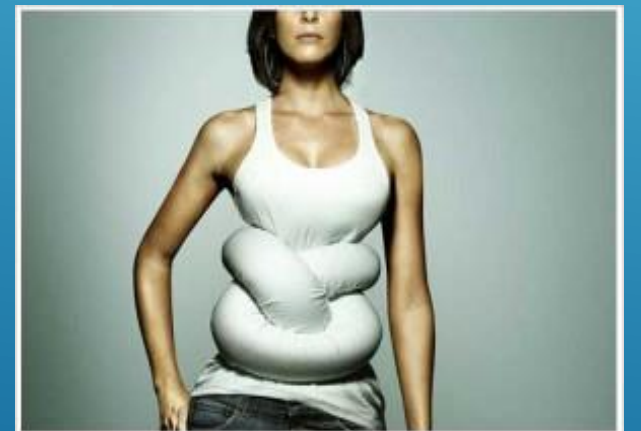



ΤΟ ΕΥΕΡΕΘΙΣΤΟ ΕΝΤΕΡΟ ΣΤΗΝ ΚΑΘΗΜΕΡΙΝΟΤΗΤΑ ΤΟΥ ΓΑΣΤΡΕΝΤΕΡΟΛΟΓΙΚΟΥ ΙΑΤΡΕΙΟΥ

Εμμ. Γρ. Συμβουλάκης, Γαστρεντερολόγος
Νοσοκομείο Ερρίκος Ντυνάν



ΣΥΝΔΡΟΜΟ ΕΥΕΡΕΘΙΣΤΟΥ ΕΝΤΕΡΟΥ

- ▶ Χρόνια λειτουργική διαταραχή του κατώτερου πεπτικού
 - ▶ *Conditio si ne qua non* : κοιλιακό άλγος
- 
- A decorative graphic consisting of several parallel white lines of varying lengths and orientations, located in the bottom right corner of the slide.

- ▶ Παγκόσμια επίπτωση 5-20% (Ελλάδα 21%)
- ▶ Γυναίκες:άνδρες OR 1.67
- ▶ Οι γυναίκες αναζητούν συχνότερα ιατρική συμβουλή

- ▶ Δεν έχει επίπτωση στην επιβίωση
- ▶ Κόστος/ασθενή/έτος 742-7547 \$, 567-862 €
- ▶ Άδειες/ασθενή/έτος 30
- ▶ 30% αναζητεί τακτική ιατρική φροντίδα
- ▶ 12% των επισκέψεων στην πρωτοβάθμια
- ▶ 30-50% των επισκέψεων σε γαστρεντερολόγο

ΚΡΙΤΗΡΙΑ ROME III

Υποτροπιάζον κοιλιακό άλγος ≥ 3 ημέρες τον μήνα
διάρκεια επεισοδίων ≥ 3 μήνες
έναρξη ≥ 6 μήνες πριν την διάγνωση

+ 2 ή περισσότερα

Ύφεση συμπτωμάτων με
την κένωση

ή/και

Έναρξη συμπτωμάτων
συνδυάζεται με αλλαγή στην
συχνότητα των κενώσεων

ή/και

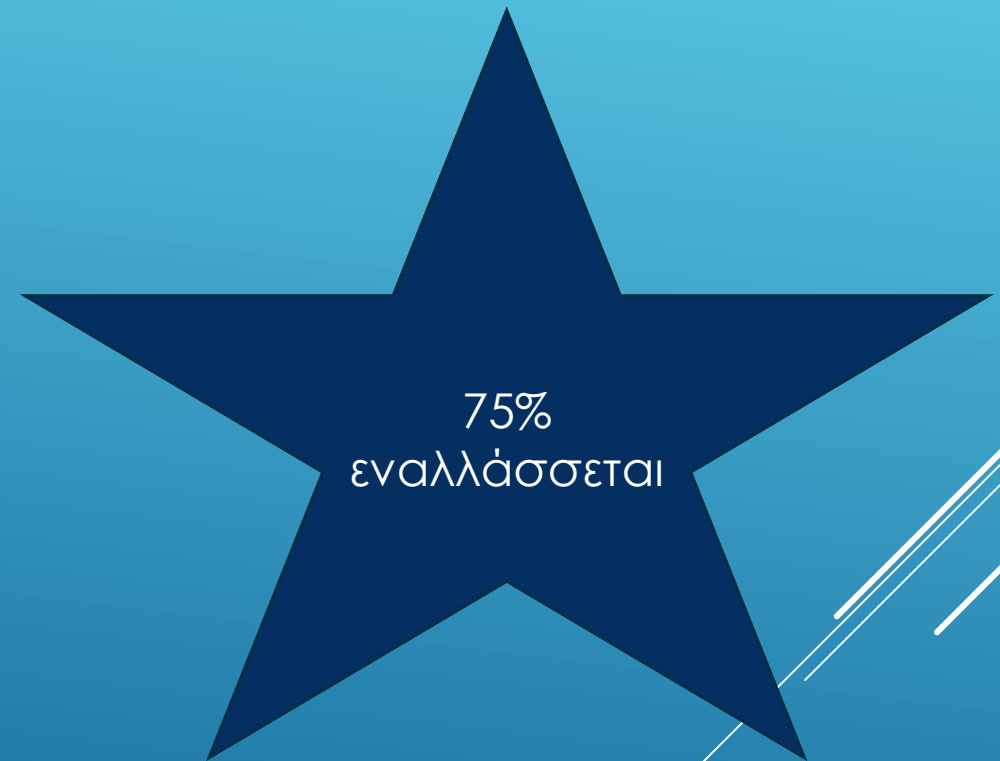
Έναρξη συμπτωμάτων
που συνδυάζεται με
αλλαγή στην σύσταση
των κενώσεων



