



# Traffic Jam Ahead

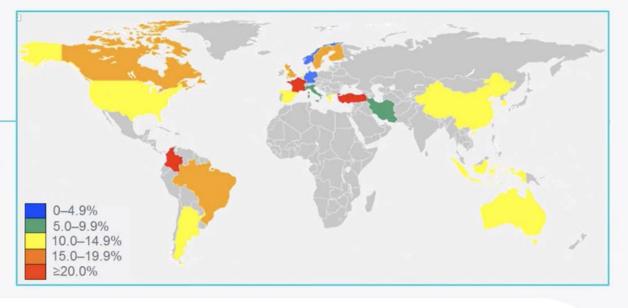
## Restoring Flow to the Mobbed Colon

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# Introduction: Epidemiology

#### Prevalence by country



#### Pooled prevalence



#### Gender

♀ 17.4% (95% CI: 13.4–21.8); OR = 2.22 (95% CI: 1.87–2.62)

3 9.2% (95% CI: 6.5–12.2)

#### Age group (years)

<29: 12.0% (95% CI: 10.0–14.0); OR = 1.0

30-44: 15.0% (95% CI: 12.0-19.0); OR = 1.20 (1.09-1.33)

45-59: 16.0% (95% CI: 11.0-21.0); OR = 1.31 (1.09-1.58)

≥60: 17.0% (95% CI: 13.0–22.0); OR = 1.41 (1.17–1.70)

#### Socioeconomic status

High: 14.0% (95% CI: 8.0–22.0); OR = 1.0

Medium: 15.0% (95% CI: 8.0–22.0); OR = 1. 01 (0.92–1.10) Low: 18.0% (95% CI: 12.0–25.0); OR = 1.32 (1.11–1.57)

### **Quality of life**

A systematic review of 8 pooled studies showed that, for both adults and children in a community or hospital setting, <u>all</u> domains of the SF-36 were negatively affected by functional constipation



The magnitude of the negative impact was comparable to that seen in patients with allergies, musculoskeletal conditions and inflammatory bowel disease

#### **Economic**

European real-life data on the economic burden of chronic idiopathic constipation are scarce.

A recent retrospective cohort study from Sweden of 4,043 patients calculated that in the 12-month follow-up period, patients with chronic constipation had:

- A mean of 2.3 ± 7.5 constipation-related contacts and a mean of 15.2 ± 19.5 other healthcare-related contacts
- Annual costs (adjusted for sex, age, mortality, and comorbidities) were €5,388, of which €951 were for constipation-related care

## What is constipation?

Infrequent passage of stools

## What is constipation?

- Healthy individuals v/s patients complaining of constipation:
  - Healthy: 6.8 BMs/week
  - Patients: 1.0 BM/week

### What is normal bowel frequency?

- Once daily?
  - Maybe
- Similar number of healthy individuals open their bowels:
  - Less than once daily
  - Once daily
  - More than once daily

## Houston, Do We Have a Problem?



 Many definitions of constipation have been used in the literature

Physicians v/s Patients

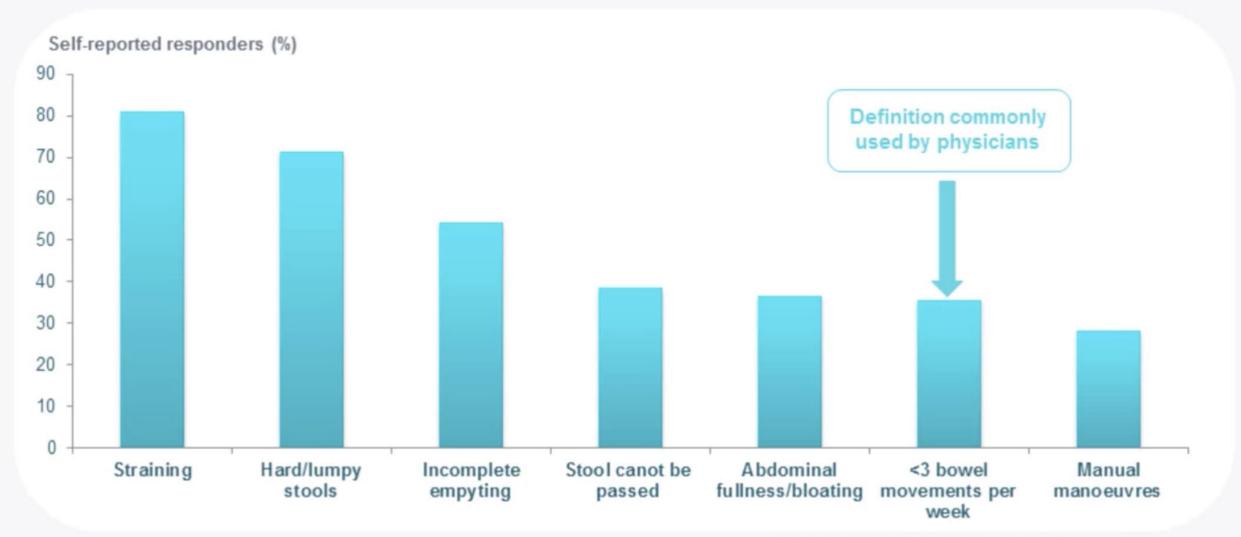
## What is constipation?

