CATILON®

Irritable bowel syndrome (IBS): Management & Case sharing

Yen-ching Wang, MD 王彥景
Chief resident, VGHTC-GI
Date: 2024/09/13

CATILON OTILONIUM BROMIDE

MENARINI ASIA-PACIFIC

Disclaimer and Copyright Statement

本演講/報告/簡報(以下稱「簡報」)為新加坡商美納里尼醫藥有限公司台灣分公司(以下稱「本公司」)的工作成果及專有智慧財產，未經本公司事前書面同意，不得複製、刊印、使用或散佈。

This presentation is the work product of A. Menarini Singapore Pte. Ltd., Taiwan Branchthe Company (“the Company”), and may not be copied, published, used, or distributed without the prior written approval of the Company".

本簡報包含講者/作者的個人獨立意見，不代表本公司及相關事業。本公司就簡報的提供已盡相當應有注意，不擔保簡報內容資訊的證據性、正確性與完整性。

This presentation contains the personal views of the author(s) and does not represent the views of the Company and/or the Menarini Group. Due care has been taken in the preparation of this presentation and the Company does not assume liability for relevance, accuracy and completeness of the information provided".

本簡報包含有關 [疾病知識及產品 教育訓練] 的機密資訊。接受資訊者應嚴格遵守：(1)不應將本簡報資訊利用於前述目的以外之任何用途；(2)未經本公司事前述面同意不得揭露予任何第3者。

This presentation contains confidential information provided for the purposes of [training for disease knowledge and product information]. The recipient is strictly prohibited from (i) using any information provided in this presentation for any other purpose and (ii) disclosing any information to third parties without the prior written consent of the Company."

CATILON®
OTILONIUM BROMIDE

Outline

- **IBS: Pathophysiology & Management**
- Case sharing
- CATILON®
  - ✔ Drug mechanism
  - ✔ Evidence
  - ✔ Safety

ROME IV (2016)

Recurrent abdominal pain, on average, at least 1 day per week (in the last three months)

That is associated with ≥ 2 of the following criteria:[1]

- **Related to defecation**
- **Associated with a change in frequency of stool**
- **Associated with a change in form (appearance) of stool**

Moayyedi P, et al. United European Gastroenterol J. 2017

CATILON® OTILONIUM BROMIDE

TW-CAT-022024-002

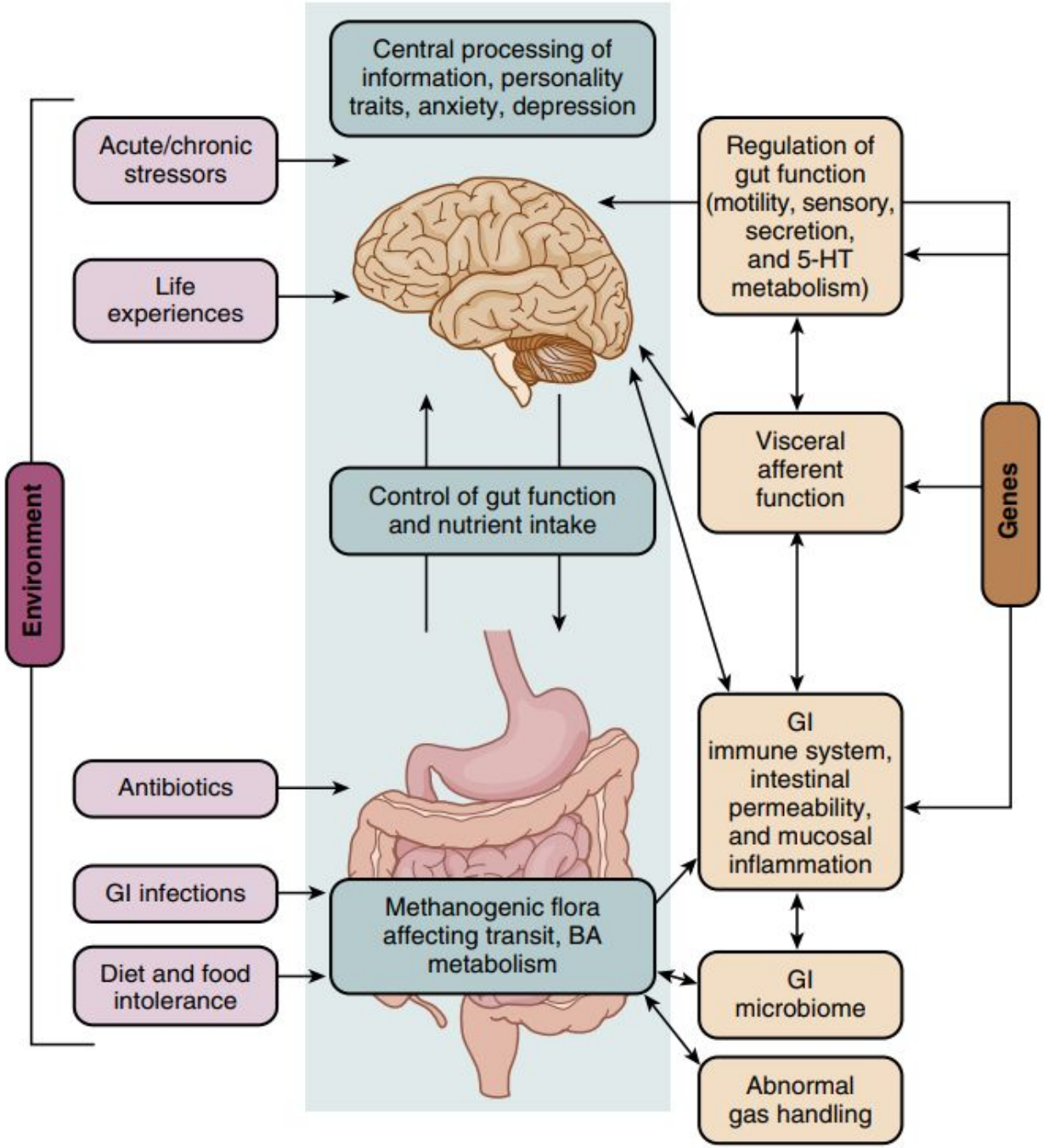
The Work has Begun- Timetable for Rome V

Mar- May 2026	Publication Gastroenterology supplement and Rome V book
May 2025	Document E sent for copyediting MDCP and Algorithms completed
Jan 2025	Begin MDCP and Algorithms Slide work completed
Oct 2024	Document D/Gastro article sent for outside review
Jan 2024	Begin Document D and Gastroenterology article
Dec 2023	Meeting in Rome – Revision and Harmonization
May, 2023	DDW symposium – Support Committee presentations Begin slide work
Jan 2023	Begin Document C
May 2022	Chapter committees review and revise Document B
May 2021	Chapter committees begin Document A Support committees begin work
Mar 2021	Editorial Board, Chapter chairs/co-chairs and committee members selected

https://theromefoundation.org/rome-iv/rome-v/

Complex mechanism…

Sleisenger & Fordtran's GI & Liver Disease, 11th Edition. 2020



Altered Motility

Gut, 1988, **29**, 1236–1243

Dysmotility of the small intestine in irritable bowel syndrome

J E KELLOW, S F PHILLIPS, L J MILLER, AND A R ZINSMEISTER

From the Gastroenterology Unit and Digestive Diseases Center, Mayo Clinic and Medical School, Rochester, MN, USA

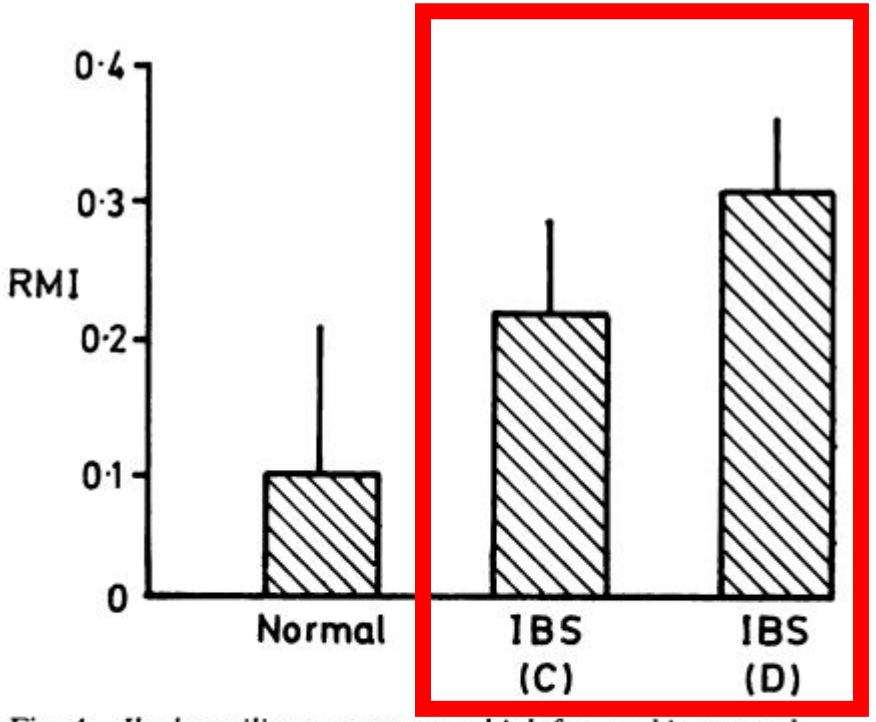


Fig. 4 *Ileal motility response to a high fat meal in control subjects and in patients with irritable bowel syndrome (IBS) with constipation (C) or diarrhoea (D). RMI (group means (SE)) is the relative motility index; postprandial motility minus basal motility divided by basal motility. Group differences were not significant; normals showed no augmentation (not different from zero, $p>0{\cdot}05$), but both groups of IBS had augmented postprandial motility ($p<0{\cdot}05$), adjusted for three comparisons.*

CCK infusion / high fat meal / ileum dilate

Kellow JE, et al. Gut 1988;29:1236–43.