▶ IBS-D (40%)

▶ IBS-C

▶ IBS-M (23%)



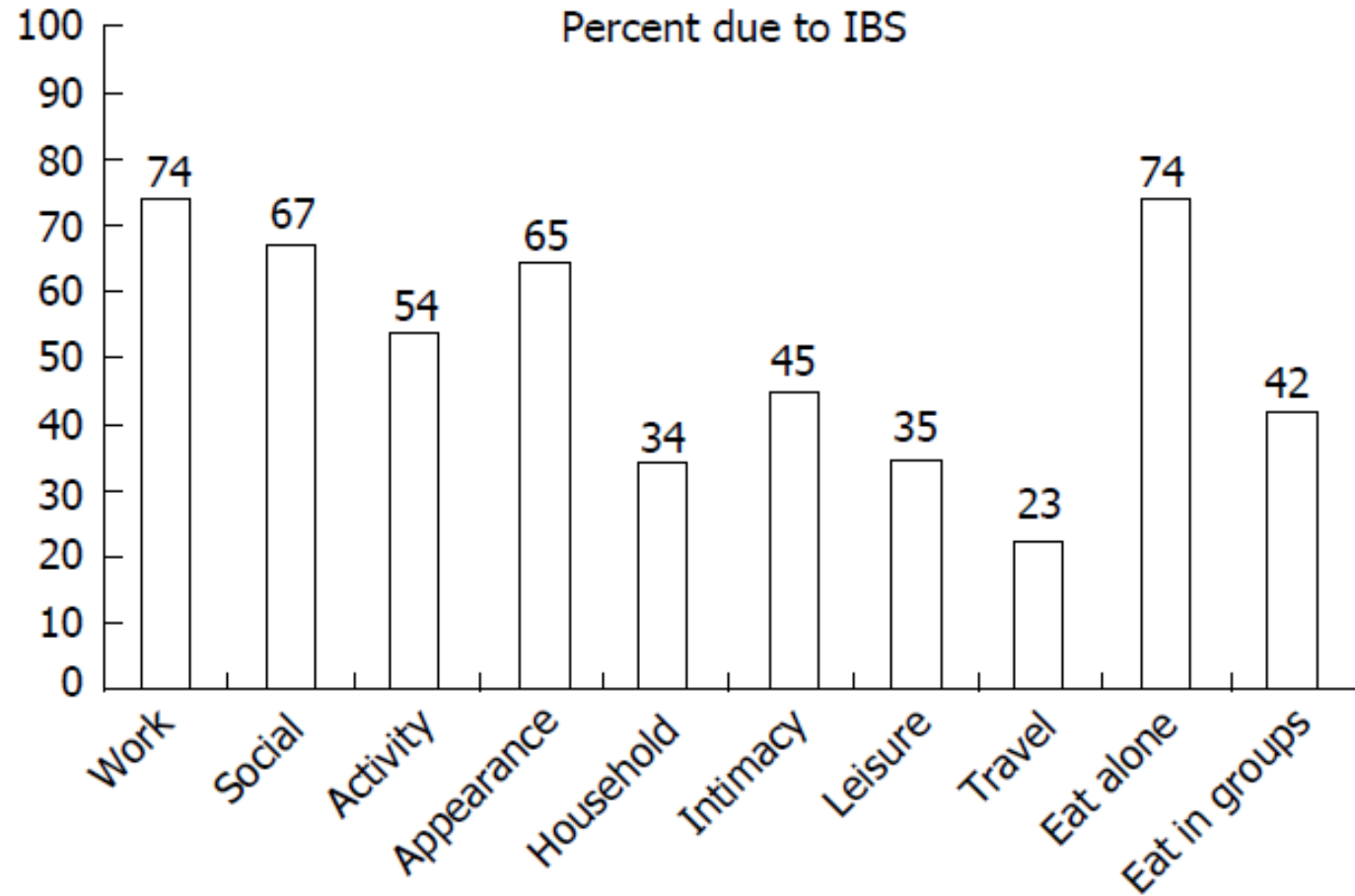
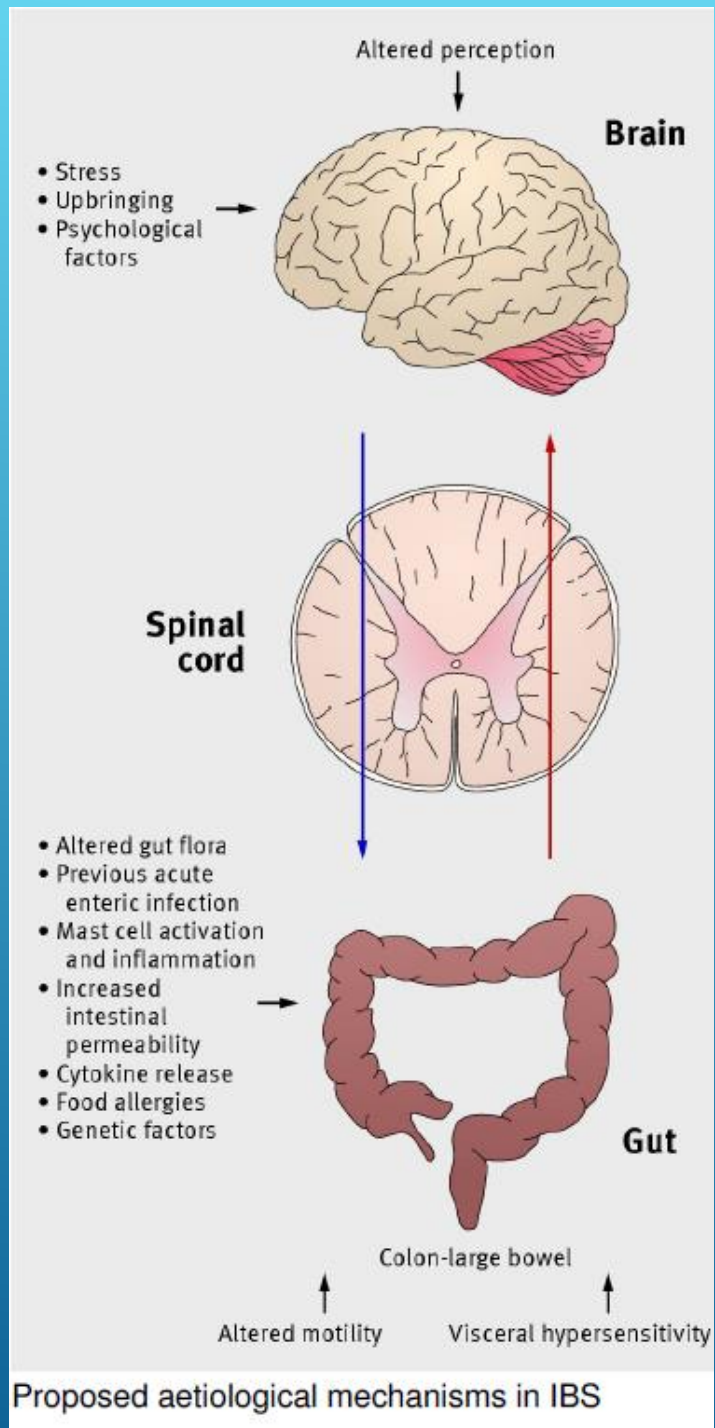


Figure 1 Percent of the sample ($n = 35$) that reported impairment in each area of daily living due to irritable bowel syndrome. IBS: Irritable bowel syndrome.

- ▶ Το 65% έχει εξωεντερικές συν-νοσηρότητες όπως ινομυαλγία, οσφυαλγία, ουρογεννητικά προβλήματα, διαταραχή ύπνου
- ▶ Το 40-60% (20% γενικός πληθυσμός) αναφέρει ψυχιατρικές διαγνώσεις όπως αγχώδη συνδρομή, κατάθλιψη, μετατραυματικό σύνδρομο
- ▶ Συχνότερα χαμηλό QoL και το 38% σε τριτοβάθμια κέντρα αναφέρει απόπειρα αυτοκτονίας λόγω των συμπτωμάτων

