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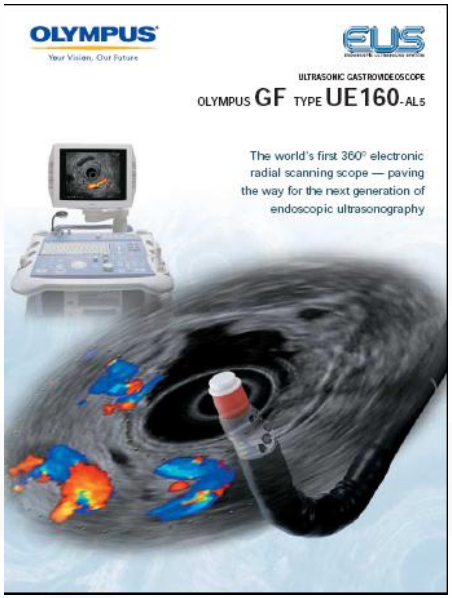
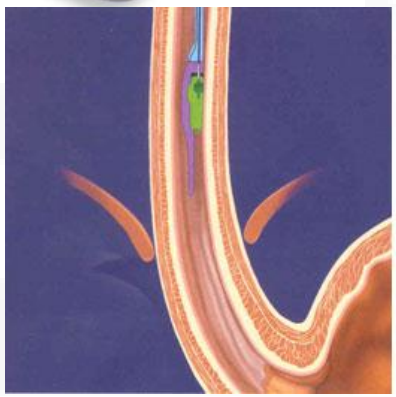
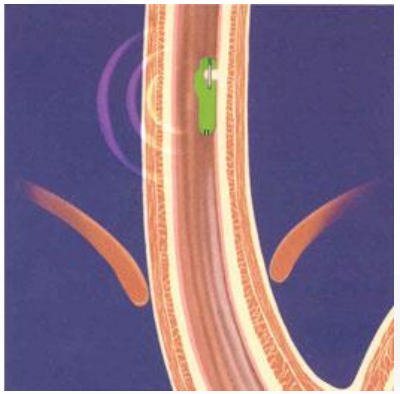
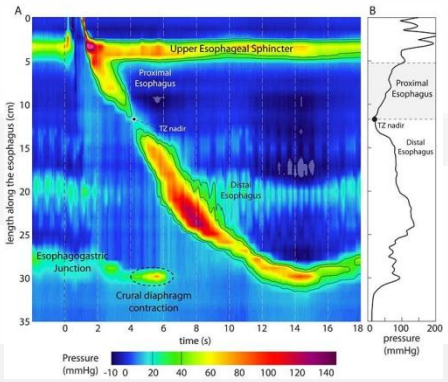
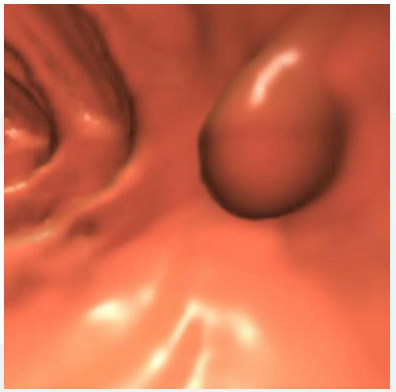
MACMURRAY
GASTROENTEROLOGY
DIGESTIVE DISEASES & ENDOSCOPY











Outline:
Food intolerances and gluten

- Case example
- Irritable bowel
    - Pathophysiology
    - Diagnosis
  - Food allergies vs. intolerances
    - Testing
    - Low FODMAP diet
- Eosinophilic Oesophagitis
- Coeliac disease

MacMurray
GASTROENTEROLOGY
DIGESTIVE DISEASES & ENDOSCOPY

Miss AC 33y receptionist

- Normal bowel function until 24y
- Sudden onset
  - diarrhoea 7X/day with urgency
  - gripey abdominal pain relieved with defecation
  - reflux / dyspepsia
  - Days with no BM but abdominal discomfort
- What would you do?
- Audience poll

Miss AC 33y receptionist

Investigations

- Routine blood tests
- Faecal cultures
- Colonoscopy X 3
- Small bowel follow through
- CT abdomen
- Gynaecological review

Treatment trials

- Metamucil / fibre supplement
- Aloe vera, slippery elm, peppermint oil, probiotics
- Gluten, dairy, meat free, Atkin's and Liver cleansing diets
- Loperamide
- Sulfasalazine

Referred for second opinion – Diagnosis IBS referred for breath testing

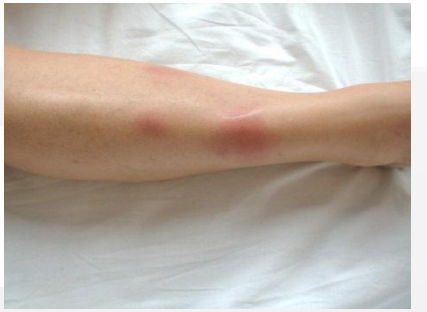
Red Flags in Gastroenterology

General Red Flags

- Unexplained weight loss
- Onset in older patients (>50)
- Family history of CRC/IBD
- Severe unremitting symptoms
- Rectal bleeding
- Nocturnal symptoms

IBD Red Flags

- Mouth ulcers
- Peri-anal disease
- Relationship of onset to smoking
- Extra-intestinal manifestations



Usefulness of red flags

- IBS vs Organic lower GI disease
  - Age 50 years at onset: OR 2.65 (1.4-5.0)
  - Blood on toilet paper: OR 2.7 (1.4-5.1)
  - Pooled sensitivity of alarm features is poor
    - 5-64%
- Dark red blood and abdominal mass
  - Sensitivity >95%
- Family history slight help

Hammer et al Gut 2004

Rome III Criteria* – Irritable Bowel Syndrome

Recurrent abdominal pain or discomfort at least 3 days/month

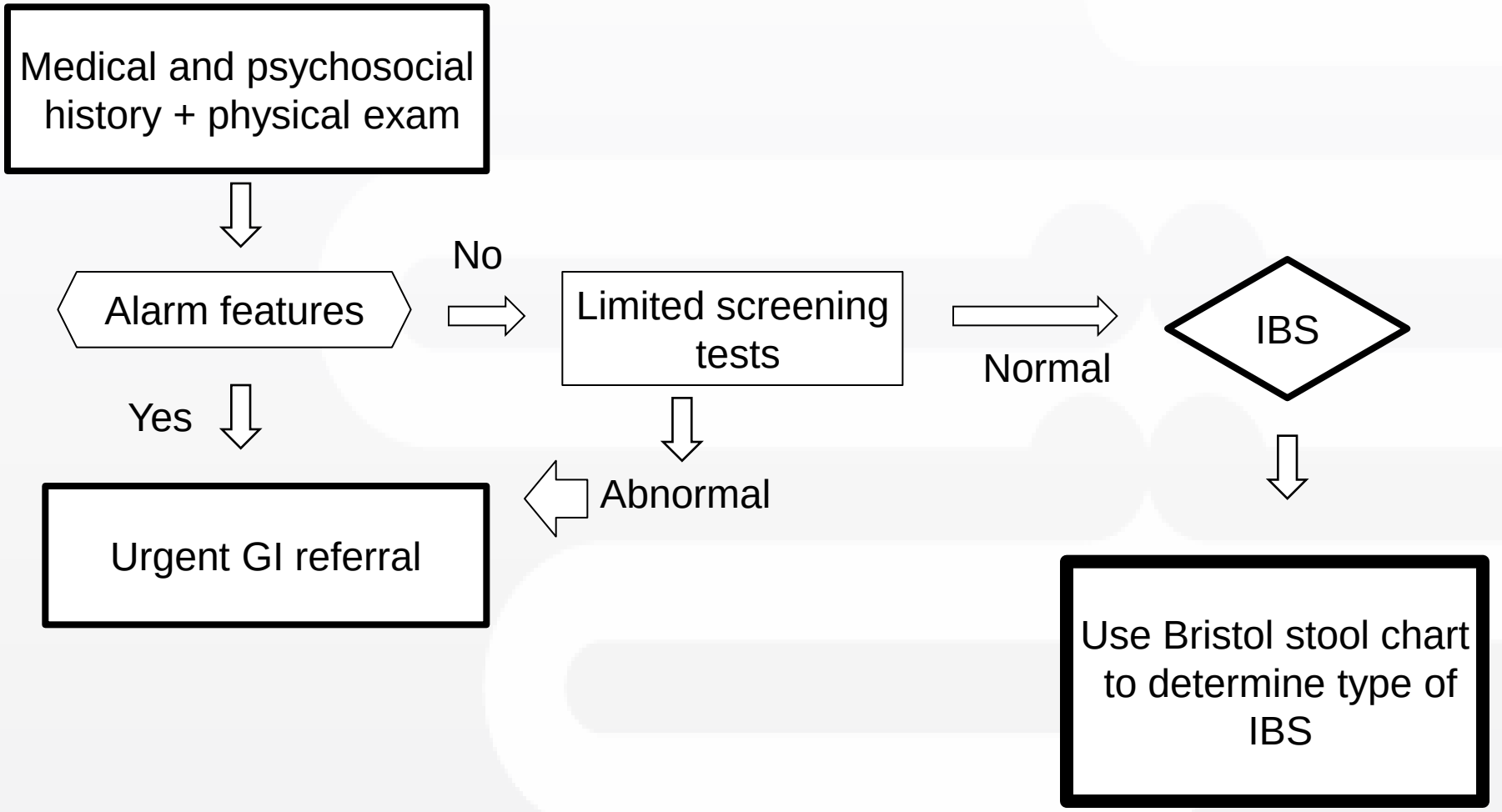
In the last 3 months associated with 2 or more :