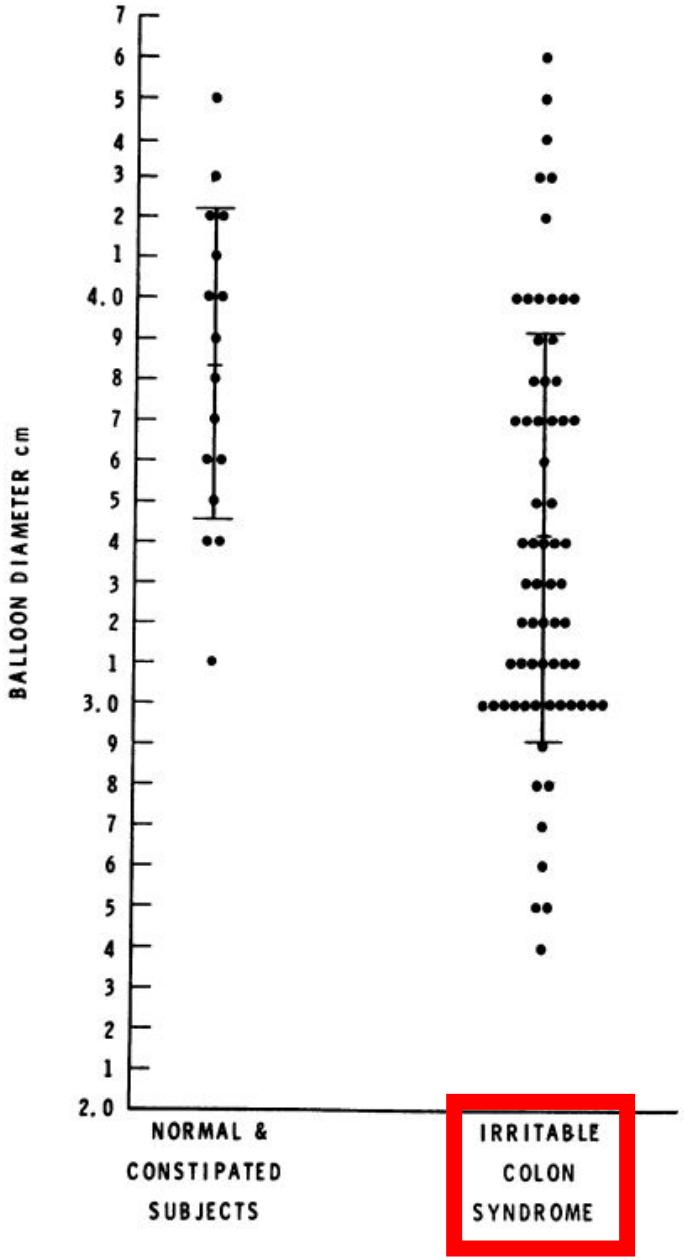
Visceral Hypersensitivity

Gut, 1973, **14**, 125-132

Pain from distension of the pelvic colon by inflating a balloon in the irritable colon syndrome[1]

JAMES RITCHIE[2]

From the Nuffield Department of Clinical Medicine, The Radcliffe Infirmary, Oxford, and the Nuffield Institute for Medical Research, Oxford



Increased perception of pain

Ritchie J. Gut 1973;14:125–32.

Abnormal Gas Handling

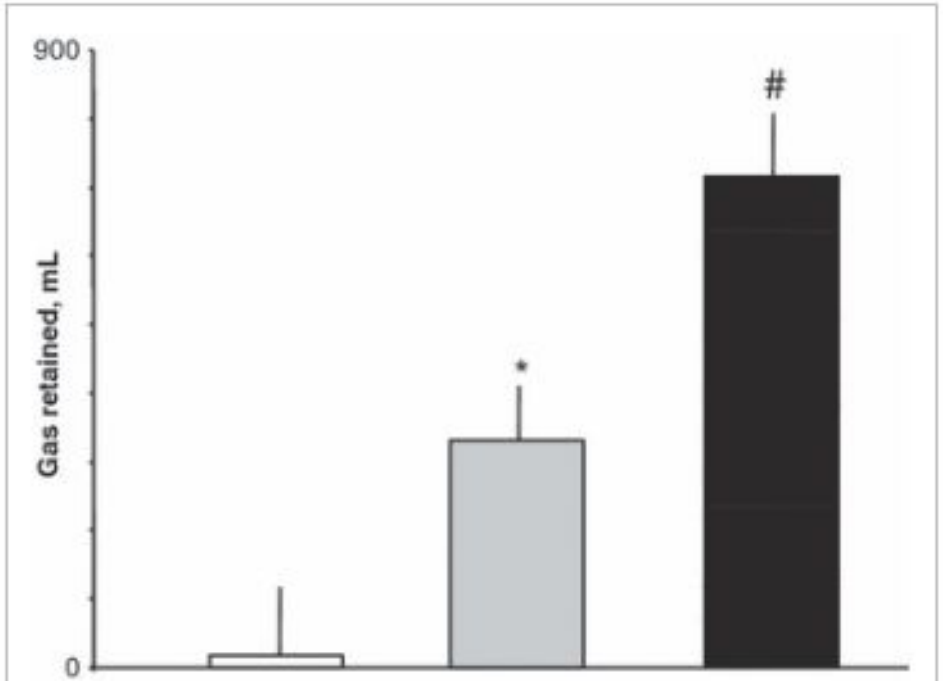
Neurogastroenterol Motil. 2010 Apr;22(4):401-6, e91-2. doi: 10.1111/j.1365-2982.2009.01447.x. Epub 2009 Dec 28.

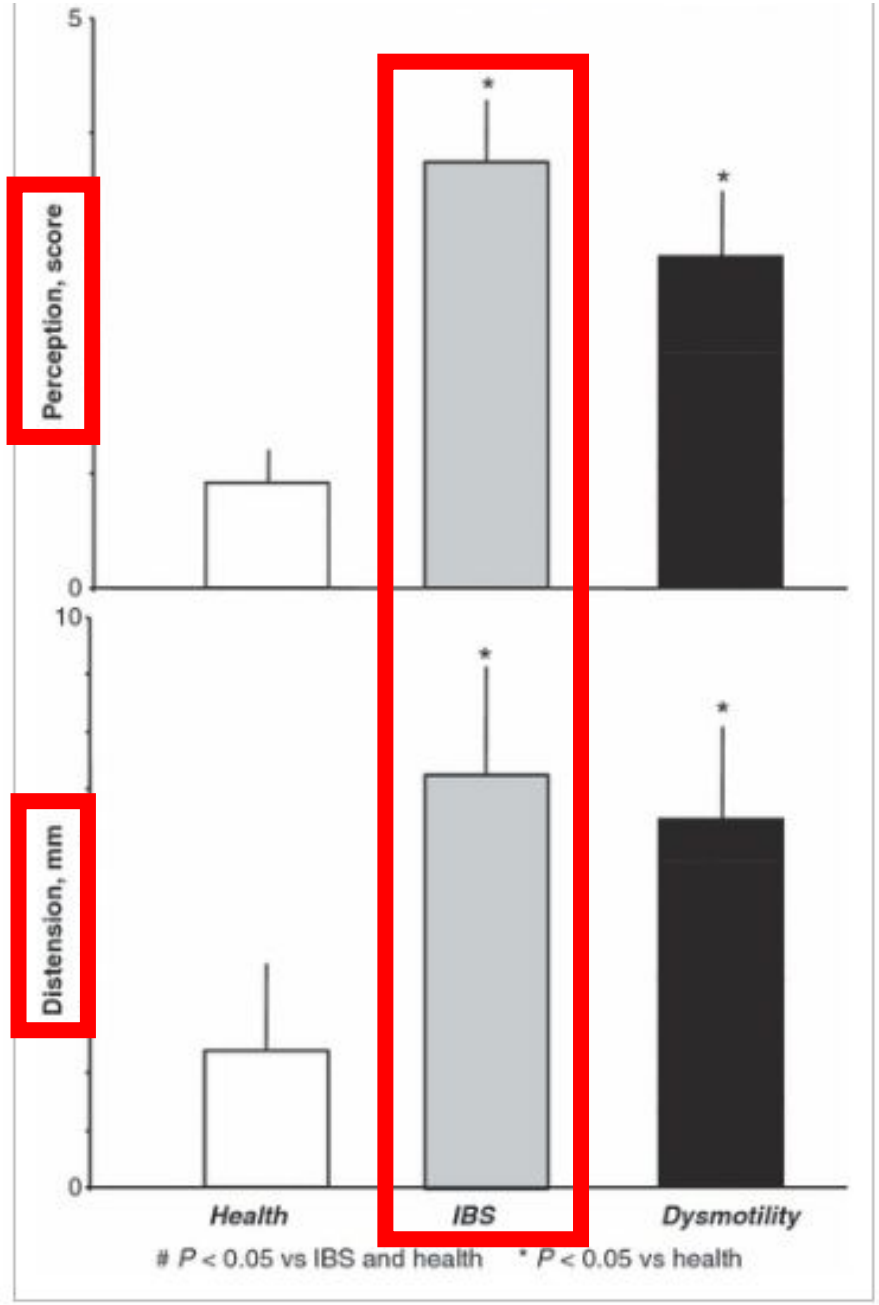
Impaired intestinal gas propulsion in manometrically proven dysmotility and in irritable bowel syndrome

J Serra [1], A Villoria, F Azpiroz, B Lobo, J Santos, A Accarino, J-R Malagelada

Affiliations + expand

PMID: 20047636 DOI: 10.1111/j.1365-2982.2009.01447.x





Serra J, et al. Neuro Gastroenterol Motil 2010;22:401–6

Potential treatment of choice…

- Altered Motility
- Visceral Hypersensitivity
- Abnormal Gas Handling

Spasmolytics

Abnormal 5-HT Metabolism

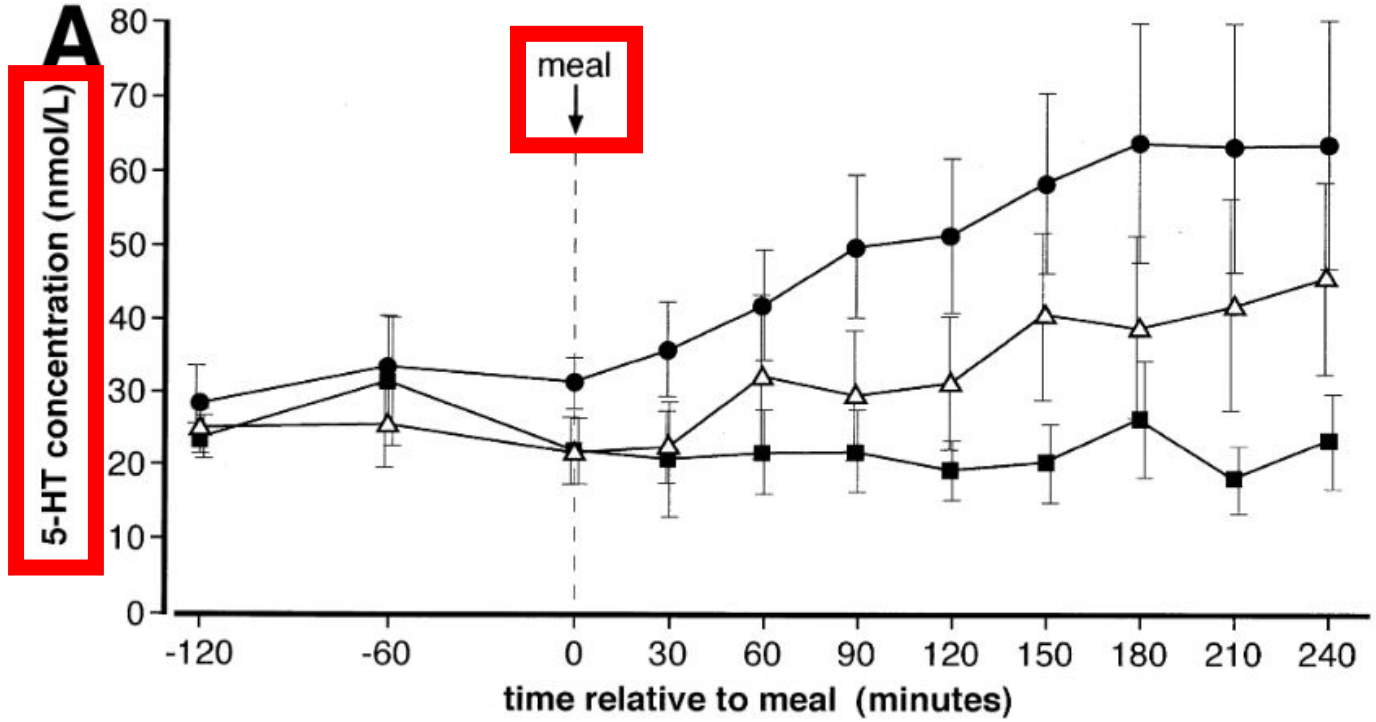
Gastroenterology. 2006 Jan;130(1):34-43. doi: 10.1053/j.gastro.2005.09.031.