 Infrequent passage of stools

- Bloating and discomfort
- Hard stools
- Straining
- Feeling of incomplete evacuation
- Abdominal pain
- Faecal incontinence
- Need for rectal or vaginal manipulation

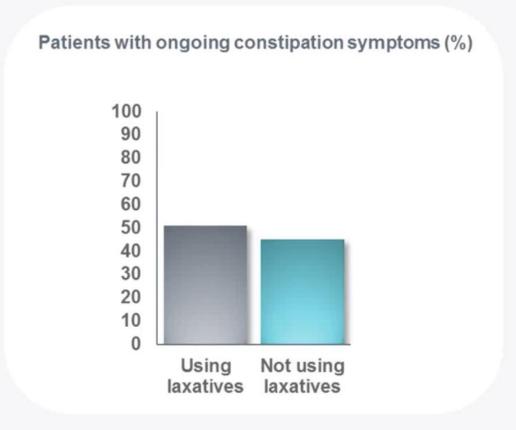
### Most bothersome self-reported symptoms in self-reported constipation

- 1,149 participants
- 27.2% self-reported constipation within the past 3 months
- 16.7% and 14.9% had constipation according to the Rome I and II criteria



## Houston, Do We Have a Problem?

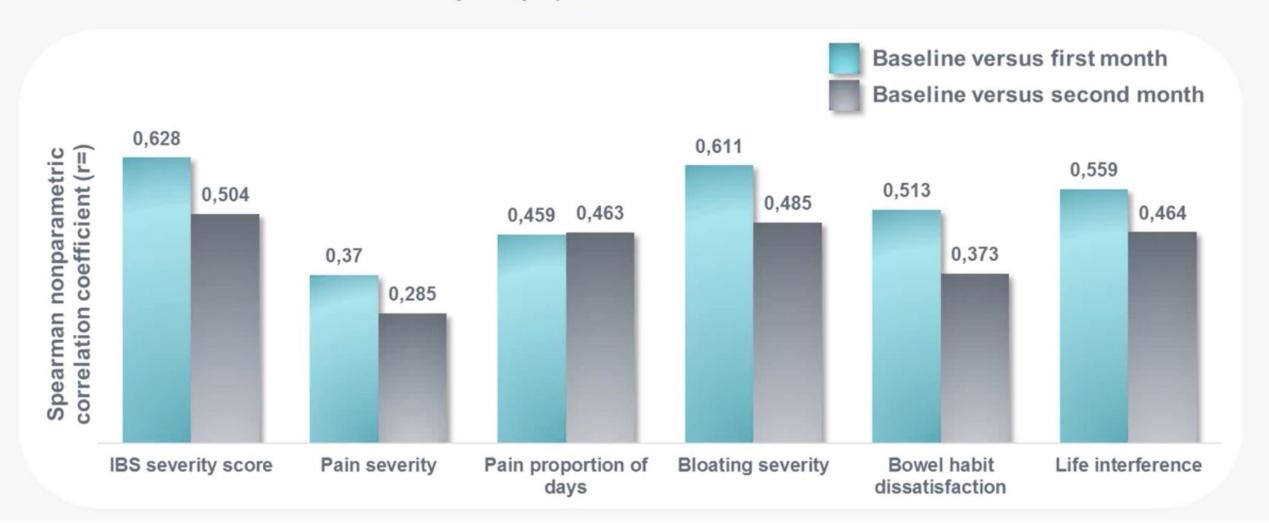




### **Bowel diary**

Value elegantly demonstrated by Palsson et al. in a prospective study of 185 well-defined (Rome III) IBS patients for an average of 73 consecutive days, yielding data on 24,642 stools

- The correlation between scores on the baseline retrospective questionnaire and the diary-based scores was poor
- Patients overestimated the severity of symptoms at baseline

