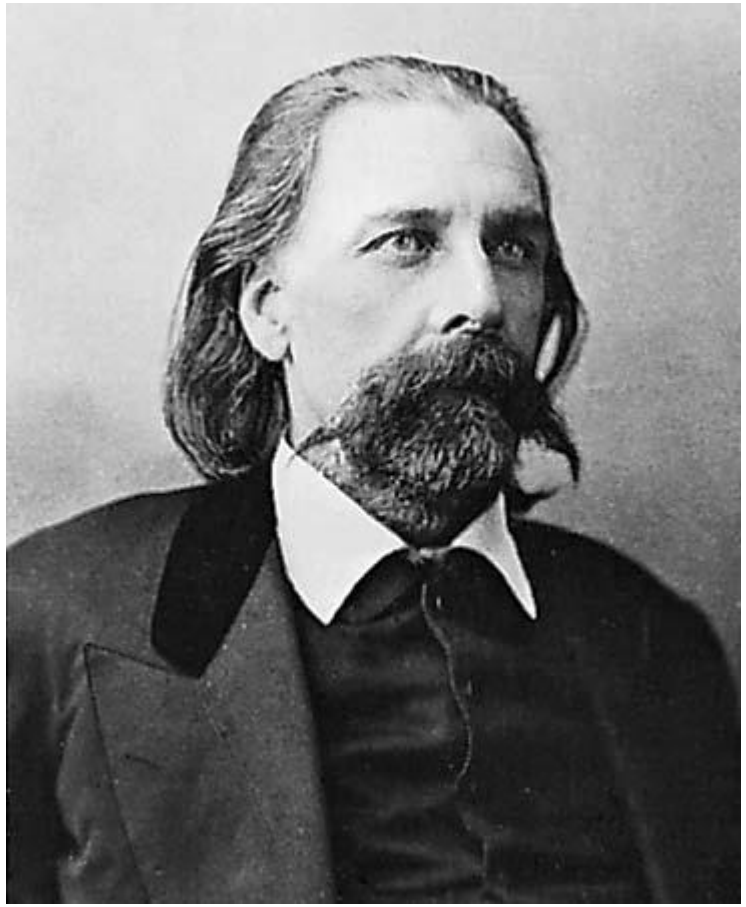
Cliniques universitaires SAINT-LUC UCLouvain BRUXELLES

Syndrome de l'intestin irritable: la théorie

Prof. Hubert Piessevaux

12 octobre 2024

Syndrome de l'intestin irritable: une banalité?



A good set of bowels is worth more to a man than any quantity of brains

Josh Billings, AD 1818-1885

SOMMAIRE

Définition

Quand il y a des douleurs abdominales chroniques inexpliquées

- Associées à des troubles du transit
- Constipation
- Diarrhée

dont l'intensité est modulée par la défécation

Définition basée sur des symptômes!

Rome II, III, IV …

Table 1. Rome Criteria for Diagnosing IBS[2,3]

Rome III Criteria	Recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months associated with two or mo of the following: • Improvement with defecation • Onset associated with a change in frequency of stool • Onset associated with a change in form (appearance) stool [a]Criterion fulfilled for the last 3 months with symptom onse at least 6 months prior to diagnosis. [b]"Discomfort" means an uncomfortable sensation not described as pain.
Rome IV Criteria	Recurrent abdominal pain, on average, at least 1 day/week the last 3 months, associated with two or more of the following criteria: • Related to defecation • Associated with a change in frequency of stool • Associated with a change in form (appearance) of stoo [c]Criteria fulfilled for the last 3 months with symptom onset least 6 months before diagnosis.

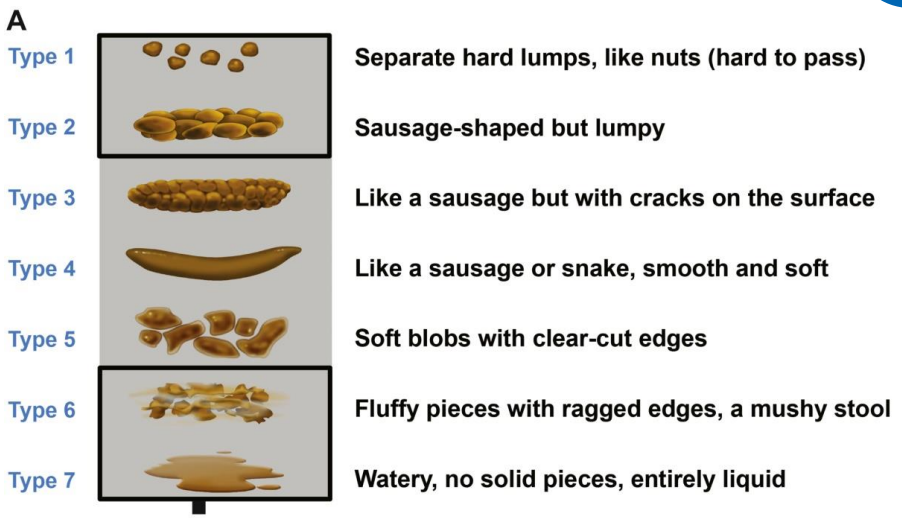
Source: Lacy BE, et al. Bowel Disorders. Gastroenterology. 2016;150:1393-1407; Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders. Accessed 8/10/16 at: https://www.theromefoundation.org/

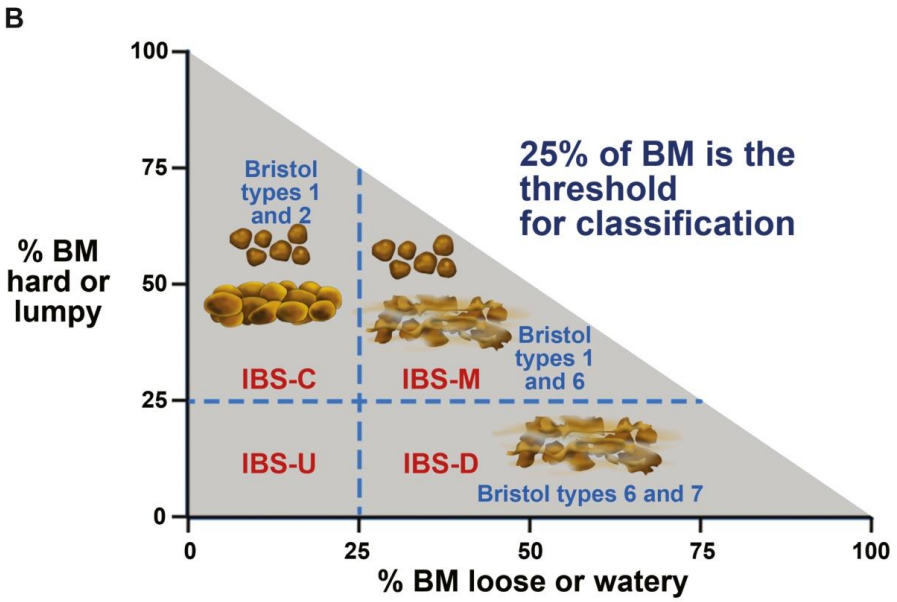
Sous-groupes

SUBTYPE	 STOOL TYPE 1 & 2	 STOOL TYPE 6 & 7
IBS with predominant constipation	More than 25%	Less than 25%
IBS with predominant diarrhea	Less than 25%	More than 25%
IBS with mixed bowel habits	More than 25%	More than 25%

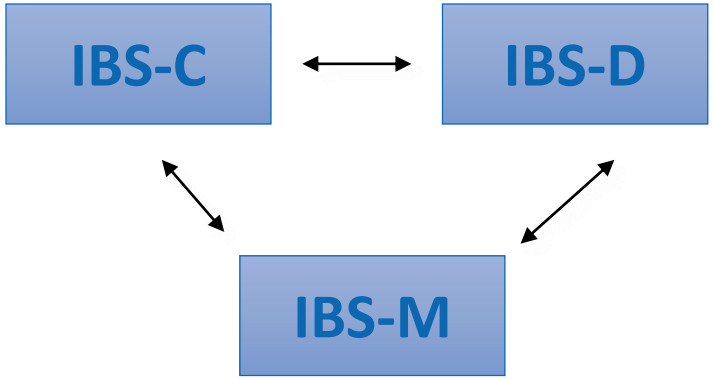
IBS Unclassified: Patient who meets diagnostic criteria for IBS but whose bowel habits cannot be accurately categorized into one of the three subtypes above.

Source: Lacy BE, et al. Bowel Disorders. Gastroenterology. 2016;150:1393-1407.

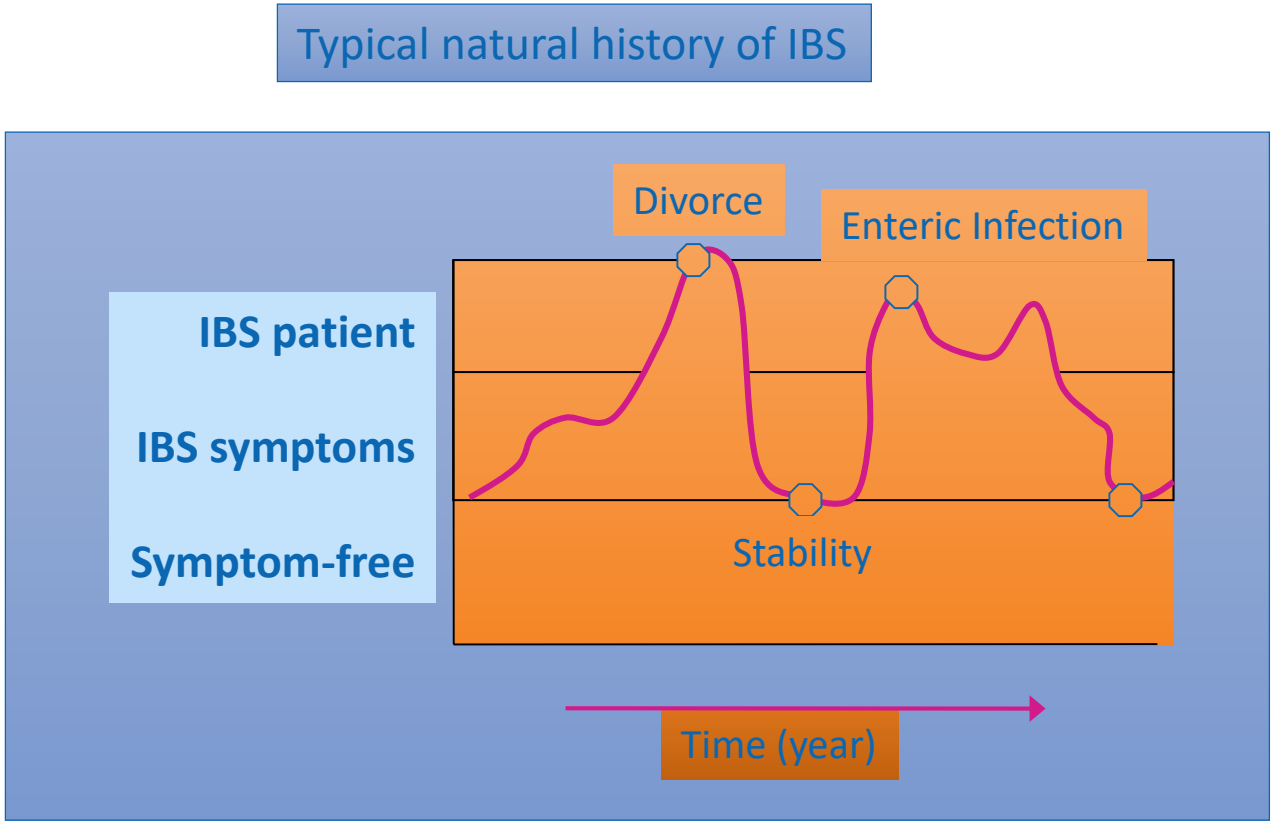




Stabilité dans le temps?



- Proportions de patients stables dans chaque sous-groupe au fil du temps mais
- dans 75% il y a eu un changement au niveau du sous-groupe.