Altered 5-hydroxytryptamine signaling in patients with constipation- and diarrhea-predominant irritable bowel syndrome

Wendy Atkinson [1], Stephen Lockhart, Peter J Whorwell, Brian Keevil, Lesley A Houghton

Affiliations + expand

PMID: 16401466 DOI: 10.1053/j.gastro.2005.09.031



Atkinson W, et al. Gastroenterology 2006;130:34–43.

CATILON® OTILONIUM BROMIDE

Disorder of Gut-Brain Interaction (DGBI)

Gut. 2012 Sep;61(9):1284-90. doi: 10.1136/gutjnl-2011-300474. Epub 2012 Jan 10.

The brain--gut pathway in functional gastrointestinal disorders is bidirectional: a 12-year prospective population-based study

N A Koloski [1], M Jones, J Kalantar, M Weltman, J Zaguirre, N J Talley

Affiliations + expand

PMID: 22234979 DOI: 10.1136/gutjnl-2011-300474

FGID(ROME II)->DGBI(ROME IV)

Table 3

Brain–gut pathway. Baseline psychological distress as a predictor of any functional gastrointestinal disorder (FGID), irritable bowel syndrome (IBS) and functional dyspepsia (FD) diagnosis at follow-up among controls free of a FGID at baseline

FGID diagnosis	Psychological distress variable	Baseline clinically elevated psychological distress		OR (95% CI)	p Value*
		Yes, mean (SD)	No, mean (SD)		
Any FGID†	Anxiety	2.7 (2.6)	1.9 (2.4)	1.11 (1.03 to 1.19)	0.006
	Depression	1.3 (2.2)	1.1 (2.2)	1.04 (0.96 to 1.13)	0.293
IBS‡	Anxiety	4.0 (3.7)	2.7 (3.0)	1.11 (1.03 to 1.18)	0.005
	Depression	2.6 (3.5)	1.5 (2.7)	1.10 (1.03 to 1.18)	0.007
FD§	Anxiety	3.9 (3.1)	2.8 (3.1)	1.09 (1.0 to 1.20)	0.057
	Depression	2.8 (3.7)	1.6 (2.9)	1.09 (1.0 to 1.20)	0.043

- * Controlling for age and gender.
- † Controls defined as no FGID.
- ‡ Controls defined as no IBS.

Higher risk for developing IBS & FGID

Koloski NA, et al. Gut 2012;61:1284–90

Potential treatment of choice…

- Abnormal 5-HT Metabolism
- Disorder of Gut-Brain Interaction (DGBI)

Neuromodulators

Altered Intestinal Permeability

Gastrointest Endosc. 2013 Apr;77(4):624-30. doi: 10.1016/j.gie.2012.11.006. Epub 2013 Jan 26.

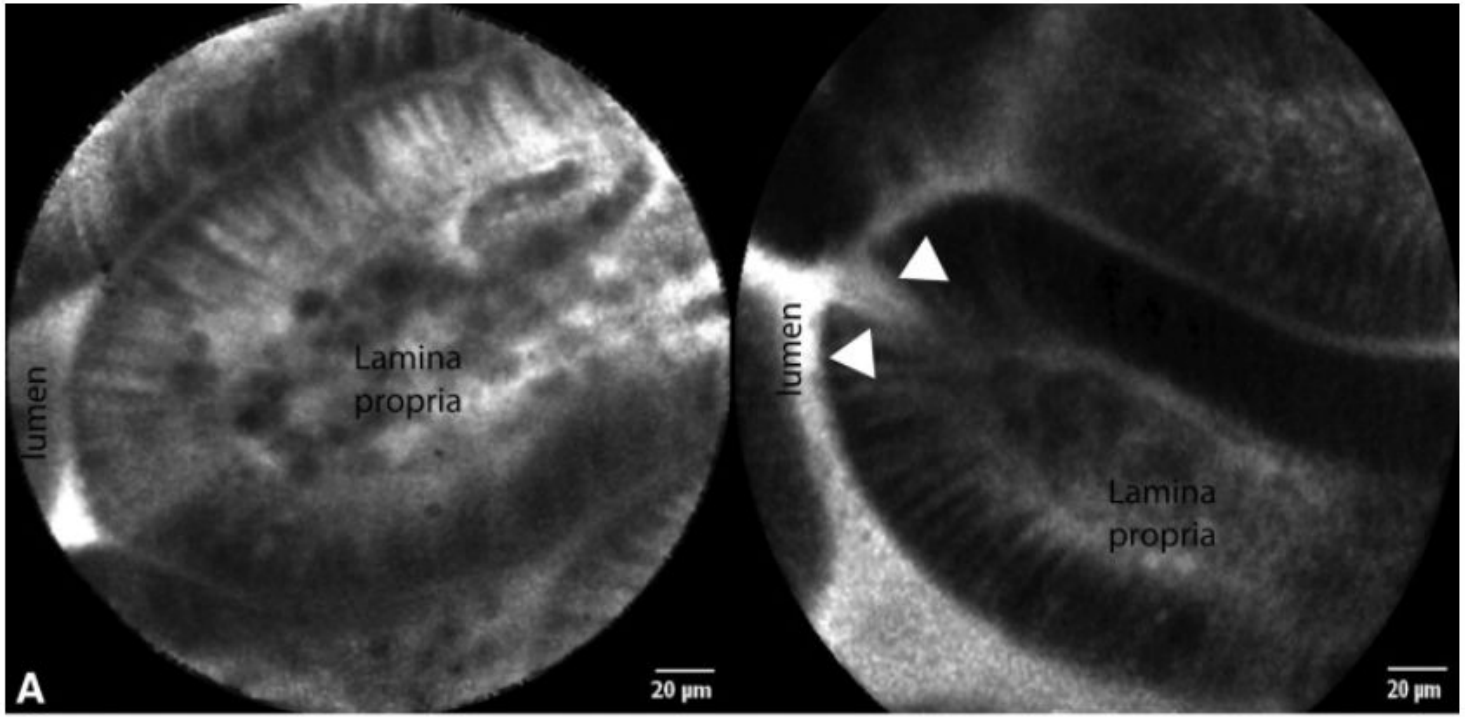
Breaks in the wall: increased gaps in the intestinal epithelium of irritable bowel syndrome patients identified by confocal laser endomicroscopy (with videos)

Jean-Francois Turcotte [1], Dina Kao, Stephanie J Mah, Brian Claggett, John R Saltzman, Richard N Fedorak, Julia J Liu

Affiliations + expand

PMID: 23357497 DOI: 10.1016/j.gie.2012.11.006

More than low-grade inflammation…



Turcotte JF, et al. Gastrointest Endosc 2013;77:624–30.

Abnormal Intestinal Microbiota

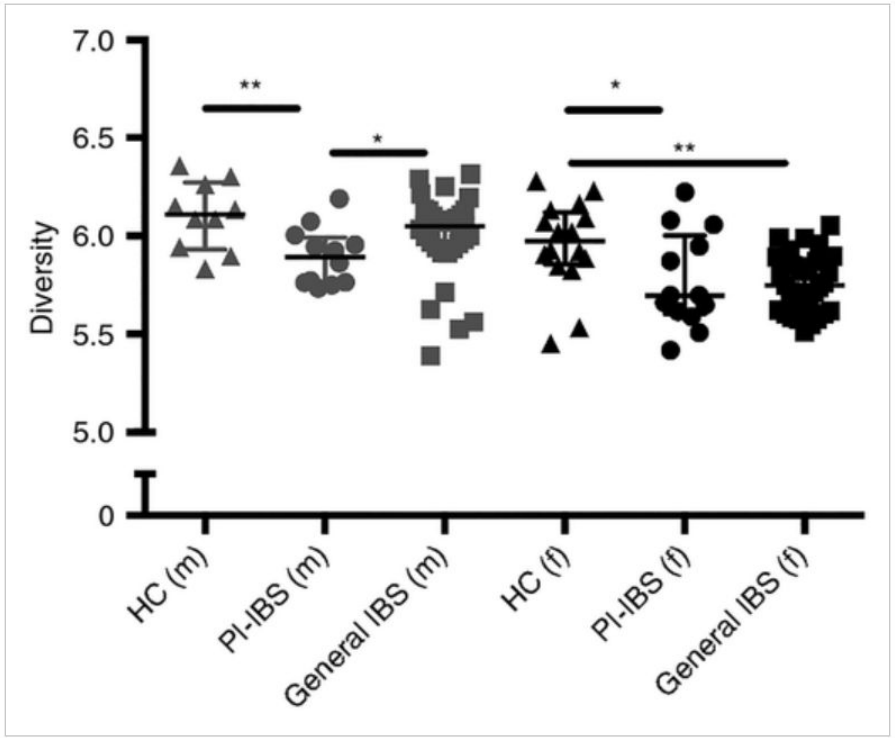
Aliment Pharmacol Ther. 2015 Feb;41(4):342-51. doi: 10.1111/apt.13055. Epub 2014 Dec 18.