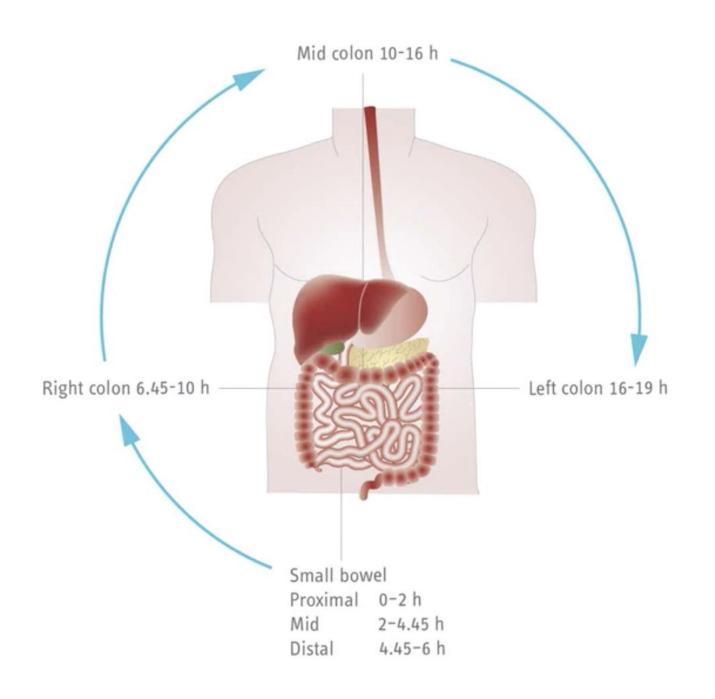


## Physiology of Defecation

 Defecation is a complex process that requires interplay between several different factors

 Control is mostly subconscious but conscious control is also involved

- Gut movement (transit)
- Pelvic floor evacuation (voiding)
- Motor function
- Social context
- Emotional context



### Proportion of different types of constipation

466 patients\* with constipation† referred to a gastroenterology referral unit 251 (54%) secondary constipation

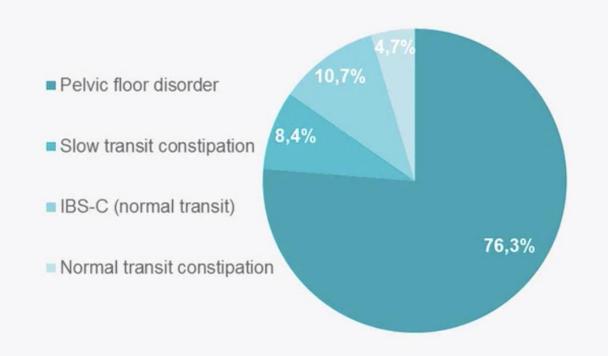
#### Including:

- Pharmacology (27%)
- Endocrine disorders (16%)
- Psychiatric disorders (13%)

\*382 women, 82 men; age range, 18-83 years, referred over a 10-year period to a centre in Buenos Aires, Argentina

†Defined using Rome I criteria

215 (46%) primary constipation



## Secondary Constipation

Medications: Opiates, antihypertensive agents, tricyclic antidepressants, iron preparations,

anti-epileptic drugs, anti-Parkinsonian agents (anticholinergic or dopaminergic)

Intrinsic/organic: Colorectal cancer, extra-intestinal mass, postinflammatory, ischaemic or surgical stenosis, anal fissure, anal strictures, inflammatory bowel disease, proctitis, diverticular disease

Metabolic/endocrine: Diabetes mellitus, hypothyroidism, hypercalcaemia, porphyria, chronic renal insufficiency,

panhypopituitarism, pregnancy

Neurological:

Spinal cord injury, Parkinson disease, paraplegia, multiple sclerosis, autonomic neuropathy, Hirschsprung disease, chronic intestinal pseudo-obstruction (CIPO), stroke

Psychological: Psychological distress (past or present), psychological disease, psychiatric disease

Myogenic: Myotonic dystrophy, dermatomyositis, scleroderma, amyloidosis, CIPO

Diet/lifestyle: Low-fibre diet, dehydration, inactive lifestyle

## **Primary Constipation**

Slow Transit

8-13%

Combinations are common

Normal Transit

>60%

Pelvic Floor Dysfn

25-76%

• IBS-C

10-25%

No abnormality

5%

## **Primary Constipation**

- Difficulty expelling stools
  - Impaired rectal contraction
  - Inadequate anal relaxation
  - Paradoxial anal contraction

Rectal/Anal Dyssynergia

Impaired rectal sensation

- Structural abnormalities
  - Rectal prolapse
  - Rectocele

## Investigations

- DRE
  - Integral to clinical evaluation
  - MUST be performed in all patients complaining of constipation
- Blood tests

Colonoscopy

- Advanced physiologic testing
  - Anal manometry
  - Balloon expulsion test
  - Colonic transit time
  - Defecography

## DRE

- Inspection:
  - Scars/skin abn/stool discharge/pus
  - Fistulae
- Squeeze the anus
  - Concentric movement of the anus and perianal skin

- Strain
  - Perineal descent
  - Rectocele
  - Prolapse of vagina or rectum
  - Bulging haemorrhoids

