Does your patient really have IBS?
(What do GI symptoms really mean?)

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Disclosures: 2005 onwards…..

Advisory board member / consultant / speaker:

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Eli Lilly
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General Electric

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Prostate Cancer UK
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East Midlands Cancer Alliance
Genzyme
Malaysian Palm Oil Board
Norgine Ltd
Philip Gould Trust
Rosetrees Trust
The Royal Marsden Charity

Hospitality

Cook Medical
SLA Pharma
Norgine
Shire Pharmaceuticals

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Mrs F

- 74 years old
- Bladder cancer – radiotherapy 1986
- Bilateral ureteric stents – 15 years
- 2008 left nephrectomy and re-implantation of right ureter
- Gall stones

- Borborygmi
- Bowels 5-10/ day since RT
- Diarrhoea / steatorrhoea
- Urgency+++
- Faecal incontinence x 1 -2 / week for years
- Flatulence +++
- Tenesmus
- Frightened to eat
- 25% body weight loss

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Mrs F

2 previous gastroenterologists

Investigations

- Colonoscopy x 3
- CT virtual colonoscopy x 1
- Blood tests

Treatments

- Trial of rifaximin (no benefit)
- Trial of colestyramine 4g od (no benefit)
- Many anti-diarrhoeals

**"Nothing can be done…. you will have to live with it…
luckily your cancer has not come back"**

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SOME
THINGS
ARE NOT
IMPORTANT

Steps to managing patients like Mrs F?

1. What symptoms do people get after cancer treatments?
2. What do individual symptoms mean?
3. What causes those symptoms?

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Symptoms

Altered taste & smell	Vomiting/ retching	Urgency of defecation
Halitosis	Cramps/ trapped wind	Faecal incontinence
Dysphagia to liquids	Upper abdominal pain	Steatorrhoea
Dysphagia to solids	Lower abdominal pain	Rectal bleeding
Belching/ burping	Rectal pain	Perianal pruritis
Heartburn	Bloating	Nocturnal defecation
Early satiety	Rectal flatulence	Constipation
Reduced appetite	Borborygmi	Loose stool
Hiccups	Tenesmus	Need to strain
Nausea	Mucus in stool	Fatigue/ lethargy

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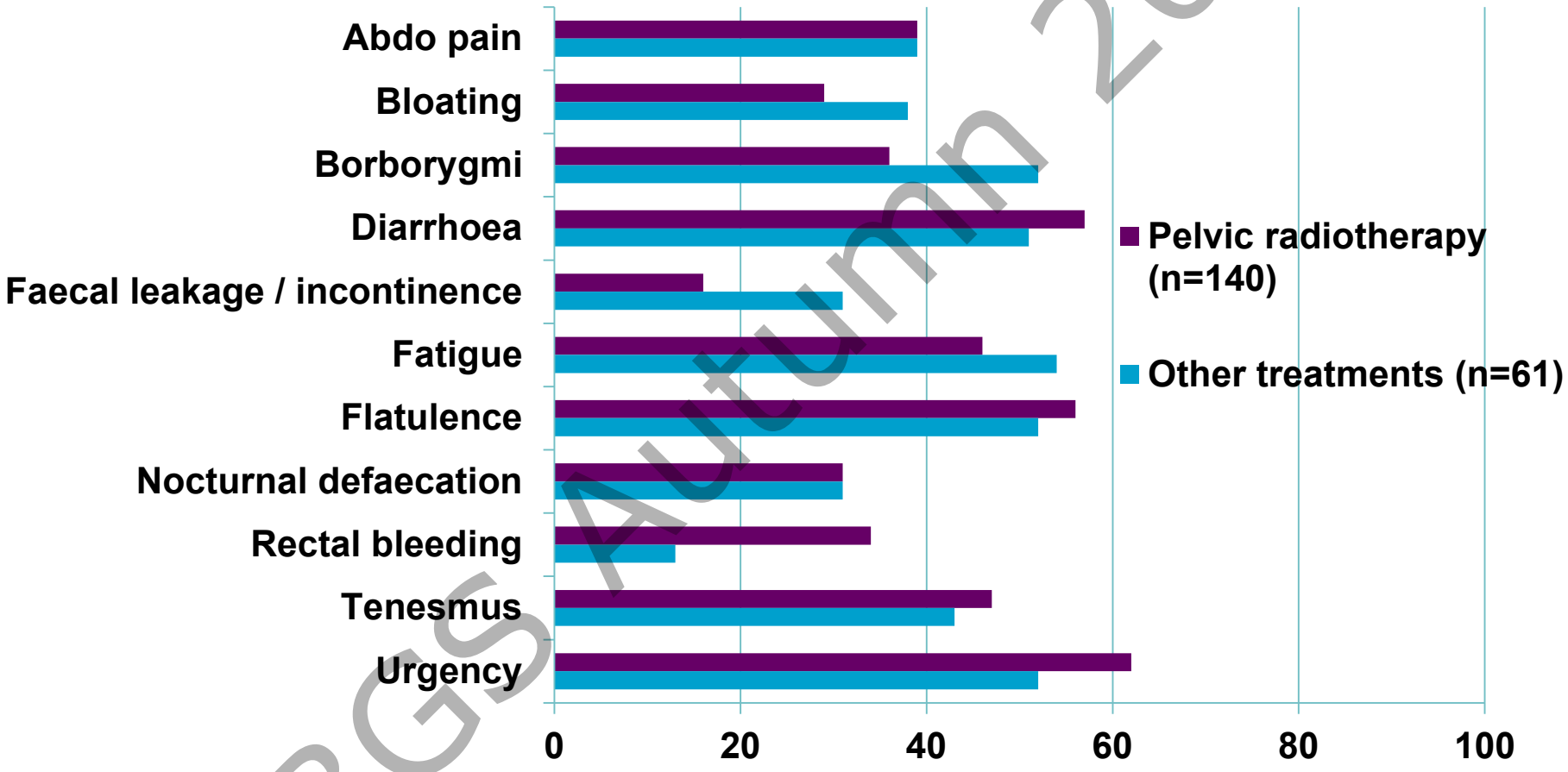
Audit: % of patients with moderate or severe GI symptoms (n=201)



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Steps to managing patients like Mrs F?