- Improvement with defecation
- and
- Onset associated with a change in frequency of stool
- and
- Onset associated with a change in form (appearance) of stool

*** Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.**

Longstreth GF, Gastroenterology 2006

Recurrent abdominal pain and disordered bowel habit



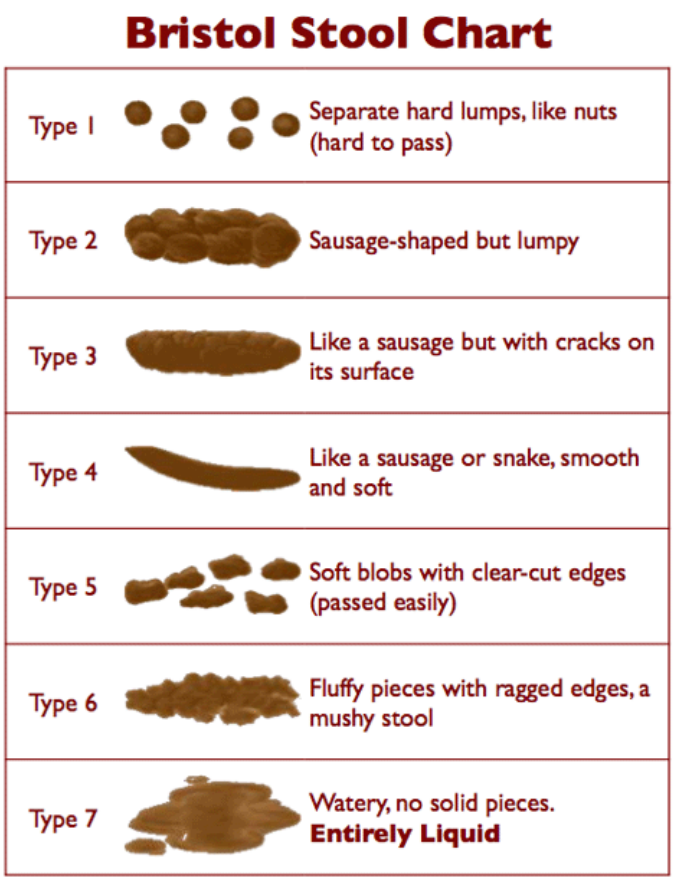
What are appropriate limited screening tests?

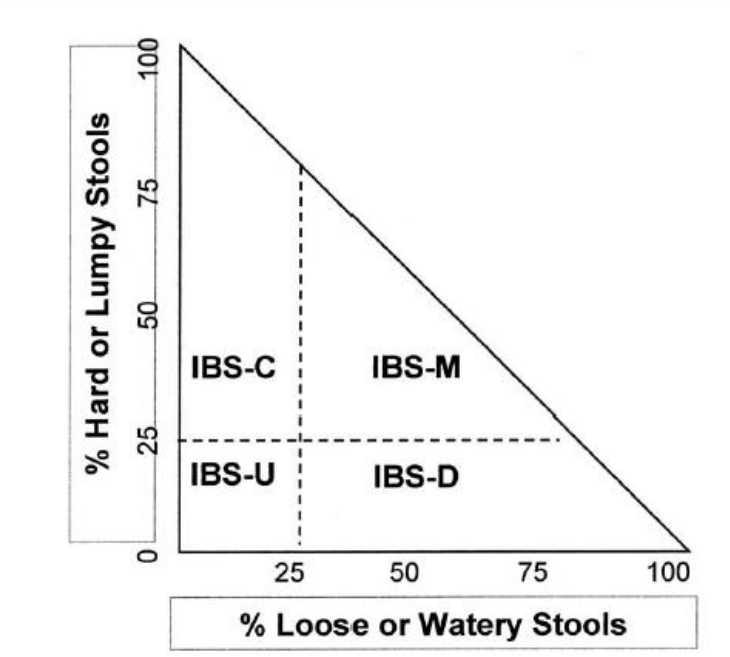
- There is insufficient evidence for any tests!
- BUT
  - FOB
  - FBC, iron studies, TFT, CRP
  - Coeliac serology (Europeans)
  - If suspicion consider US
  - If severe symptoms or an older patient consider referral

What about faecal calprotectin?

- Is pretty good inflammatory marker for GI tract
- Very stable molecule
  - Lasts 7 days
- For cutoff over 150
  - Sensitivity 95%, specificity 91%
  - NPV 96% in primary care
    - 4.8 year FU
      - » Turvil Front Gastro 2011

pes of IBS



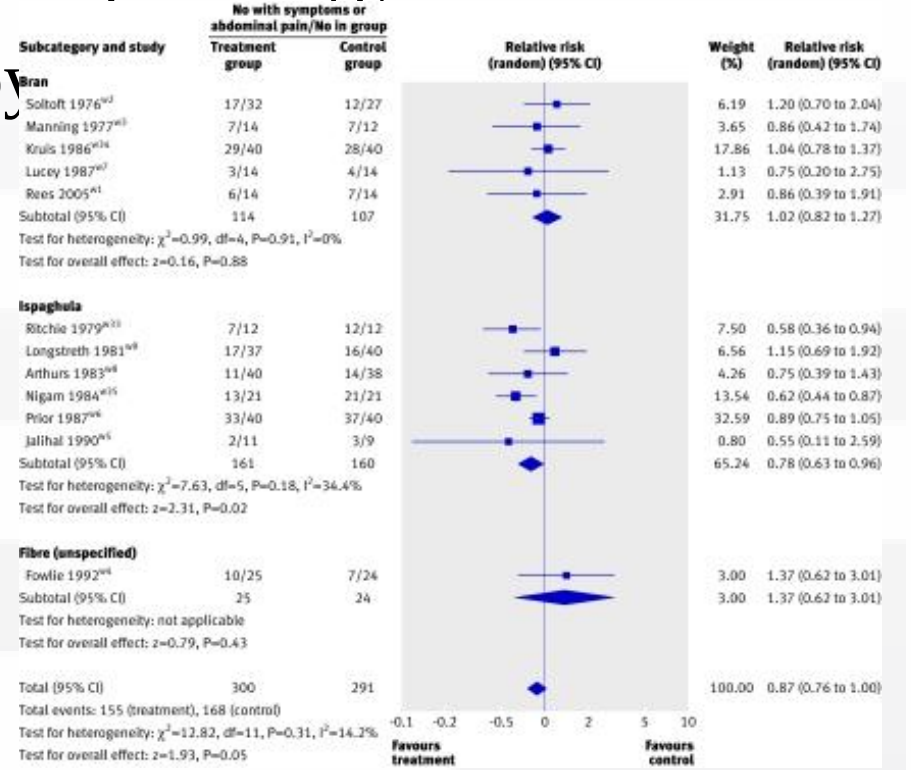


» Longstreath et al Gastro 2006, 130 (5) 1480

- (Antidepressants NNT 4)

IBS-C

- Trial of simple laxatives
  - Generally risks of serious pathology low
  - Usually no colonoscopy
- What about fiber?