## Colonoscopy

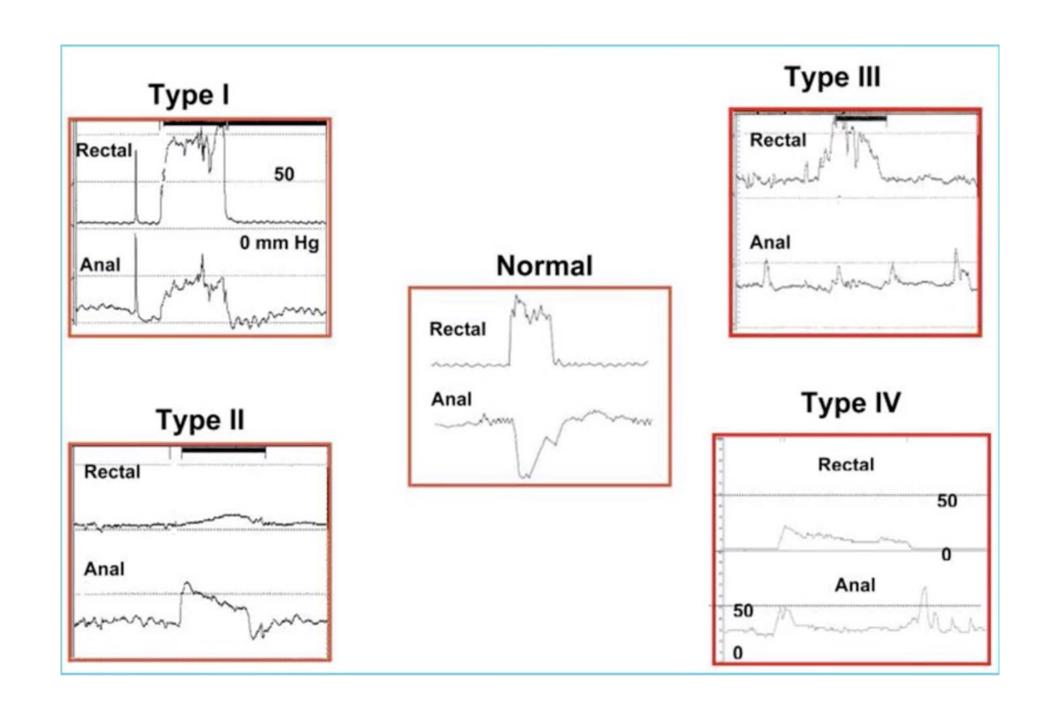
 Yield is VERY low for constipation as sole indication

#### ALARM SYMPTOMS

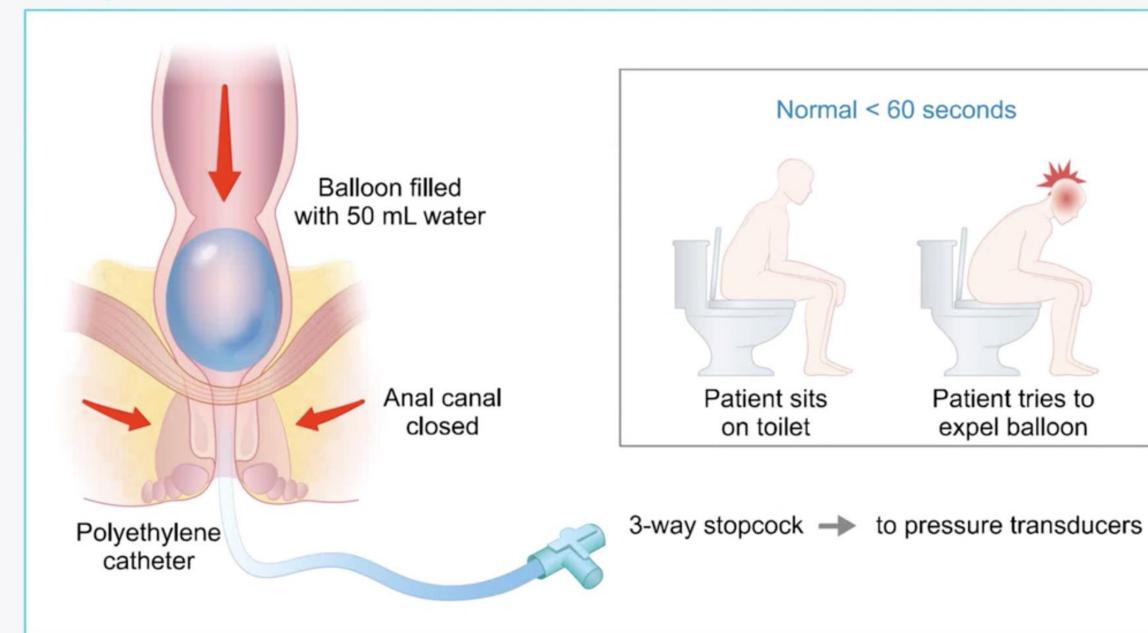
- Age >50
- Anaemia
- Blood in stools
- Weight loss
- Fhx
- Abd/rectal mass
- Change in bowel habits