1. What symptoms do people get after cancer treatments?
   - many and all need treating

2. What do individual symptoms mean?

3. What causes those symptoms?

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Mr. H

- 84 year old, normal bowel function pre-RT
- Prostate cancer, 1 year after conformal RT
- Normal PSA
- Bowels open x4 per day
- Urgency
- Often loose stool
- Faecal incontinence weekly
- Tenesmus
- Perianal soreness

Too much fibre

Mr. J

- 72 year old, normal bowel function pre-RT
- Prostate cancer, 1 year after IMRT
- Bowels open 3-6 per day
- Urgency
- Often loose stool
- x2 faecal incontinence / month
- Tenesmus
- Perianal soreness

Giardia
&
2cm sigmoid polyp

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Hannah

Stem Cell Transplant for Leukaemia

Week 7	**diarrhoea:**	**Flexi sig**	**GvHD**
Rx tacrolimus + steroids - settled			
Week 11	**diarrhoea:**	**OGD/Flexi sig**	**SIBO**
Rx ciprofloxacin – settled		**+D2 aspirate**	**(Klebsiella)**
Week 14	**diarrhoea:**	**OGD/Flexi sig**	**SIBO**
Rx doxycycline – settled		**+D2 aspirate**	**(Ecoli)**
Week 17	**diarrhoea :**	**OGD/Flexi sig**	**CMV**
valgancyclovir – settled		**+D2 aspirate**	
Week 20	**diarrhoea**	**OGD/Flexi sig**	**SI Candida**
Rx fluconazole/amphotericin- settled		**+D2 aspirate**	**Glabrata**
Week 35	**diarrhoea**	**History**	**Lansoprazole**

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Steps to managing patients like Mrs F?

1. **What symptoms do people get after cancer treatments?**

- many and all need treating

2. **What do individual symptoms mean?**

- Its impossible to say

3. **What causes those symptoms?**

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Why GI symptoms?

Any insult

Pathological change

Cell death
Atrophy
Ischaemia
Oedema
Inflammation
Fibrosis

Affects specific GI physiological functions depending on the affected site

Symptoms

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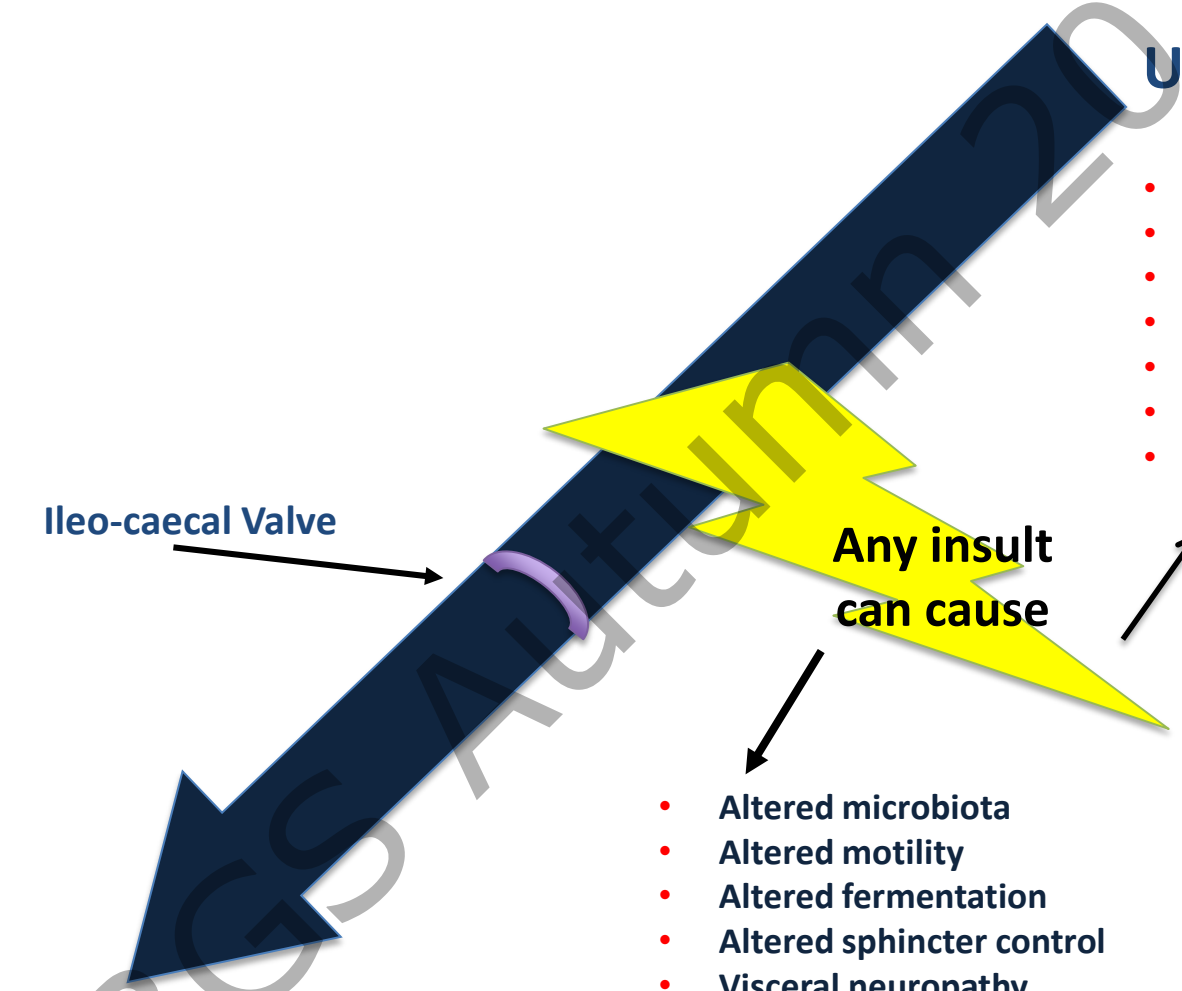
Modigliani Gastroenterology 1990, Hovdenak Int J Radiat Oncol Biol Phys. 2000
Shen Gastroenterology 2001, Osada J Gastroenterol Hepatol 2008, Lemmens Inflamm Bowel Dis 2013

