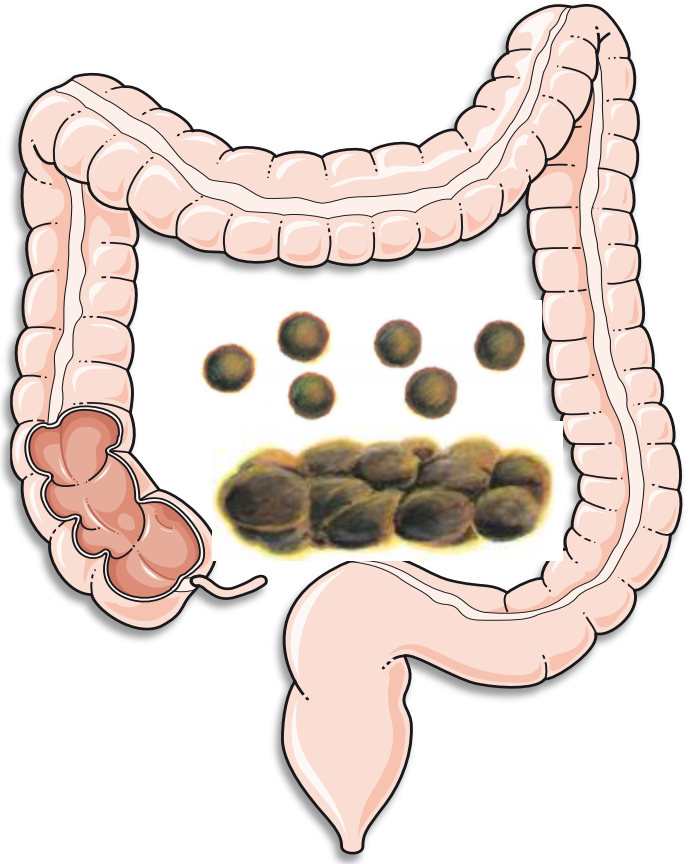
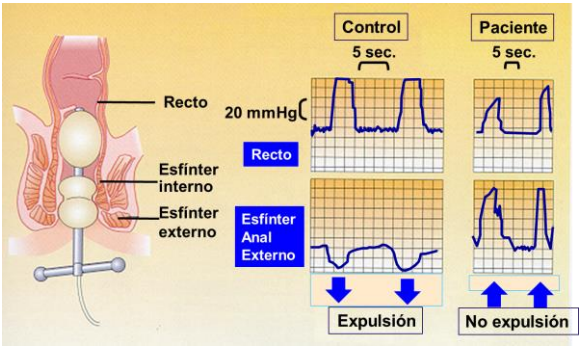
II Tecnofarma Adium Summit Bogotá junio2-3 2023



Estreñimiento Crónico
Manejo actual 2023

William Otero R MD, FAGA FACP, FASGE
Profesor titular de Medicina
Universidad Nacional de Colombia
Hospital Universitario Nacional



Youtoube “William otero gastroenterólogo”

Conflicto de intereses
Conferencista, Bristol
Takeda, Abbott, Tecnoquimica
Tecnofarma, Menarini, Procaps

Esta actividad es asuspiciada por
Tecnofarma sin injerencia en su contenido

Estreñimiento

Mitos y tradiciones

Produce intoxicación
Produce cáncer, igual que laxantes
Se debe al consumo de agua
Se debe a poca fibra en la dieta
La colonoscopia es necesaria
Se alivia cambiando el estilo de vida
La vida sedentaria lo produce
El ejercicio es terapéutico

Muller-Lisner SA, Am J Gastroenterol 2005;100:231-42
Staller K, Am J Gastroenterol 2020;115:1741-5