Prévalence

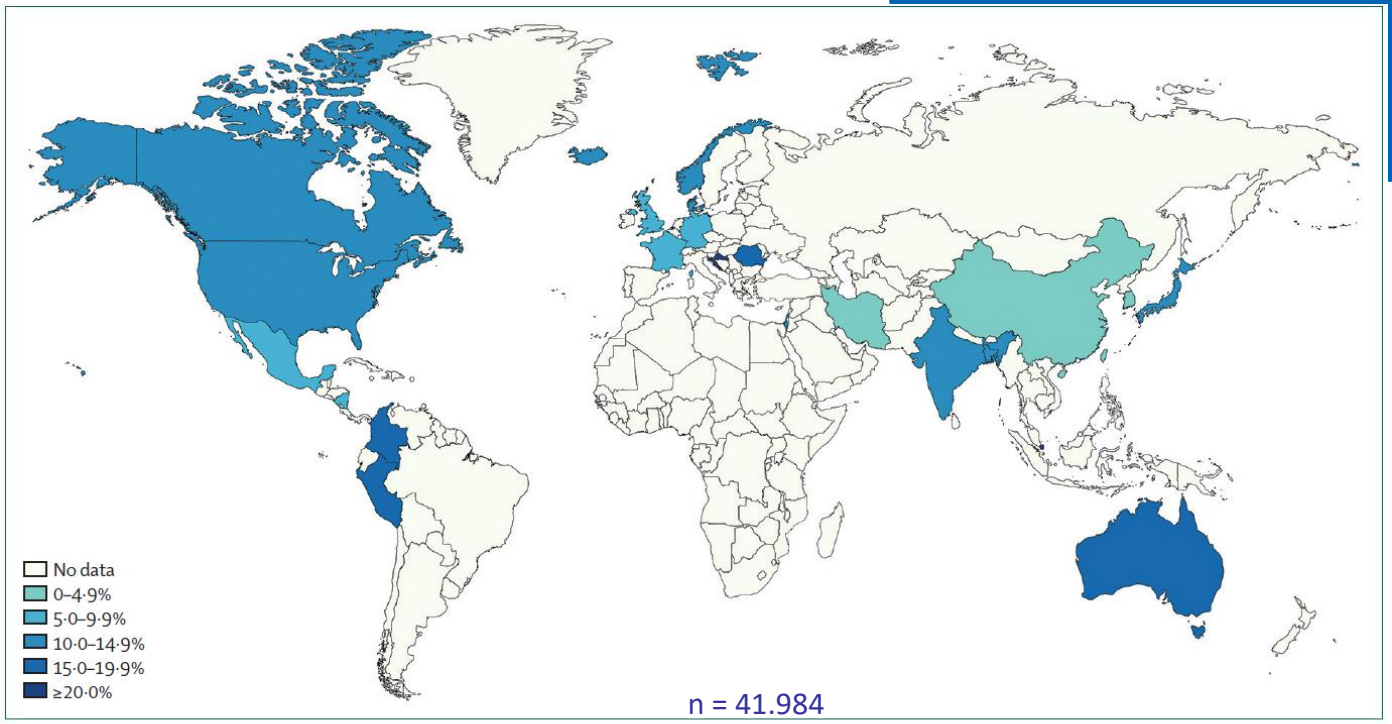
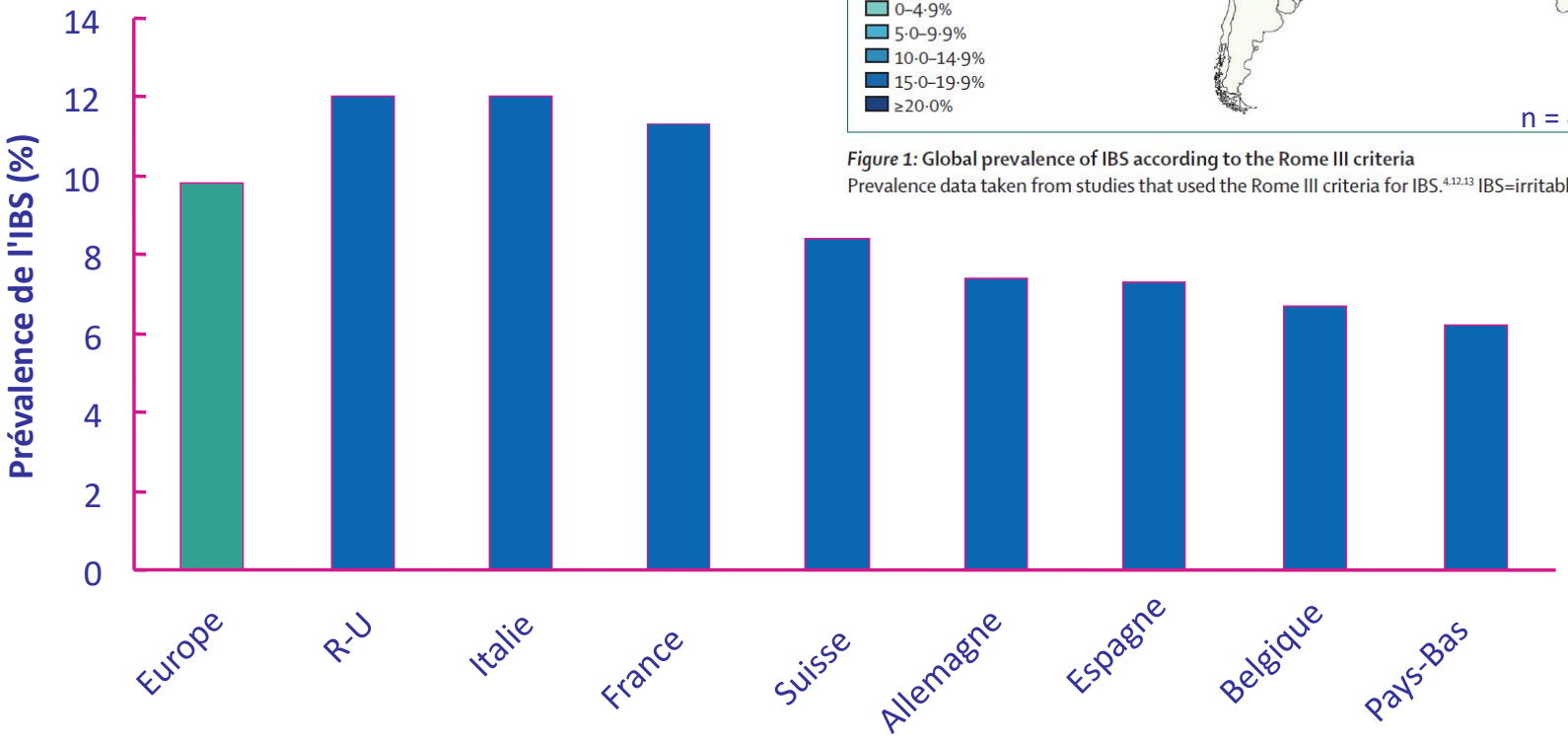
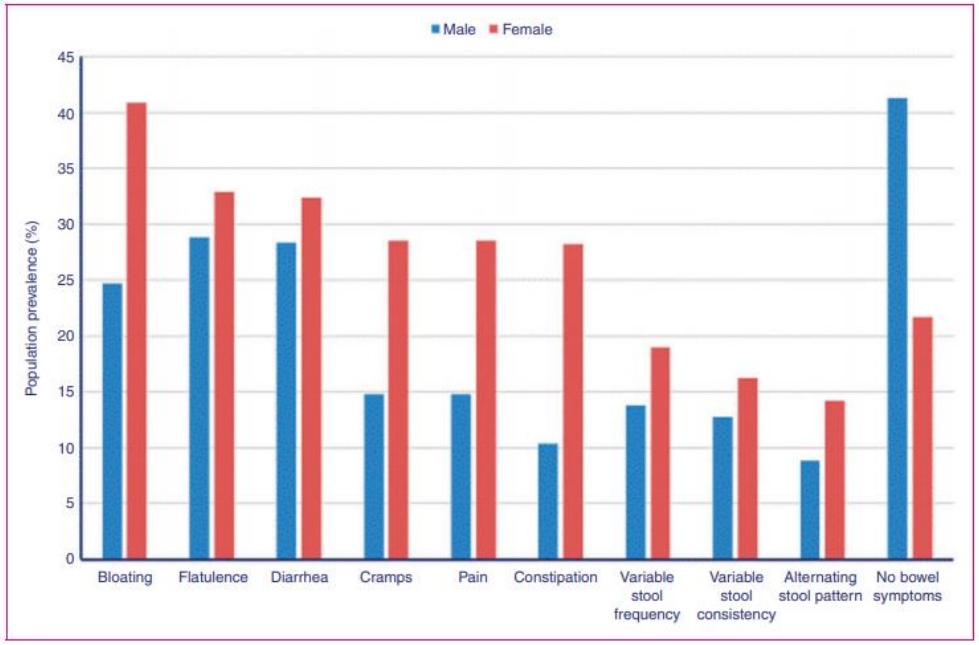


Figure 1: **Global prevalence of IBS according to the Rome III criteria**
Prevalence data taken from studies that used the Rome III criteria for IBS.[4,12,13] IBS=irritable bowel syndrome.



Hungin et al., 2002

En Belgique?



e 1. Prevalence of bowel symptoms as reported by the general population in men and women.

Table 2. Comparison between patients fulfilling Rome IV criteria and the self-reported irritable bowel syndrome (IBS) group.

	IBS according to Rome IV	Self-reported IBS
Prevalence	5.5%	17.6%
Employment state:		
Employed	63%	45%
Symptoms		
Diarrhea	37%	39%
Constipation	34%	35%
Alternating stool pattern	28%	28%
Abdominal pain	100%	48%
Bloating	74%	65%
Abdominal cramps	69%	51%
Problems with frequency of bowel symptoms	49%	27%
Problems with consistency of bowel movements	37%	24%

Facteurs de risque

- Sexe F > M
- Age
- Statut socio-économique
- Co-morbidité

Table 5. Pooled Prevalence of IBS According to Age, Gender, and Socioeconomic Status

	No. of subjects	Pooled prevalence of IBS (95% CI)	Odds ratio for IBS (95% CI)
Age band (*y*)			
<30	6909	11.0 (6.0–18.0)	1.00
30–39	7247	11.0 (7.0–16.0)	1.04 (0.85–1.27)
40–49	7543	9.6 (6.0–14.0)	0.86 (0.59–1.24)
50–59	5434	7.8 (5.0–11.1)	0.68 (0.40–1.17)
≥60	5540	7.3 (4.3–11.0)	0.63 (0.38–1.04)
Gender			
Male	78,913	8.9 (7.3–10.5)	1.00
Female	83,330	14.0 (11.0–16.0)	1.67 (1.53–1.82)
Socioeconomic status			
High	866	14.0 (9.0–19.0)	1.00
Medium	1732	14.0 (8.0–22.0)	1.02 (0.72–1.44)
Low	2663	13.0 (7.0–22.0)	0.99 (0.71–1.36)

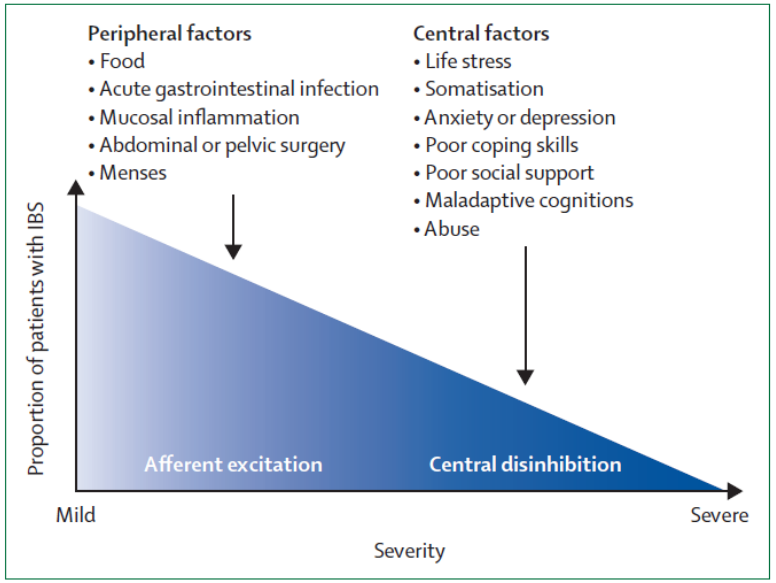


Figure 2: **Factors affecting symptom severity in IBS**
Adapted from Sperber and colleagues.[16] IBS=irritable bowel syndrome.