What physiological changes?



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Using the concept of symptoms are due to “physiological upset”

Management of complex symptoms becomes straightforward

Assess each of the 30 symptoms accurately

For abnormal symptoms arrange appropriate tests to identify which physiological deficits are present

->obvious treatment options

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Algorithm-based management of patients with gastrointestinal symptoms in patients after pelvic radiation treatment (ORBIT): a randomised controlled trial

H Jervoise N Andreyev, Barbara E Benton, Amyn Lalji, Christine Norton, Kabir Mohammed, Heather Gage, Kjell Pennert, James O Lindsay

Summary

Background Chronic gastrointestinal symptoms after pelvic radiotherapy are common, multifactorial in cause, and affect patients' quality of life. We assessed whether such patients could be helped if a practitioner followed an investigative and management algorithm, and whether outcomes differed by whether a nurse or a gastroenterologist led this algorithm-based care.

Published Online September 23, 2013 http://dx.doi.org/10.1016/S0140-6736(13)61648-7

See Online/Comment

Funded by: "Research for Patient's Benefit", a programme of the National Institute for Health Research

The Lancet December 2013

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Aims of this RCT (n=218):

1. Is using management checklist followed systematically for new onset GI symptoms after pelvic radiotherapy effective?

   Yes p=0.006

2. Outcomes when patients are managed by a specialist nurse are not inferior to those managed by a gastroenterologist?

   Yes p=0.2

3. Is it cost effective?

   £ 1,000

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Mrs F

- 74 years old
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- Gall stones

- Borborygmi
- Bo…

…ontinence for years

…ce +++

Tenesmus

- Frightened to eat
- 25% body weight loss

Complicated symptoms

=

Lots of simple symptoms

Endoscopy alone without other investigations only adequate in 4% patients

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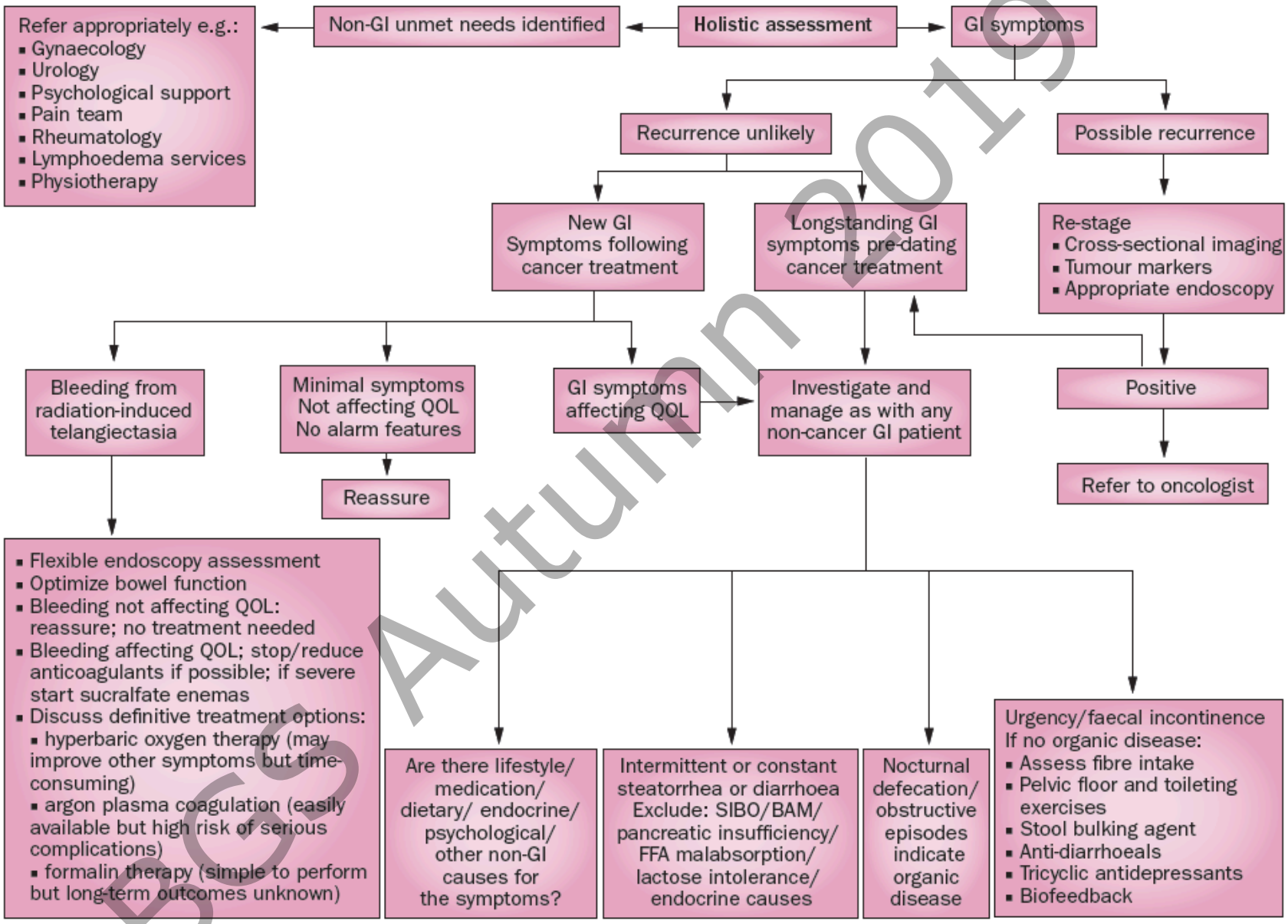