## Advanced Physiologic Testing

To be considered in patients not responding to conventional therapy



### **Balloon expulsion test**

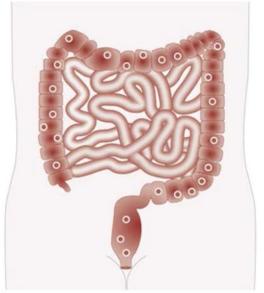


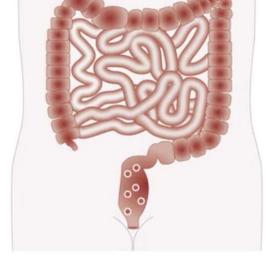
## Colonic Transit Time

- Ingestion of 1 capsule per day for 3 days
- Each capsule contains 24 markers

PFA on day 4 and 7

Distribution of radiopaque markers may add valuable information





Markers scattered about the colon is most likely slow transit constipation

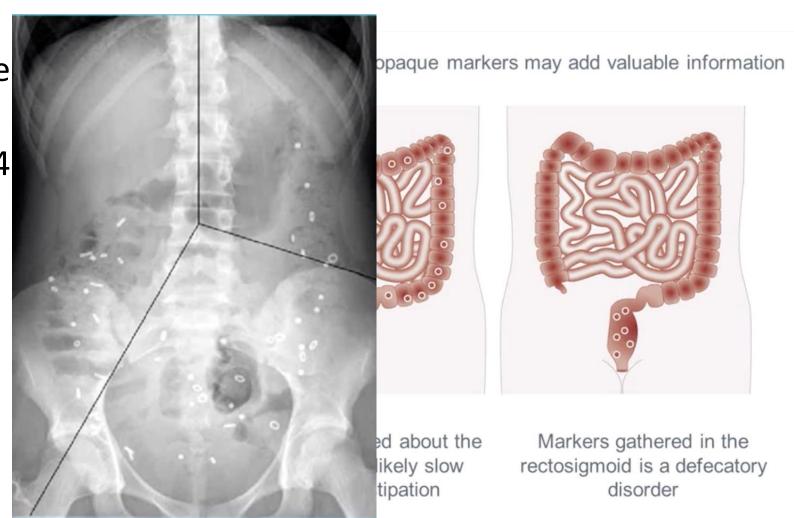
Markers gathered in the rectosigmoid is a defecatory disorder