Ford BMJ 2008

IBS-D and IBS-M

- Bowel flora are probably important
- Food plays a greater role than genetics in shaping human microbiota

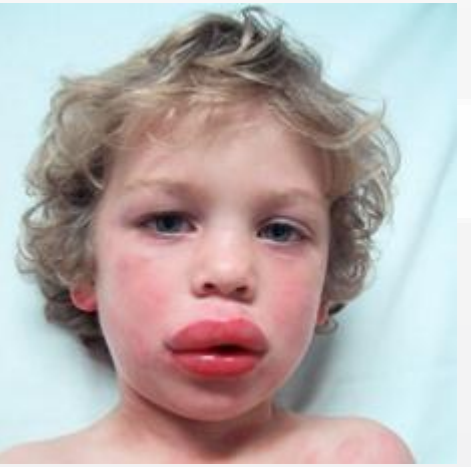
Wu et al, Science Sept 2011

How diet can effect IBS symptoms

- By changing micoflora over time in the gut
  - This is probably why probiotics work at least in the short term
  - Microflora thought to return to baseline when stop treatment
- By acutely changing GI tract function
  - Food intolerance and the FODMAPs

Food Allergy vs Intolerance

- Allergies
  - Immunologic over reaction
  - IgE antibodies
    - Type 1 immune response
  - Immediate
  - Eg Hives, anaphylaxis
- Intolerances
  - Response to food
  - Not immunologic
  - Eg lactose intolerance
    - Lack enzyme lactase



Food allergies

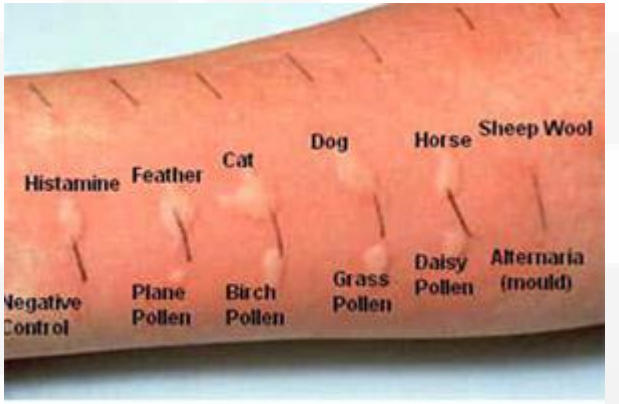
- Big eight
  - Milk, egg, peanuts, tree nuts, seafood, shellfish, soy and wheat
  - True allergy in children aged 2 is about 2-4% and is less common in adults

How do you test for food allergy?

- Skin prick testing
  - **Relevant Inhalant allergens in New Zealand in the skin prick test**

    House dust mite 1 (*D. pteronyssinus)*
    House dust mite 2 *(D. farinae)*
    Perennial rye
    Cat
    Macrocarpa
    Oak
    Birch
    Cedar
    Plantain
    Moulds (Individually) – *Alternaria, Aspergillus*
    Dog
  - **Food allergens reliably tested by skin prick test**

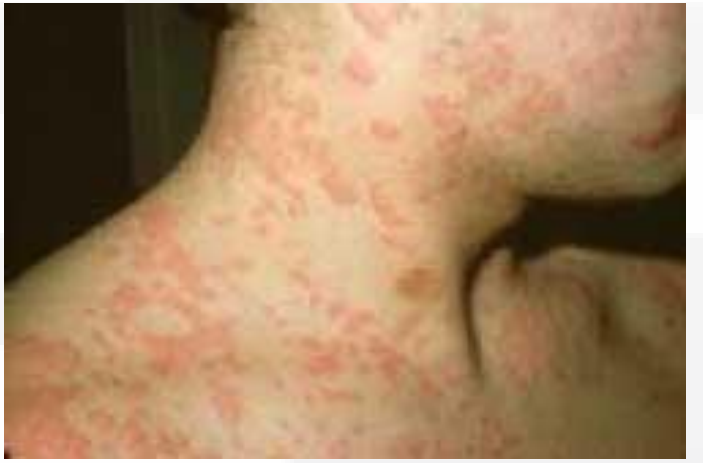
    Milk
    Eggs
    Peanut
    Wheat
    Soy
    Fish & shellfish



Skin Allergy Test

Allergy tests

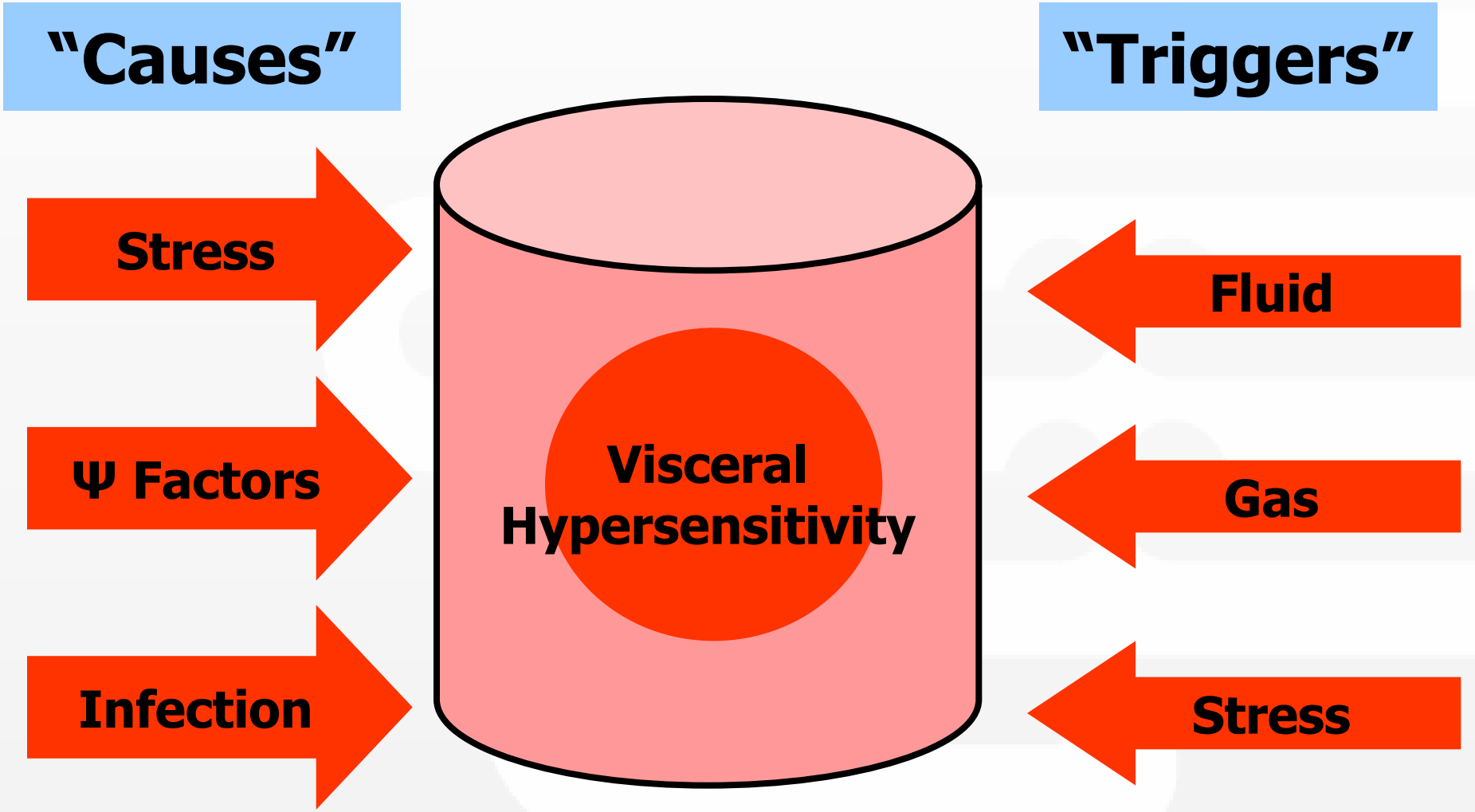
- RAST blood testing
  - Radioallergosorbant test
    - Detects specific IgE antibodies to known allergens
    - A large number are available
      - Standard one 96



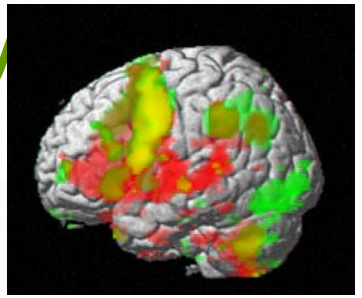
Food allergy does not cause IBS!

Food intolerance does not cause IBS but can exacerbate IBS symptoms

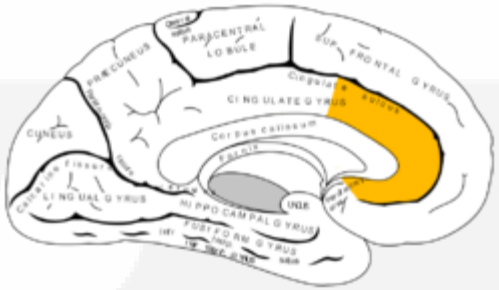
IBS Pathophysiology



Pathophysiology of IBS- Visceral hypersensitivity



- Rectal balloon distention and fMRI scanning have shown increased brain activation and symptom generation in IBS patients
  - Mertz Gastroenterology 2000
- Anterior cingulate cortex
  - Error detection, task anticipation
  - Motivation, modulates emotion



Causes: Post infectious IBS

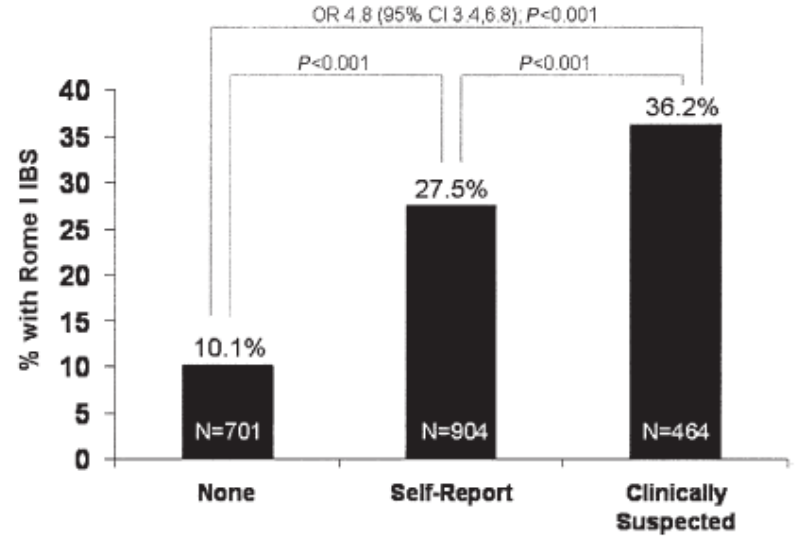


Figure 1. Rate of Rome I IBS 2–3 years after acute gastroenteritis from exposure to contaminated drinking water (between-group comparisons reported; overall 3-way comparison by χ^2 analysis, $P <$ .001).