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Hauer-Jensen, Denham, Andreyev Nat Rev Gastroenterology & Hepatology 2104

Mrs F

Holistic needs assessment

- Depressed -> psychological support (citalopram)
- Vaginal bleeding -> gynaecology (topical hormone therapy)
- Profound hypoMg^{2+} & hypoCa^{2+} (optimally replaced)

Gastroenterological evaluation

- Faecal elastase low – (pancreatic supplements)
- SeHCAT scan – severe bile acid malabsorption (colesevelam and low fat diet)
- Breath test confirmed SIBO (ciprofloxacin)
- Severe biliary gastritis (mucaine)
- Vit B12 and vitamin D deficiency (replaced)

Outcome

- Thriving
- Weight gain

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Treatment decisions: is experience enough?

- Prospective study new patients n=47
- 92 GI diagnoses were predicted
- 168 new GI diagnoses were made
- 41 (24%) diagnoses matched the prediction
- 62% of patients > 3 GI diagnoses
- No clinicians predicted the correct combination

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Muls European J Cancer Care 2017

Symptoms of BAM

- Abdominal pain/cramps
- Bloating
- Flatulence
- Frequency
- Incontinence
- Loose stool
- Nocturnal defaecation
- Steatorrhoea
- Urgency
- Weight loss/ gain

Symptoms of EPI

- Abdo pain/cramps
- Bloating
- Borborygmi
- Flatulence
- Foul smelling stool
- Loose stool
- Nocturnal defaecation
- Steatorrhoea
- Urgency
- Wind
- Weight loss

Symptoms of carbohydrate malabsorption

- Abdo pain/cramps
- Bloating
- Borborygmi
- Diarrhoea
- Flatulence
- Nocturnal defaecation
- Urgency
- Wind
- Weight loss

Symptoms of SIBO

- Abdo pain
- Belching
- Bloating
- Borborygmi
- Constipation
- Diarrhoea
- Flatulence
- Gastric stasis
- Mucus discharge
- Nausea/vomiting
- Nocturnal defaecation
- Steatorrhoea

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Wedlake Clinical Therapeutics 2009

Grace Aliment Pharm & Therapeutics 2013

Are there any lessons to learn from this approach to the patients with GI consequences of cancer treatment ……

for the most frequent patient in the GI clinic,

the person with Irritable Bowel Syndrome?

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Joanna

- 76 years old
- 2 week wait pathway: ‘change in bowel habit’
- Hypothyroid, Hypertension, Osteoarthritis, Type 2 DM
  Cholecystectomy 192
- DH: Thyroxine, Ramipril, Amlodinine, Atorvastatin, Laxido
- 3 children, 5 grandchildren
- Thoroughly miserable

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Joanna

- 3rd Colonoscopy – normal

- Bowels open x1 in 3 days - 6 times / day +/- urgency
- Stool constipated -> normal -> pellety -> loose
- Bloating
- Pains helped by bowels being open
- Pain associated with loose stool
- Need to strain
- Leakage every 2-3 weeks

- Symptoms for 30 years

Happy this is IBS?

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What is Irritable Bowel Syndrome?

- “Typical symptoms”
- No other disease detected in the bowel
- Affects 1 in 5 people

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What are those typical symptoms?

Rome IV Criteria

Pain or discomfort in the belly + change in bowel habit

- Longer than 6 months
- More than 3 days in 3 months

AND two of the following:

- Pain is relieved by bowel movement
- Start of pain is linked to a change in the frequency of stool
- Start of pain is linked with change in stool appearance

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Irritable Bowel Syndrome symptoms?

1 in 3 people have CONSTIPATION

1 in 3 people have DIARRHOEA

1 in 3 have mixed DIARRHOEA & CONSTIPATION

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NICE approach

Recommended tests

- FBC
- ESR
- CRP
- Coeliac screen

Unnecessary tests

- Ultrasound
- Sigmoidoscopy
- Colonoscopy
- TFTs
- Faecal ova and parasites
- Faecal occult bloods
- Hydrogen breath testing

Advise on lifestyle modifications

- Reduce stress
- Fibre intake 30g
- Regular m
- Flu
- rch
- fruit
- oid sorbitol
- Trial wheat / lactose exclusion
- Increase activity
- Use of probiotics

There is a lack of good quality evidence on the role of lifestyle modification

Drug treatments?