COLORPLATE 76

GEORGE CRUIKSHANK. *The Cholic*. 1819. Hand-colored etching. 10⅛ × 8⅛ in. (25.7 × 20.6 cm). SmithKline Beckman Corporation Collection, Philadelphia Museum of Art. *Influenced by the political and social satires of James Gillray, Cruikshank found favorite themes in the fashionable overindulgence in food and drink.*

Facteur de risque: infection

- Observé chez +/- 10%

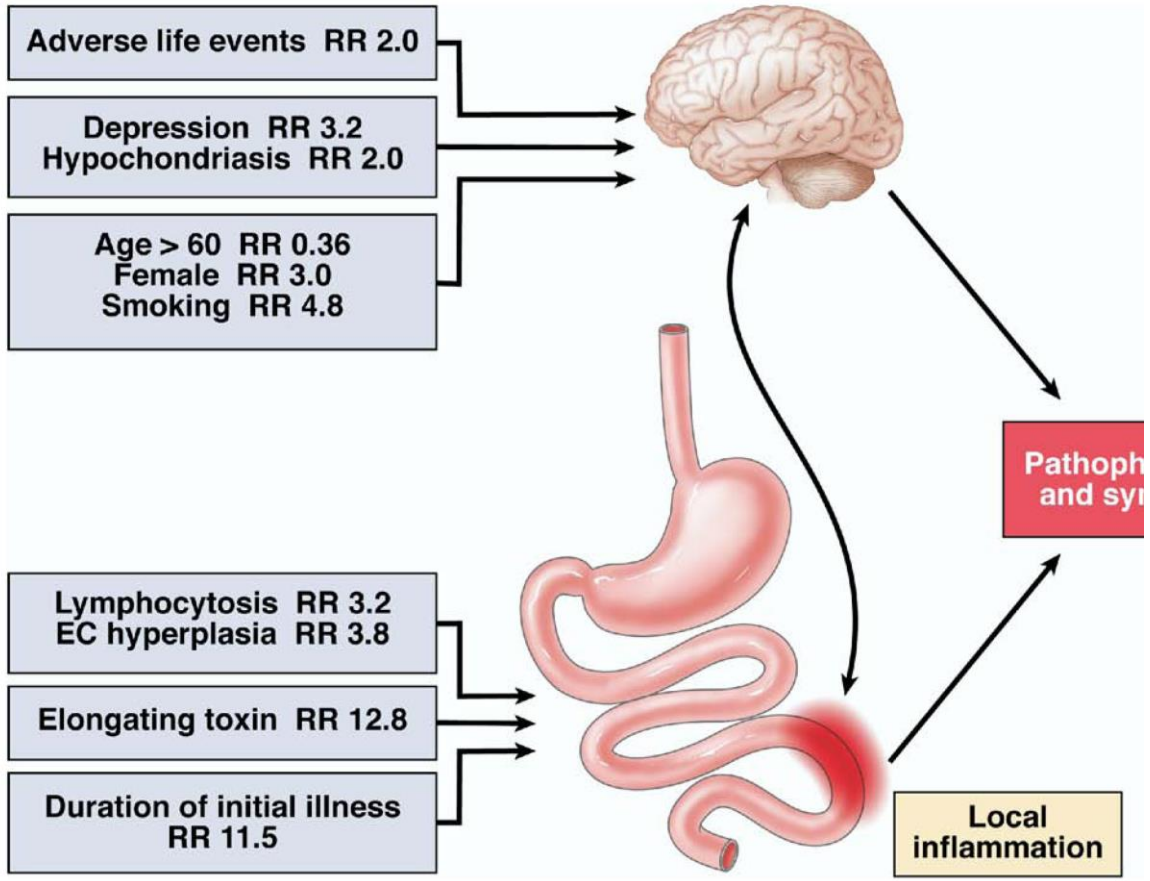
Key summary

Established knowledge on this subject

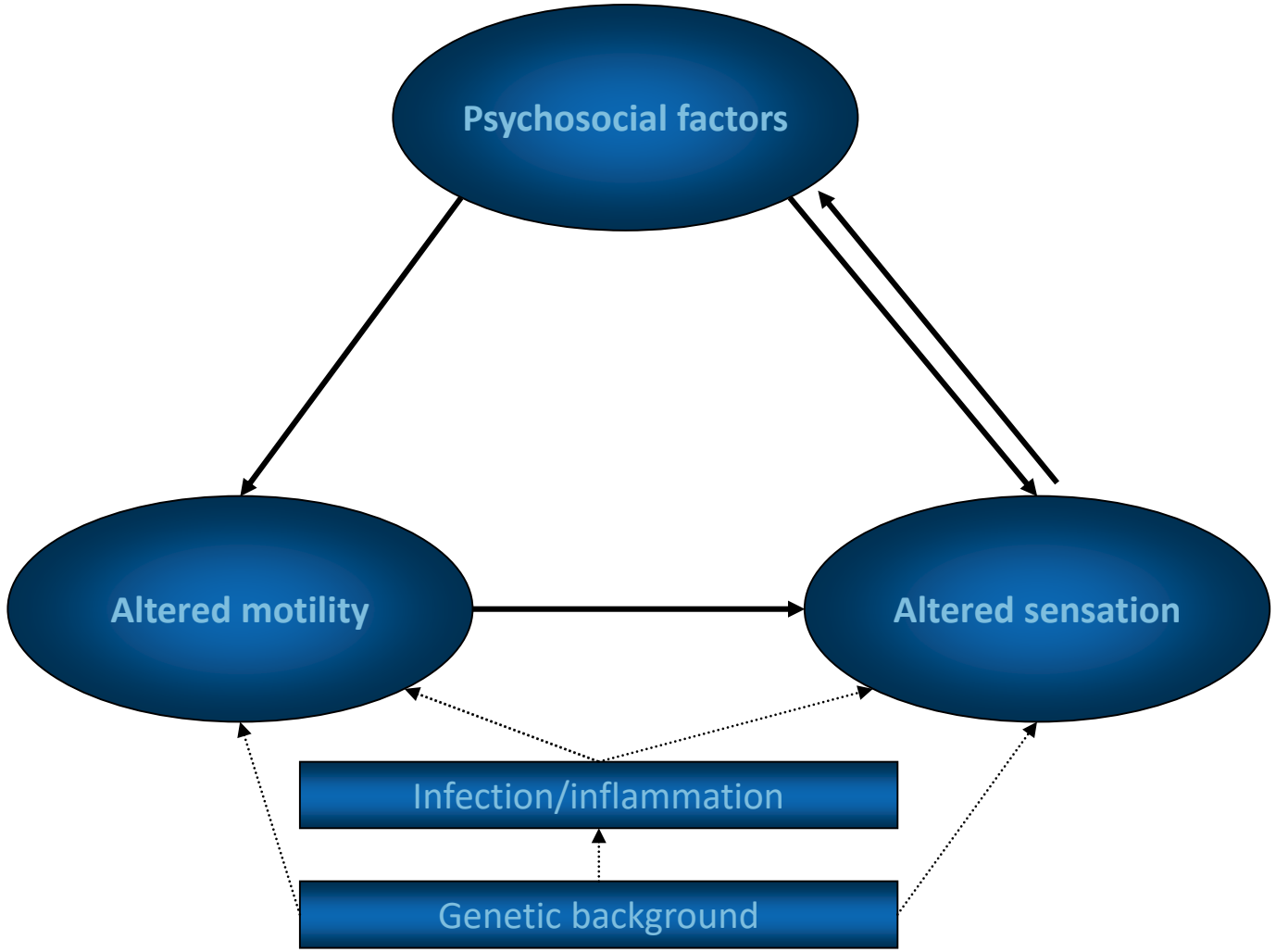
- Bacterial gastroenteritis quadruples the risk of developing irritable bowel syndrome (IBS) but the proportion of all IBS that is post-infectious (PI) is unclear.
- Risk factors include severity of initial illness, female gender and adverse psychological factors.
- What determines prognosis is uncertain.

What are the significant and/or new findings of this study?

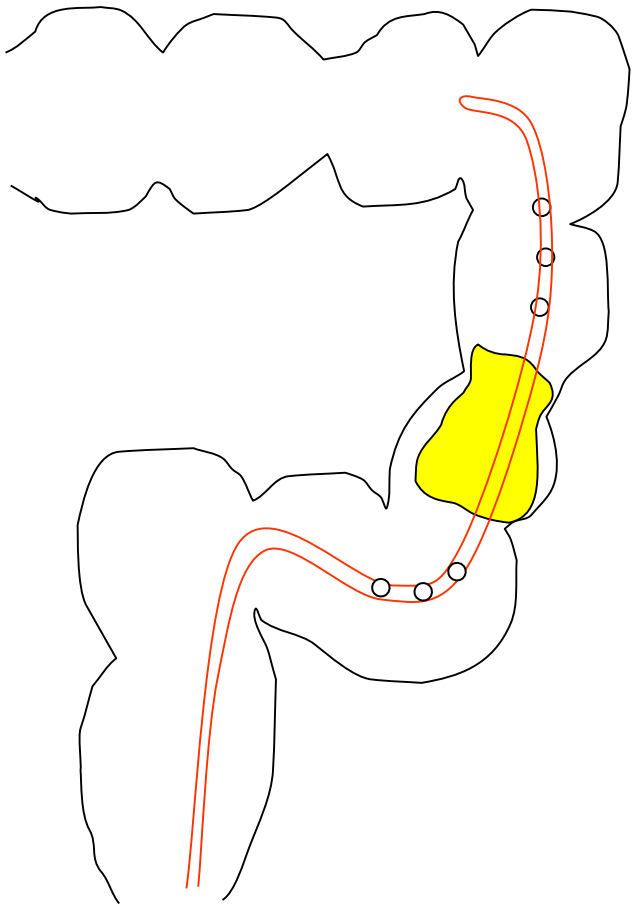
- Thirteen per cent of 7811 IBS patients met criteria for PI-IBS.
- PI-IBS was associated with childhood hygiene, somatisation and living in Northern Europe/America.
- Prognosis in PI-IBS was not different from non-PI-IBS.
- High somatisation, female gender and living in North America and Northern Europe were associated with lower recovery rates.