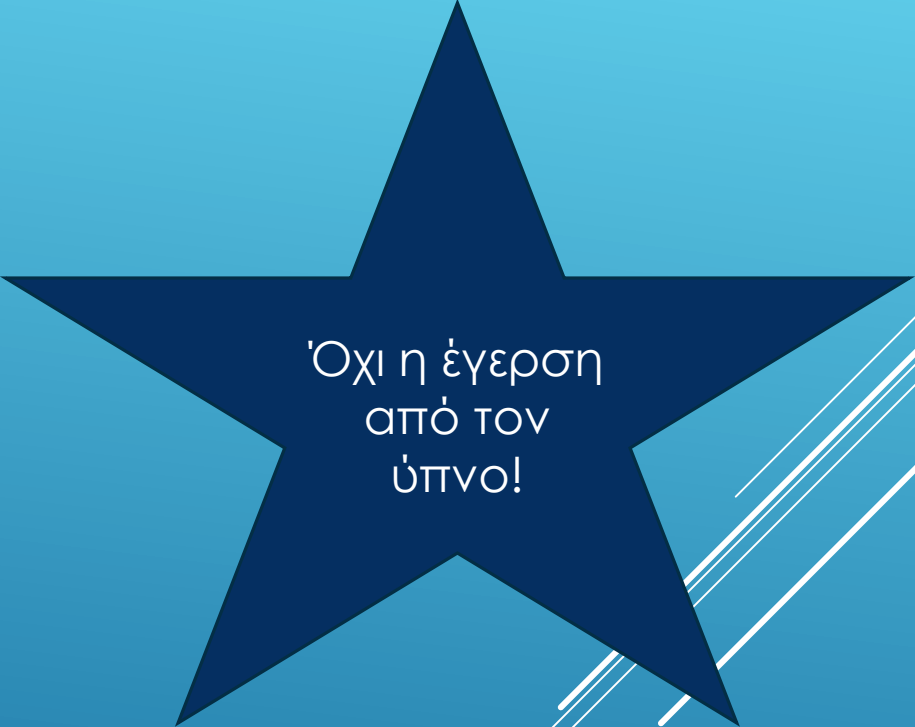




Proposed aetiological mechanisms in IBS

ALARM SYMPTOMS

- ▶ ≥50 ετών
- ▶ Οικογενειακό ιστορικό για ΚΠΕ
- ▶ Απώλεια βάρους
- ▶ Αιματοχεσία
- ▶ Αναιμία
- ▶ Ψηλαφητή μάζα
- ▶ Πυρετός
- ▶ Πρόσφατη αλλαγή στις εντερικές συνήθειες



Όχι η έγερση
από τον
ύπνο!

- ▶ Γενική αίματος, CRP
- ▶ Ορολογικό έλεγχο για κοιλιοκάκη (αν 5% των πασχόντων από IBS έχουν κοιλιοκάκη, cost effective)

Table 2 | Recommendations for the treatment of IBS from National Institute for Health and Care Excellence (NICE), American College of Gastroenterology (ACG), and American Gastroenterological Association (AGA)

Therapy	NICE ¹⁴²	ACG recommendation ⁹²	ACG (quality of evidence) ⁹²	AGA ¹⁴¹
Specialized diets	N/A	Weak	Very low	N/A
Fiber	Recommends soluble fiber	Weak	Moderate	N/A
Probiotics	Should not be discouraged	Weak	Low	N/A
Peppermint oil	N/A	Weak	Moderate/Low	N/A
Loperamide	Recommends as first line therapy	Strong recommendation against	Very low	Very low
Polyethylene glycol	Recommends	Weak	Very low	Low
Antispasmodics	Recommends as first line	Weak	Low	Low
Antidepressants	Recommends as second line	Weak	High	Low
			Very low	
Psychological Interventions	Recommends in refractory patients	Weak	High	N/A
Alosetron (US only)	N/A	Weak recommendation in women with IBS-D	Moderate	Moderate
5-HT ₄ agonists/5-HT ₃ antagonists	N/A	Strong recommendation against	Low	N/A
Linaclotide	N/A	Strong	High	High
Lubiprostone	N/A	Strong	Moderate	Moderate
Rifaximin	N/A	Weak	Moderate	Moderate
			Very low	

5-HT= 5 hydroxytryptamine; IBS-D= diarrhea predominant irritable bowel syndrome; N/A=not applicable.