- Antispasm
- TCA
- SSRI

The evidence base for drug treatments is generally poor

AND >50% will still have their symptoms after 7 years

NICE 2017

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Organic disease misdiagnosed as IBS-D

1.	Small bowel bacterial overgrowth	41%
2.	Bile acid malabsorption	28-32%
3.	Carbohydrate malabsorption	35-64%
4.	Pancreatic insufficiency	6%
5.	Non-coeliac gluten sensitivity	0.6-6%
6.	Coeliac disease	2.8-5%
7.	Infectious diarrhoea	<1%
8.	Inflammatory bowel disease	<1%
9.	Cancer	<1%

Cash 2002, Whitehaead 2006, Jellema 2009, Jadallah 2009, Wedlake 2009, Leeds 2010, Tang 2013, Goebel-Stenglel 2014

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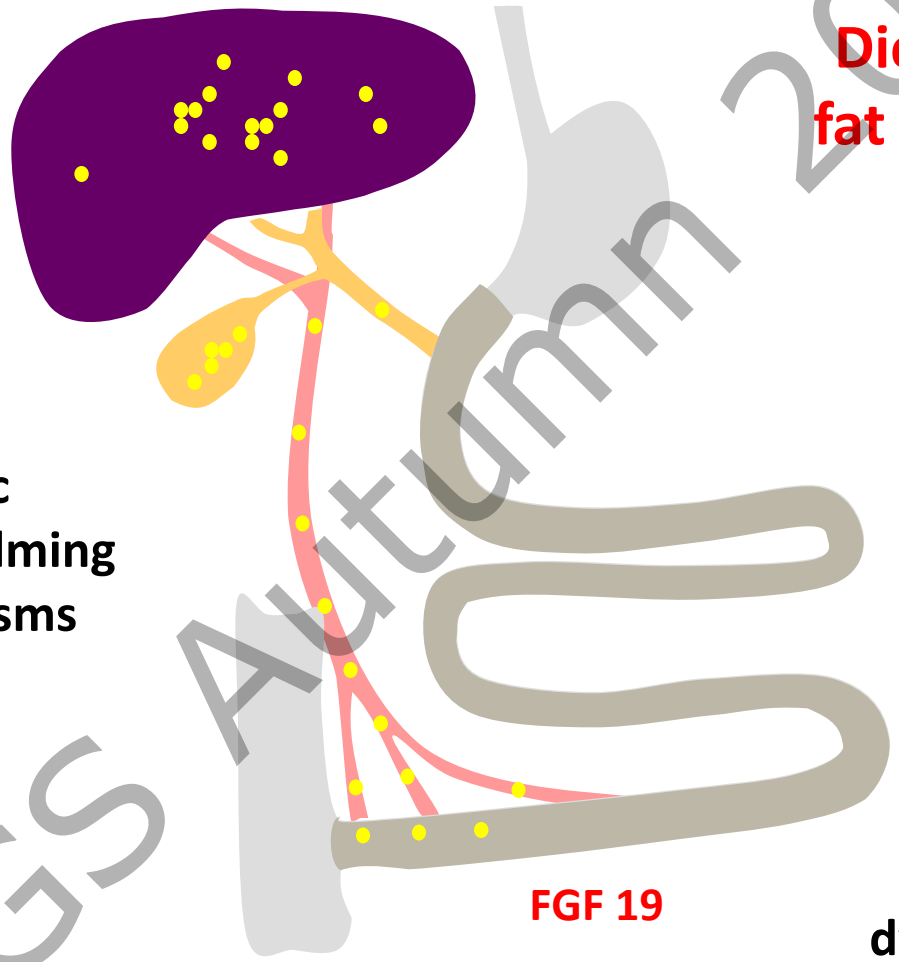
Enterohepatic circulation of bile acids



Dietary fat intake

increased hepatic production, overwhelming absorptive mechanisms = BAD

FGF 19

terminal ileal dysfunction = BAM

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Bajor A 2006, Walters 2009, Hoffman 2009

Frequency of bile acid malabsorption misdiagnosed as IBS-D?

A systematic review:

- **18 papers over 30 years**
- **1223 patients**

- **32% were misdiagnosed**

- **Condition more common than coeliac disease**
- **Affects >1% of the British Population**

Wedlake Alimentary Pharmacology & Therapeutics 2009

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Survey of gastroenterologists

- 706 consultant gastroenterologists in the UK (hepatologists excluded)
- Response rate = 62%

Showed ->

- In the large majority of patients with possible primary bile acid diarrhoea, the diagnosis was not considered

Khalid Clinical Medicine 2010

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What is the response of BAM /BAD to treatment

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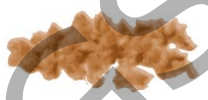
Gupta J Supportive Care Cancer 2015

Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on the surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. **Entirely Liquid**