## Colonic Transit Time

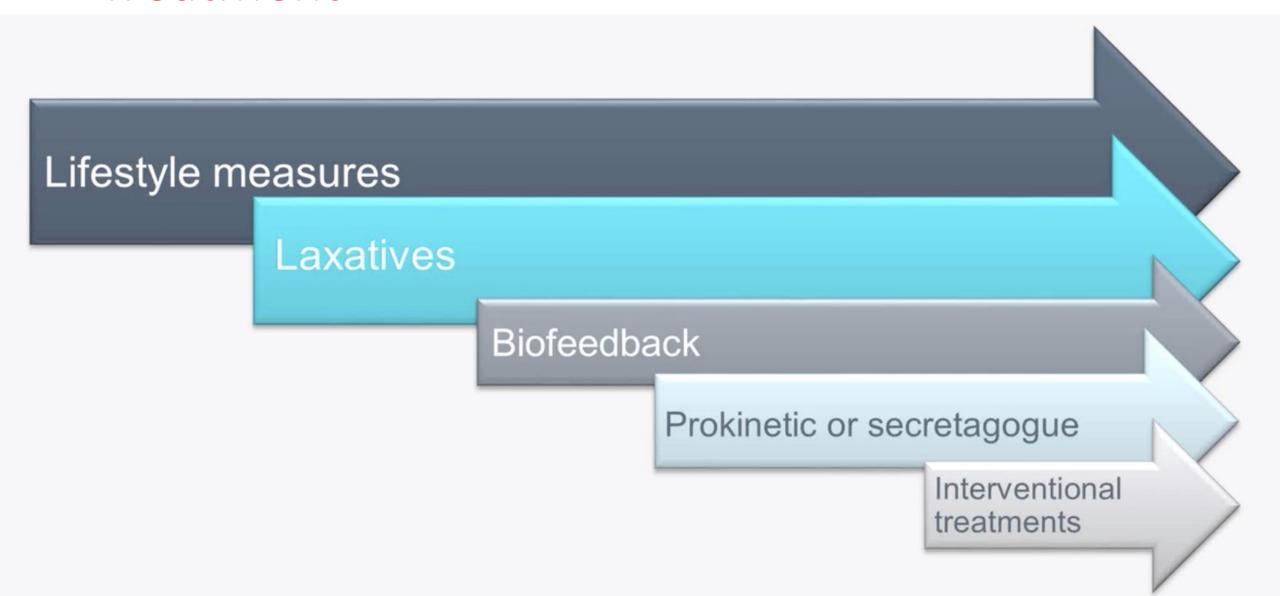
 Ingestion of 1 capsule pe days

Each capsule contains 24

PFA on day 4 and 7



## Treatment



## Lifestyle Measures

### Dietary Fibre

• Unchanged 56%

• Improved 22%

• Symptom free 22%

#### Exercise

Modest effect

### Fluid consumption

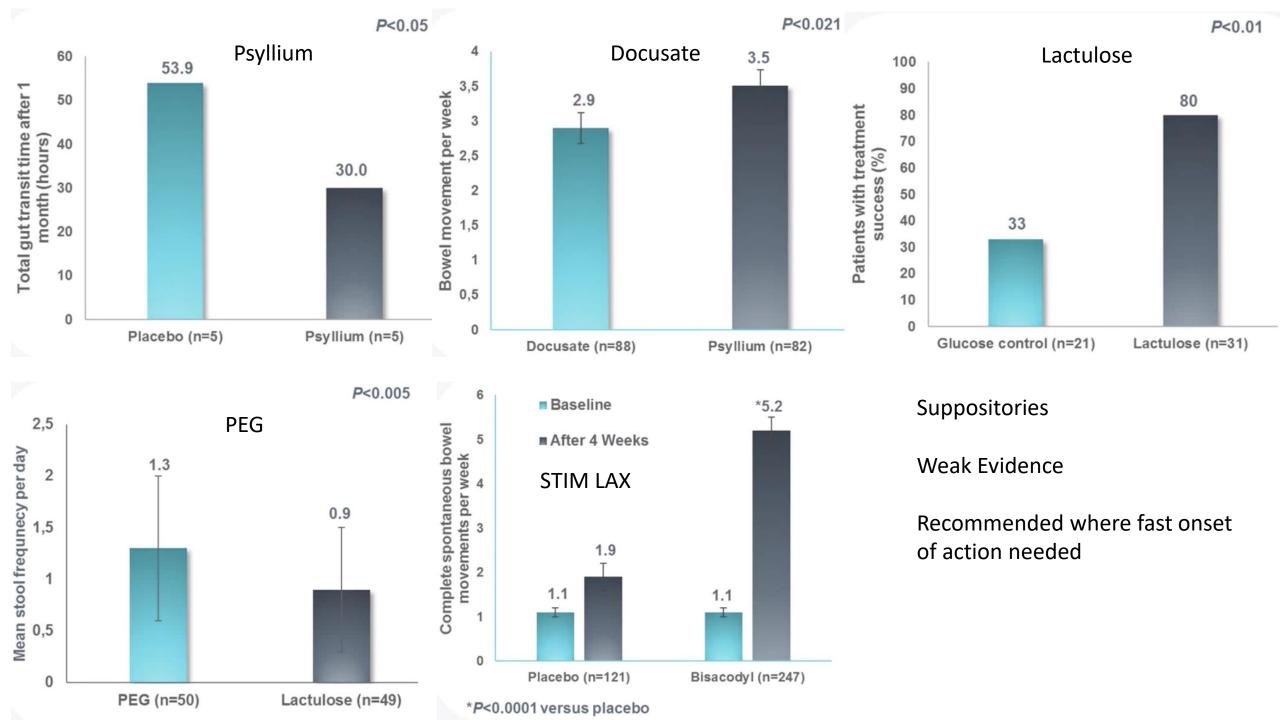
Modest effect

### Laxatives

### **Current therapeutic options for chronic constipation**

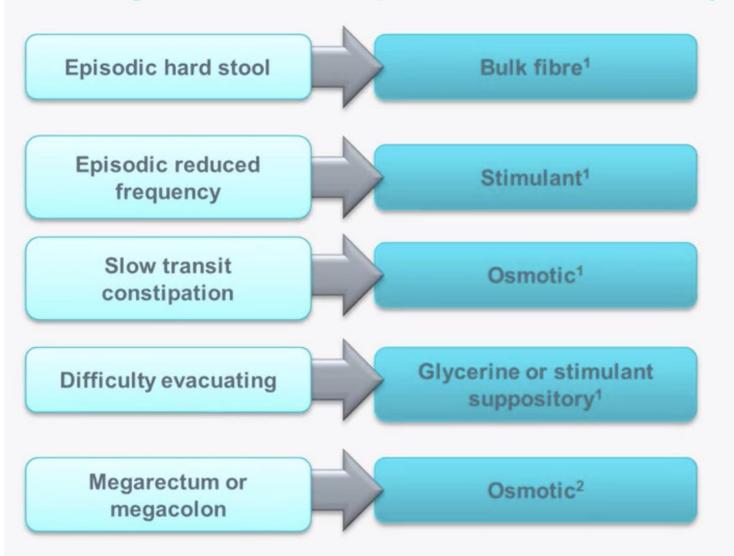
Agent and mechanism of action	Example	Therapeutic response
Bulking agent Increases stool volume making it easier to pass	Pysillium	Decreased gut transit time and increased stool frequency <sup>1,2</sup>
Stool softener Softens the stools making it easier to pass	Docusate	Less effective than pysillium at improving bowel movements <sup>3</sup>
Osmotic laxative Increases fluids within the intestine making stools softer and easier to pass	Lactulose	Decreased transit and reduced faecal impaction <sup>4</sup>
	Polyethylene	Increased stool frequency and decreased straining <sup>5</sup>
Stimulant laxative Stimulates muscles helping them to move stools and waste products along the large intestine	Bisacodyl	Increased frequency of bowel movement <sup>6</sup>
	Sennoside	Increased frequency of bowel movements in elderly patients <sup>7</sup>