ΔΙΑΙΤΑ-LIFESTYLE NICE GUIDANCE

- ▶ Ενημέρωση, ενθάρρυνση
- ▶ Ενθάρρυνση για φυσική άσκηση NNT 6
- ▶ Καλός ύπνος (μελατονίνη versus placebo)
- ▶ Τακτικά γεύματα ικανής διάρκειας
- ▶ Τουλάχιστον 1,5L νερό/d
- ▶ Καφές και τσάι ως 3 κούπες/d
- ▶ Αλκοόλ/αναψυκτικά εντός ορίων

ΔΙΑΙΤΑ-LIFESTYLE NICE GUIDANCE

- ▶ Επί μετεωρισμού/διάρροιας αποφυγή τροφίμων πλουσίων σε ίνες
 - ▶ Ως 3 φρούτα/d
 - ▶ Σε IBS-D αποφυγή σορβιτόλης (γάλα ;)
 - ▶ Αποφυγή αδιάλυτων ινών (whole grains,wheat)
 - ▶ Καλύτερα διαλυτές (βρώμη, ψύλλιο, λιναρόσπορος) NNT 10
-
- ▶ Όσοι παίρνουν προβιοτικά τουλάχιστον για 1 μήνα
 - ▶ Αποφυγή aloe vera
 - ▶ Αποφυγή ρεφλεξολογίας,βελονισμού
-
- ▶ All based on moderate and low quality evidence from RCT's and controlled trials