Triggers:
Distention causes symptoms

- Distention caused by:
  - Solids
    - Dietary fibre content and bacterial mass
  - Liquids
    - Due to osmotic load of diet
  - Gas
    - Air swallowing
    - Due to bacterial fermentation

Causes of distention

- Air swallowing
  - Aerophagia
- Influence of food
  - Gluten sensitivity
  - Food malabsorbtion /intolerance
    - Fermentation by large bowel flora
- Pancreatic exocrine dysfunction
- Small bowel bacterial overgrowth

Aerophagia

- Main way that air enters the GI tract
  - 17mls of air for every 10mls of water
  - N2 is not absorbed so unless belched passes through
  - Air transit at 10cm/sec therefore can reach the other end in 15-35 minutes

Can food be a trigger of IBS?

- Well described that certain foods cause symptoms in some individuals

- Many patients describe a specific food trigger

Food intolerances

- Population study in UK
  - 20% complained of intolerances
    - Of these 20% were real on objective testing
      - » Young et al Lancet 1994
- Large placebo effect but this explains why individual exclusions diets do not often work

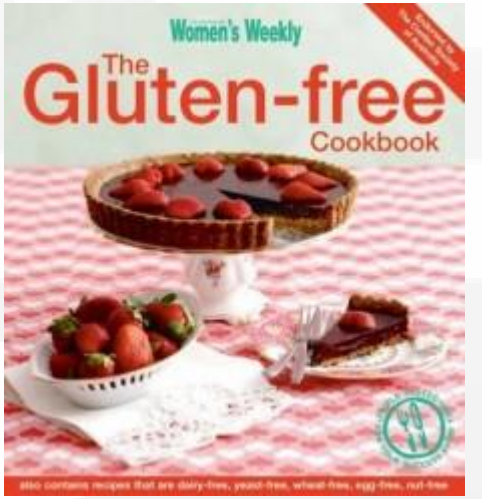
Food that effect transit

- Foods that cause diarrhoea
  - Beer
  - Broccoli
  - Coffee
  - Spicy foods
  - Prunes
  - Fruit and vegetables
  - Spinach
- Foods that thicken the stool
  - Cheese
  - Peanut butter
  - Rice
  - Pasta

What about gluten?

- Gluten is a non absorbed protein that appears in foods that are processed from wheat and related species

- Mechanism is not known



Gluten sensitivity

- Double blind, placebo re-challenge trial
- Coeliac excluded
- 2 slices of bread and a muffin
- 6 week study

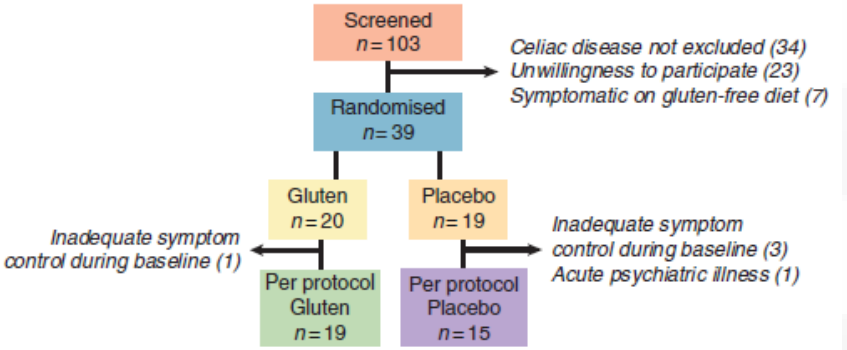
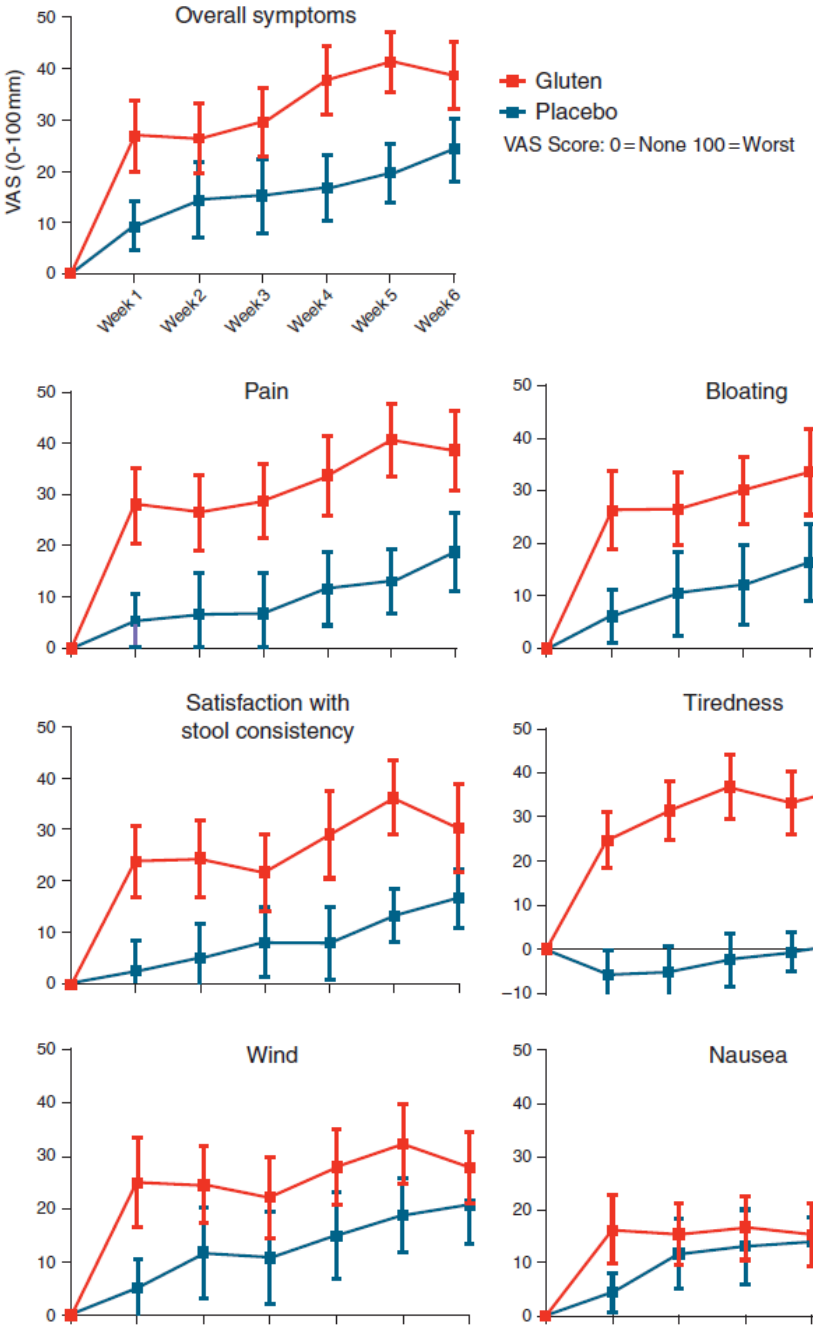


Figure 1. Recruitment pathway and reasons for screen failure and withdrawals.

»Biesiekierski et al: Am J gastro 2011



»Biesiekierski et al: Am J gastro 2011

Dietary triggers: FODMAPs

- A group of previously un-grouped short chain carbohydrates that share properties:
  - Poorly absorbed in small intestine
  - Small and osmotically active
  - Rapidly fermented by bacteria

What are FODMAPs?