Altered faecal and mucosal microbial composition in post-infectious irritable bowel syndrome patients correlates with mucosal lymphocyte phenotypes and psychological distress

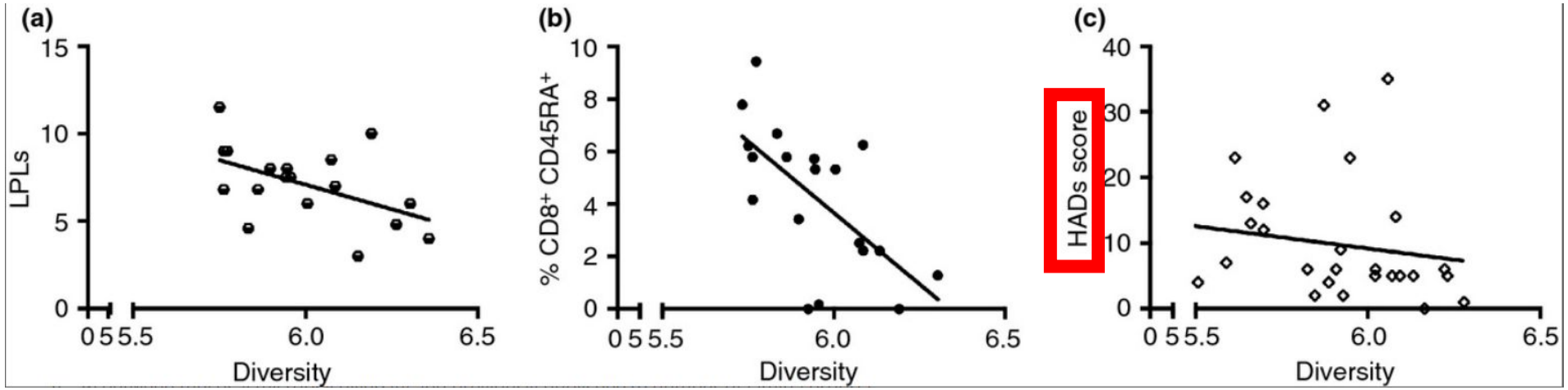
J Sundin [1], I Rangel, S Fuentes, I Heikamp-de Jong, E Hultgren-Hörnquist, W M de Vos, R J Brummer

Affiliations + expand

PMID: 25521822 DOI: 10.1111/apt.13055



lamina propria / intraepithelial lymphocytes



Sundin J, et al. Aliment Pharmacol Ther 2015;41:342–51.

Potential treatment of choice…

- Altered Intestinal Permeability
- Abnormal Intestinal Microbiota

Microbiome-based therapeutics

Fermentable Oligo-, Di-, Mono-saccharides And Polyols (FODMAP) Foods

› Lancet. 1994 Jul 2;344(8914):39-40. doi: 10.1016/s0140-6736(94)91055-3.

Bran and irritable bowel syndrome: time for reappraisal

C Y Francis [1], P J Whorwell

Affiliations + expand

PMID: 7912305 DOI: 10.1016/s0140-6736(94)91055-3

Fibre source	Better	Worse	Unchanged
Bran	10 (10%)	55 (55%)	35 (33%)
Cornflakes	0	0	88 (100%)
Rice Crispies	0	0	81 (100%)
Porridge	0	9 (12%)	66 (88%)
Muesli	0	21 (27%)	58 (73%)
Vegetables	3 (3%)	24 (25%)	71 (72%)
Fruit	5 (5%)	42 (45%)	47 (50%)
Pulses	0	22 (25%)	65 (75%)
Nuts	0	23 (27%)	61 (73%)
Proprietary fibre	27 (39%)	15 (22%)	27 (39%)

Table: **Symptomatic response to fibre**

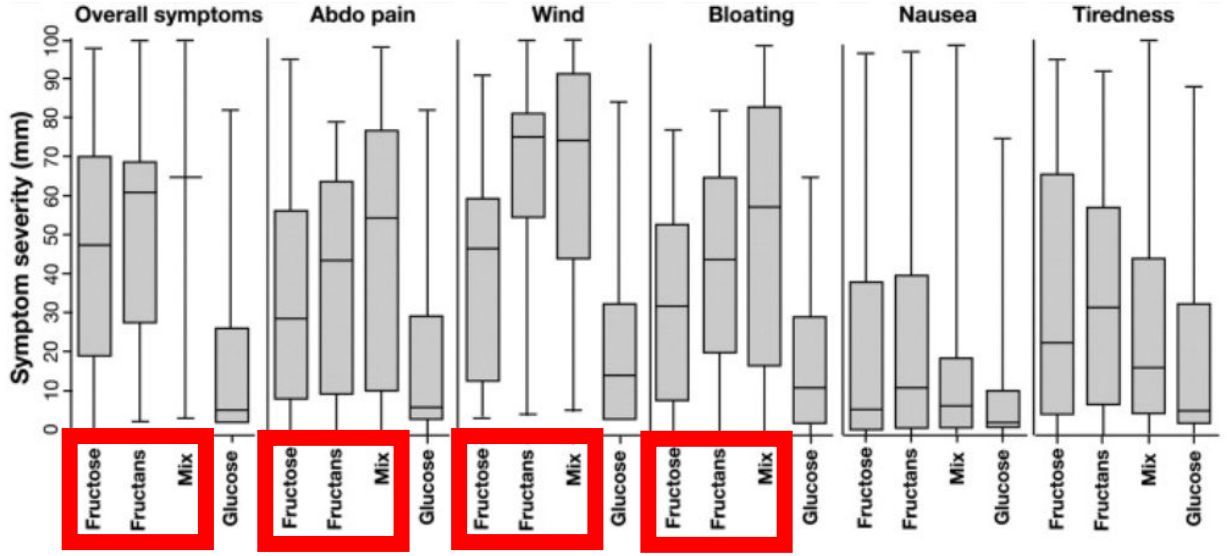
Randomized Controlled Trial › Clin Gastroenterol Hepatol. 2008 Jul;6(7):765-71.
doi: 10.1016/j.cgh.2008.02.058. Epub 2008 May 5.

Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence

Susan J Shepherd [1], Francis C Parker, Jane G Muir, Peter R Gibson

Affiliations + expand

PMID: 18456565 DOI: 10.1016/j.cgh.2008.02.058



Francis CY, et al. Lancet 1994;344:39–40.
Shepherd SJ, et al. Clin Gastroenterol Hepatol 2008;6:765–71.

CATILON® OTILONIUM BROMIDE

More RCTs for diet intervention...

Randomized Controlled Trial > Lancet Gastroenterol Hepatol. 2024 Jun;9(6):507-520.
doi: 10.1016/S2468-1253(24)00045-1. Epub 2024 Apr 18.

A low FODMAP diet plus traditional dietary advice versus a low-carbohydrate diet versus pharmacological treatment in irritable bowel syndrome (CARIBS): a single-centre, single-blind, randomised controlled trial

Sanna Nybacka [1], Hans Törnblom [2], Axel Josefsson [2], Johann P Hreinsson [2], Lena Böhn [2], Åsa Frändemark [2], Cecilia Weznaver [2], Stine Störsrud [2], Magnus Simrén [3]

Affiliations + expand

PMID: 38643782 DOI: 10.1016/S2468-1253(24)00045-1

Diet intervention:
it is possible & effective

Randomized Controlled Trial > Aliment Pharmacol Ther. 2024 Feb;59(4):492-503.
doi: 10.1111/apt.17791. Epub 2023 Nov 15.

Clinical trial: A Mediterranean diet is feasible and improves gastrointestinal and psychological symptoms in irritable bowel syndrome

Heidi M Staudacher [1], Sophie Mahoney [1], Kim Canale [1], Rachelle S Opie [1], Amy Loughman [1], Daniel So [1 2], Lauren Beswick [3 4], Chris Hair [3 4], Felice N Jacka [1 5]

Affiliations + expand

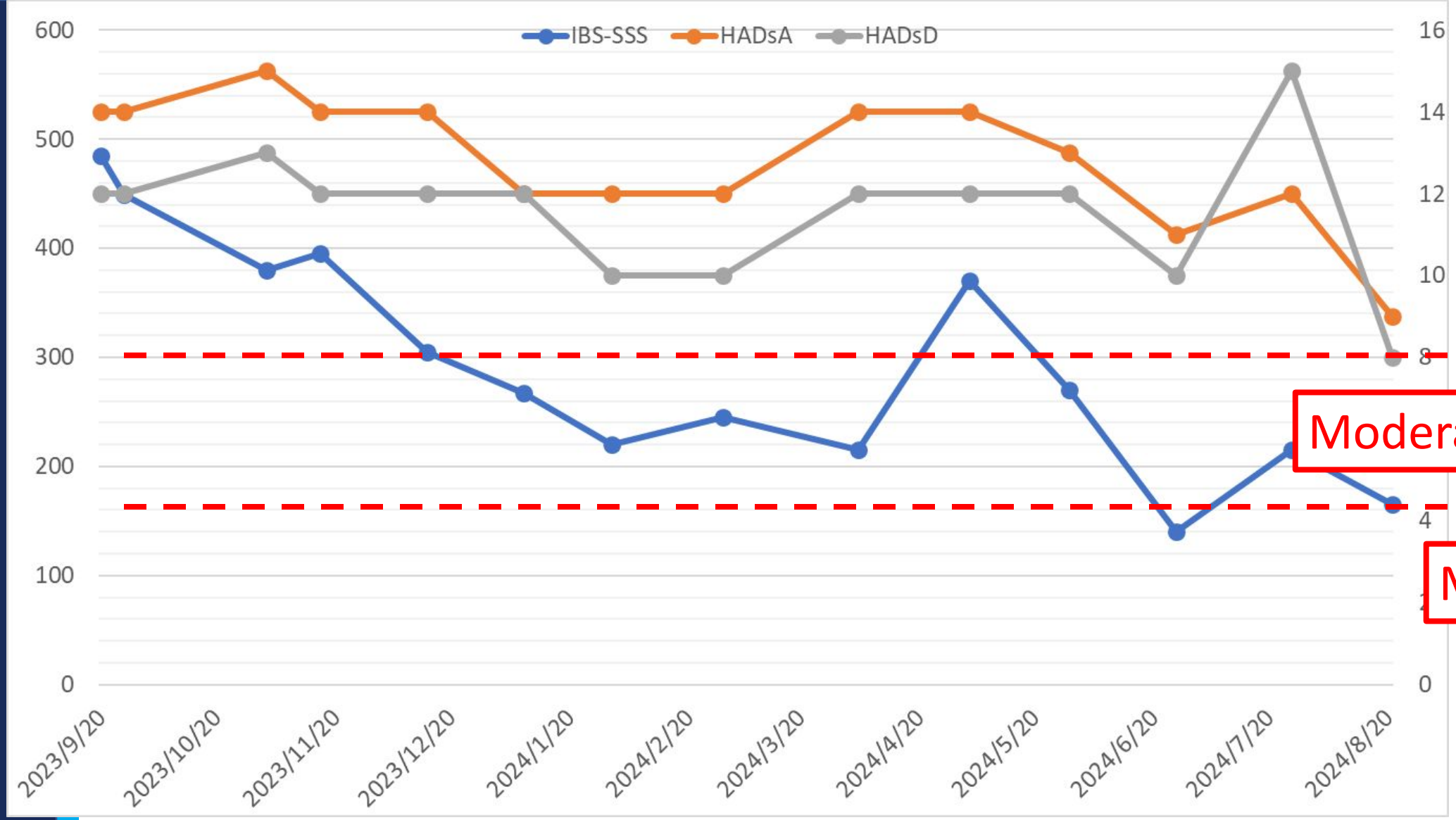
PMID: 37969059 DOI: 10.1111/apt.17791

Outline

- IBS: Pathophysiology & Management
- **Case sharing**
- CATILON®
  - ✔ Drug mechanism
  - ✔ Evidence
  - ✔ Safety