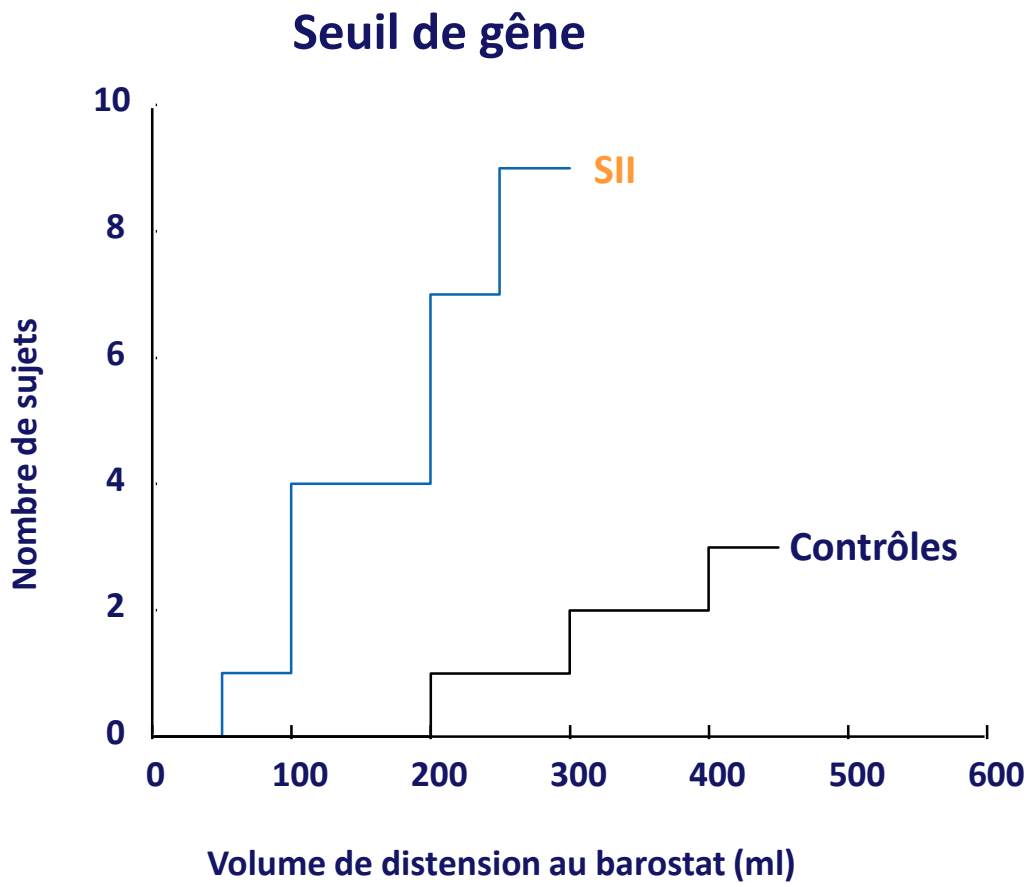


Modèle bio-psycho-social



Hypersensibilité viscérale





Bradette et al., 1994

Inhibition descendante

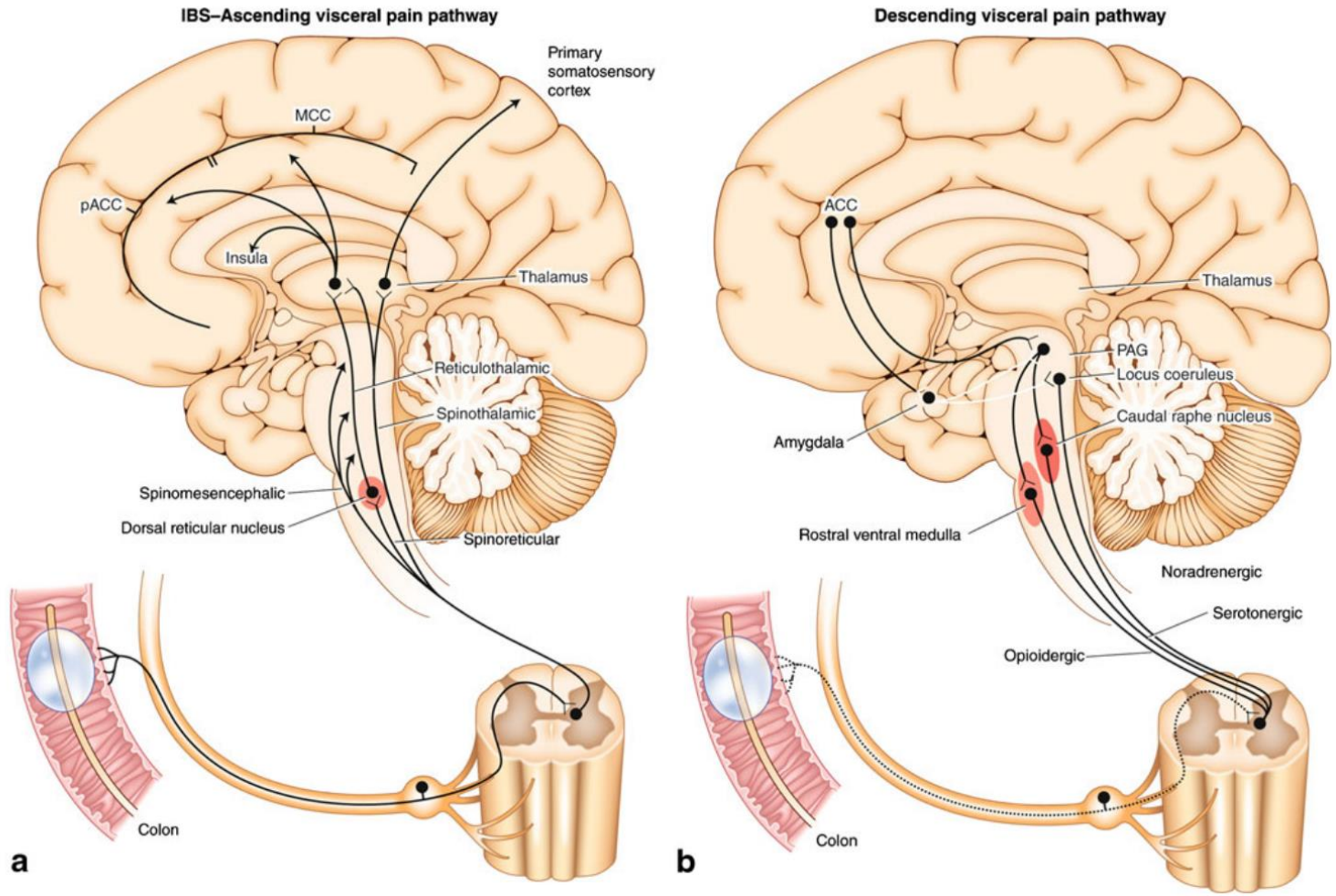
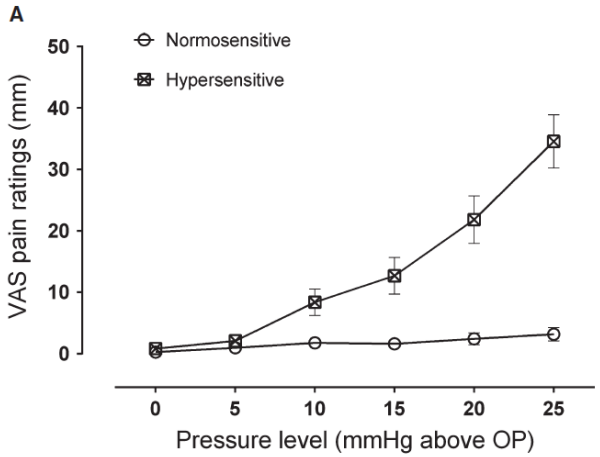
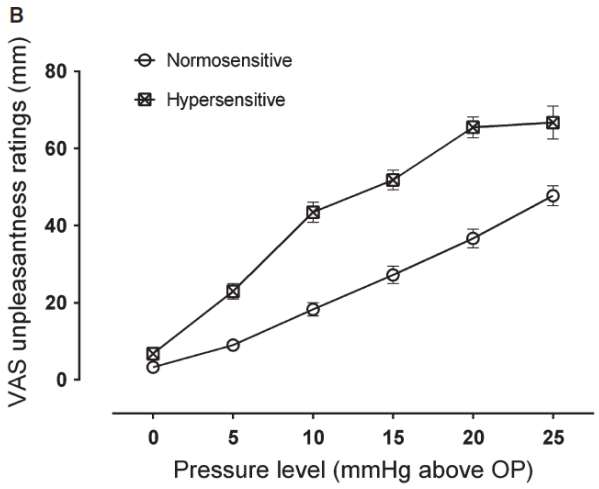
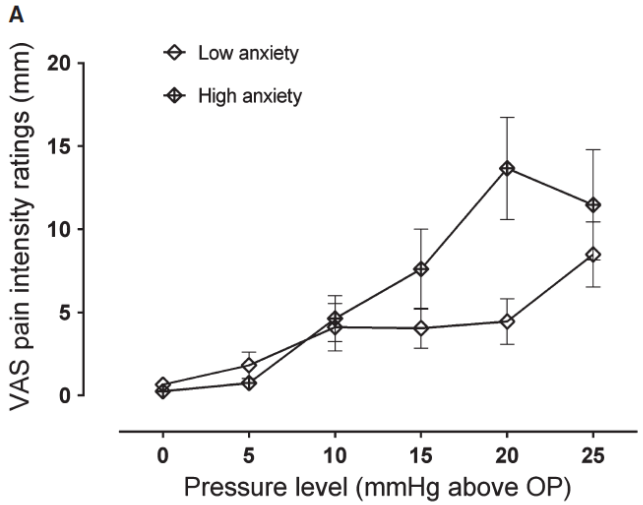


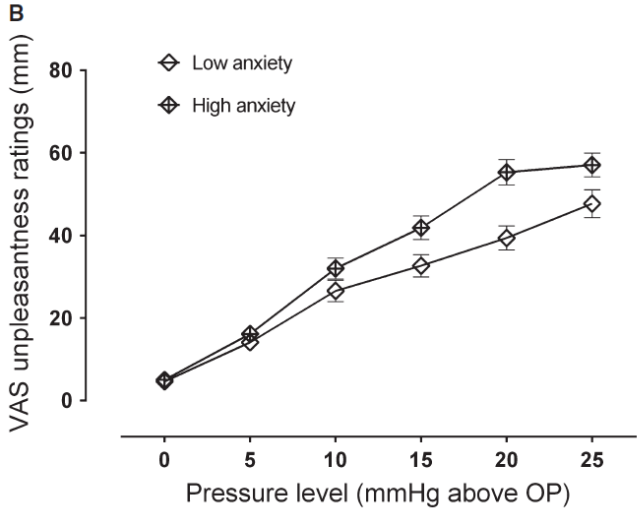
Fig. 1 **a** Neuroanatomic pathways mediating visceral pain sensation. **b** Descending inhibitory pathway for visceral pain. ACC—anterior cingulate cortex; IBS—irritable bowel syndrome; MCC—midcingulate cortex; pACC—perigenual anterior cingulate cortex; PAG—periaqueductal gray