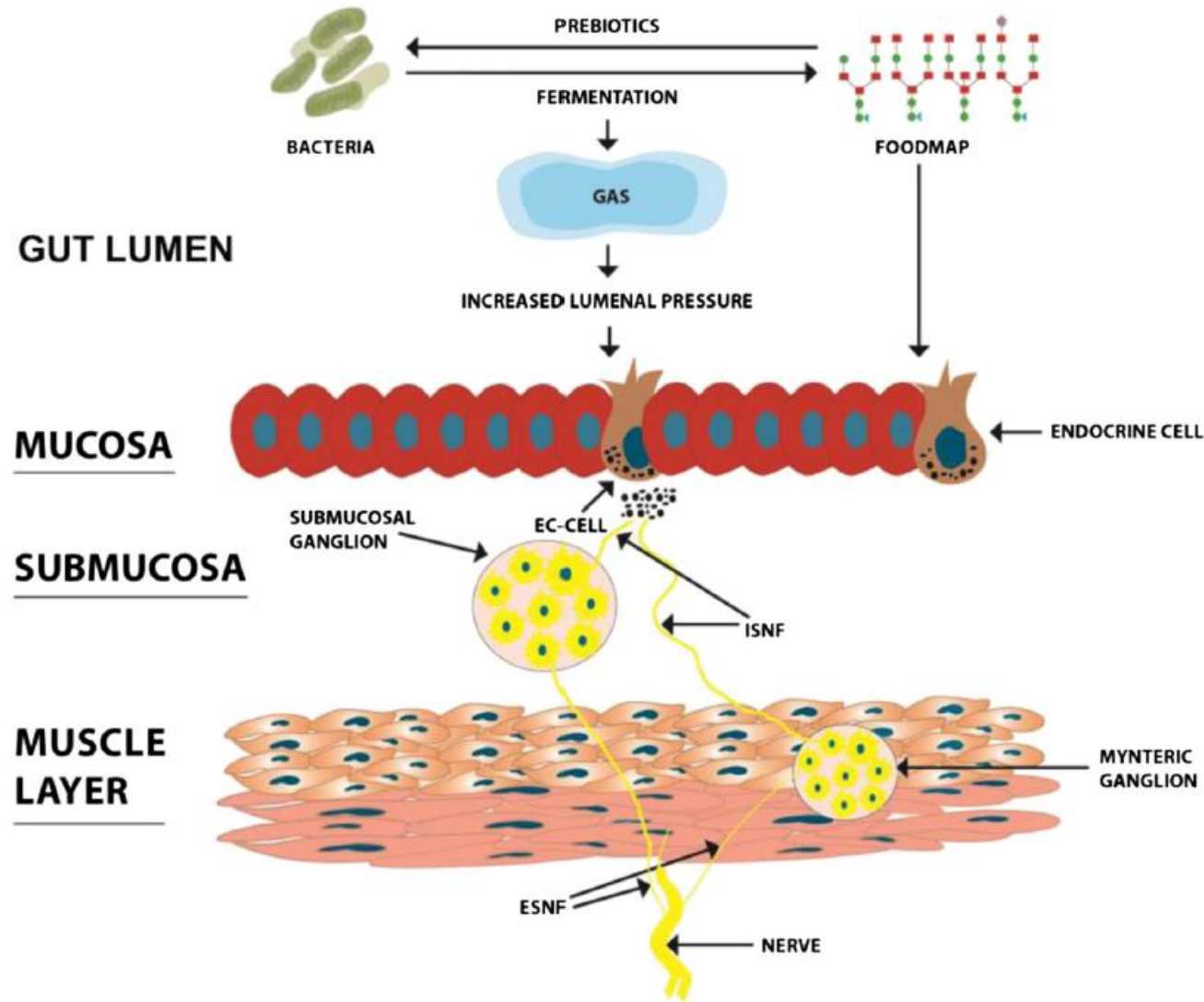








Figure 6 Schematic illustration for the possible mechanisms by which FODMAPs can trigger IBS symptoms. Upon reaching the large intestine FODMAPs can exert direct or indirect effect on the intestinal endocrine cells. They act as prebiotics and change the intestinal flora and they are fermented by the intestinal microbiota with gas production. The production of gas increases the luminal pressure and stimulates the release of serotonin from serotonin (EC) cells. Serotonin act on the intrinsic sensory nerve fibres (ISNF) of the submucosal and myenteric ganglia, which in turn convey the activation to the extrinsic sensory nerve fibres (ESNF) to the central nervous system.

Food category	Low FODMAP examples	High FODMAP examples
Dairy products 	<ul style="list-style-type: none"> • Lactose-free dairy products • Hard cheeses 	<ul style="list-style-type: none"> • Ice cream • Milk (including goats' milk) • Soft cheeses (camembert/brie) • Yoghurt • Cream
Vegetables 	<ul style="list-style-type: none"> • Bean sprouts, bok choy • Capsicum, carrots, celery, cucumber, corn • Eggplant, lettuce, leafy greens • Pumpkin, potatoes • Tomatoes, zucchini, all fresh herbs 	<ul style="list-style-type: none"> • Artichokes, asparagus • Beetroot, broccoli, brussel sprouts • Cabbage, cauliflower, fennel, green beans, garlic • Mushrooms, okra, onions • Snow peas, squash
Fruits 	<ul style="list-style-type: none"> • Bananas, berries, cantaloupe melon • Grapes, grapefruit, honeydew melon, kiwi • Lime, passion fruit, pineapple • Rhubarb, all citrus fruits 	<ul style="list-style-type: none"> • Avocado, apples, apricots • Cherries, dates, dried fruits, figs • Mango, nectarines • Papaya, peaches, pears, plums, prunes • Watermelon