Fermentable

Oligosaccharides

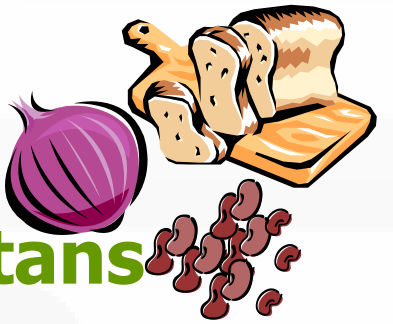
Disaccharides

Monosaccharides

And

Polyols

What are FODMAPs?



F

Oligosaccharides fructans, galactans

D

M

A

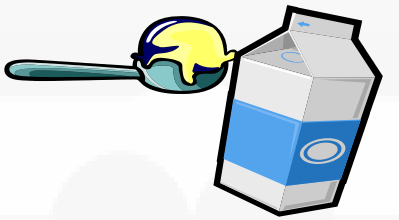
P

What are FODMAPs?

F

O

Disaccharides — lactose



M

A

P

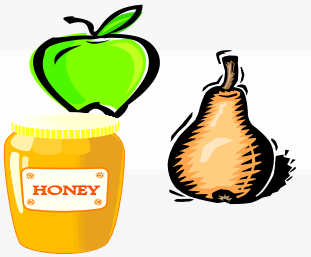
What are FODMAPs?

F

O

D

Monosaccharides **fructose**
(in excess of glucose)



A

P

What are FODMAPs?