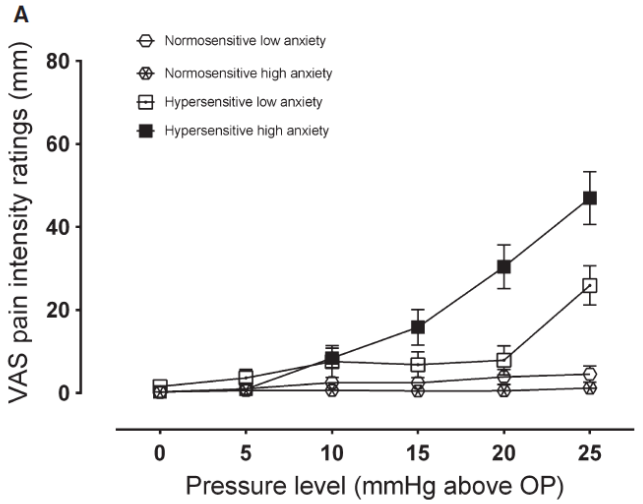
Relation anxiété - hypersensibilité

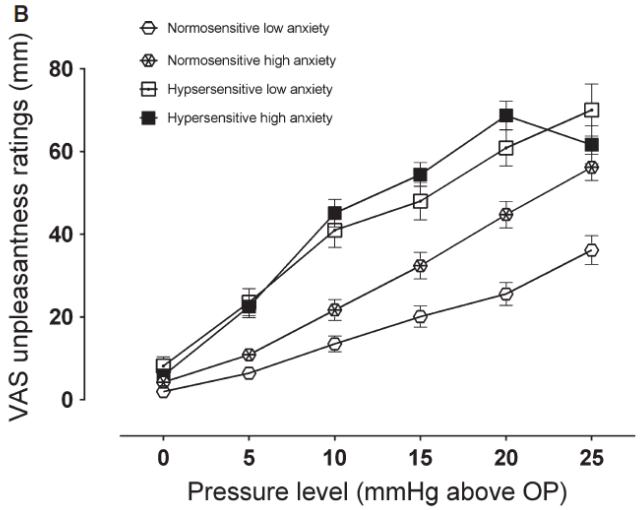




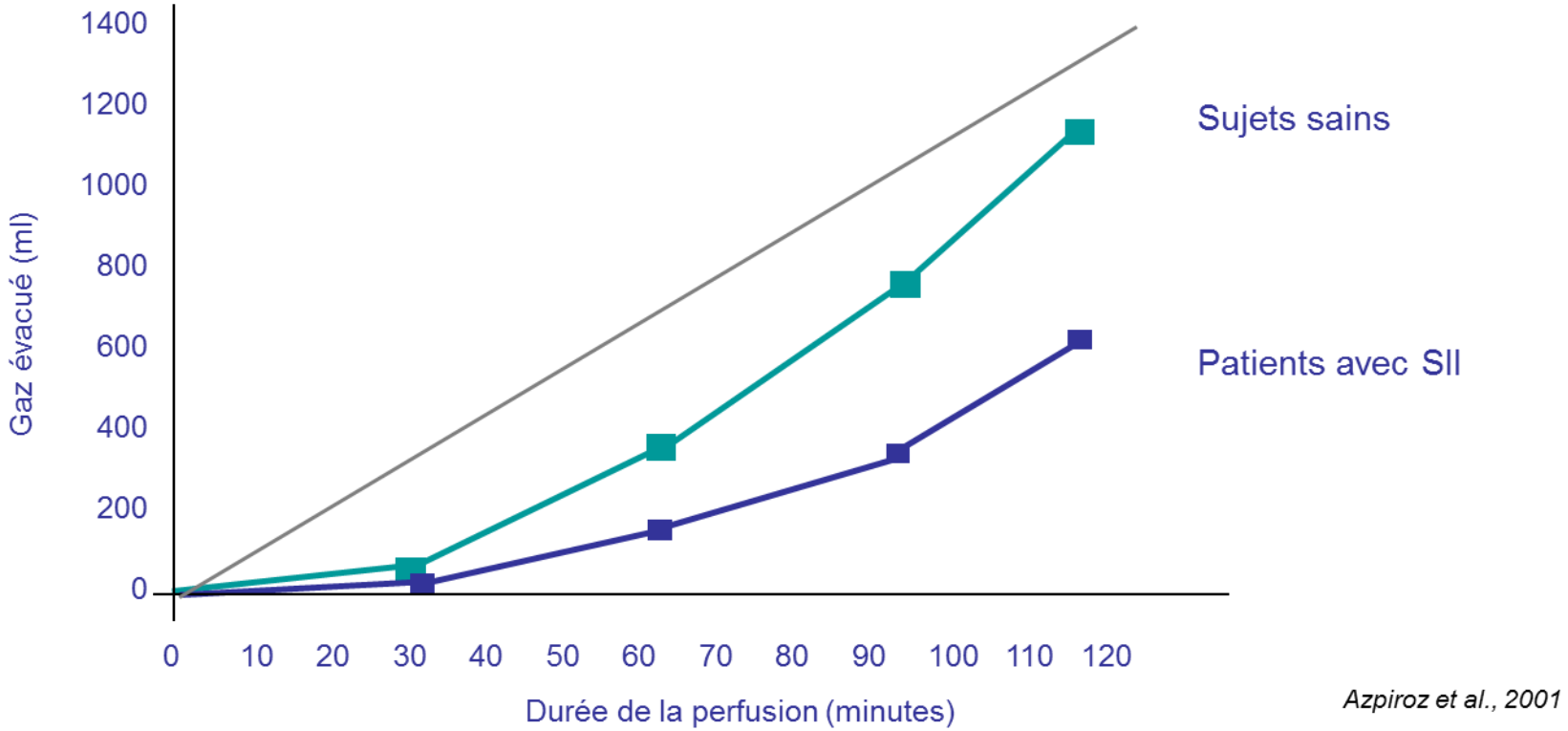






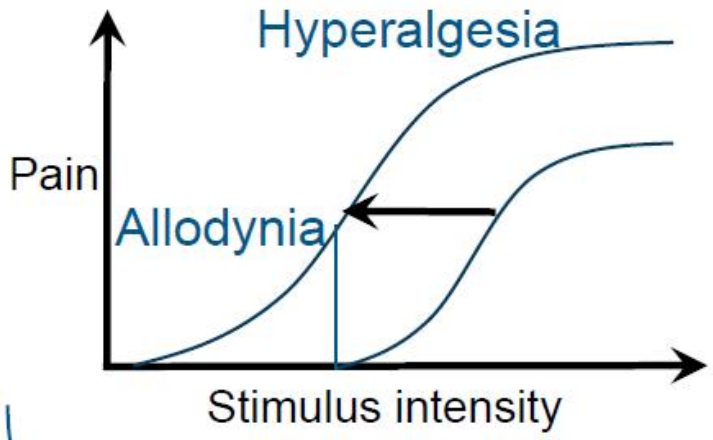


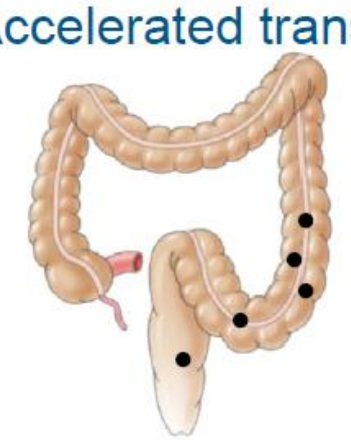
Transport du gaz

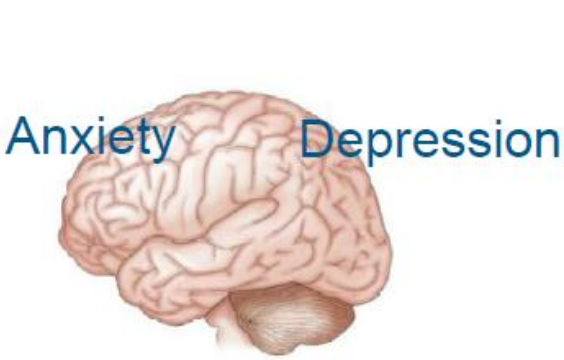


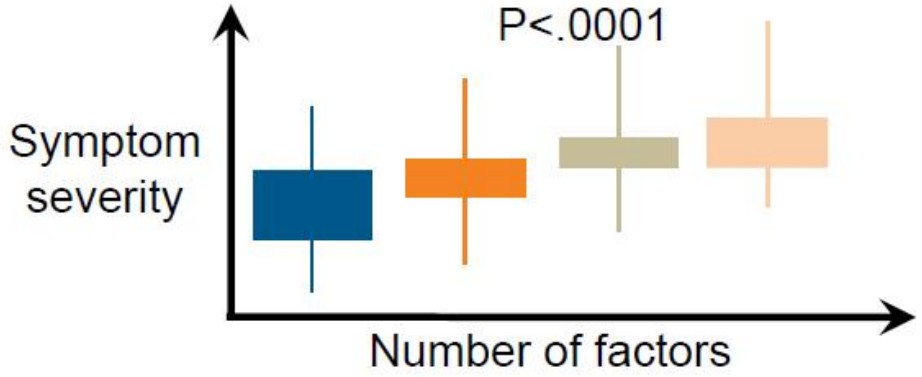
Azpiroz et al., 2001

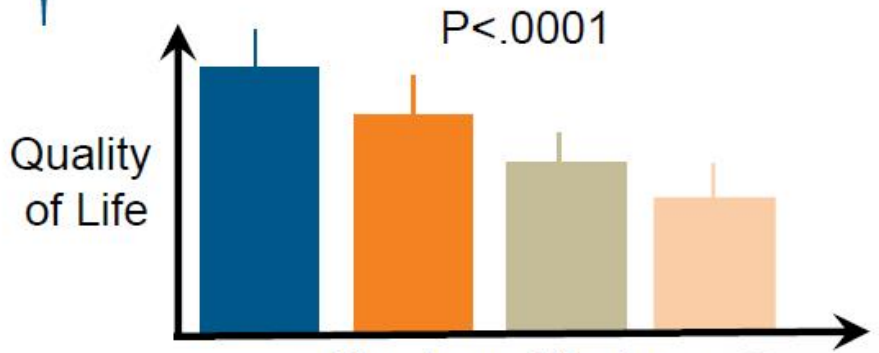
Physiopathologie











Gastroenterology

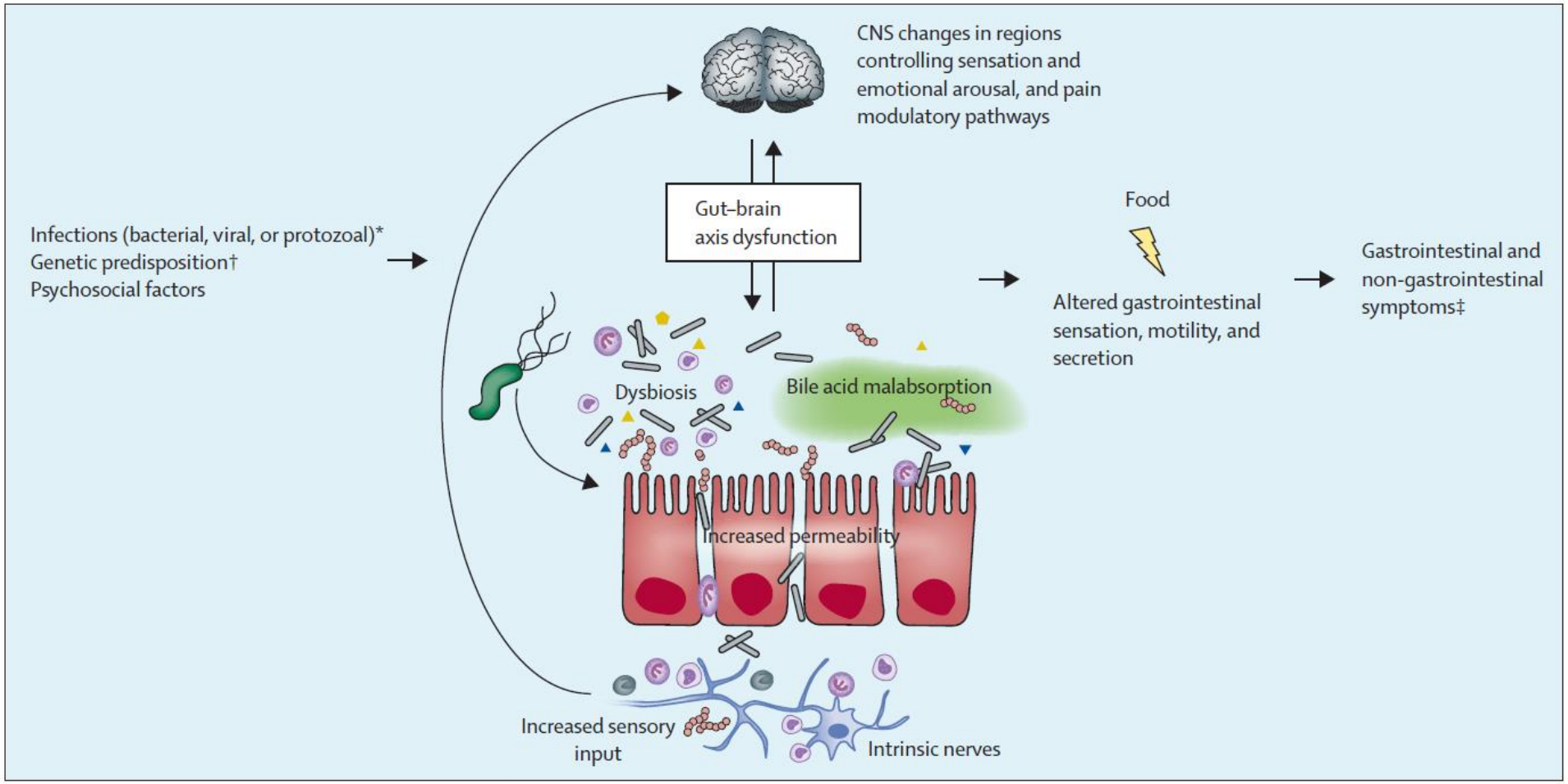
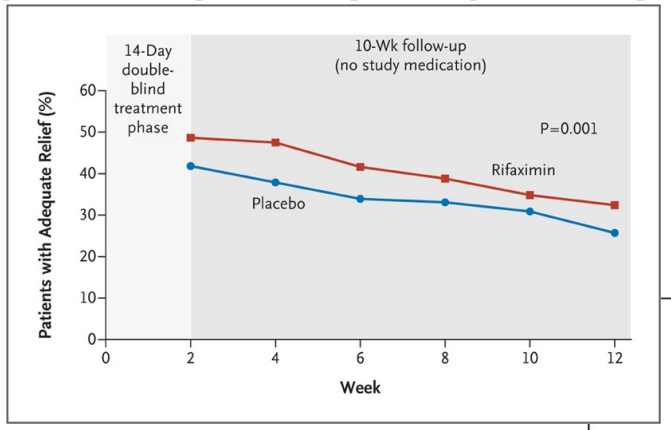


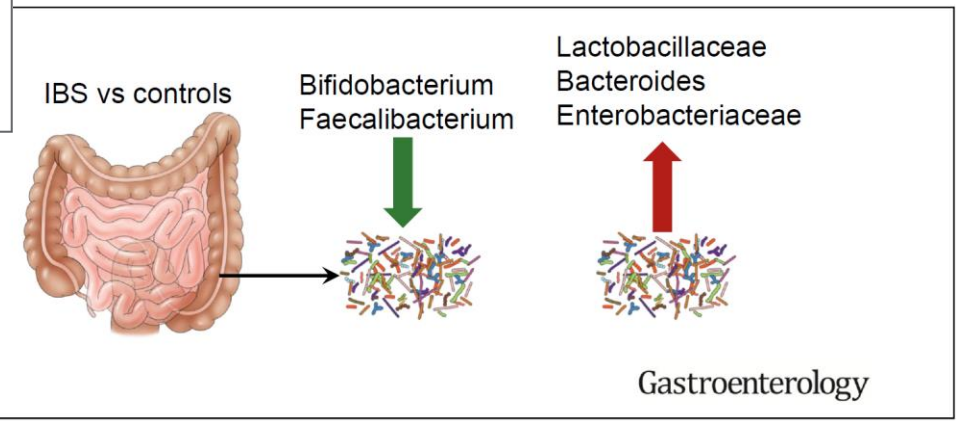
***Figure 3*: Pathophysiological mechanisms involved in IBS**

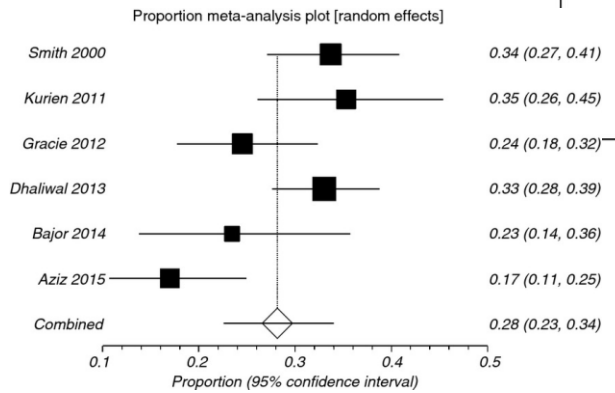
IBS=irritable bowel syndrome. *See references 17 to 20. †Genome-wide association studies have shown associations with variants of chromosome 9 and mutations in the sucrase-isomaltase gene.[21–23] Other studies have shown that approximately 2% of patients with IBS carry mutations in *SCN5A*,[24] which alters the function of the voltage-gated mechanosensitive sodium ion channel NaV1.5. ‡Gastrointestinal symptoms include abdominal pain; abnormal stool form, stool frequency, or both; and bloating.[5] Non-gastrointestinal symptoms include back pain, gynaecological and bladder symptoms, headache, and fatigue.[25]

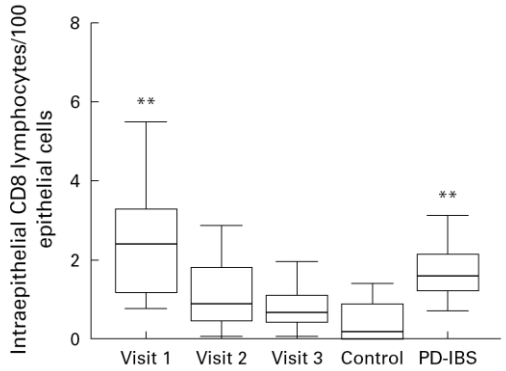
Le micro-environnement intestinal

- FODMAP et disaccharides
- Le microbiote
- Acides biliaires dans IBS-D
- Fonction barrière et immunité