Meats and protein sources 	<ul style="list-style-type: none"> • Fish, meat, chicken, tofu, shellfish, eggs 	<ul style="list-style-type: none"> • Legumes, pulses
Breads and cereal 	<ul style="list-style-type: none"> • Spelt and gluten-free bread • Rice cereal, rice quinoa, gluten-free pasta 	<ul style="list-style-type: none"> • Wheat and wheat based bread • Cereals, rye, wheat, pasta
Food additives, spices, and condiments 	<ul style="list-style-type: none"> • Most spices and herbs • Mayonnaise • Olives, onion powder, olive oil, pepper, salt • Maple syrup without high fructose corn syrup, mustard • Soy sauce, chili sauce • Sugar • Vinegar (including balsamic vinegar) 	<ul style="list-style-type: none"> • Any food with high fructose corn syrup or agave syrup content • Artificial sweeteners including sorbitol, mannitol, isomalt, xylitol (cough drops, gums, mints) • Chutneys, coconut, honey, jams, jellies • Molasses, pickles, relishes

- ▶ RCT 41 άτομα για 4 εβδομάδες
- ▶ ACS 68% v 23%

- ▶ RCT 30 άτομα για 3 εβδομάδες
- ▶ VS 22mm v 45mm

- ▶ Σοβαρή κριτική στις μελέτες

- ▶ Σε πάσχοντες που συσχετίζουν το φαγητό με τα συμπτώματα (φούσκωμα, αέρια)

Shepherd et al. Clin Gastroenterol Hepatol 2008

Halmos et al. Gastroenterology 2014

ΦΑΡΜΑΚΟΛΟΓΙΚΗ ΘΕΡΑΠΕΙΑ

- ▶ Σπασμολυτικά σε IBS-D, υπακτικά / καθαρτικά σε IBS-C
- ▶ Μετα-ανάλυση 22 RCT's NNT 5 NNH 17,5
- ▶ Peppermint oil (αναστολέας Ca) NNT 2,5

Ford et al. BMJ 2008

Hookway et al. BMJ 2015

Khanna et al. J Clin Gastroenterology 2014

ΣΕΡΟΤΟΝΙΝΕΡΓΙΚΟΙ ΑΓΩΝΙΣΤΕΣ / ΑΝΤΑΓΩΝΙΣΤΕΣ

- ▶ Alosetron 5-HT₃ ανταγωνιστής σε γυναίκες με σοβαρό IBS-D (ισχαιμική κολίτιδα)
- ▶ Προυκαλοπρίδη (Resolor) 5-HT₄ αγωνιστής **NNT 6** σε γυναίκες με σοβαρή δυσκοιλιότητα