Type 6 or 7

-> SeHCAT scan

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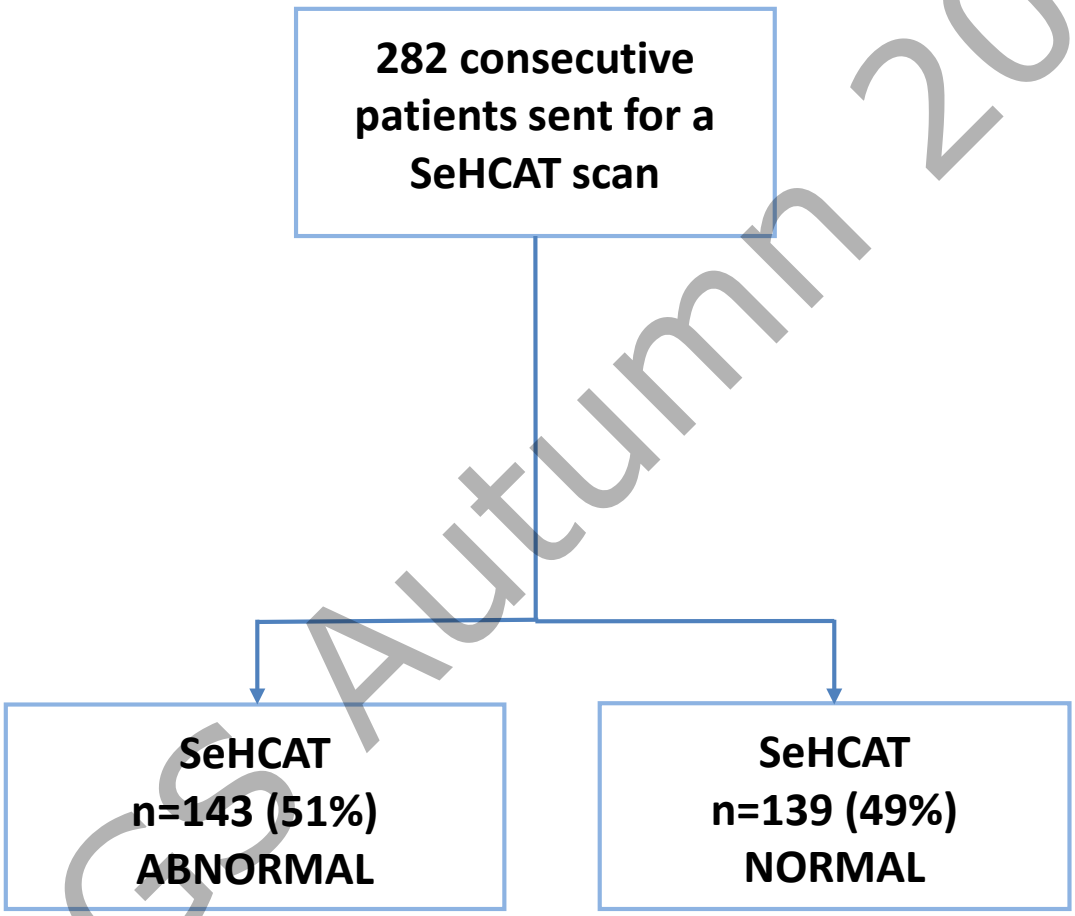

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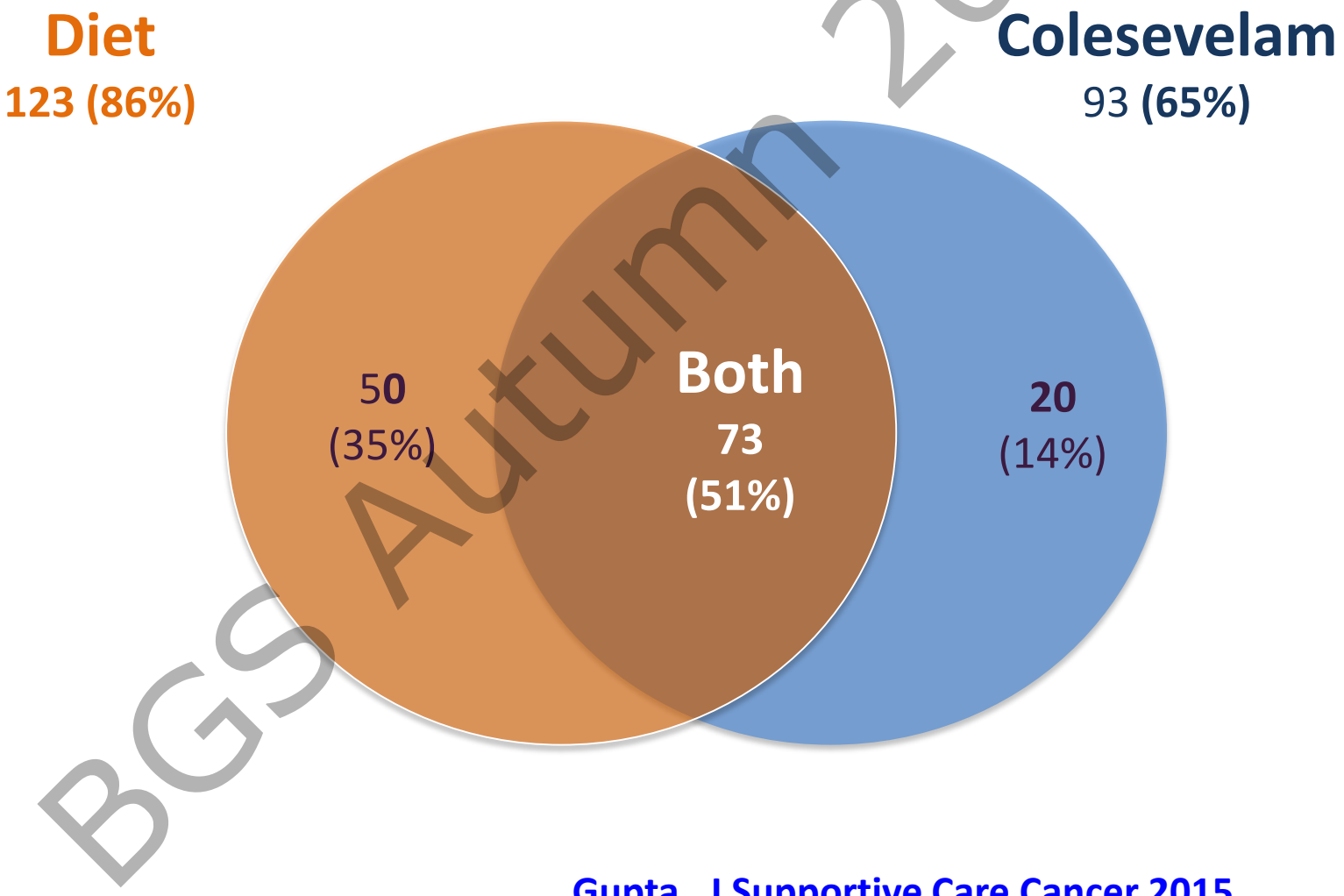
Gupta J Supportive Care Cancer 2015

Treatment prescribed in BAM cohort:



Gupta J Supportive Care Cancer 2015

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Which symptoms improved?