鍾○琴 58 year-old female

- Chief complaint:
  - lower abdominal pain (10/10 VAS) for decades, severe cramping off and on
  - loose stool, bowel movement 4-5 days interval; accompanied with nausea and belching (frequent ER visit)
  - UE/CE negative findings in LMD, no BWL
- Past history:
  - insomnia (regular hypnotics & anxiolytics); s/p appendectomy; no family history
  - Initial survey: sonography(-), lab(-); **IBS-SSS** / **HADs** / **T-MEDAS**

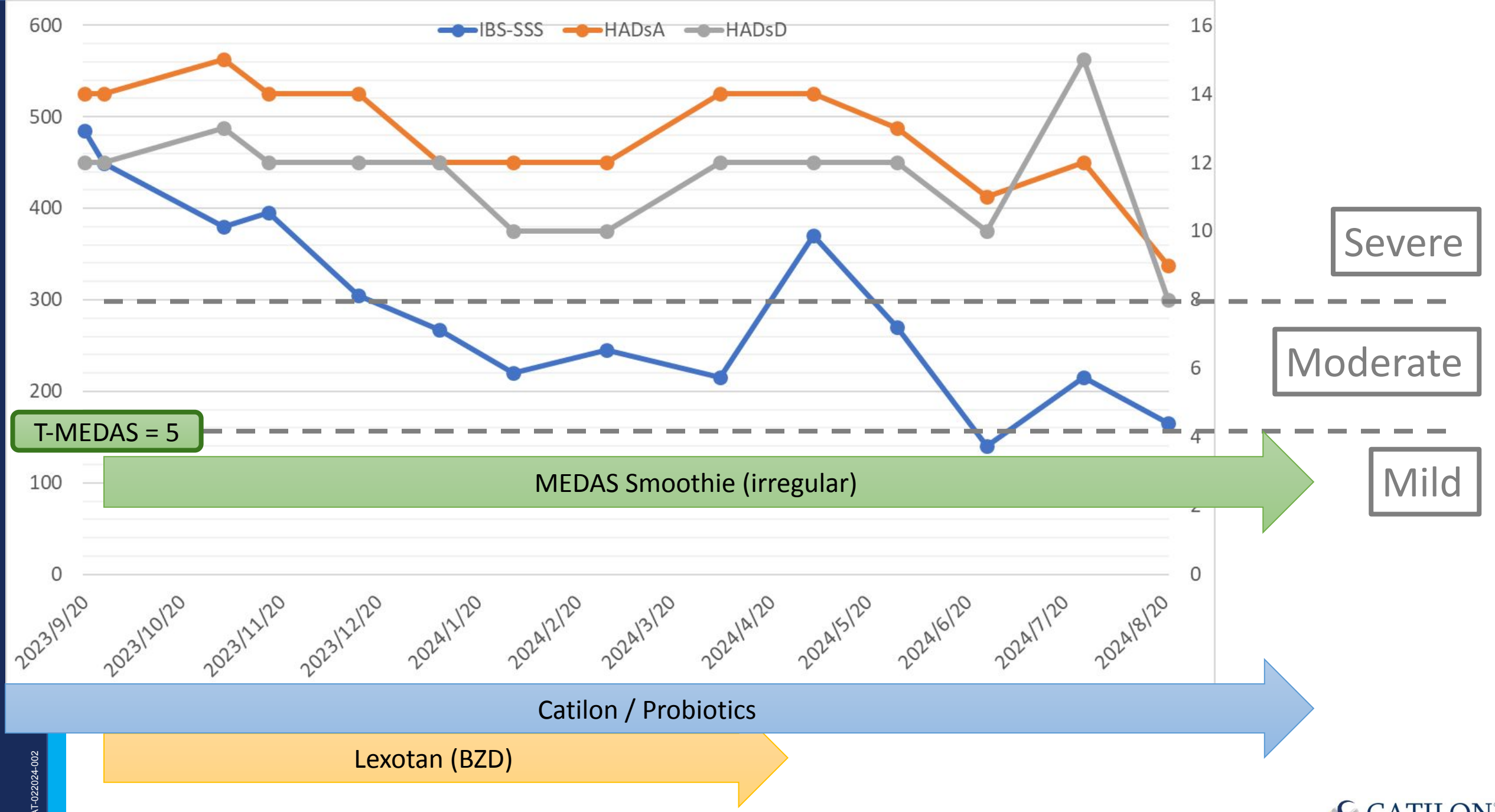


Severe > 300

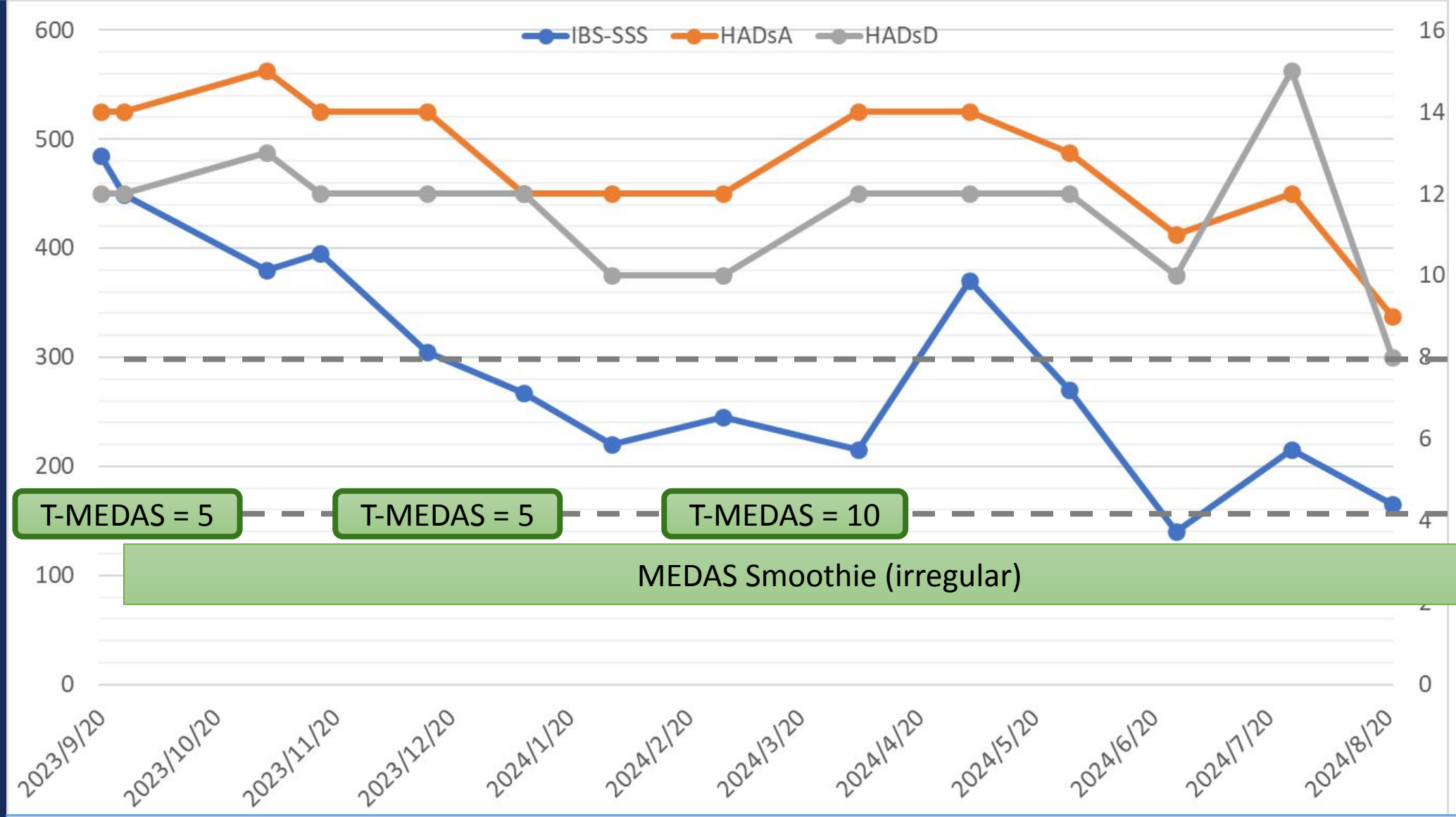
Moderate = 175-300

Mild = 75-175

CATILON®
OTILONIUM BROMIDE



CATILON® OTILONIUM BROMIDE



Severe

Moderate

Mild

T-MEDAS = 5

T-MEDAS = 5

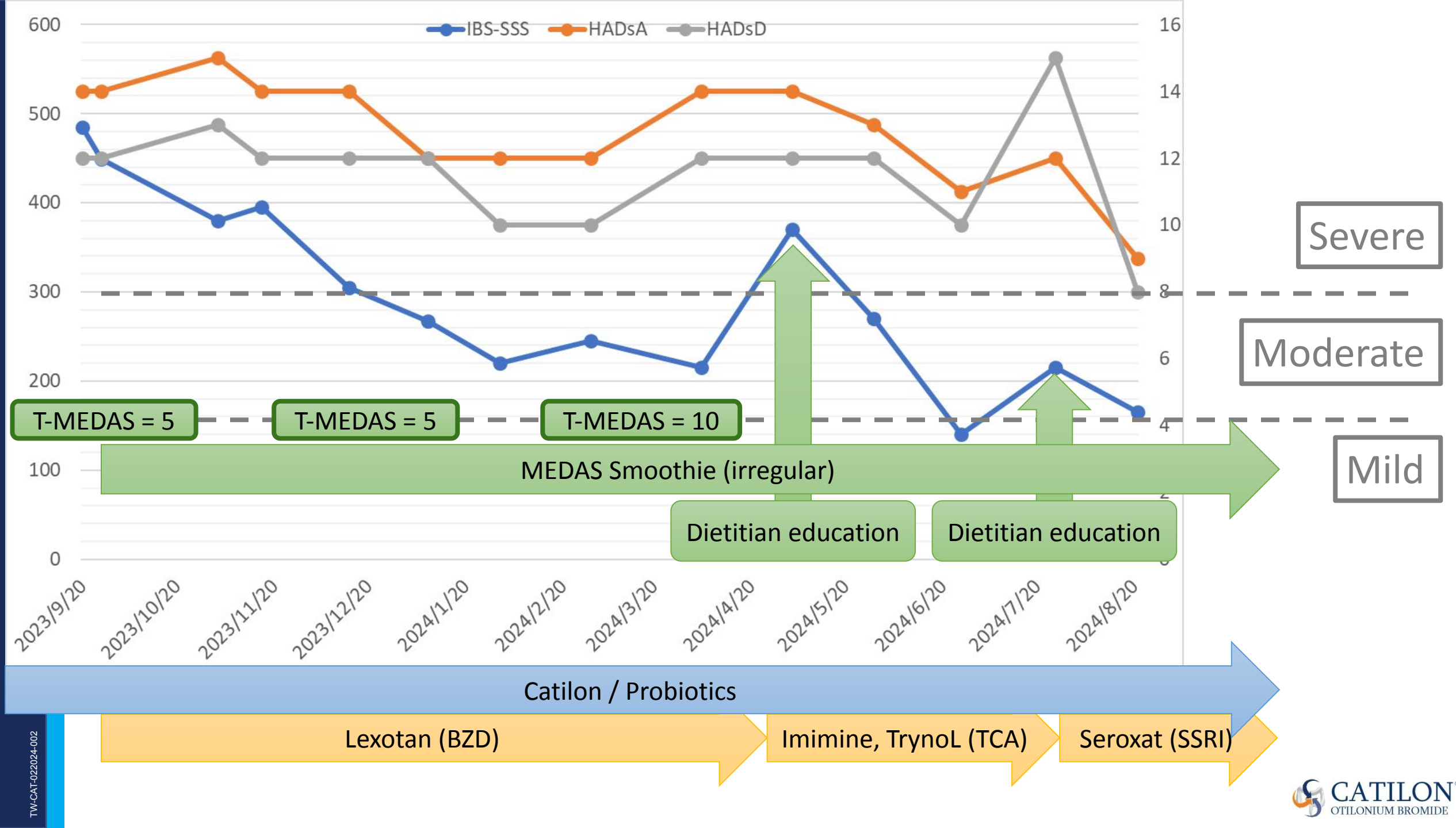
T-MEDAS = 10

MEDAS Smoothie (irregular)

Catilon / Probiotics

Lexotan (BZD)

CATILON® OTILONIUM BROMIDE



CATILON® OTILONIUM BROMIDE

2023/09/20

T0	紅肉
T1	紅肉
T3	白肉
T4	加工澱粉
T5	精緻澱粉
T6	水果
T7	蔬菜
T8	全穀類
T9	種子油
T10	豆類
T11	堅果
T12	種子油
T13	含糖飲料
T14	奶油

2023/12/19

T0	紅肉
T1	紅肉
T3	白肉
T4	加工澱粉
T5	精緻澱粉
T6	水果
T7	蔬菜
T8	全穀類
T9	種子油
T10	豆類
T11	堅果
T12	種子油
T13	含糖飲料
T14	奶油

2024/03/05

T0	紅肉
T1	紅肉
T3	白肉
T4	加工澱粉
T5	精緻澱粉
T6	水果
T7	蔬菜
T8	全穀類
T9	種子油
T10	豆類
T11	堅果
T12	種子油
T13	含糖飲料
T14	奶油

2023/09/20

- 豆漿
- 甘蔗汁
- 水梨
- 麵

CATILON® OTILONIUM BROMIDE

2023/12/19

- 花椰菜
- 麵
- 柳丁
- 芹菜
- 豆漿

CATILON® OTILONIUM BROMIDE

2024/03/05

- 豆漿
- 豆腐

CATILON®
OTILONIUM BROMIDE

Bottom line: Personalized approach is crucial

- **Good communication**
- **Spasmolytics**
- **Neuromodulators**
  - Anxiolytics, TCAs, SSRIs
- **Microbiome**-based therapeutics