LUBIPROSTONE

- ▶ Type 2 chloride channel activator
- ▶ FDA approved for IBS-C
- ▶ 4 μελέτες, όλες με θετικά αποτελέσματα
- ▶ 8μg x 2/d
- ▶ Ναυτία,διάρροια

Johanson et al. Aliment Pharmacol Ther 2008
Drossman et al. Aliment Pharmacol Ther 2009
Fukudo et al. Neurogastroenterol Motil 2011

LINACLOTIDE

- ▶ Αγωνιστής γουανιλικής κυκλάσης C
- ▶ FDA approved for IBS-C
- ▶ 4 μελέτες, όλες με θετικά αποτελέσματα
- ▶ 290 µg/d
- ▶ διάρροια

ΔΕΥΤΕΡΗ(;) ΓΡΑΜΜΗ ΘΕΡΑΠΕΙΑΣ

- ▶ Τα αντικαταθλιπτικά χρησιμοποιούνται σε καταστάσεις χρόνιου πόνου και αλλάζουν το bowel transit time (προσοχή σε IBS-C)
- ▶ Τρικυκλικά και SSRI's NNT 4
- ▶ Adverse events

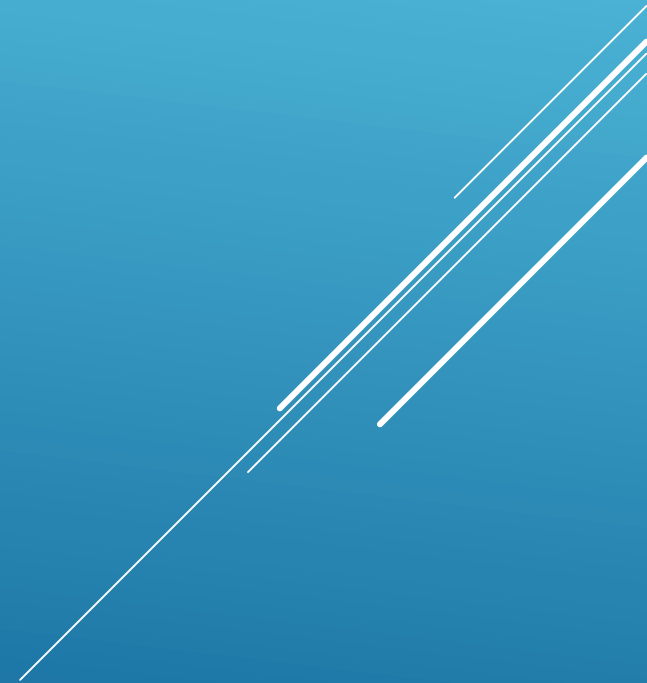


Ford et al. BMJ 2012
Hookway et al. BMJ 2015

ΑΛΛΑΓΗ ΜΙΚΡΟΒΙΑΚΟΥ ΠΕΡΙΒΑΛΛΟΝΤΟΣ

▶ Αντιβιοτικά

▶ Προβιοτικά



ΡΙΦΑΞΙΜΙΝΗ

- ▶ Target I,II 2 εβδομάδες θεραπεία
- ▶ IBS-D,M
- ▶ Βελτίωση σε συνολικά συμπτώματα/μετεωρισμό στις 4 εβδομάδες και διαρκεί 12
- ▶ NNT 10
- ▶ No adverse effects

Pimmentel et al. Ann Intern Med 2006

Menees et al. Am J Gastroenterol 2012

ΠΡΟΒΙΟΤΙΚΑ

- ▶ Lactobacillus, Bifidobacterium
- ▶ 6 μετα-αναλύσεις
- ▶ NNT4




- ▶ Ποιός πάσχων θα ωφεληθει
 - ▶ Optimal dose and organism (bifidobacteria)
 - ▶ Διάρκεια Θεραπείας
- 
- A decorative graphic consisting of several parallel white lines of varying lengths, slanted upwards from left to right, located in the bottom right corner of the slide.