F

O

D

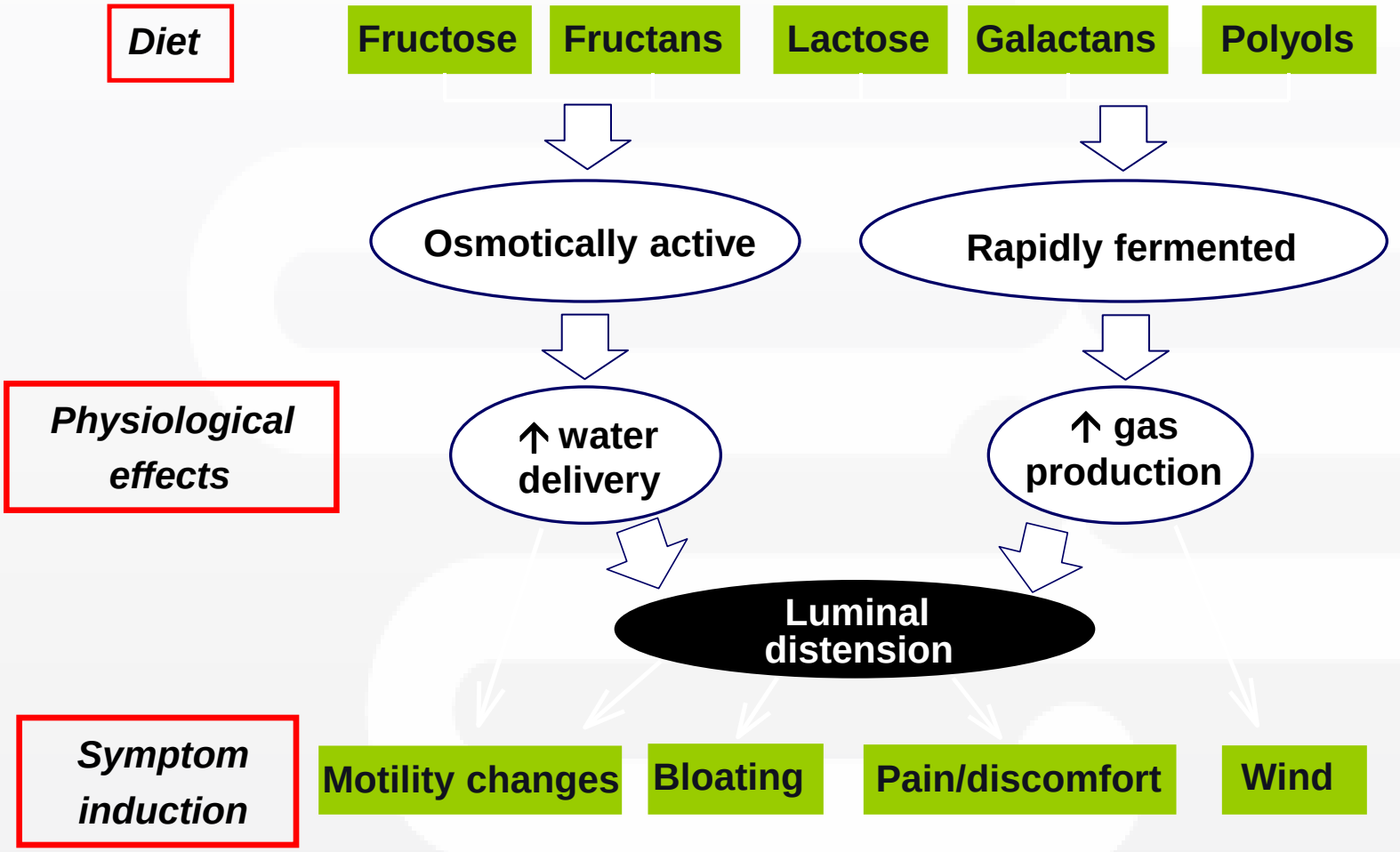
M

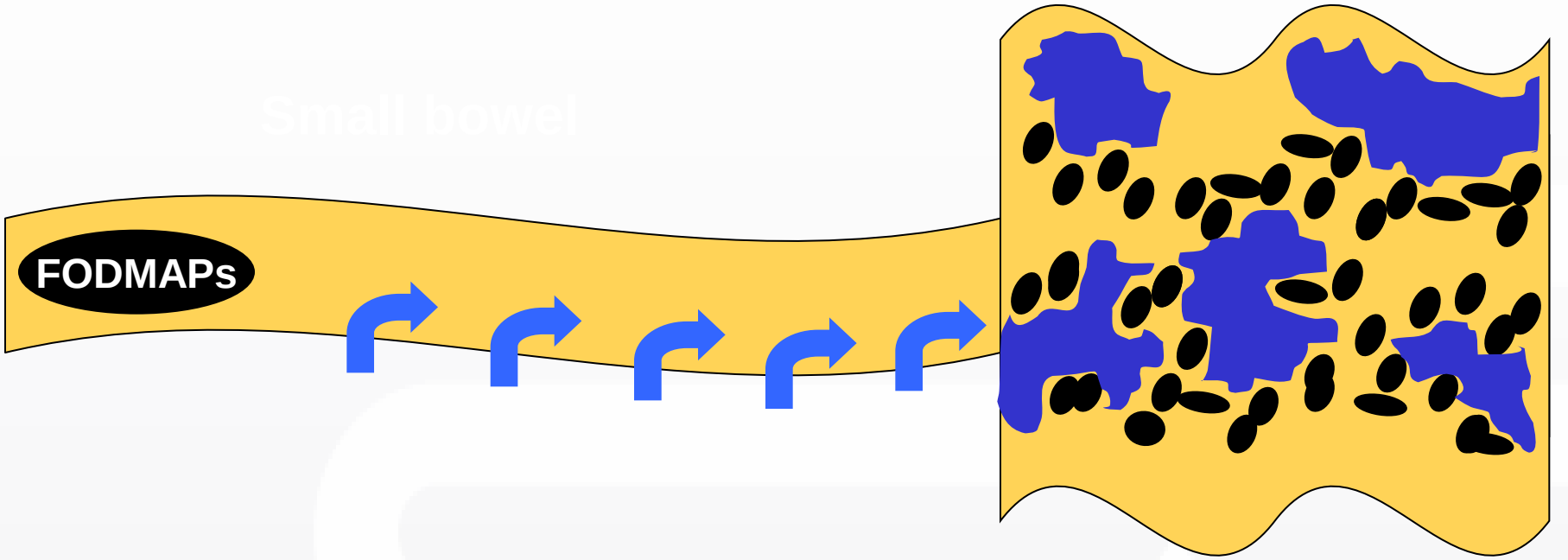
And

Polyols

sorbitol

The FODMAP hypothesis




FODMAPs
Luminal distension
gas
fluid
Bloating
Diarrhoea
Wind
Pain

Low FODMAP diet in IBS

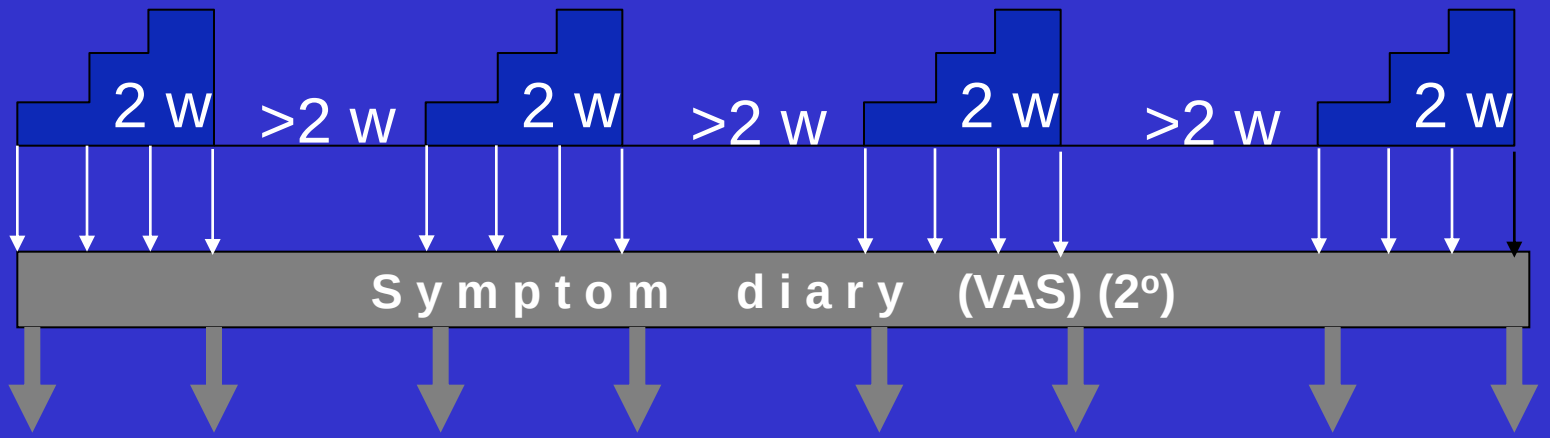
- n = 25
- 23-60 years, 4 male
- IBS (Rome II)
- FM +ve breath test
- Previous symptom improvement on low FODMAP diet

Study design

- **Fructan 7 g tds**
- **Fructose 14 g tds**
- **Fructose + fructan tds**
- **Glucose (placebo) 7 g tds**

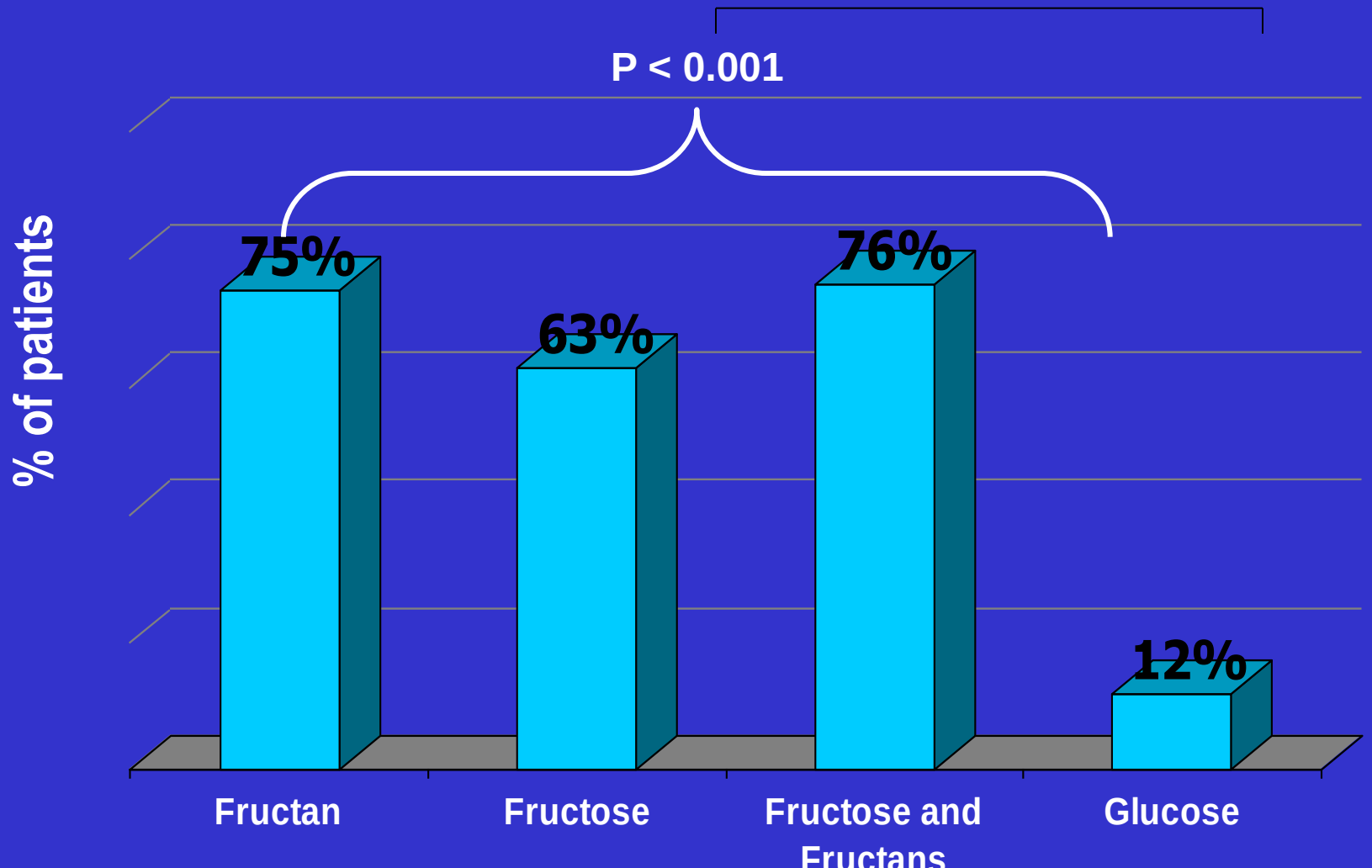
L O W F O D M A P D I E T (supplied to patient)

>2 week run-in

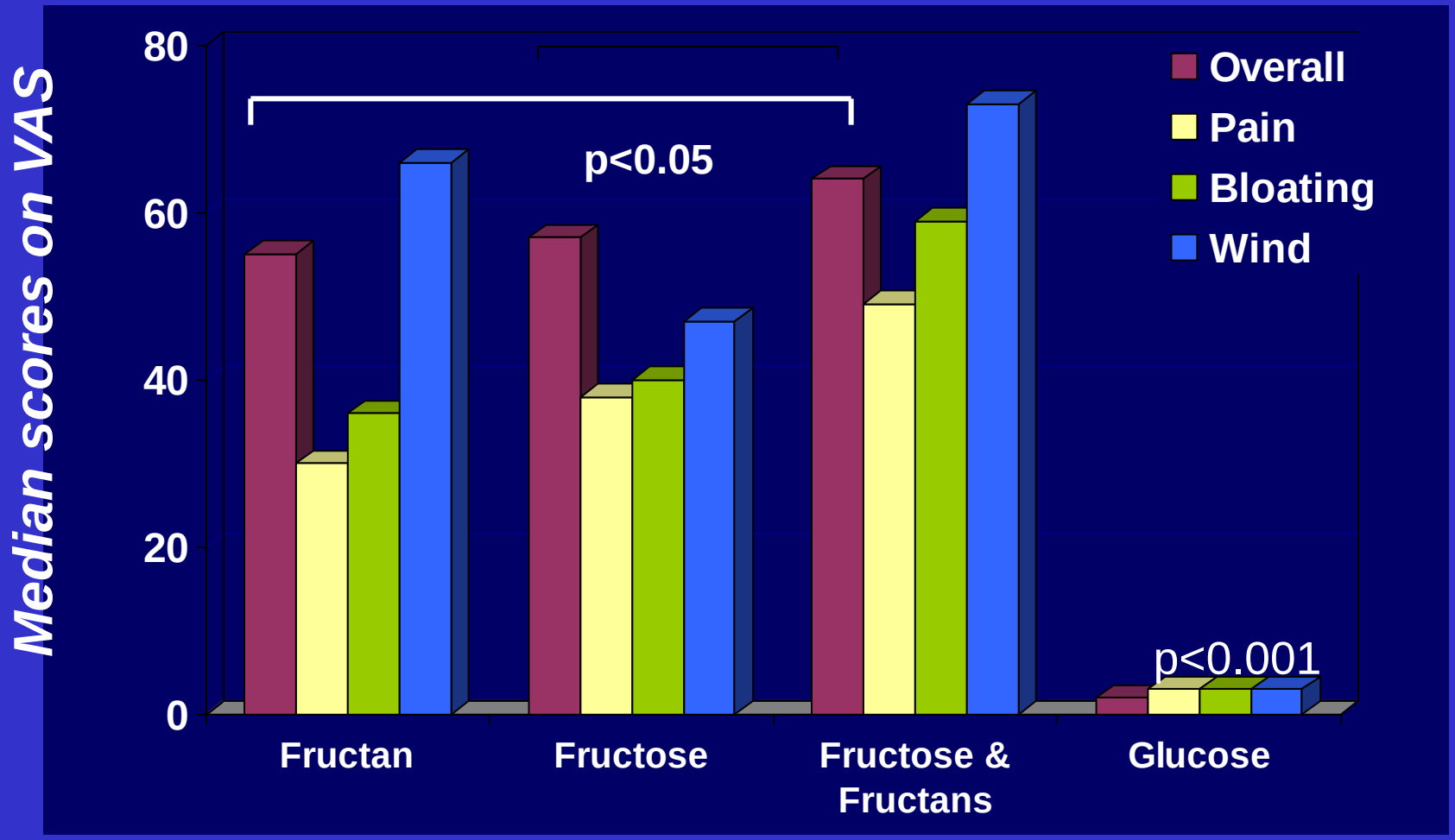


1º end-point:

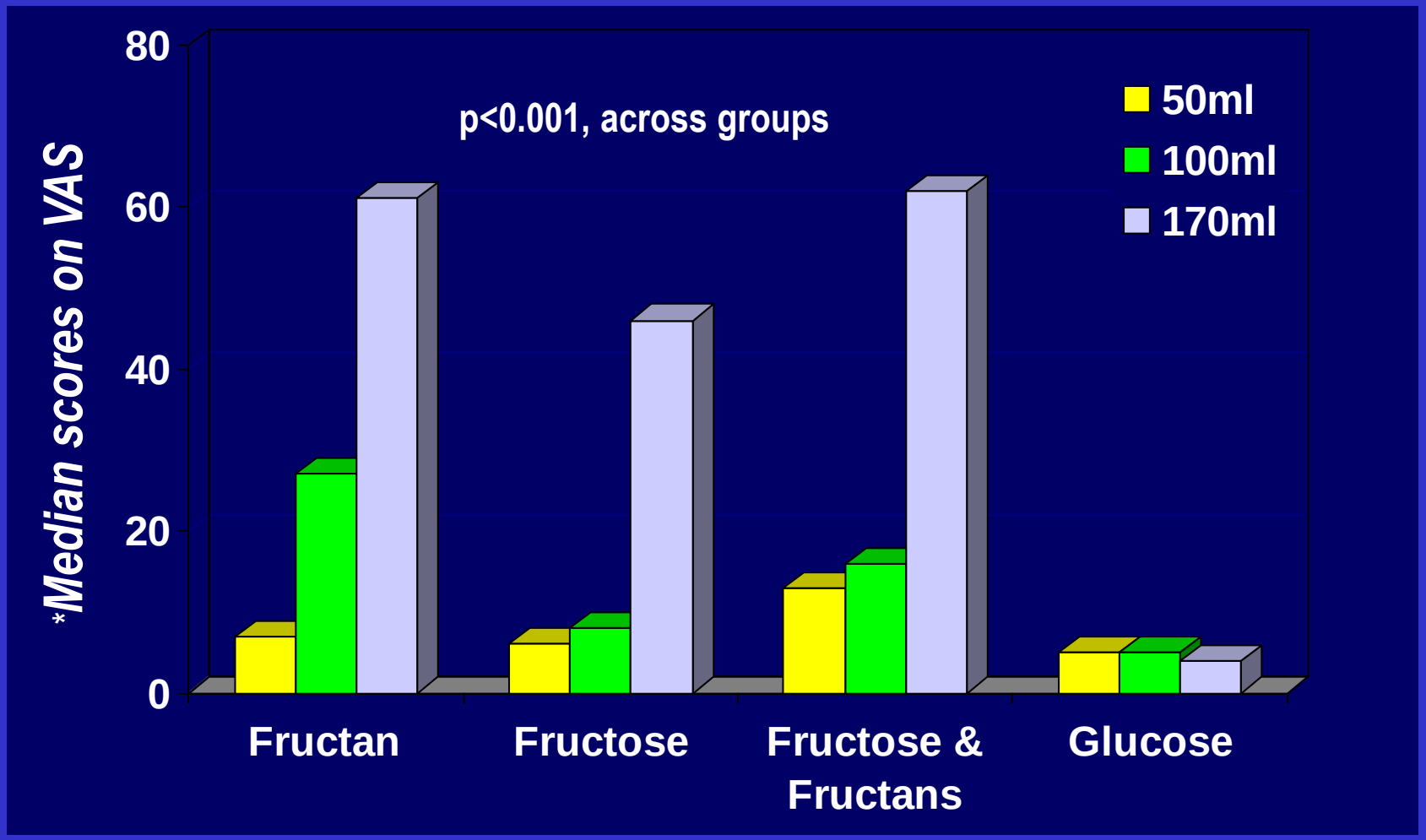
Symptoms not adequately controlled



2º end-point: Symptom scores



Effect of dose on overall symptom score



The low FODMAP diet is difficult- What is a H_2/CH_4 breath test?

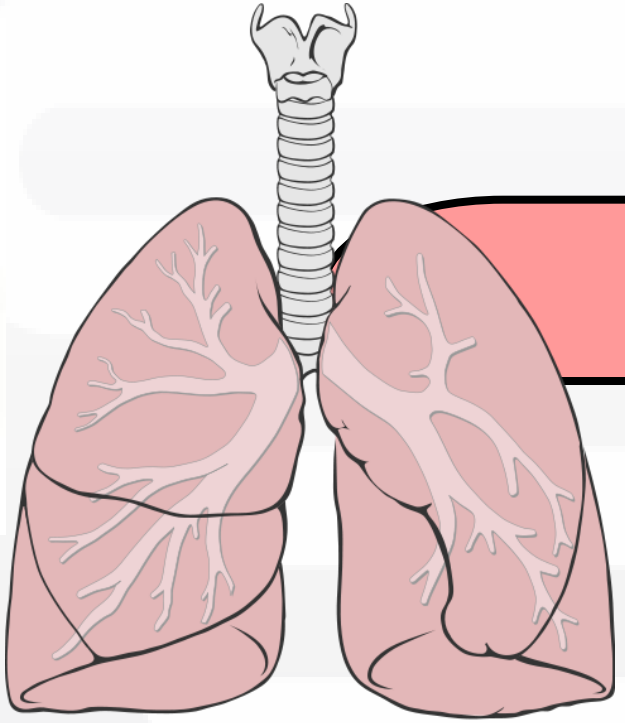
- 24 hours of low fermentable diet
- Lactulose test (positive control)
  - ? H_2 / CH_4 producer
  - ? Small intestinal bacterial overgrowth
- Fructose (35g)
- Lactose
- Glucose (proximal SIBO)
- Also look for symptoms
- Sequential breath tests Q15min until +/-

Colon

Small bowel

Lactulose

H_2 H_2 H_2 H_2 H_2 H_2



Must be able to measure methane too - 10% of people produce CH_4 not H_2

Positive Hydrogen Breath Test

Time (minutes)

Sugar	0	15	30	45	60	75	90	105	120	135	150	165	180	Symptoms
Lactulose 29-1-2007	0	0	0	0	3	21	15	24	23					None reported
Fructose 30-1-2007	0	0	0	12	22	38	37	46	20					Abdominal pain and diarrhoea
Lactose 10-2-2007	1	0	0	0	0	0	0	0	0					None reported