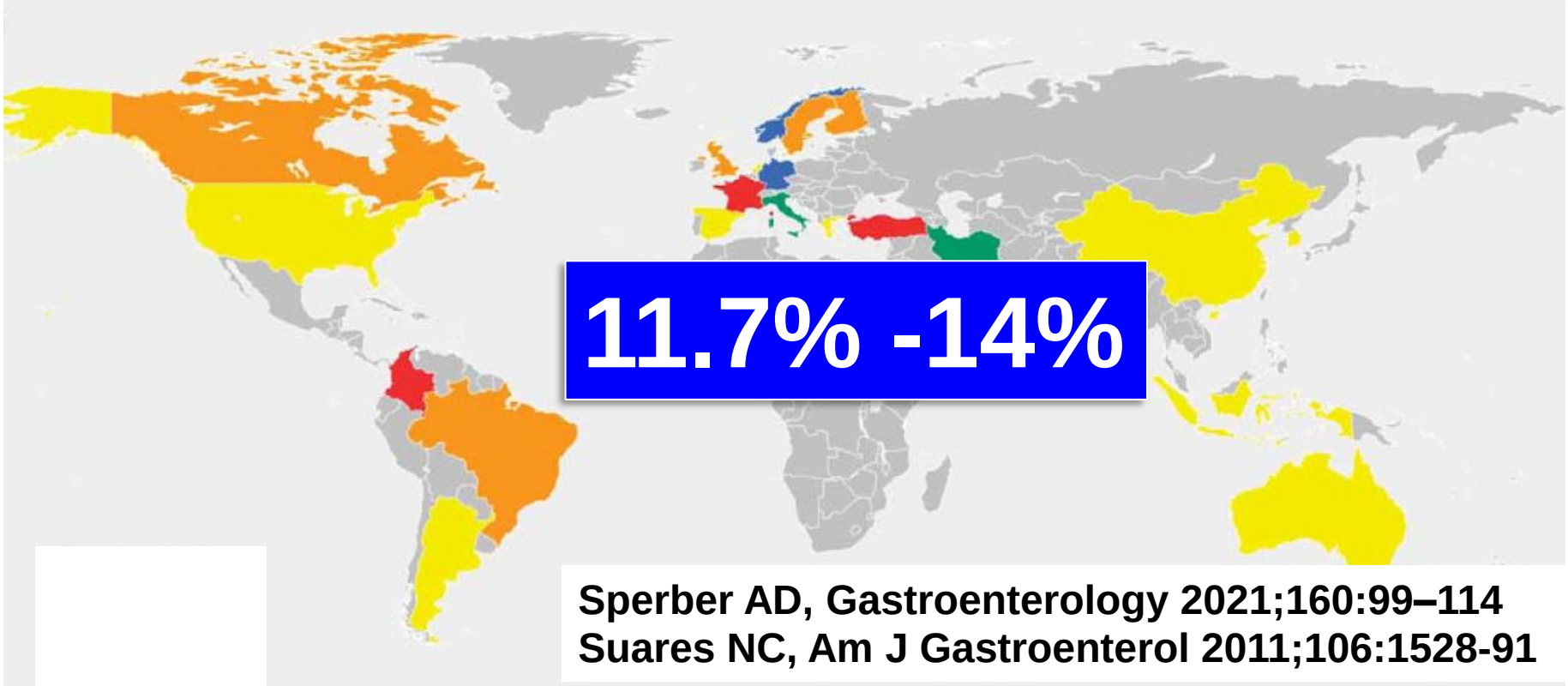
Tendrían diarrea !

Impacto USA

8 millones de consultas
1 millón remisiones gastroenterología
230 millones US$ anuales

Bharucha AE, Gastroenterology 2020;158:1232-49

Estreñimiento a nivel mundial



Sperber AD, Gastroenterology 2021;160:99–114
Suares NC, Am J Gastroenterol 2011;106:1528-91

35%, 60-101 años

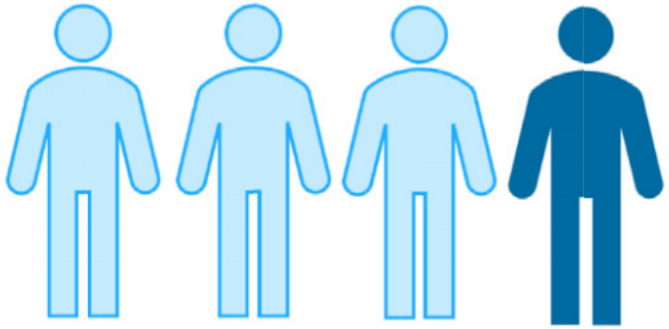
Mugie, S, Best Pract. Res. Clin. Gastroenterol 2011;25:3–18

Prevalence of Rome IV Functional Bowel Disorders Among Adults in the United States, Canada, and the United Kingdom