	Change in symptom score [n= (%)] Improvement	Wilcoxons test p-value
BAM cohort (n=143)		
Urgency	97 (68)	0.0001
Incontinence	79 (55)	0.0001
Wind	62 (43)	0.0001
Nocturnal BO	62 (43)	0.0001
Tiredness	58 (41)	0.0001
Abdominal pain	57 (40)	0.0001
Bloating	47 (33)	0.0001
Steatorrhoea	45 (31)	0.001

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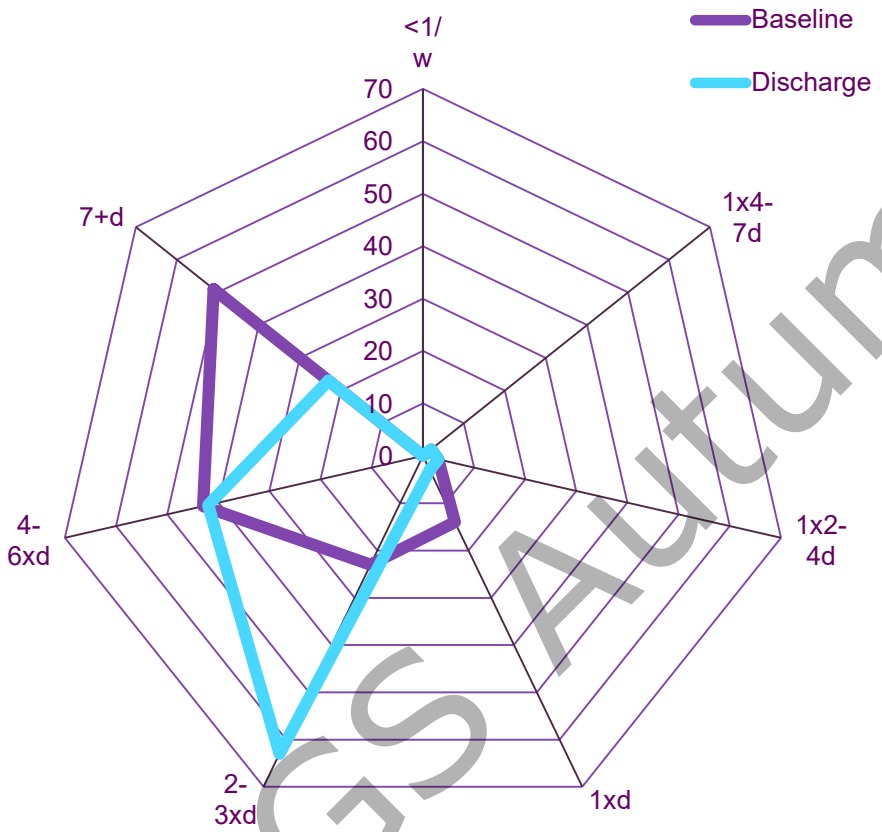
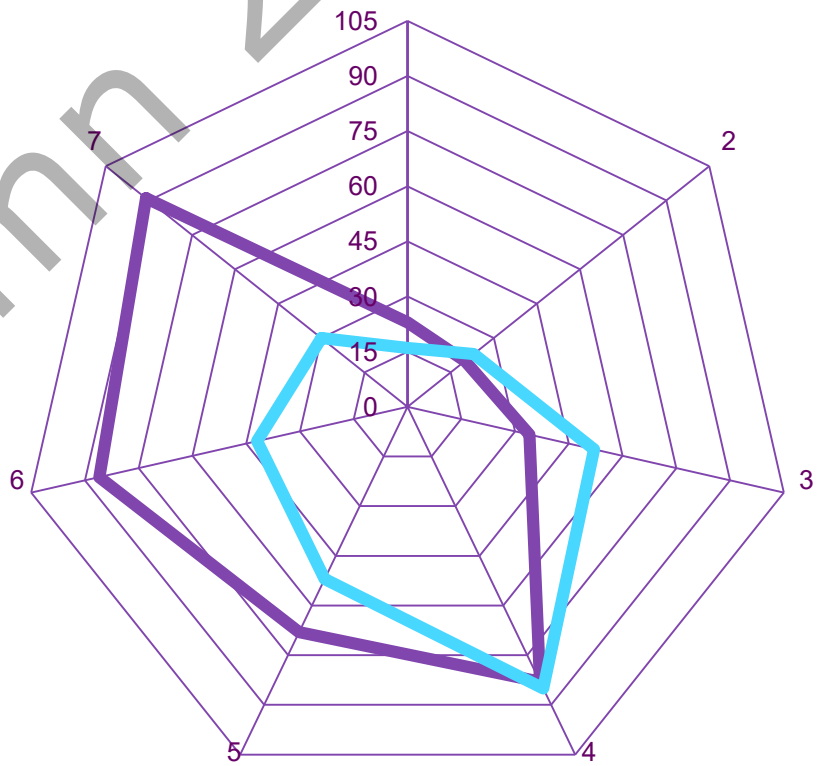
Gupta J Supportive Care Cancer 2015