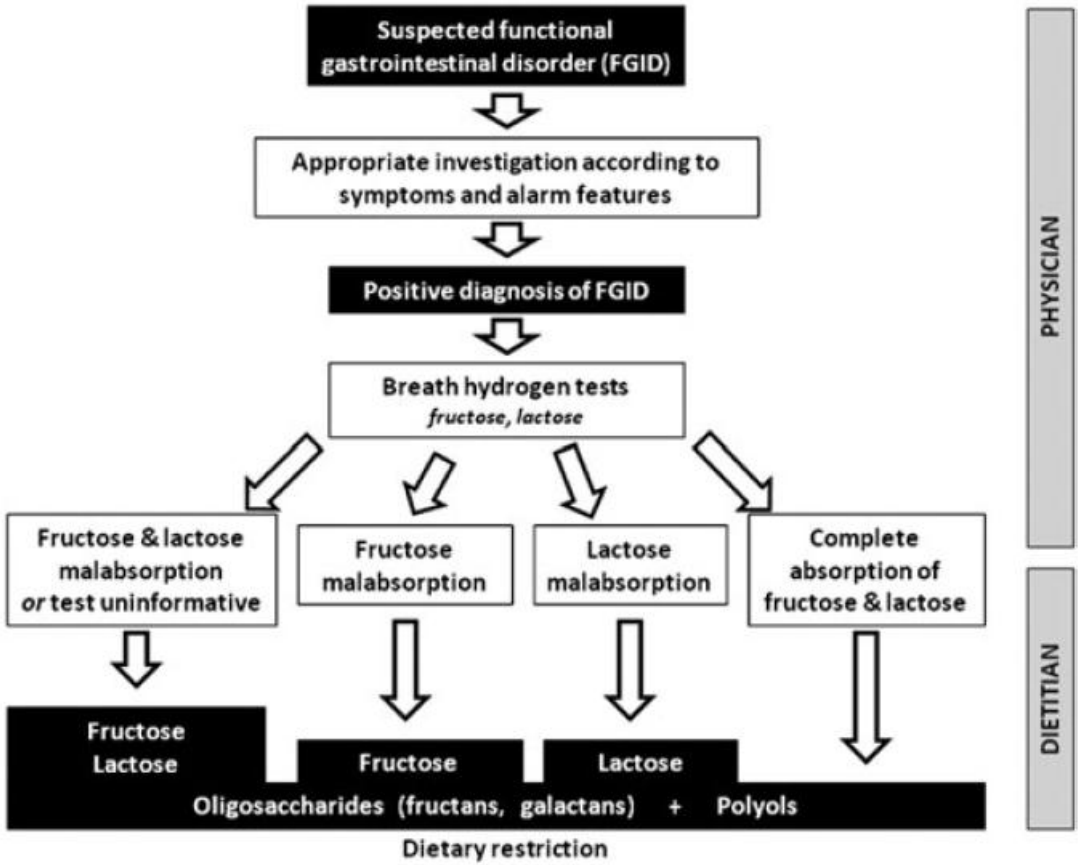


Figure 1 A bi-disciplinary approach to the patient with functional gastrointestinal disorder (FGID), especially irritable bowel syndrome or functional bloating. Breath hydrogen tests determine the degree of dietary restriction necessary by defining who can completely absorb fructose and/or lactose. Other FODMAP (oligosaccharides and polyols) are malabsorbed by all.

Other GI symptoms and diet

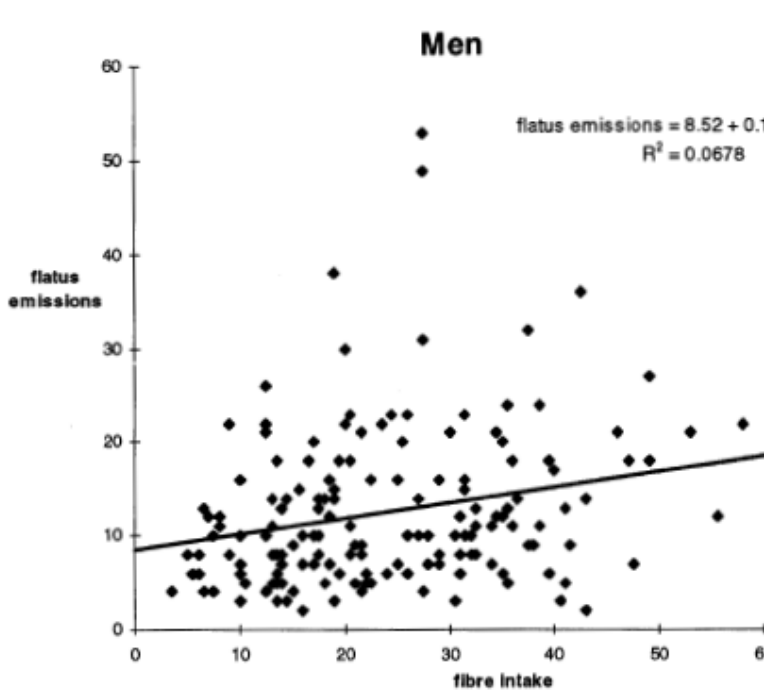
- Flatulence

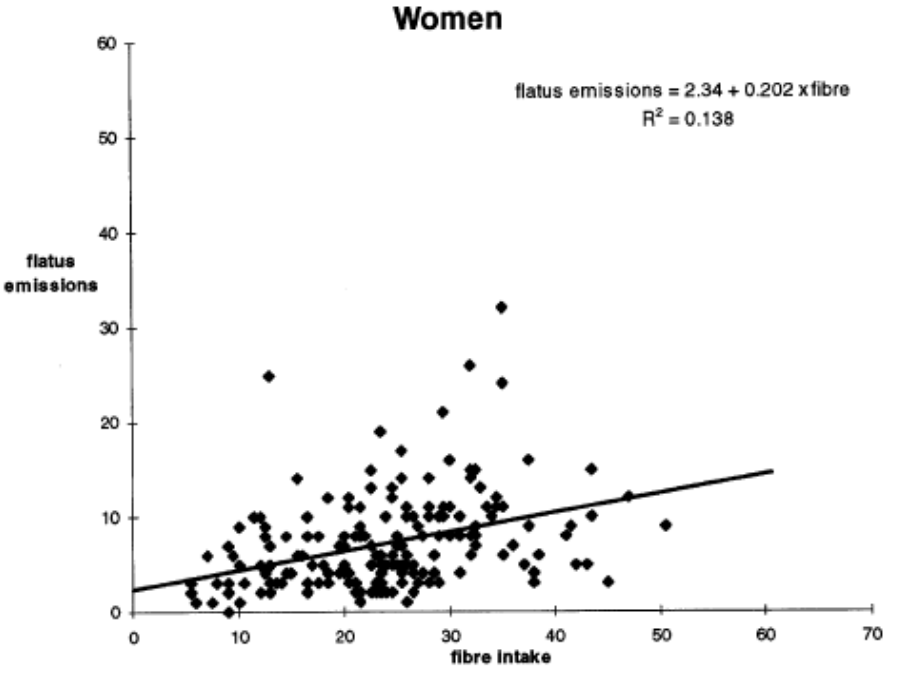
Foods that cause gas

- Beer
- Broccoli
- Cabbage
- Cauliflower
- Corn
- Cucumber
- Dried beans
- Milk
- Mushrooms
- Nuts
- Onions
- Peas
- Soda
- Spicy foods

Dietary fibre

- 120 normal individuals kept a flatus diary
  - Also measure aromatic content!





Dietary fibre

- Beer made no difference to frequency but increased aroma

- Men reported more aroma than woman

Baked beans

- A diet containing half of calories from baked beans
  - Increased flatus from 15 to 176mls/hour
- Due to bacterial fermentation

Foods that cause odour

- Asparagus
- Broccoli
- Brussels sprouts
- Cabbage
- Cheese
- Eggs
- Fish
- Garlic
- Horseradish
- Spices

Due to phenols, amines and sulphur

Other advice

- Avoid supplements
- Small regular meals
- Mix moist and dry foods
- Reduce protein
- Use rice as sole carbohydrate
- Regular exercise

Case example

- 52 year old CEO with an 8 year history of occasional burning epigastric pains
- No alarm symptoms
- Takes occasional Omeprazole and Mylanta

- Does this man need a Gastroscopy?
- Now presents with food bolus obstruction

Eosinophilic Oesophagitis

- Chronic immune/antigen mediated oesophageal disease characterised clinically by symptoms related to oesophageal dysfunction and histiologically by eosinophil-predominant inflammation

- Managed by PPI, steroids and dilatation

EE and diet

- Also treated by 6 food elimination diet
  - Cows milk, soy, wheat, eggs, nuts and fish

- Excluded then re-introduced
  - 64% reduction in Eo counts
    - Wheat and milk
  - 94% reduction in symptoms
    - Skin prick only predicted 13%
      - » Gonsalves et al gastro 2012

Case Example

- 39 year old lady with IBS symptoms has a positive ‘blood test’ for coeliac disease

- Does she need further investigation?
- What about her children?

Coeliac disease

- It is estimated that only 10-15% of cases in the USA are diagnosed

- Retrospective testing of stored serum in Olmsted county
  - Prevalence 4-4.5X compared to 50 years ago
    - » Rubio-Tapa A et al Gastro 2009

Changing picture of disease

- Classic form now rare
- Average age of diagnosis in 5th decade
- Many are overweight
- Sero-prevalence M=F
- Other presentations increasingly recognised
  - Anaemia
  - Osteoporosis
  - Obstetric problems
  - Neuropsychiatric
  - Autoimmune conditions

Testing for Coeliac disease

- Transglutaminase antibodies are best
  - Sensitivity 89%
  - Specificity 98%
    - » Van Der Windt et al JAMA 2010
  - Has replaced older tests
- Biopsy is gold standard

What about HLA DQ testing?

- Only HLA DQ2 or DQ8 are at risk
  - Test helpful for negative predictive value
  - If positive then 20% chance of developing disease
    - DQ2 homo 31X
    - DQ2/DQ8 14X
    - DQ8 homo 10X
    - DQ2 hetero 10X
    - DQ8 hetero 2X
      - » Pietzak Clin Gastro Hepatol 2009

What about diet in coeliac disease?

- Need to be completely gluten free
  - Serology starts to improve in 6 weeks
- Has been shown to reduce cancer risks
  - » Loftus and Loftus Gastro 2004
- My approach
  - Baseline DEXA scan
  - Can eat oats and ‘traces’ of gluten
    - Re-biopsy at 1 year and then advise from there

Conclusion

- Diet is important in many diseases
  - Food allergies vs intolerance
    - Role of breath testing
      - Guides dietary advice
      - Is helpful if positive or negative
- Eosinophilic oesophagitis
- Coeliac disease

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