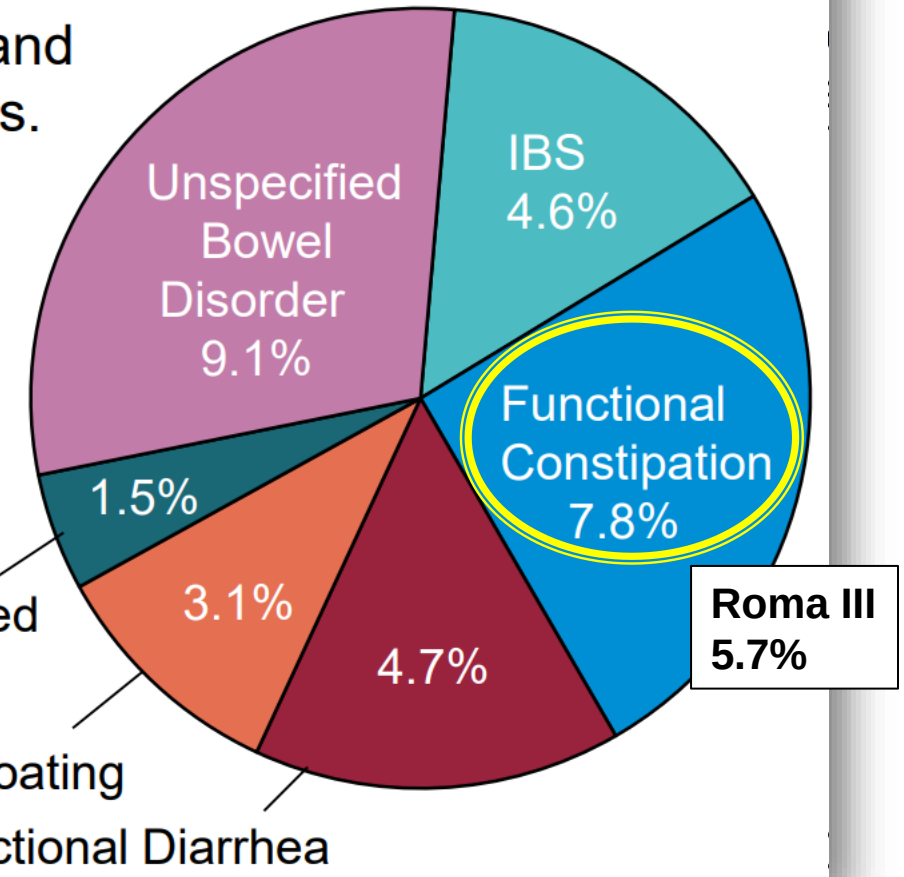
Olafur S. Palsson,[1] William Whitehead,[1] Hans Törnblom,[2] Ami D. Sperber,[3] and Magnus Simren[1,2]

Prevalence of Functional Bowel Disorders

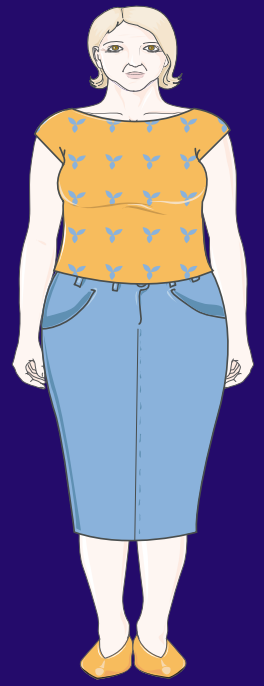
More than **1 in every 4 adults** in the U.S., Canada and the U.K. has one of the six functional bowel disorders.



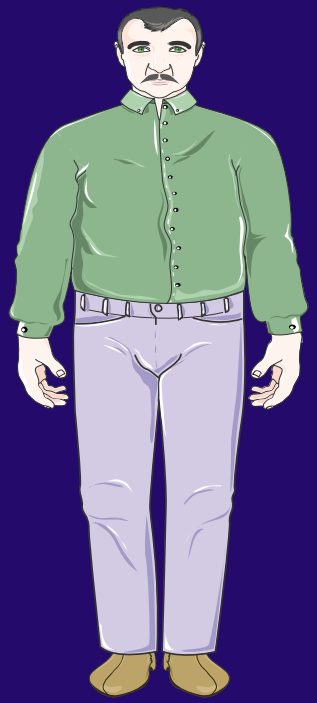
- ✓ Functional bowel disorders are more common in women than men
- ✓ They become less common after mid-life



Palsson OS, Gastroenterology 2020;158:1262–1273



1.5:1



Bharucha AE, Gastroenterology 2020;158:1232-49

Roma IV 2016

Esfuerzo
Heces duras o como “terrones” 25%

Sensación de evacuación incompleta 25%
Sensación obstrucción/ ano-rectal 25%
Maniobras manuales 25%
Menos de 3 deposiciones/semana