Facteurs génétiques

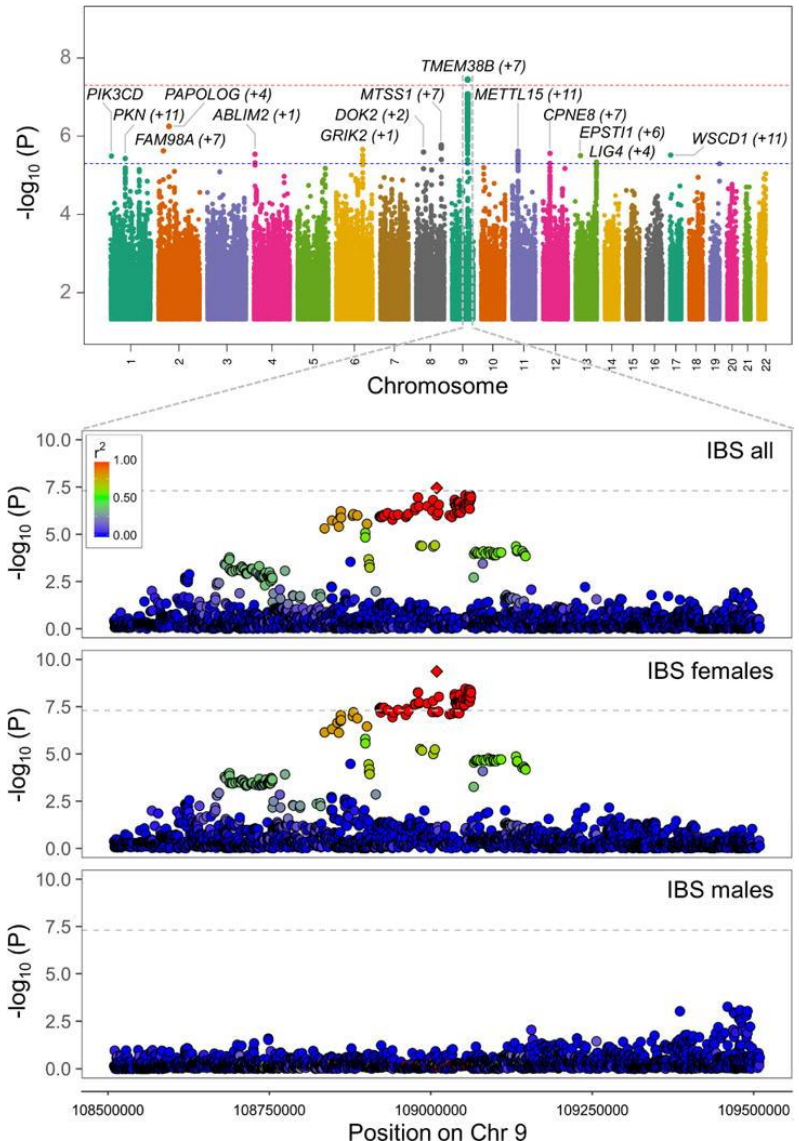


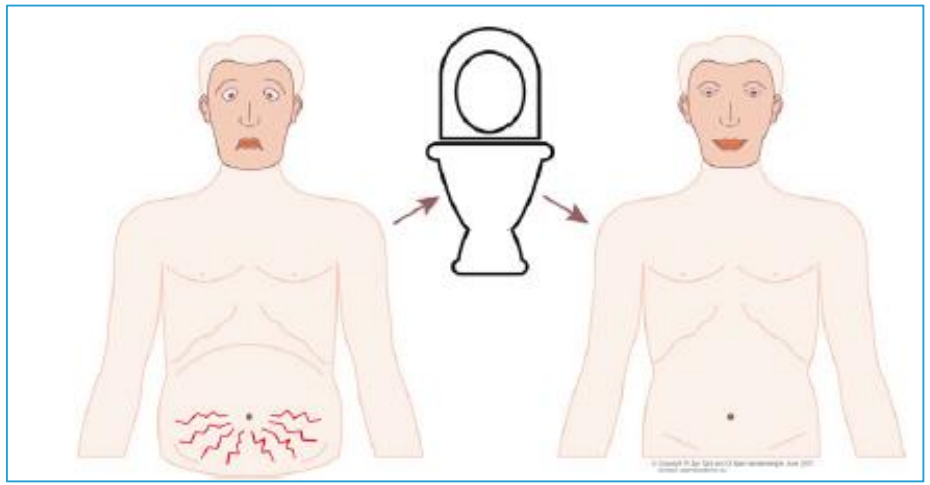
Table 1. Patient Cohort Characteristics

	IBS cases (n = 584)	IBS cases with SCN5A mutation (n = 13)
Median age, *y* (range)	49.5 (18.0–70.0)	49.8 (30.0–62.0)
Female, n (%)	484 (83)	11 (85)
Race		
Caucasian, n (%)	549 (94)	12 (92)
Non-Caucasian, n (%)	35 (6)	
Not stated, n (%)		1 (8)
Region		
Local, n (%)	396 (68)	10 (77)
National, n (%)	187 (32)	3 (23)
Met Rome II criteria, n (%)	328 (59)	
IBS subtype		
IBS-C, n (%)	59 (10)	4 (31)
IBS-D, n (%)	143 (25)	3 (23)
IBS-M, n (%)	181 (31)	3 (23)
Other, n (%)	201 (34)	3 (23)

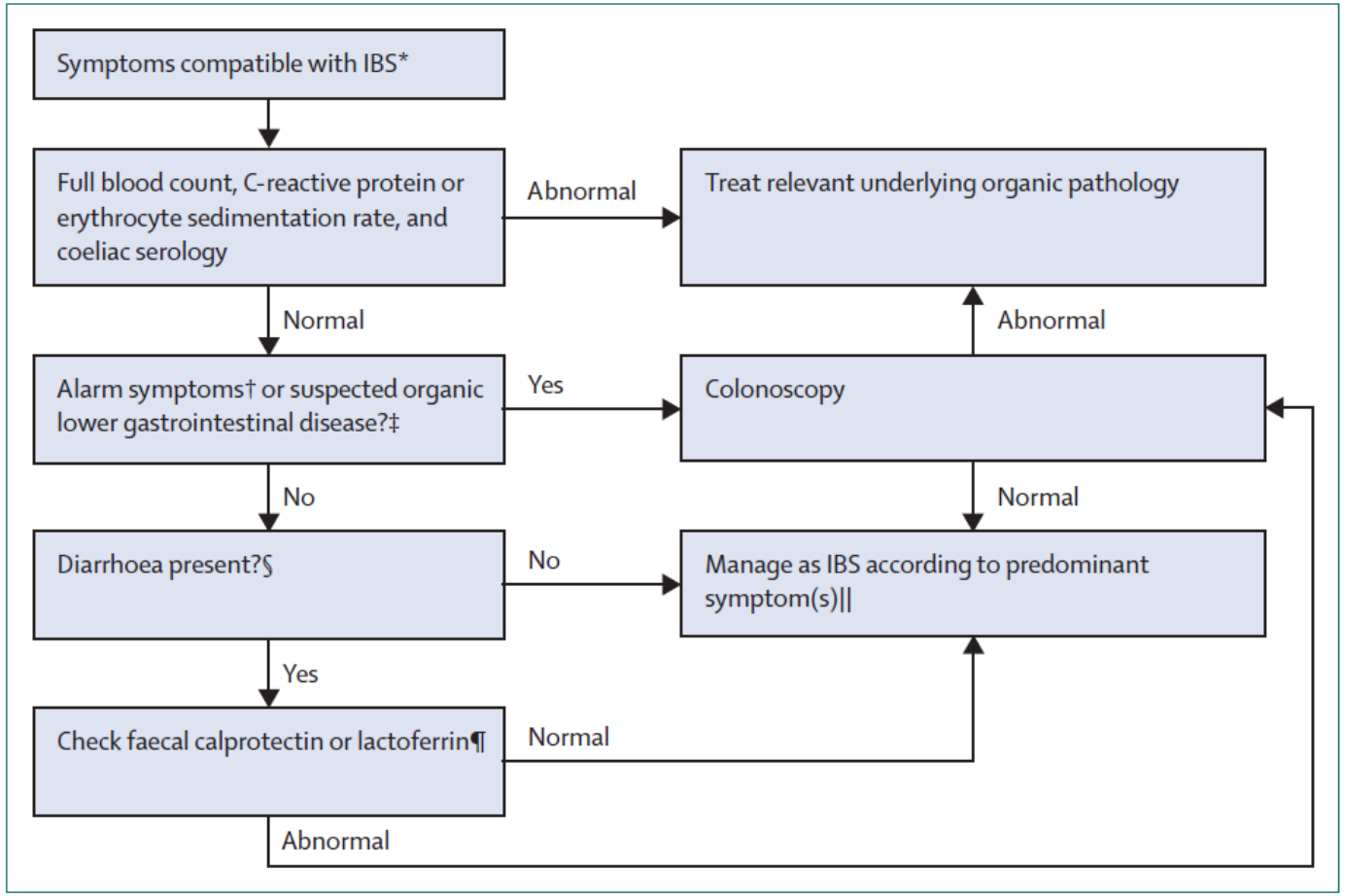
IBS-M, mixed-subtype IBS.

Présentation clinique

- La douleur est clé
  - Pas de IBS en cas de douleur aiguë
  - Récidivante et fluctuante plutôt que continue
  - Le plus souvent dans l'abdomen inférieur
  - Modifiée par le transit
- Le ballonnement est fréquent mais pas indispensable pour le diagnostic



Investigations
NON INDISPENSABLES



Approche

Table 3 Treatment approach for functional abdominal pain syndrome

Establishing an effective patient-physician relationship

1. Empathize
2. Educate
3. Validate
4. Reassure
5. Negotiate the treatment
6. Set reasonable limits

The treatment plan

1. Set reasonable treatment goals
2. Help the patient take responsibility
3. Base treatment on symptom severity and degree of disability
4. Medications
5. Mental health referral
6. Specific psychological treatments
7. Multidisciplinary pain treatment center referral

Cliniques universitaires SAINT-LUC
UCLouvain BRUXELLES

Consensus belge dans la prise en charge de l'intestin irritable:

Stratégies thérapeutiques

Prof. Hubert Piessevaux, MD PhD

Explanation is a crucial part of the management of IBS.

Lifestyle modifications are effective in the first-line approach of IBS.

- De nombreuses études montrent le déficit en information des patients
- L'éducation et l'information forment une base pour l'engagement du patient dans sa prise en charge
- Une étude randomisée montre un bénéfice d'une intervention psycho-éducative

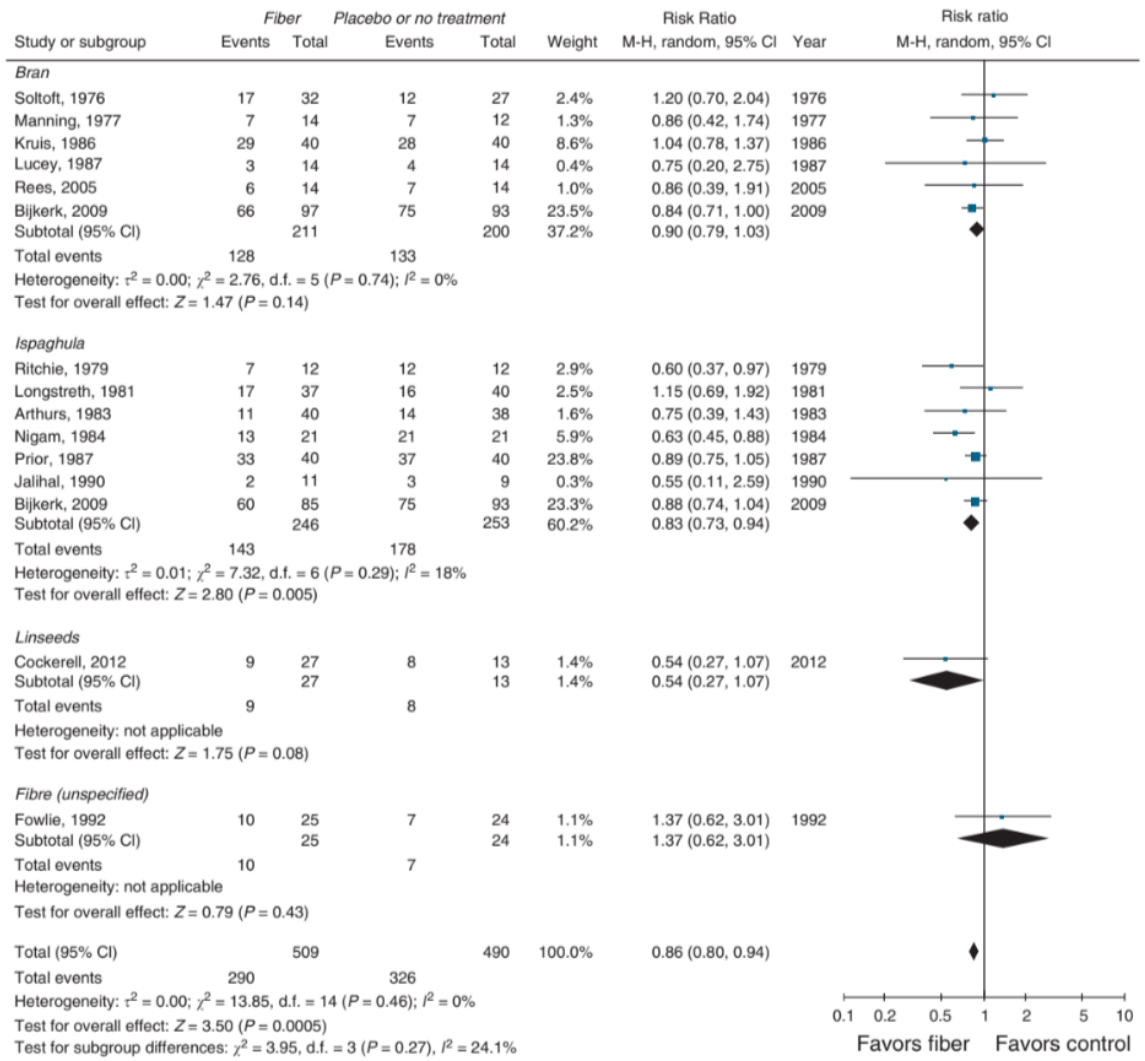
  A warm patient practitioner interaction with more time spent on explanations and questions, allowing patient understanding his or her condition, produces better outcome in comparison with a limited interaction, as demonstrated in a randomized controlled trial
- Explique en partie l'effet placébo
- 'Lifestyle modification' est mal défini
- Bénéfice persistant démontré pour l'effort physique (stimulé par kiné) (mais étude unique et faible nombre de patients)
- Yoga: pas d'évidence