  - Probiotics, Mediterranean diet
- **Diet** intervention
  - Mediterranean diet, FODMAP-simple restriction diet

› Clin Gastroenterol Hepatol. 2024 May 9:S1542-3565(24)00428-2. doi: 10.1016/j.cgh.2024.04.021. Online ahead of print.

Is a Simplified, Less Restrictive Low FODMAP Diet Possible? Results from a Double-Blind, Pilot Randomized Controlled Trial

Prashant Singh [1], Samuel W Chey [1], Judy Nee [2], Shanti Eswaran [1]; Dietary Therapy in IBS Working Group; Anthony Lembo [3], William D Chey [4]

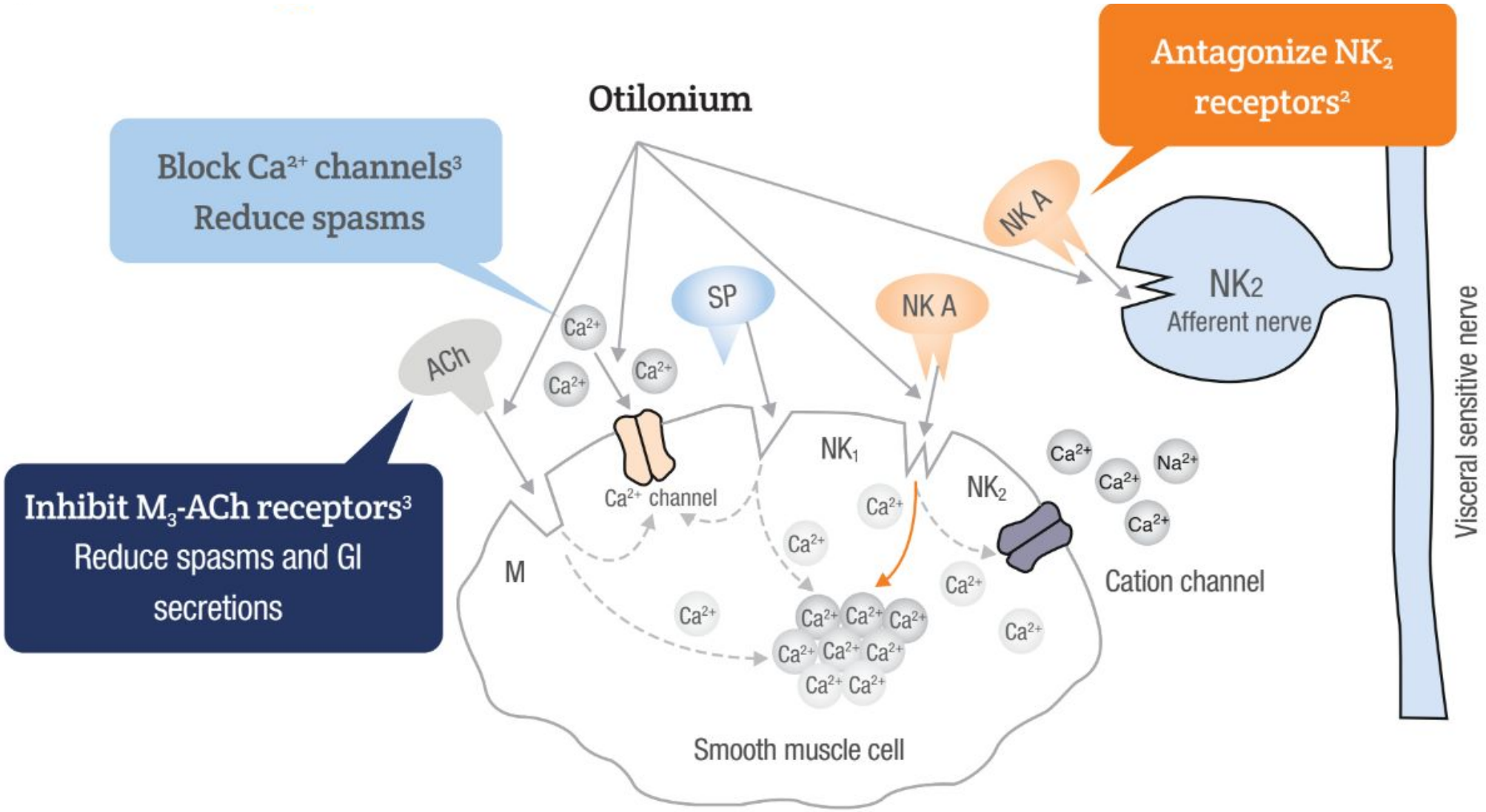
Collaborators, Affiliations + expand

PMID: 38729393 DOI: 10.1016/j.cgh.2024.04.021

Outline

- IBS: Pathophysiology & Management
- Case sharing
- **CATILON®**
  - ✔ Drug mechanism
  - ✔ Evidence
  - ✔ Safety

Drug mechanism: reduce spasm & visceral pain



Evangelista S. et al. Curr Pharm Des. 2018;24(16):1772-1779.

CATILON® OTILONIUM BROMIDE

Evidence during ROME I (1994): provide fewer pain

Clinical Trial > Aliment Pharmacol Ther. 1998 Oct;12(10):1003-10.
doi: 10.1046/j.1365-2036.1998.00397.x.

Otilonium bromide in irritable bowel syndrome: a double-blind, placebo-controlled, 15-week study

G Battaglia [1], A M Morselli-Labate, E Camarri, A Francavilla, F De Marco, G Mastropaolo, R Naccarato

Affiliations + expand

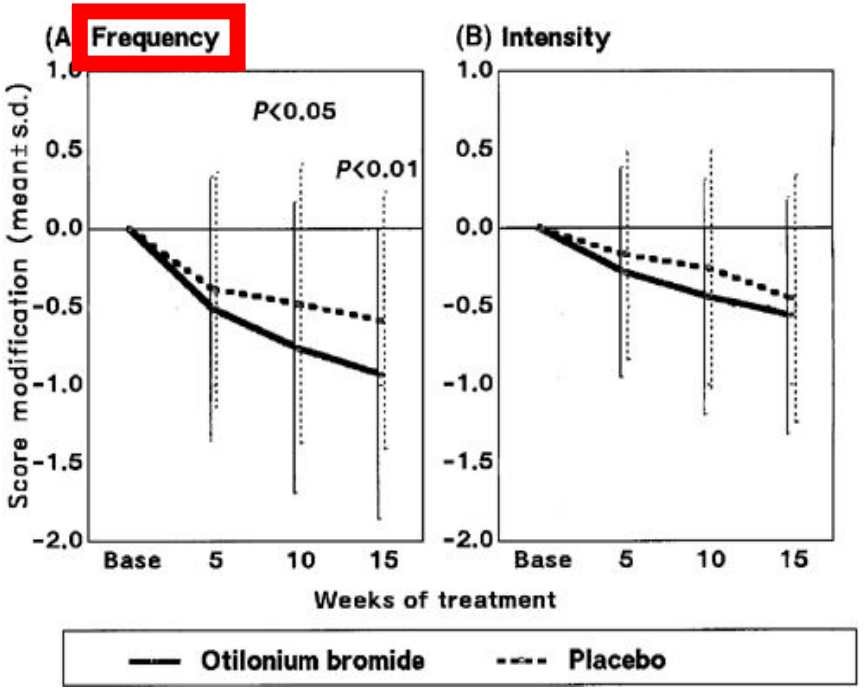
PMID: 9798806 DOI: 10.1046/j.1365-2036.1998.00397.x

Free article

Abstract

Aim: To evaluate the efficacy of otilonium bromide, a spasmolytic agent, in the treatment of irritable bowel syndrome using modern and validated diagnostic criteria.