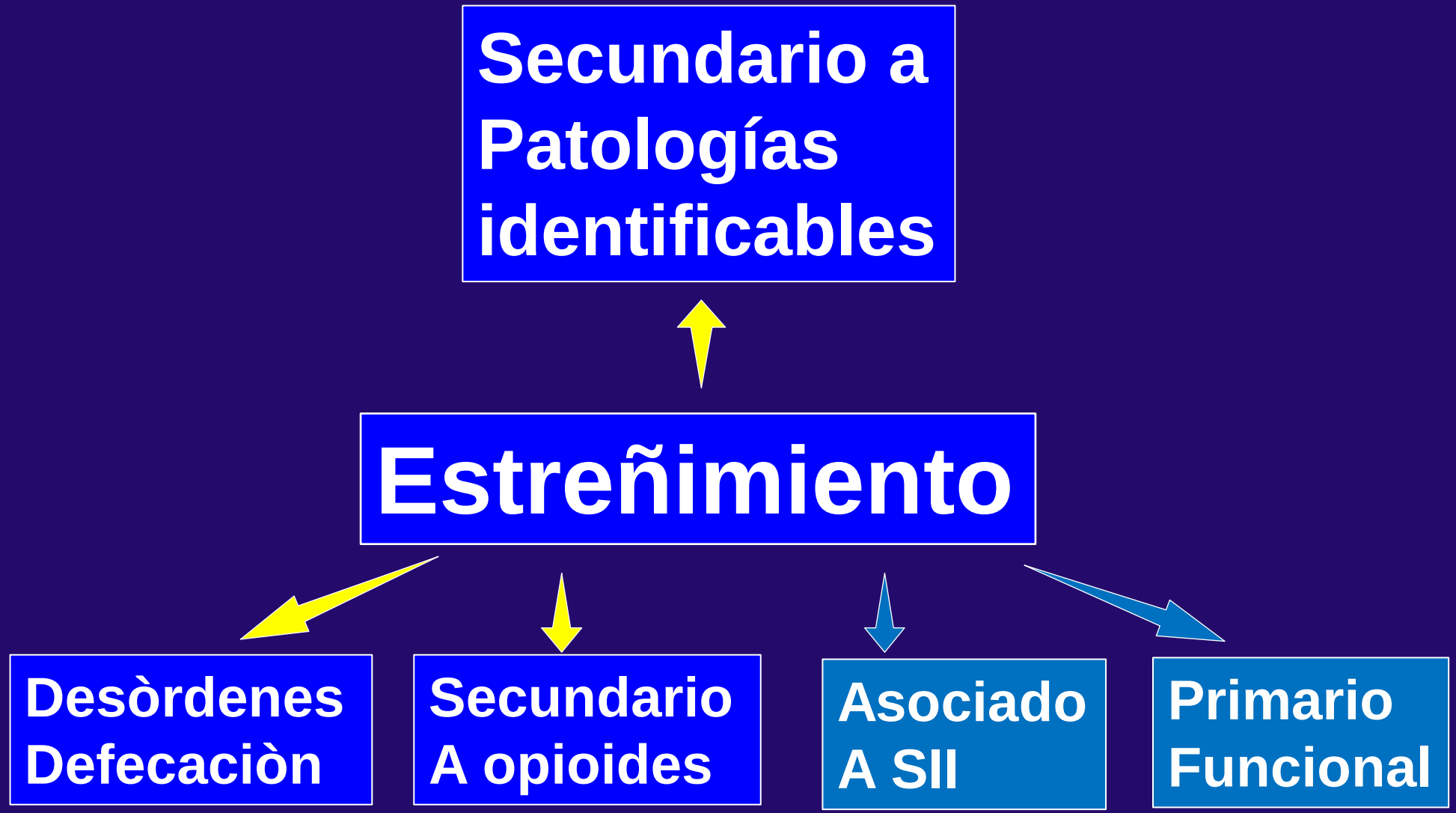
NO heces “sueltas”
Criterios insuficientes para SII