Table 1 Overview of different non-pharmacological treatments for IBS patients

Ref/year	Treatment modalities
Stress management [66]/1987	PMR, thermal biofeedback, education, training in stress coping strategies, home practice, individual treatment
[67]/1991	Relaxation exercises (PMR), stress theory, individual treatment
Relaxation [68]/1993	PMR, home practice, individual treatment
[77]/2007	PMR, home practice (audio tape), small group treatment
Meditation [71]/2001	Relaxation response meditation, homework, individual treatment
Cognitive behaviour therapy [69]/2000	Cognitive education, PMR, isometric relaxation, home practice (audio tape), individual treatment
[70]/2000	Cognitive education, PMR, training assertiveness and coping strategies, individual treatment
[73]/2003	Biopsychosocial IBS theory, stress theory, homework, group treatment
[75]/2006	Psychoeducational theory, IBS theory, stress coping, homework diary, group treatment
Functional relaxation [79]/2010	For explanation see body text, small group
Mindfulness [80]/2011	Mindfulness stress reduction program specialized to IBS, <i>i.e.</i> , mindfulness training + cognitive behaviour theory, group treatment
[82]/2013	Mindfulness stress reduction with cognitive therapy program better than unspecified mindfulness alone, group treatment
Hypnotherapy [64]/1984, [65]/1987, [74]/2005	Hypnosis and PMR, audiotape daily, individual treatment
[72]/2002	Hypnosis and PMR, audiotape daily, individual treatment
[76]/2006	Guided imagery, PMR, individual treatment
[81]/2012	Hypnosis and PMR, audiotape daily, individual treatment
Body awareness therapy [18]/2002	Body awareness training, psychosomatic theory, IBS theory, group treatment
[22]/2007	Body awareness training, psychosomatic theory, IBS theory, group treatment

PMR: Progressive muscle relaxation; IBS: Irritable bowel syndrome.

ΨΥΧΟΛΟΓΙΚΕΣ ΘΕΡΑΠΕΙΕΣ-ΘΕΡΑΠΕΙΕΣ ΣΥΜΠΕΡΙΦΟΡΑΣ

- ▶ Ψυχιατρικές διαταραχές Χ3
- ▶ Cochrane review : no benefit
- ▶ Meta-analysis NNT4



(Sorrow Voca.) Glorious practice this mesmerism is, because it gives us so much power over the imagination of the patient; it is really very satisfactory. The public have been kept so completely in the dark, as regards the *true cause of diseases*, that we doctors can impose any thing we please upon them. None of these impositions could take place under Mr. Morison's Hygeian System of Medicine, and therefore it wont do for us. What would become of our Guinea Trade, if we, for one moment, admitted that he was in the right? Hurrab, then for confusion and mystery in medicine.



THE MESMERIC M. D.

Table 1 | Selected new treatments for IBS*

Treatment	Dosing and administration	Comments on effect	NNT
Exercise ⁶³	20-60 minutes of moderate to vigorous physical activity 3-5 days/week	IBS-SSS score dropped by >50 points in 43% of patients randomized to exercise versus 26% in control arm	6
Biofeedback for IBS-C ⁶⁹	Refer to specialist center; 2-3 sessions of 45-60 minutes	Overall biofeedback therapy led to symptom relief in 12 of the 29 patients with IBS symptoms before treatment	Unknown
Probiotics	Wide variety of strains and formulations available (see Hungin et al for selection based on main symptom) ⁷⁸	Magnitude of benefit and the most effective species and doses remain uncertain	4
Iberogast (STW-5) ⁸⁷	20 drops in half a glass of water 3 times daily; available without prescription in many European countries and Australia; online vendors good option for US patients	In observational studies abdominal scores decreased by 65-80%; about 80% of physicians and patients assessed the effectiveness of STW-5 as very good or good; superiority over placebo confirmed in an RCT	5
Hypnotherapy/CBT	Refer to specialist providers; many different programs exist; recommend exploring local options as 6-12 sessions usually needed	Several RCTs in different settings and populations support long term efficacy	2-4
Rifaximin ¹⁰⁷	400-550 mg three times daily for 10-14 days (prescription only)	A meta-analysis found rifaximin to be more efficacious than placebo for global IBS symptom improvement; therapeutic gain over placebo= 9.8%	7-11
Lubiprostone ¹¹⁴	8 µg twice daily (prescription only)	IBS-C patients on lubiprostone endorsed greater symptom relief (17.9% v 10.1%)	12
Linacotide ¹¹⁷	290 µg daily (prescription only)	34% of patients on linacotide responded versus 14% of patients randomized to placebo	5

CBT=cognitive behavioral therapy; IBS=irritable bowel syndrome; IBS-C=constipation predominant IBS; IBS-SSS=irritable bowel syndrome severity scoring system; NNT=number needed to treat; RCT=randomized controlled trial.

- ▶ Γυναίκα 47 ετών, προεμμηνοπαυσιακή
- ▶ Κοιλιακό άλγος, δυσκοιλιότητα, φούσκωμα (IBS-C OR:2.38)
- ▶ Το κοιλιακό άλγος δεν σχετίζεται με συγκεκριμένες τροφές
- ▶ Έχει συμβουλευθεί 1 παθολόγο και 2 γαστρεντερολόγους
- ▶ Έχει λάβει σπασμολυτικά, προβιοτικά, υπακτικά χωρίς αποτέλεσμα