Although 16–40% of patients use laxatives, symptoms persist despite laxative use in up to 70% of patients<sup>8</sup>



### Laxatives: Summary

### Tailoring laxatives to the patient based on their symptoms and diagnosis



### If no improvement:

- Increase dose<sup>1</sup>
- Rational combination:
  - Stool softener and stimulant laxative<sup>3,4</sup>
  - Bulking agent<sup>1</sup>

### Biofeedback

#### **Therapy**

#### Rectal balloon

Expansion of balloon mimics sensation of rectal filling

#### **Electrodes**

On an anal plug record motor activity of EAS contractions

#### **Feedback**

Information conveyed to patient via visual or auditory feedback

#### **Patients**

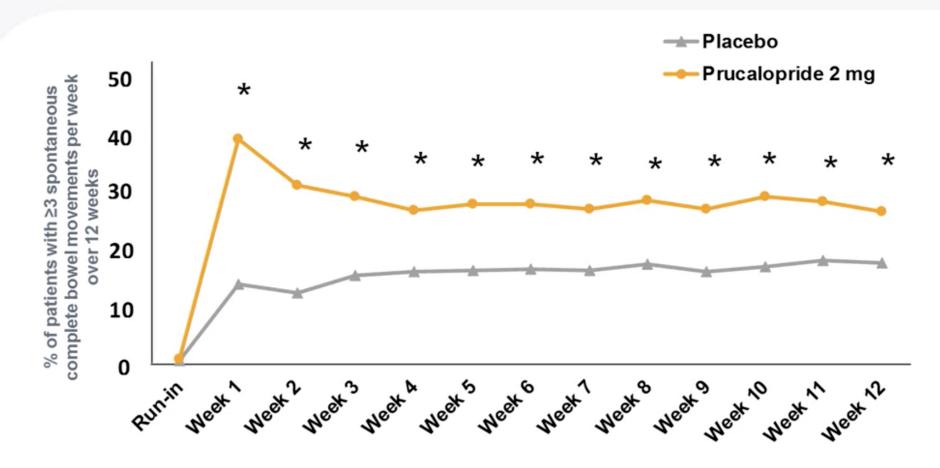
Are trained to achieve maximal relaxation of the EAS





### Prokinetics and secretagogues

#### Prucalopride in chronic constipation: Response over a 12-week treatment period<sup>†</sup>



<sup>\*</sup>P<0.001 versus placebo

†Primary end point

The 4 mg dose has not been licensed since no incremental benefit was demonstrated versus the 2 mg dose

