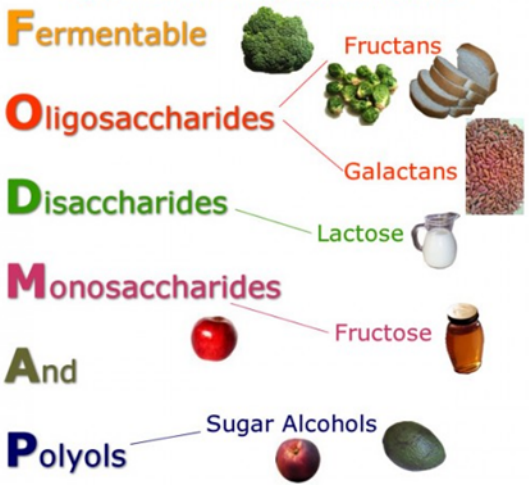
Posserud et al UEG Journal 2013

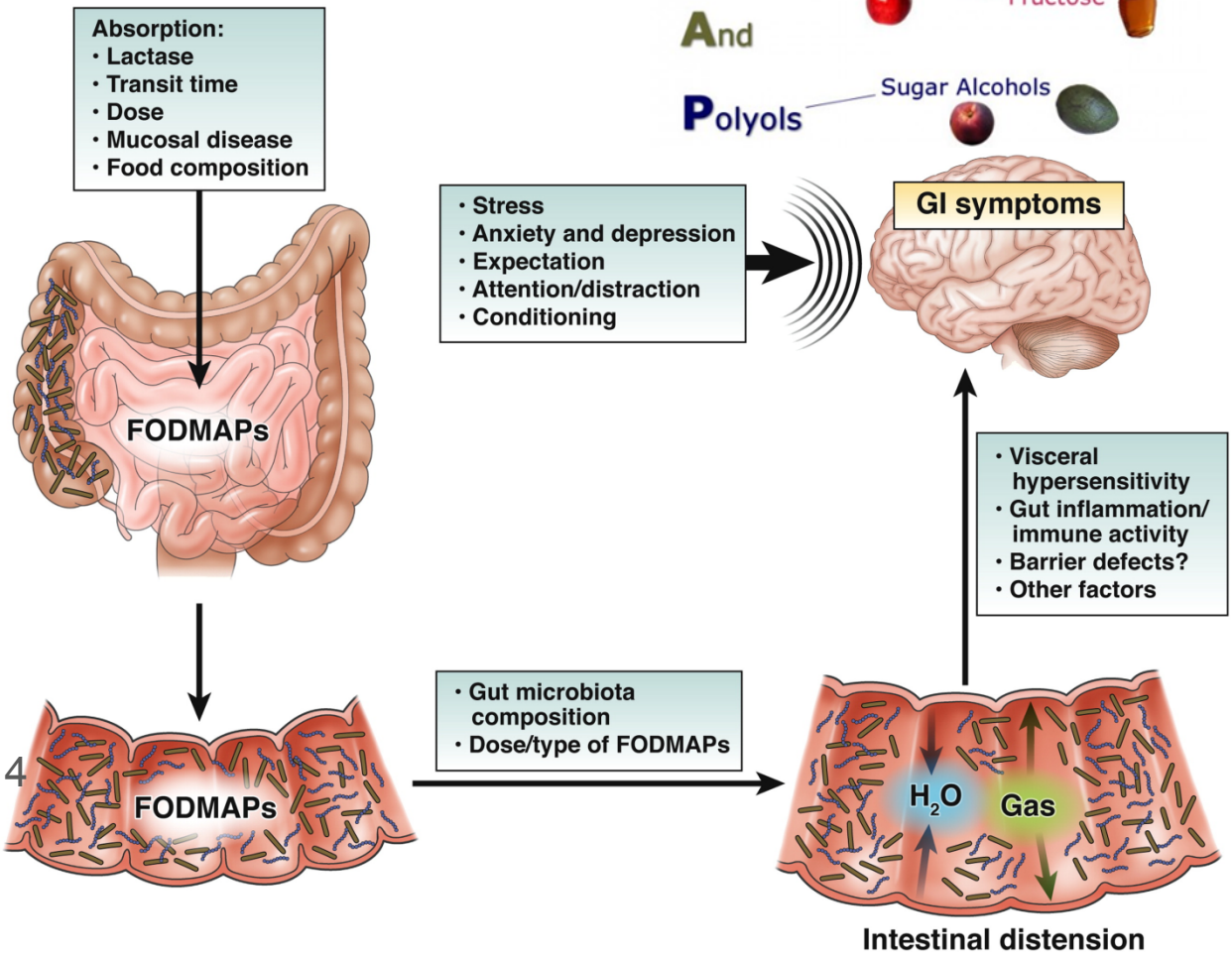
FODMAPs – IBS





Halmos et al Gastroenterology 2014

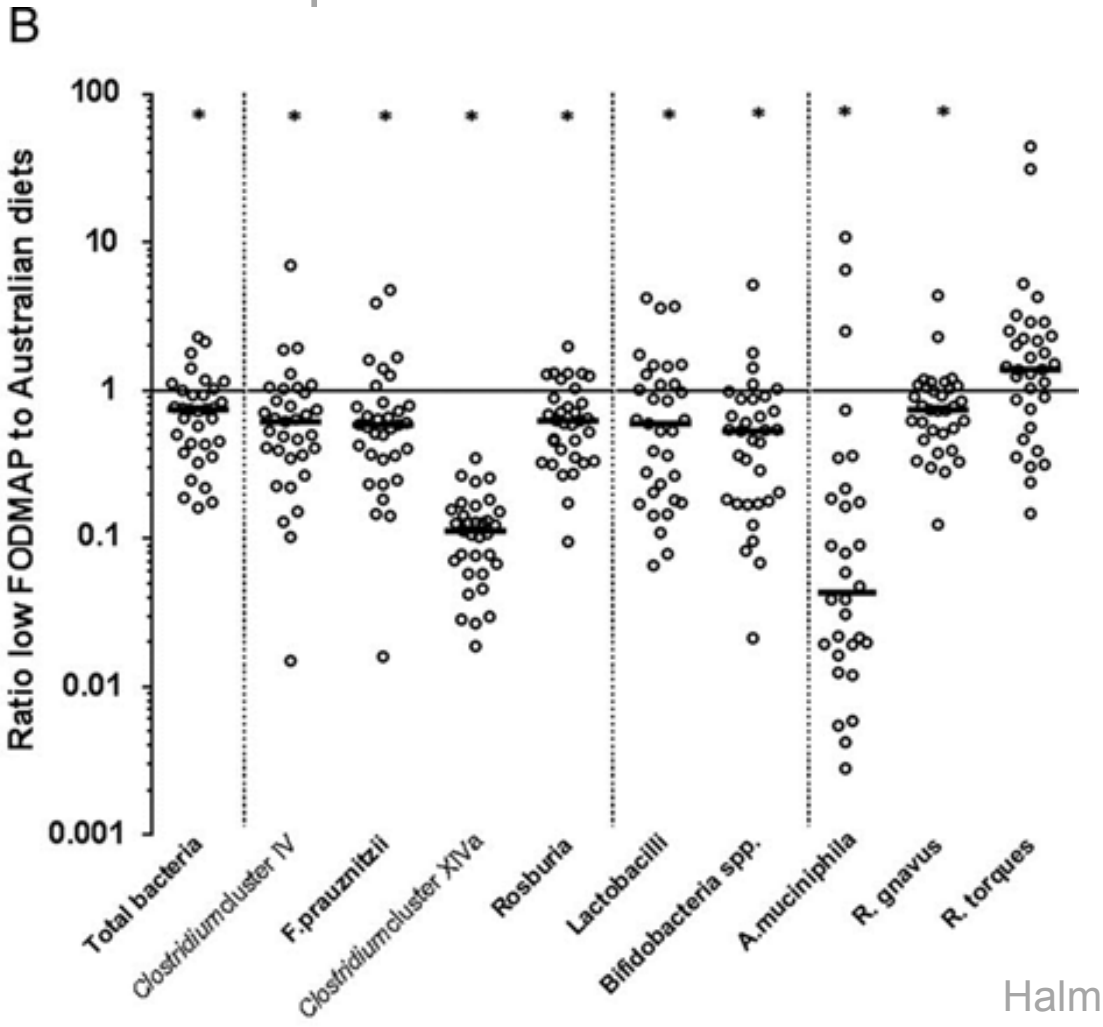




Simrén Gastroenterology 2014

Low FODMAPs diet – gut microbiota

Total and specific bacterial abundance



Halmos et al Gut 2014

Conclusion

- Alterations in gut microbiota composition and function exist in GI diseases
  - No uniform pattern detected yet
  - Association with symptom pattern
  - … not yet a biomarker…
  - Prognostic factor