Lacy BE, et al. Gastroenterology 2016;150:1393–1407

Estreñimiento

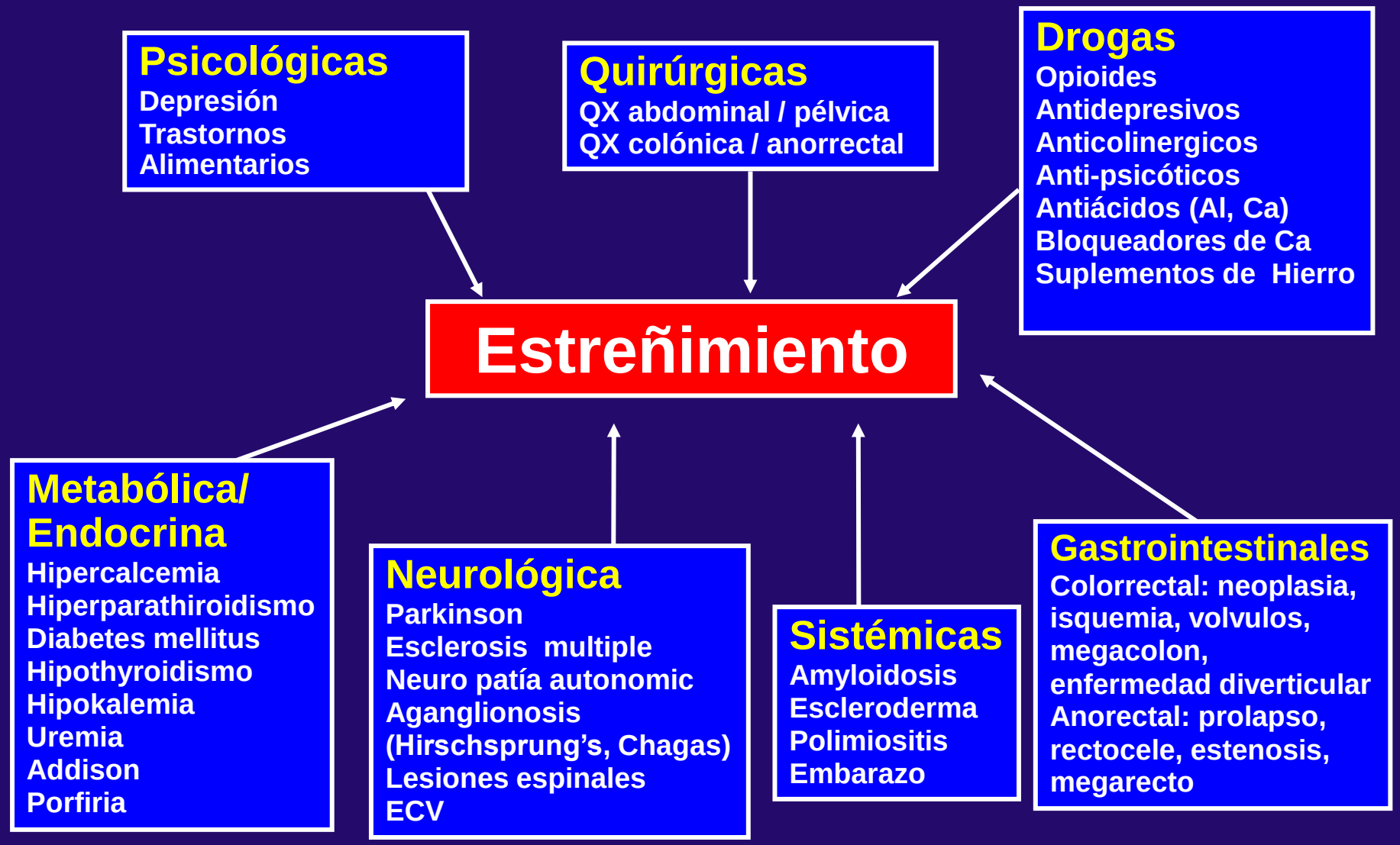
Es un síntoma

No es una enfermedad



Lacy BE, Gastroenterology 2016;150:1393–407 . Roma IV 2016.
Barucha E, Gastroentrrology 2020;158:1232-49. AGA 2020