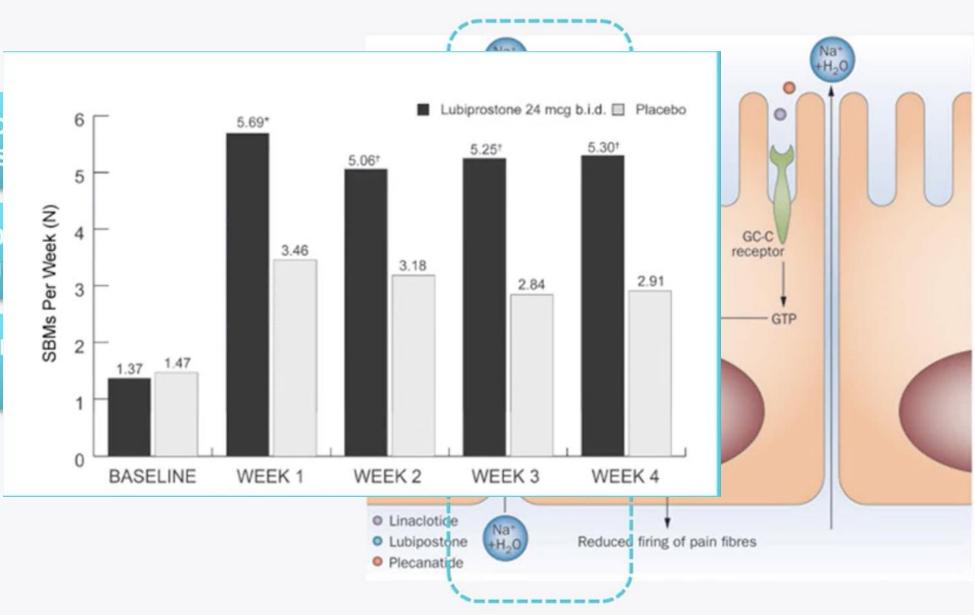
## Prokinetics and secretagogues

### Lubiprostone

A bicyclic fatty ac derived from pros

Primarily works b CIC-2 chloride ch

Secretion of chlor the lumen



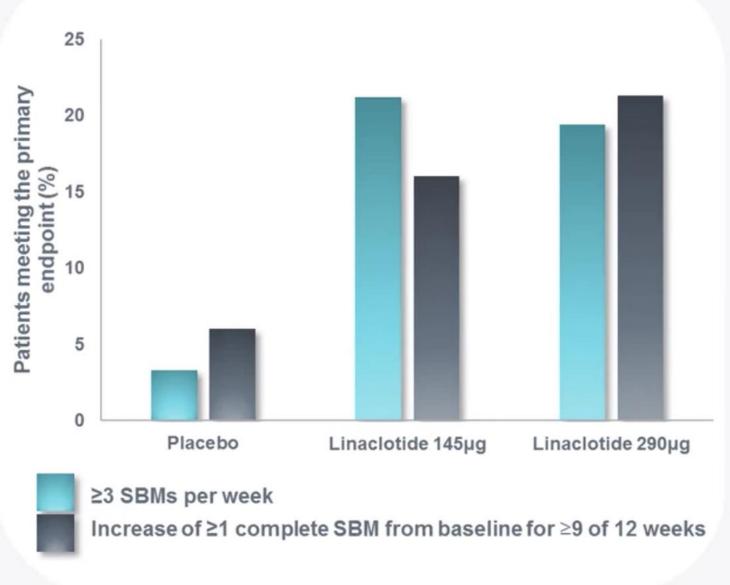
### Prokinetics and secretagogues

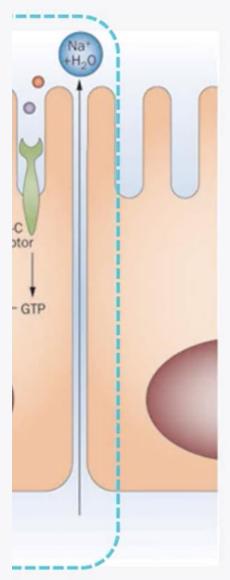
#### Linaclotide

Acts on guanyl is selectively exborder membra mucosa cells from to the rectum

Finally opens the channel

Reduces depola fibres



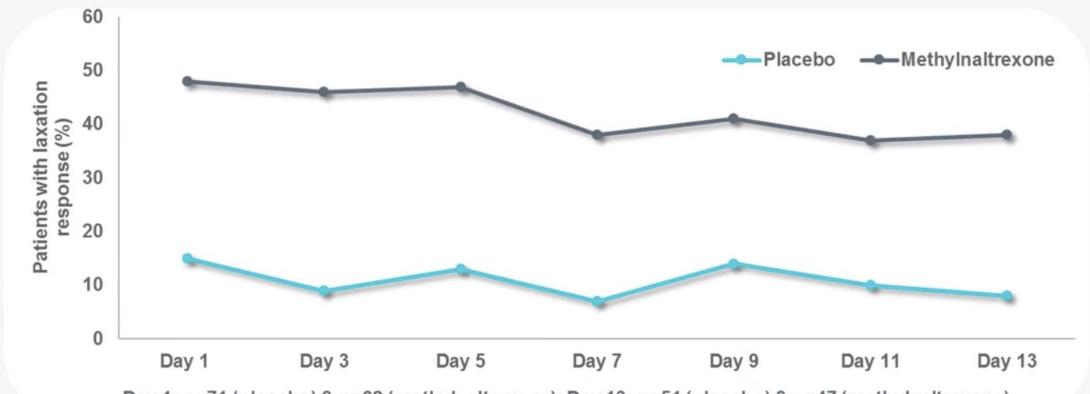


#### Methylnaltrexone

A μ-opioid receptor antagonist that cannot pass the blood brain barrier

Belongs to the PAMORA medication group (peripheral µ-opioid receptor antagonists)

Limited evidence for subcutaneous methylnaltrexone in non-opioid constipation<sup>1</sup>



Day 1: n=71 (placebo) & n=62 (methylnaltrexone); Day 13: n=51 (placebo) & n=47 (methylnaltrexone)

## Constipation in Pregnancy

• Up to 40%

• 1<sup>st</sup> trimester: 35%

• 2<sup>nd</sup> trimester: 39%

• 3<sup>rd</sup> trimester: 21%

• Post partum: 17%

## Take Home Messages

• WHAT DO YOU MEAN YOU ARE CONSTIPATED?

## Take Home Messages

- Healthy Lifestyle recommended (despite lack of evidence)
  - Exercise
  - Diet rich in fibre
  - Adequate water intake
- Laxatives
  - Tailor to patient's needs
  - PEG is first choice for most

 Prokinetics and secretagogues are 2<sup>nd</sup> line agents

 Surgical treatment in highly selected cases

# **Hépatite C**

- Ena traitement
- Ena guerison



## Ou concerné?

Zis ene sel comprimé par jour pou 3 mois

- Li disponible
- Li gratuit
- Li efficace

Pou plis renseignements – coz ek ou docteur