  - Therapeutic target – pre-, pro- & antibiotics, diet, FMT etc.

Conclusion II

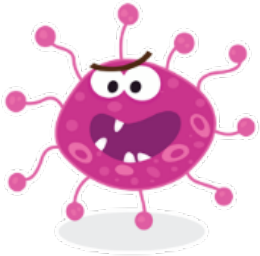
- Therapeutic interventions aiming at correcting the intestinal flora in patients with functional GI disorders seem promising:
  - Non-absorbable antibiotics; probiotics
  - Pre/synbiotics?
  - Diet
  - Other ways
- More trials needed
  - Larger, high-quality trials
  - Head-to-head comparisons
  - Antibiotic resistance
  - …

Thank you for your attention!

Tummy Buddy

Vs

Tummy Baddy



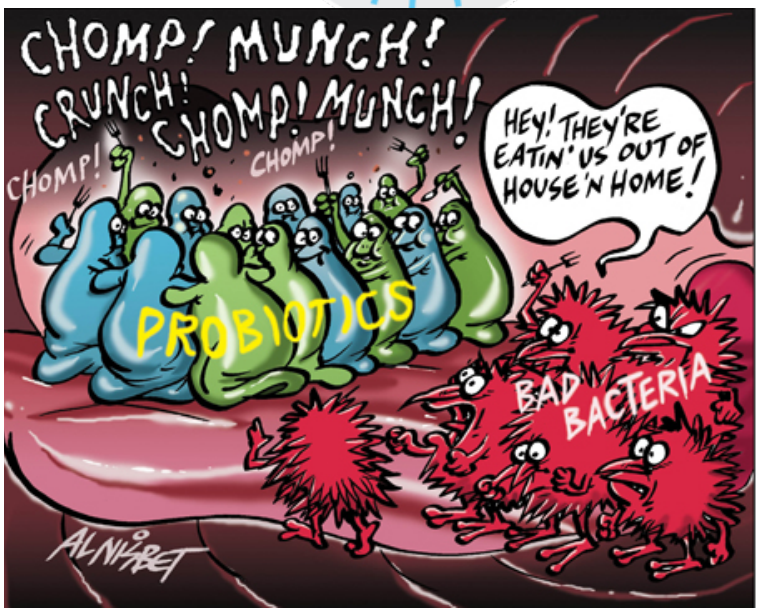


Illustration: Don Smith