Reported stool frequency



Reported stool consistency



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Gupta J Supportive Care Cancer 2015

Diet to help manage BAM

- 40 patients
- 20 male, 20 female
- Mean age 61 (range 22-90 years)
- Definite bile acid malabsorption
- 25 Colesevelam and still symptomatic
- Willing to consider fat as max 20% of calories

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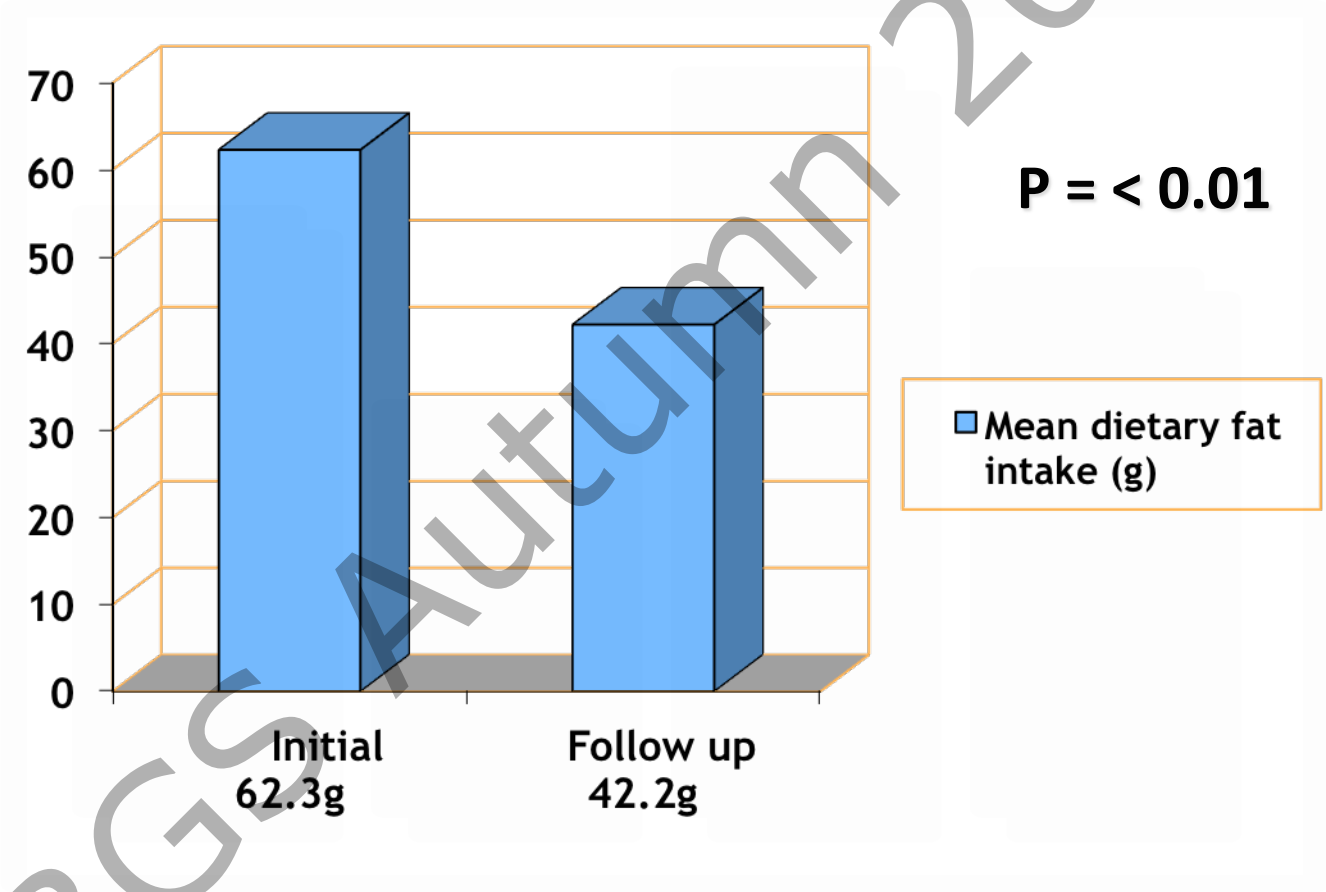
Watson Clin Medicine 2015

Change in reported dietary fat intake



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Watson Clin Medicine 2015

Improvement in symptoms

	p value
Urgency to open bowels	<0.01
Bloating & distension	<0.01
Lack of control	<0.01
Frequency of opening bowels	<0.01
Flatulence & wind	<0.05
Abdominal pain	<0.05
Steatorrhoea	<0.05
Abdominal gurgling	<0.05

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Watson Clin Medicine 2015

Joanna

- Nocturnal defecation x1 every 6 weeks
- Sensitivity to richer foods
- Significant improvement in her symptoms for 3 weeks after her colonoscopy
- AXR & SeHCAT scan

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Joanne – clear diagnoses

- **AXR – faecal loading**

- **SeHCAT scan 7 day retention 6%**
  -> Moderate bile acid malabsorption

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Joanne

Management of the faecal loading

- **Picolax**
- **Change her position on the lavatory**

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Joanne

Management

- Picolax
- Change her position on the lavatory
- Pelvic floor exercises
- Use regular Normacol™
- Use of a regular glycerine suppositary
- Added bile acid sequestrant - Colesevelam

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Joanne

6 weeks later

- **“I feel great”**
- **“I’m a different person”**

3 months later

- **“You have transformed my life after 30 years”**

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