Estreñimiento Secundario



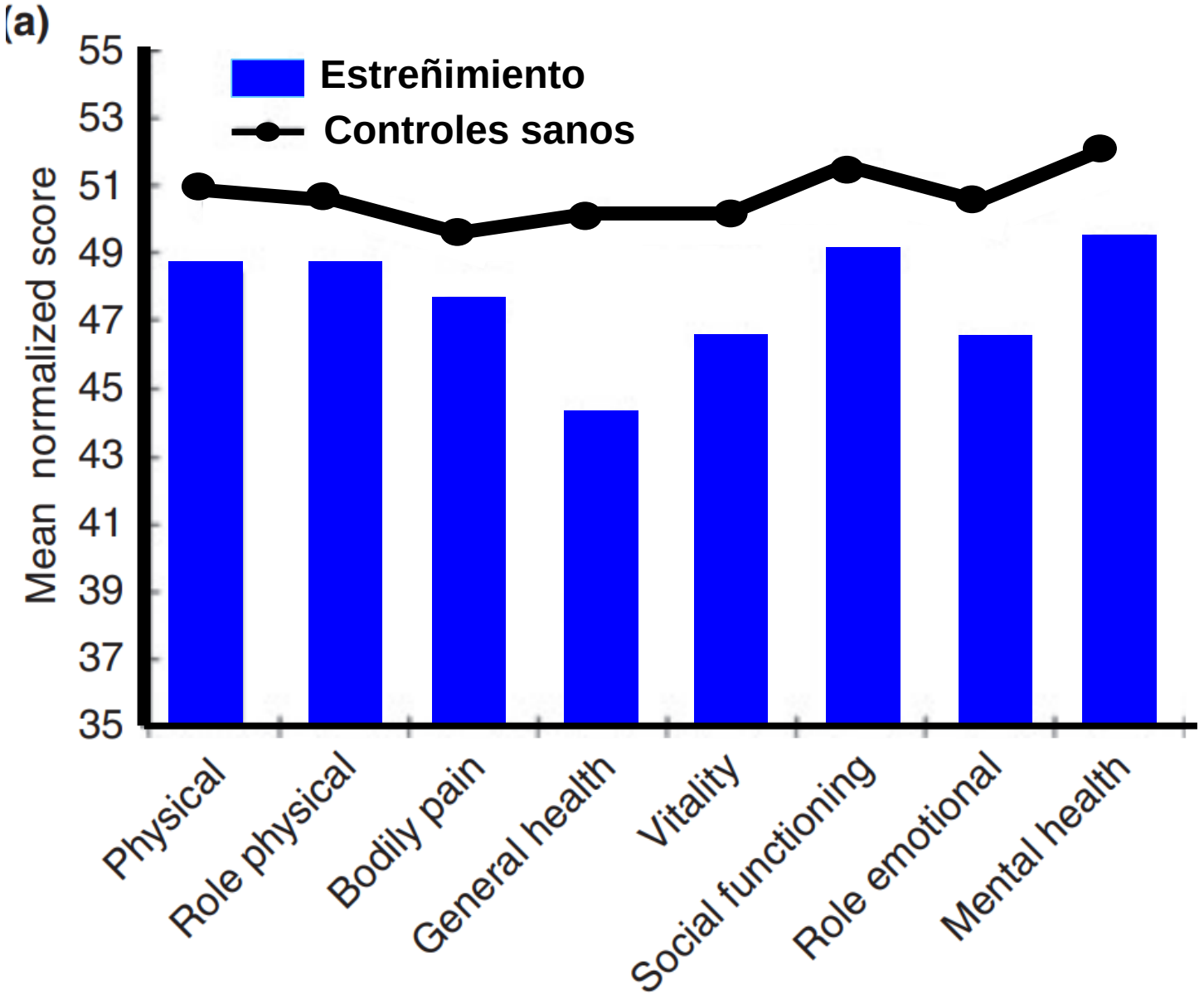
Candelli M, *Hepatogastroenterology*. 2001;48:1050-1057,
Locke GR, *Gastroenterology*. 2000;119:1761-1766.

Medicamentos estreñimiento

5-HT_3-receptor antagonists	Ondansetron
Analgesics	
Opiates[a]	Morphine
Nonsteroidal anti-inflammatory agents[a]	Ibuprofen
Anticholinergic agents	Librax, belladonna
Tricyclic antidepressants[a]	Amitriptyline > nortriptyline
Antiparkinsonian drugs	Benzatropine
Antipsychotics	Chlorpromazine
Antispasmodics[a]	Dicyclomine
Antihistamine[a]	Diphenhydramine
Anticonvulsants[a]	Carbamazepine
Antihypertensives	
Calcium channel blockers	Verapamil, nifedipine
Diuretics[a,b]	Furosemide
Centrally acting	Clonidine
Antiarrhythmics	Amiodarone
β-adrenoceptor antagonist	Atenolol
Bile acid sequestrants	Cholestyramine, colestipol
Cation-containing agents	
Aluminum[a]	Antacids, sucralfate
Calcium	Antacids, supplements
Bismuth	
Iron supplements	Ferrous sulfate
Lithium	
Chemotherapy agents	
Vinca alkaloids	Vincristine
Alkylating agents	Cyclophosphamide
Miscellaneous compounds	Barium sulfate, oral contraceptives, polystyrene resins
Endocrine medications	Pamidronate and alendronic acid
Other antidepressants	Monoamine oxidase inhibitors
Other antipsychotics	Clozapine, haloperidol, risperidone
Other antiparkinsonian drugs	Dopamine agonists
Other antispasmodics	Mebeverine, peppermint oil
Sympathomimetics	Ephedrine, terbutaline