Collins, Clin Gastroenterol Hepatol 2009; Abus, Aliment Pharmacol Ther 2013; Johannesson Am J Gastroenterol 2011

Première ligne

Fibres (hydro-)solubles

- Toutes les fibres ne sont pas égales
- NNT= 7 pour Ispaghula/psyllium
- Faible risque
- Si pas de bénéfice, passer rapidement à la ligne suivante



Moayyedi, Am J Gastroenterol 2014

Première ligne

Spasmolytiques

1.5. Spasmolytics are effective in IBS.	95%, Yes
1.6. Spasmolytics are the preferred first-line treatment in IBS.	80%, Yes

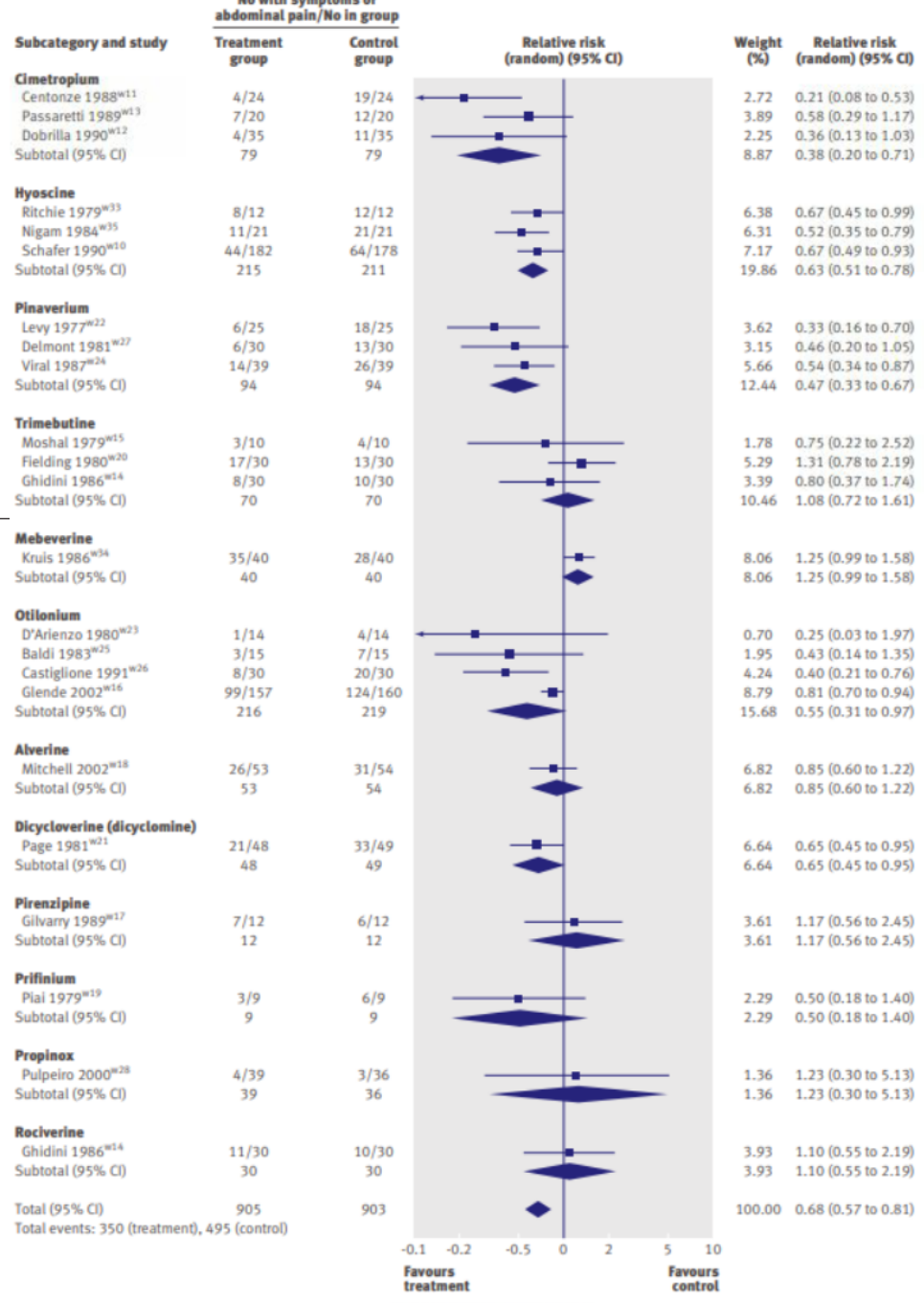
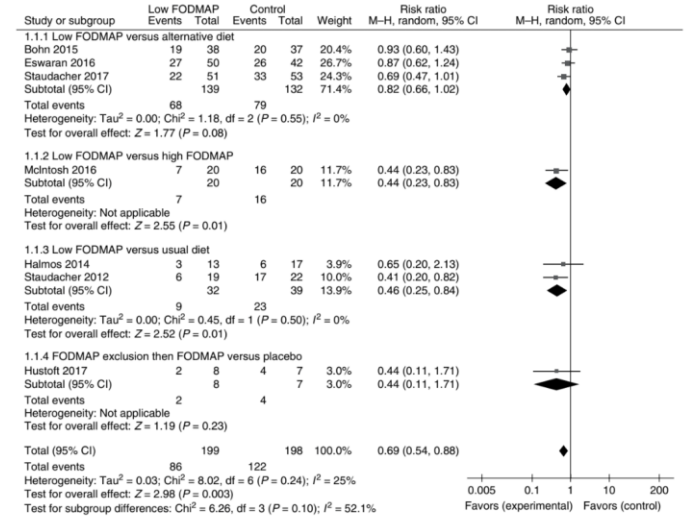


Fig 3| Forest plot of randomised controlled trials of antispasmodics versus placebo in treatment of irritable bowel syndrome. Events are number of patients with either global symptoms of irritable bowel syndrome or abdominal pain unimproved or persistent after treatment. See bmj.com for individual tests for heterogeneity and for overall effect

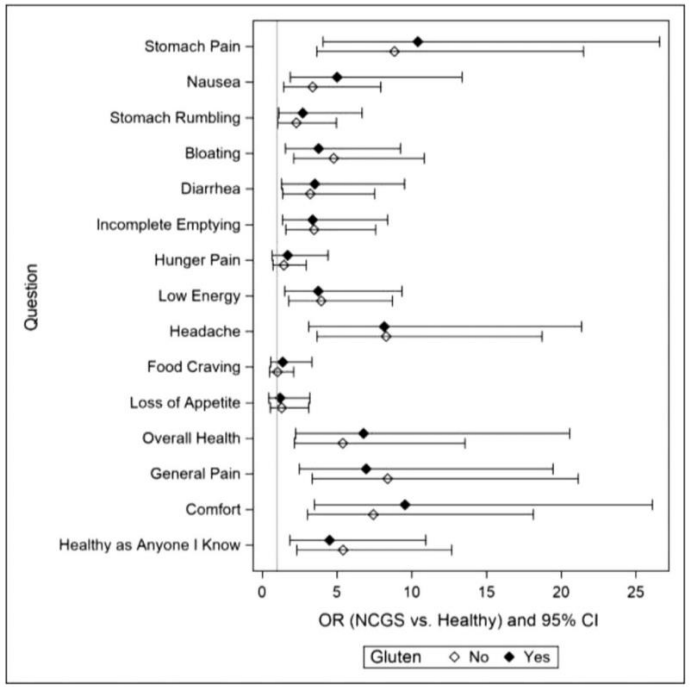
Ford, BMJ 2008

Interventions diététiques

1.5.	Irrespective of specific food intolerance, eating can exacerbate symptoms in some IBS patients.	100%, Yes	B	A+ 80%, A 20%, A- 0%, D- 0%, D 0%, D+ 0%	20-23
1.5.	A fructose reduced diet is effective in the treatment of IBS.	65%, No	C	A+ 20%, A 45%, A- 15%, D- 10%, D 10%, D+ 0%	96-97
1.6.	We advise against the gluten-free diet for the management of IBS.	85%, Yes	C	A+ 60%, A 25%, A- 10%, D- 0%, D 5%, D+ 0%	100-110
1.7.	A low FODMAP diet is effective in the treatment of IBS.	100%, Yes	B	A+ 70%, A 30%, A- 0%, D- 0%, D 0%, D+ 0%	111-115
1.8.	A low FODMAP diet is the preferred first-line treatment in IBS.	50%, No	D	A+ 15%, A 35%, A- 15%, D- 20%, D 5%, D+ 10%	111-117



3 Low FODMAP diet and irritable bowel syndrome (IBS) symptoms. CI confidence interval, FODMAP fermentable oligo-, di- and monosaccharides d polyols



Evidence of high sugar intake, and low fibre and mineral intake, in the gluten-free diet

D. Wild*, G. G. Robins*, V. J. Burley† & P. D. Howdle*

Moleski, Nutrition 2021; Wild, Aliment Pharmacol Ther 2010; Dionne, Am J Gastroenterol 2018

Modifications du microbiome

1.4. Prebiotics are not effective in IBS.	75%, No	D	A+ 30%, A 45%, A- 5%, D- 15%, D 5%, D+ 0%	213-215
1.5. Selected probiotics are effective in IBS	80%, Yes	C	A+ 35%, A 45%, A- 15%, D- 0%, D 5%, D+ 0%	42,213,216-218
1.6. Poorly resorbable antibiotics are effective in IBS-D.	75%, No	B	A+ 35%, A 40%, A- 25%, D- 0%, D 0%, D+ 0%	50,211,219-222
1.7. Faecal microbiota transplantation may have a temporary effect in IBS.	70%, No	B	A+ 30%, A 40%, A- 30%, D- 0%, D 0%, D+ 0%	223-229
1.8. Faecal microbiota transplantation is not effective in the treatment of IBS.	15%, No	B	A+ 10%, A 5%, A- 10%, D- 30%, D 30%, D+ 15%	223-229
1.9. We advise against faecal microbiota transplantation for the treatment of IBS.	90%, Yes	B	A+ 70%, A 20%, A- 0%, D- 0%, D 10%, D+ 0%	223-229

Pré-/Pro-/Antibiotiques

- Data for prebiotics and synbiotics were sparse
- Which particular combination, species or strains of probiotics are effective for IBS remains, for the most part, unclear
- Both single-strain and multi-strain trials have demonstrated benefits
- Only a few probiotics available in Belgium have demonstrated efficacy (e.g. Bifidobacterium animalis subsp lactis (Activia), L plantarum 299v (Bion Transfit), Bifidobacterium bifidum HI-MIMBb75 (Kijimea Pro), Bifidobacterium infantis 35624 (Alflorex), Bacillus coagulans MTCC 5856 (SporixX Pro), Escherichia coli (Symbioflor 2)).

- Rifaximin has modest efficacy in improving symptoms in non-constipated IBS.