Methods: Three hundred and seventy-eight patients with irritable bowel syndrome were enrolled in the study. At entry, endoscopy/barium enema, clinical examination and laboratory tests were used to rule out organic diseases. After a 2-week placebo run-in, 325 patients were randomly assigned to receive either otilonium bromide 40 mg t.d.s. or placebo for 15 weeks. Abdominal pain, abdominal distension and disturbed defecation were scored at the beginning of the study and every 5 weeks. A global determination of well-being by visual analogue scale and the tenderness of the sigmoid colon were also scored.



Battaglia G, et al. Aliment Pharmacol Ther. 1998 Oct;12(10):1003-10.

Evidence during ROME II (2002): relieve not just pain

Clinical Trial > Eur J Gastroenterol Hepatol. 2002 Dec;14(12):1331-8.
doi: 10.1097/00042737-200212000-00008.

Extended analysis of a double-blind, placebo-controlled, 15-week study with otilonium bromide in irritable bowel syndrome

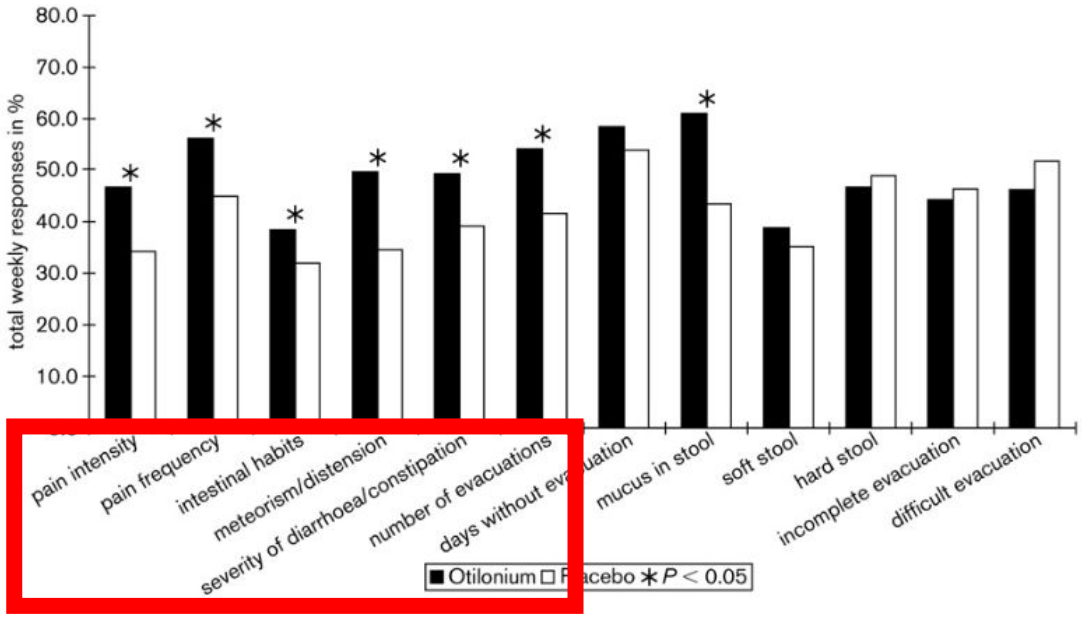
Manfred Glende, Antonio M Morselli-Labate, Giuseppe Battaglia, Stefano Evangelista

PMID: 12468954 DOI: 10.1097/00042737-200212000-00008

Abstract

Background/objective: In order to follow the most recent developments and recommendations in trial methodology for drug evaluation in patients with irritable bowel syndrome, we performed an extended analysis of a large clinical trial from a previously published study of otilonium bromide, using an assessment that integrates the key symptoms of irritable bowel syndrome.

Materials and methods: A large-scale clinical trial with a double-blind, placebo-controlled, parallel-group study design was conducted in 378 patients, treated for 15 weeks with the recommended standard dose of 40 mg otilonium bromide or placebo three times daily. The study was based on the collection of 12 single efficacy endpoints. The new efficacy assessment was based on the data reported by the patients. Rather than demonstrating score differences between the treatment groups of the study, we carried out an assessment that integrates the most frequent symptoms reported (pain frequency and intensity, presence of meteorism and distension) by the patient.



Rates of total weekly responses in the single endpoints of IBS in months 2–4 of treatment in the ITT patients with respective baseline scores > 0. *$P < 0.05$ otilonium bromide *vs* placebo group.

Glende M, Evangelista S, et al. Eur J Gastroenterol Hepatol. 2002;14(12):1331-1338.

Evidence during ROME III (2006): provide some durability?

Randomized Controlled Trial > Aliment Pharmacol Ther. 2011 Aug;34(4):432-42.
doi: 10.1111/j.1365-2036.2011.04730.x. Epub 2011 Jun 16.

Randomised clinical trial: otilonium bromide improves frequency of abdominal pain, severity of distention and time to relapse in patients with irritable bowel syndrome

P Clavé [1], M Acalovschi, J K Triantafillidis, Y P Uspensky, C Kalayci, V Shee, J Tack; OBIS Study Investigators

Collaborators, Affiliations + expand

PMID: 21679214 DOI: 10.1111/j.1365-2036.2011.04730.x

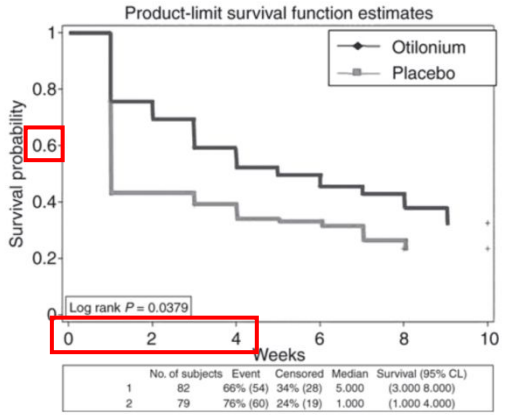
Free article

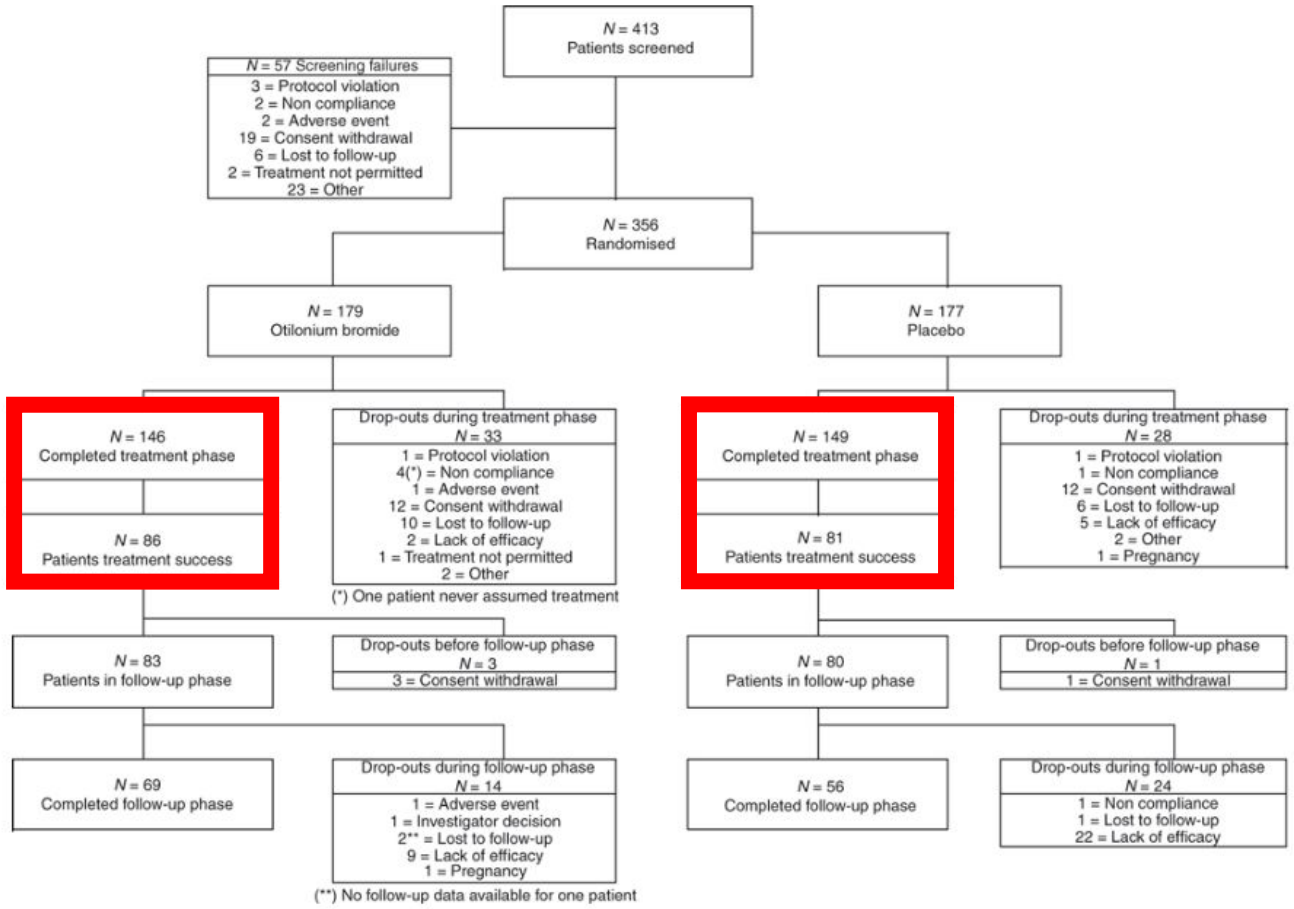
Abstract

Background: Otilonium bromide (OB) is a spasmolytic agent that blocks L-Type Calcium channels in human colonic smooth muscle.

Aim: To study the efficacy of OB in symptom control in irritable bowel syndrome (IBS).

Methods: A total of 356 patients (46.16±19years, 71% female) with IBS participated in a double-blind, randomised, parallel placebo-controlled phase IV study. OB (40mg t.d.s.) or placebo was administered for 15weeks, and follow-up was extended 10 additional weeks.