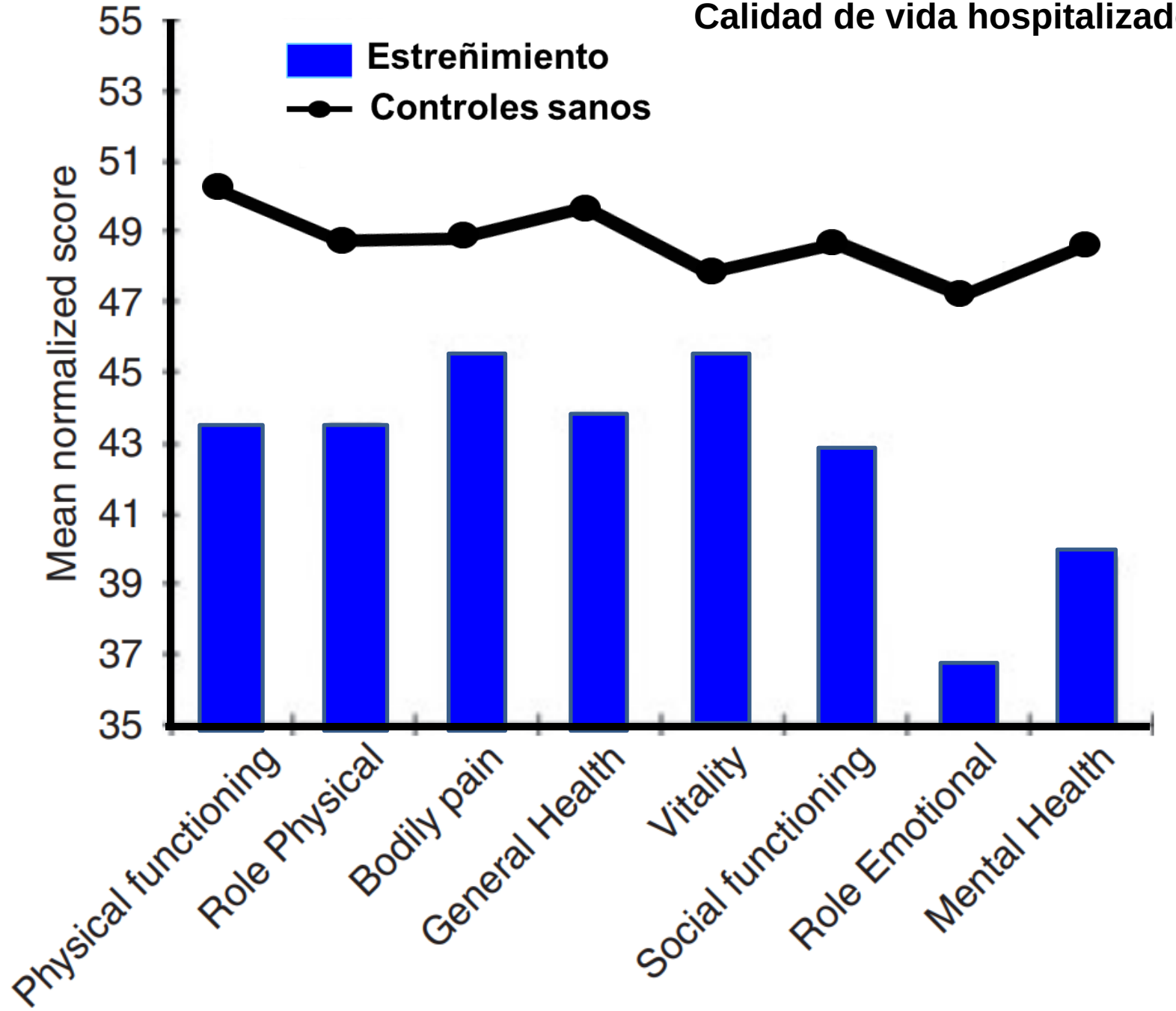
Bharucha AE, Gastroenterology 2013;144:218–238.