Ford, Aliment Pharmacol Ther 2018

Transplantation fécale

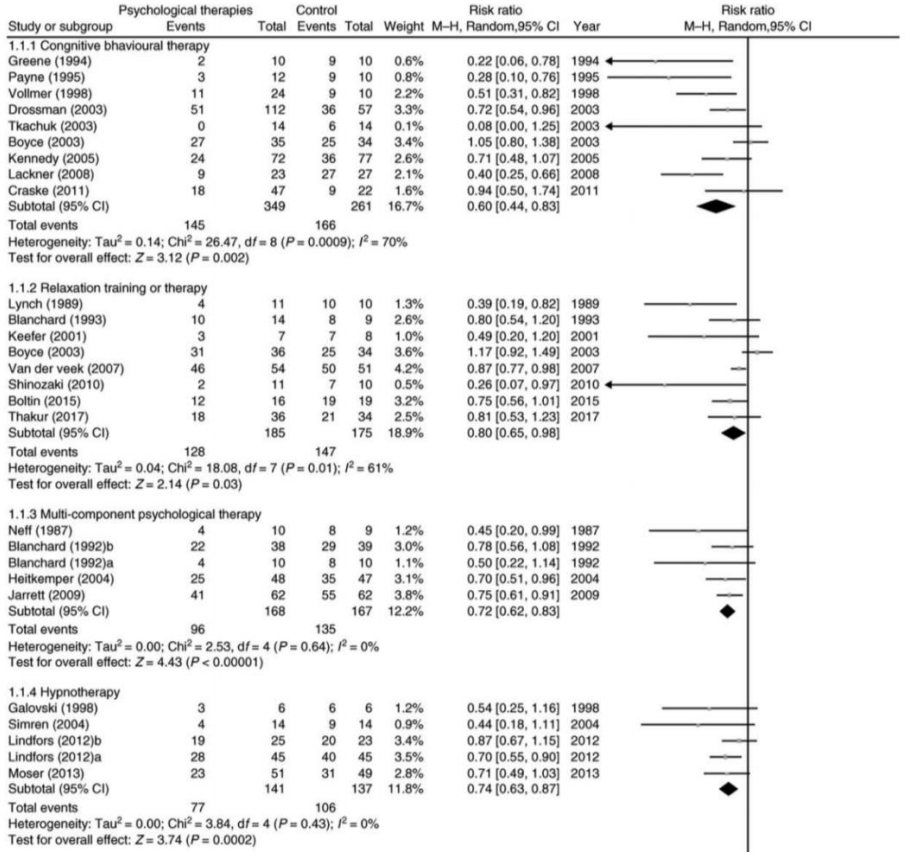
Author/country (reference)	N (act/plac)	Inclusion / IBS types	Fecal transplant	Placebo	Administration	Donor	Follow-up (months)	Primary endpoint	Results
Halkjaer / Denmark (2)	51 (25/26)	IBS-SS≥175 D-C-M	12 g feces 12 days	Saline / glycerol	Frozen capsules	Mix of 4	3	Decline in IBS-SS	Placebo better than active (p=0,012)
Arionades / US (3)	48 (crossover)	IBS-SS≥175 D-C-M	0-38g feces 3 days	Saline / glycerol	Frozen capsules	?	3	Decline in IBS-SS	No difference active vs. placebo
Johnsen / Norway (1)	83 (55/28)	IBS-SS≥175 D-M	50-80g feces (fresh/frozen)	Own feces	Coloscopy caecum	Mix of 2	3	IBS-SS decline ≥75 points	Active 36/55=65% vs. placebo 12/28=43% (<p 0,05)
Holster / Sweden (4)	16 (8/8)	IBS-SS≥175 D-C-M	30 g frozen feces	Own feces	Coloscopy caecum	1 (high butyrate production)	6	IBS-SS decline ≥30%	Active=placebo No influence on visceral sensitivity
Lahtinen / Finland (5)	49 (23/26)	Not specified D - M	30 g frozen feces	Own feces	Coloscopy caecum	1 (healthy)	12	IBS-SS decline ≥50 points	Active=placebo Decrease IBS-SS in active group at 3m (p=0,01)
El-Salhy / Norway (6)	164 (109/55)	IBS-SS≥175 D-C-M	30g or 60 g frozen feces	Own feces	Duodenal endoscope	1 (healthy profile)	3	IBS-SS decline ≥50 points	Active 30g 76,9% vs. active 60 g 89,1% vs.placebo 23,6% (vs placebo <p 0,0001)
Holvoet / Belgium (7)	62 (43/19)	Refractory IBS + bloating D-M	Fresh feces (quantity?)	Own feces	Nasoduodenal/nasojejunal probe	2 (high diversity)	3/12	Self-reported improvement	Active 24/43=56% vs. placebo 5/19=26% (p=0,03)

IBS-SS= IBS-symptom score. D-C-M= diarrhea – constipation – mixed.

Interventions non-médicamenteuses visant l'axe intestin-cerveau

10.	Statements on non-pharmacological treatment targeting the brain-gut axis	Overall agreement, Endorsement	Grade of evidence	Voting distribution	References
1.1.	Cognitive behavioural therapy is effective in IBS.	95%, Yes	B	A+ 60%, A 35%, A- 5%, D- 0%, D 0%, D+ 0%	242,244-246
1.2.	Medical hypnotherapy is effective in IBS.	70%, No	B	A+ 35%, A 35%, A- 25%, D- 5%, D 0%, D+ 0%	248-254
1.3.	Yoga is effective in IBS.	35%, No	C	A+ 10%, A 25%, A- 40%, D- 0%, D 15%, D+ 10%	255-258
1.4.	Mindfulness is effective in IBS.	50%, No	C	A+ 10%, A 40%, A- 30%, D- 5%, D 15%, D+ 0%	260-263
1.5.	Osteopathy is not effective in IBS.	85%, Yes	C	A+ 40%, A 45%, A- 5%, D- 10%, D 0%, D+ 0%	265-266

Limitations of psychological treatment are the need for longer treatment durations, patients' motivation and the availability of specialised mental health professionals



Neuromodulateurs

9. **Statements on neuromodulators and pain management**	Overall agreement, Endorsement	Grade of evidence	Voting distribution	References
1.1. Tricyclic antidepressants are effective in IBS.	100%, Yes	B	A+ 85%, A 15%, A- 0%, D- 0%, D 0%, D+ 0%	128,230-234
1.2. Selective serotonin reuptake inhibitors are effective in IBS.	95%, Yes	B	A+ 70%, A 25%, A- 5%, D- 0%, D 0%, D+ 0%	230-231
1.3. Selective serotonin and noradrenalin reuptake inhibitors are effective in IBS.	65%, No	B	A+ 30%, A 35%, A- 25%, D- 5%, D 5%, D+ 0%	235-237
1.4. Delta-ligands (pregabalin and gabapentin) are effective in IBS.	65%, No	B	A+ 30%, A 35%, A- 20%, D- 10%, D 0%, D+ 5%	238
1.5. Centrally-acting opioids are not effective in IBS.	100%, Yes	D	A+ 80%, A 20%, A- 0%, D- 0%, D 0%, D+ 0%	232,239-240

Neuromodulateurs

SNRI – duloxetine open label placebo run in

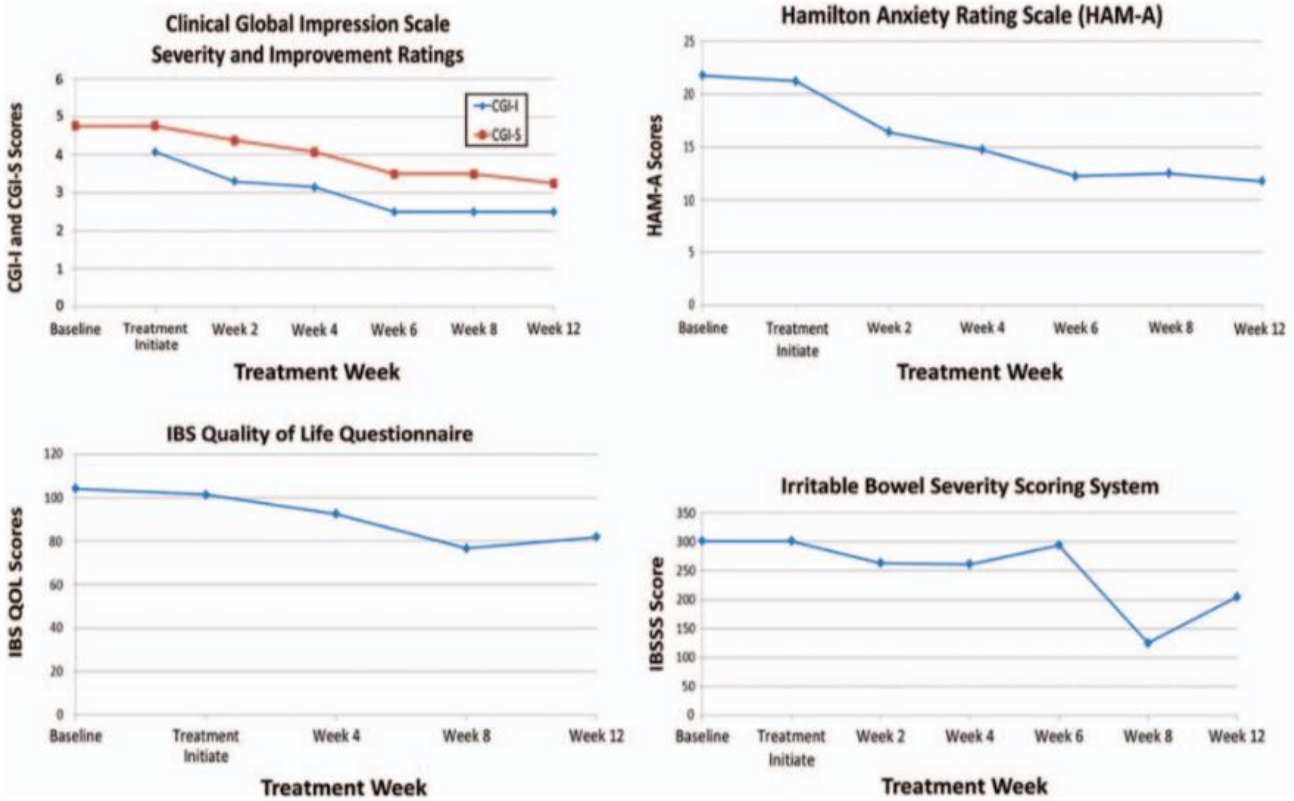


Figure 1. Treatment Outcome Measures.

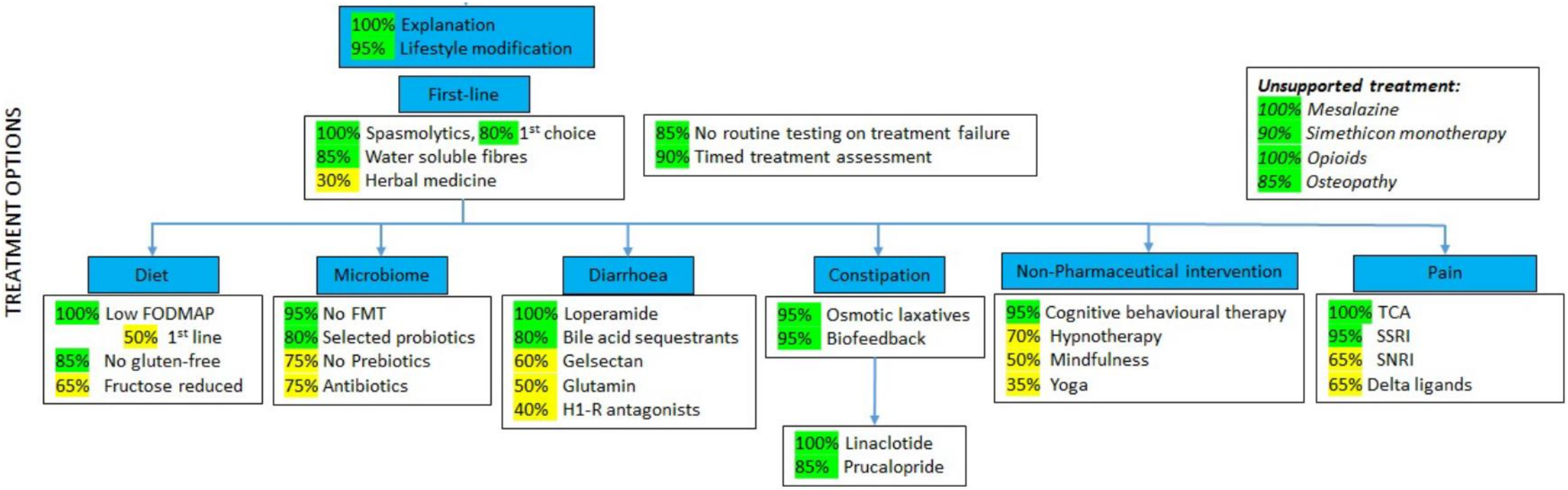
Kaplan, Int J Psychiatry Clin Pract. 2014

Question de la durée du traitement

Table 14. — **Suggested treatment duration before assessing its efficacy. A non-exhaustive list of frequently used IBS therapies**

Treatment	Assessment of treatment success	Reference
Otilonium bromide	10-15 weeks	52
Low FODMAP diet	1-2 weeks	112
Linaclotide	6 weeks	67
Amitriptyline	5-10 weeks	233
Citalopram	3-6 weeks	128

Algorithme de prise en charge



Conclusion: do's and dont's

- Faites un diagnostic positif et partagez-le avec vos patients
- Ayez conscience de la physiologie gastro-intestinale
- Expliquez la physiopathologie
- Prenez le temps d'une bonne anamnèse
- Recherchez les craintes et les agendas cachés
- Adaptez le traitement au profil des symptômes

Merci pour votre attention

Si vous avez des questions, n'hésitez pas à les poser