Clavé P et al. Aliment Pharmacol Ther. 2011;34(4):432-442

Evidence during ROME IV (2016): globally effective

Therap Adv Gastroenterol. 2017 Mar;10(3):311-322. doi: 10.1177/1756283X16681708.
Epub 2017 Jan 16.

Efficacy of otilonium bromide in irritable bowel syndrome: a pooled analysis

Pere Clavé [1], Jan Tack [2]

Affiliations + expand

PMID: 28246548 PMCID: PMC5305018 DOI: 10.1177/1756283X16681708

Abstract

Background: Otilonium bromide (OB) is a spasmolytic agent acting as an L-type calcium channel antagonist in intestinal and colonic smooth muscle cells (SMCs). We analyzed three independent clinical trials with homogeneous design on patients with irritable bowel syndrome (IBS). After 2 weeks receiving placebo, patients were randomized to receive OB (3 × 40 mg daily) or placebo for 15 weeks. We aimed to perform a pooled analysis of the data from these homogeneous clinical trials to evaluate the efficacy of OB treatment on symptoms and global response of patients.

Methods: A total of 883 patients with IBS (69.8% women, mean age 46.2 years, 43.8% mixed type) were included, 442 treated with OB and 441 with placebo. The efficacy results from the three studies at weeks 5, 10 and 15 were pooled in an intention-to-treat (ITT) strategy, analyzed with a logistic regression model and described by forest plots.

Jan Tack, MD, PhD, RFF | President

Professor of Medicine
Head, Department of Clinical and Experimental Medicine
Head of Clinic, Department of Gastroenterology
University Hospital KU Leuven
Translational Research Center for Gastrointestinal Disorders (TARGID)
Leuven, Belgium

Reduction in pain intensity / episodes global symptoms/ bloating at **Week 10/15**

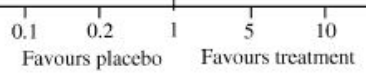
Clavé P & Tack J. Therap Adv Gastroenterol, 2017 10(3), 311-322.

Meta-analysis (2001)

Poynard T et al. Aliment Pharmacol Ther. 2001

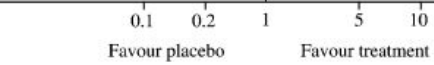
Efficacy on pain

Study	Treatment n/N	Control n/N	Peto OR (95% CI Fixed)	Weight %	Peto OR (95% CI Fixed)
01 Mebeverine					
Kruis	9/40	11/40		5.7	0.77[0.28, 2.10]
Secco	12/15	9/15		2.5	2.51[0.54, 11.66]
Tasman-Jones	15/24	7/24		4.6	3.72[1.21, 11.45]
Subtotal (95% CI)	36/79	27/79		12.8	1.70[0.87, 3.34]
Chi-squared 4.51 (d.f. = 2) P = 0.21 Z = 1.55 P = 0.12					
02 Cimetropium					
Piai	13/15	4/15		2.9	10.61[2.57, 43.90]
Subtotal (95% CI)	13/15	4/15		2.9	10.61[2.57, 43.90]
Chi-squared 0.00 (d.f. = 0) P = 1.00 Z = 3.26 P = 0.001					
03 Trimebutine					
Fielding	18/30	19/30		5.4	0.87[0.31, 2.44]
Moshal	6/20	2/20		2.5	3.38[0.73, 15.62]
Subtotal (95% CI)	24/50	21/50		7.9	1.33[0.57, 3.13]
Chi-squared 2.08 (d.f. = 1) P = 0.35 Z = 0.65 P = 0.5					
04 Otilium					
Baldi	7/15	2/15		2.5	4.64[1.00, 21.54]
Barbier	16/36	7/36		6.0	3.11[1.16, 8.31
Battaglia	76/160	53/165		29.4	1.90[1.22, 2.96]
Subtotal (95% CI)	99/211	62/216		37.9	2.17[1.47, 3.21]
Chi-squared 1.80 (d.f. = 2) P = 0.61 Z = 3.89 P = 0.00010					
05 Hyoscine					
Schafer	106/182	104/178		33.1	0.99[0.65, 1.51]
Subtotal (95% CI)	106/182	104/178		33.1	0.99[0.65, 1.51]
Chi-squared 0.00 (d.f. = 0) P = 1.00 Z = −0.04 P = 1					
06 Pinaverium					
Delmont	22/30	15/30		5.4	2.64[0.94, 7.41]
Subtotal (95% CI)	22/30	15/30		5.4	2.64[0.94, 7.41]
Chi-squared 0.00 (d.f. = 0) P = 1.00 Z = 1.84 P = 0.07					
Total (95% CI)	300/567	233/568		100.0	1.65[1.30, 2.10]
Chi-squared 23.62 (d.f. = 10) P = 0.01 Z = 4.09 P = 0.00004					



Global assessment

Study	Treatment n/N	Control n/N	Peto OR (95% CI Fixed)	Weight %	Peto OR (95% CI Fixed)
01 Mebeverine					
Connel	11/22	1/22		2.1	9.39[2.53, 34.86]
Tasman-Jones	15/24	7/24		2.8	3.72[1.21, 11.45]
Berthelot	31/36	24/33		2.6	2.26[0.70, 7.25]
Kruis	6/40	12/40		3.3	0.43[0.15, 1.21]
Subtotal (95% CI)	63/122	44/119		10.8	2.04[1.15, 3.63]
Chi-squared 14.96 (d.f. = 3) P = 0.00 Z = 2.43 P = 0.01					
02 Cimetropium					
Piai	8/15	1/15		1.5	8.57[1.85, 39.79]
Centonze	20/24	5/24		2.8	11.61[3.79, 35.62]
Passaretti_c	9/13	4/12		1.5	3.98[0.85, 18.53]
Passaretti_d	4/7	4/8		0.9	1.31[0.18, 9.32]
Dobrilla	21/35	24/35		3.8	0.69[0.26, 1.83]
Subtotal (95% CI)	62/94	38/94		10.6	2.87[1.61, 5.13]
Chi-squared 16.96 (d.f. = 4) P = 0.00 Z = 3.56 P = 0.0004					
03 Trimebutine					
Luttecke	27/40	2/40		4.4	14.45[5.84, 35.76]
Moshal	11/20	4/20		2.2	4.29[1.21, 15.18]
Luttecke_2	11/26	5/26		2.6	2.89[0.90, 9.29]
Fielding	13/30	17/30		3.6	0.59[0.22, 1.61]
Subtotal (95% CI)	62/116	28/116		12.8	3.45[2.03, 5.86]
Chi-squared 21.65 (d.f. = 3) P = 0.00 Z = 4.59 P < 0.00001					
04 Otilonium					
Barbier	10/36	3/36		2.5	3.65[1.11, 12.04]
Castiglione	22/30	10/30		3.5	4.86[1.78, 13.28]
Battaglia	90/160	66/165		18.9	1.91[1.24, 2.96]
Subtotal (95% CI)	122/226	79/231		25.0	2.33[1.60, 3.40]
Chi-squared 3.38 (d.f. = 2) P = 0.34 Z = 4.38 P = 0.00001					
05 Hyoscine					
Ritchie	22/48	14/48		5.3	2.02[0.89, 4.60]
Nigam	38/84	25/84		9.2	1.93[1.03, 3.59]
Schafer	106/182	91/178		20.8	1.33[0.88, 2.02]
Subtotal (95% CI)	166/314	130/310		35.3	1.56[1.14, 2.15]
Chi-squared 1.38 (d.f. = 2) P = 0.71 Z = 2.74 P = 0.006					
06 Pinaverium					
Levy	19/25	17/25		2.4	1.48[0.43, 5.01]
Delmont	24/30	17/30		3.1	2.89[0.98, 8.49]
Subtotal (95% CI)	43/55	34/55		5.5	2.15[0.96, 4.83]
Chi-squared 0.65 (d.f. = 1) P = 0.72 Z = 1.86 P = 0.06					
Total (95% CI)	518/927	353/925		100.0	2.13[1.77, 2.58]
Chi-squared 67.10 (d.f. = 20) P = 0.00 Z = 7.86 P < 0.00001					



Safety: no much concern by current data

Review > Clin Exp Gastroenterol. 2014 Apr 7:7:75-82. doi: 10.2147/CEG.S46291. eCollection 2014.

Long-term efficacy and safety of otilonium bromide in the management of irritable bowel syndrome: a literature review

John K Triantafillidis [1], George Malgarinos [1]

Affiliations + expand

PMID: 24741324 PMCID: PMC3984067 DOI: 10.2147/CEG.S46291

In Human = placebo-like tolerability without systemic anticholinergic effects

- two trials did not report any adverse effect[1,2]
- mild **nausea** was reported[3]
- low incidence of **weakness** and **dizziness**[4]
- only two adverse reactions (**urticaria**) have been reported so far[5]

1. Villagrasa M, et al. Ital J Gastroenterol. 1991;23(8 Suppl 1):67–70.
2. Heading R, et al. Aliment Pharmacol Ther. 2006;24(2):207–236.
3. Baldi F, et al. Ital J Gastroenterol. 1991;23(8 Suppl 1):60–63.
4. Defrance P, et al. Ital J Gastroenterol. 1991;23(8 Suppl 1):64–66.
5. Spinelli A. Clin Drug Invest. 2007;27(1):15–33.

CATILON® Tablets 40mg 腸必寧錠

- **【適應症】**腸躁症腹痛症狀之緩解。每次1錠，每日2～3次。伴水服用通常成人用於治療腸躁症的腹痛症狀的口服劑量是一次40mg，每日三次。
- **【禁忌症】**已知對本藥之活性成分或賦形劑過敏者禁用。腸阻塞 (intestinal obstruction)。本藥在嬰孩及小於18歲之孩童的安全性和有效性尚未確立。
- **【不良反應與注意事項】**臨床研究於臨床試驗中，與安慰劑/參考藥物組相比較，使用otilonium bromide具有良好之耐受性，發生非常少數不良事件。這些不良反應之發生可能與使用otilonium bromide有關，發生頻率: 不常見: ≥1 / 1000至< 1/100，有輕微的疲倦、噁心、口乾、嘔吐、頭暈、頭痛、上腹痛、瘙癢、紅斑及眩暈。上市後經驗曾有下述其他不良反應報告:蕁麻疹及血管性水腫。但這些反應，無法於現有數據估算其發生頻率。
- Otilonium可能引起anti-cholinergic effect之不良反應，如視力模糊、便秘或尿滯留等。使用otilonium可能引起過敏反應。老年人、服用多種藥物、青光眼、攝護腺肥大或幽門狹窄患者需小心調整使用劑量。
- 孕婦、授乳婦:尚無完整的人體懷孕及授乳婦女研究試驗資料，於此期間不建議使用本藥物。但動物實驗並無致畸胎性報告。

Fin (^A^)y~

CATILON package insert