Calidad de vida comunidad

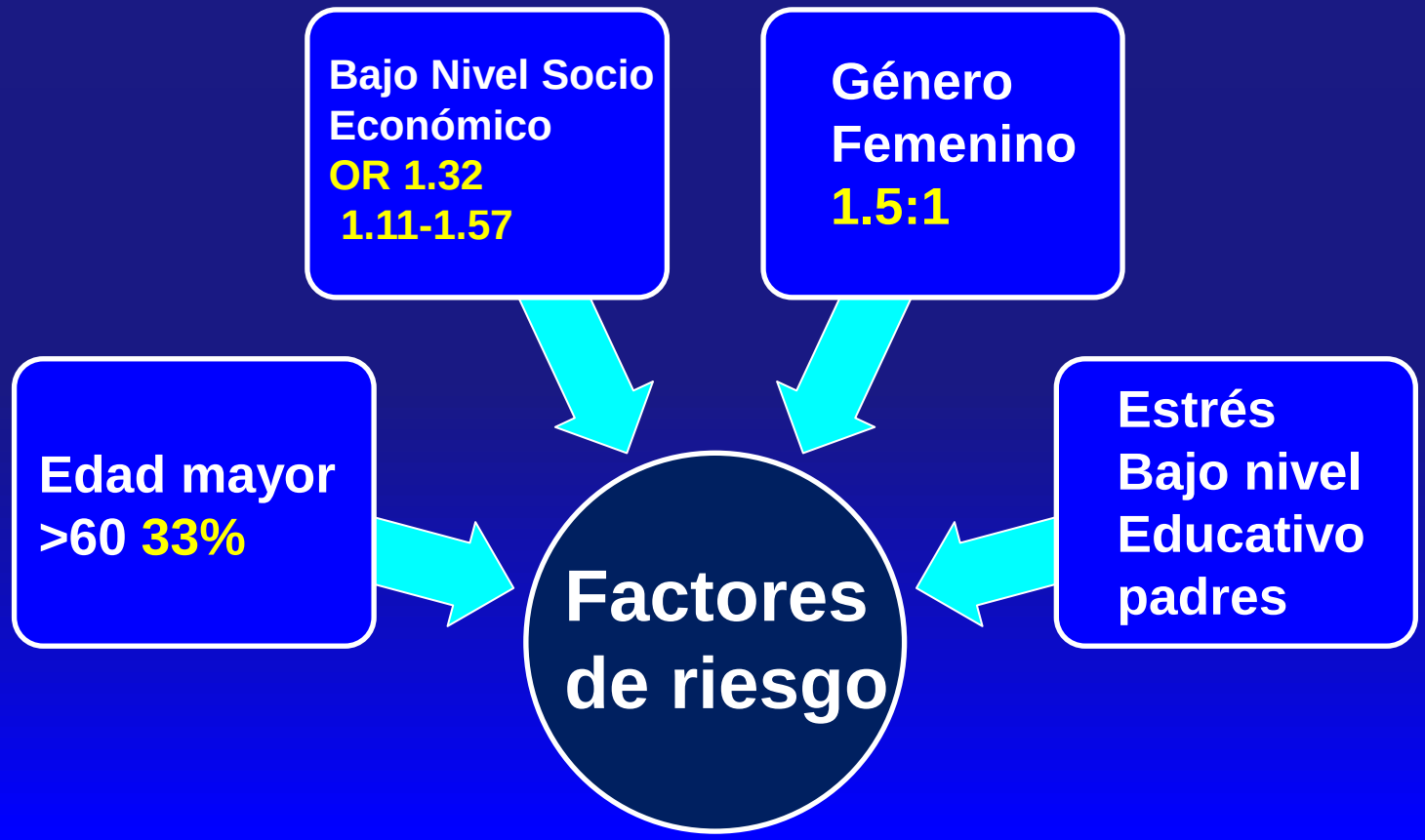


Belsey J, Aliment Pharmacol Ther 2010;31:938–49

Calidad de vida hospitalizados

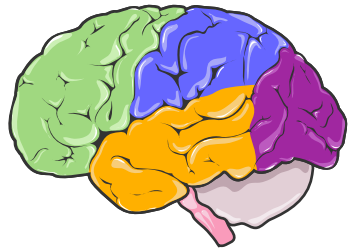


Belsey J, Aliment Pharmacol Ther 2010;31:938–49



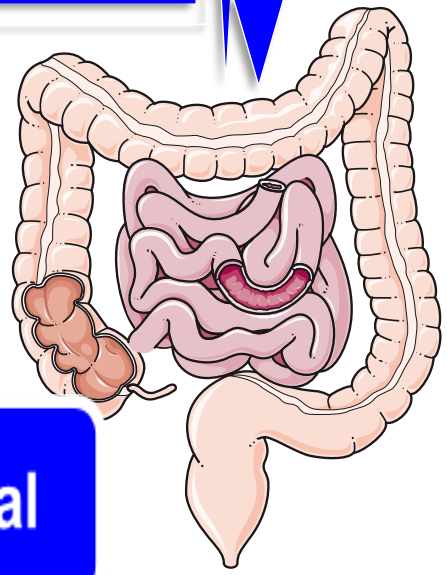
Barucha AE, Mayo Clin Proc. 2019;94:2340-2357
Bharucha AE, Gastroenterology 2020;158:1232-49

Estreñimiento Crónico Primario Fisiopatología



Vía eferente

Vía eferente



Estilos de vida ?
Dieta?
Obesidad

Factores genéticos

Alteración de la motilidad

Alteración de la microbiota

Alteración función ano-rectal

Disfunciòn piso pèlvico
Desòrdenes defecaciòn

Wald A, JAMA 2016;315:185-91
Barucha AE, Mayo Clin Proc. 2019;94:2340-57
Vriesman MH, Nat Rev Gastroenterol Hepatol. 2020;17:21-39

Fisiopatología

Microbioma

Ratones libres de gérmenes

Tránsito Colónico Lento

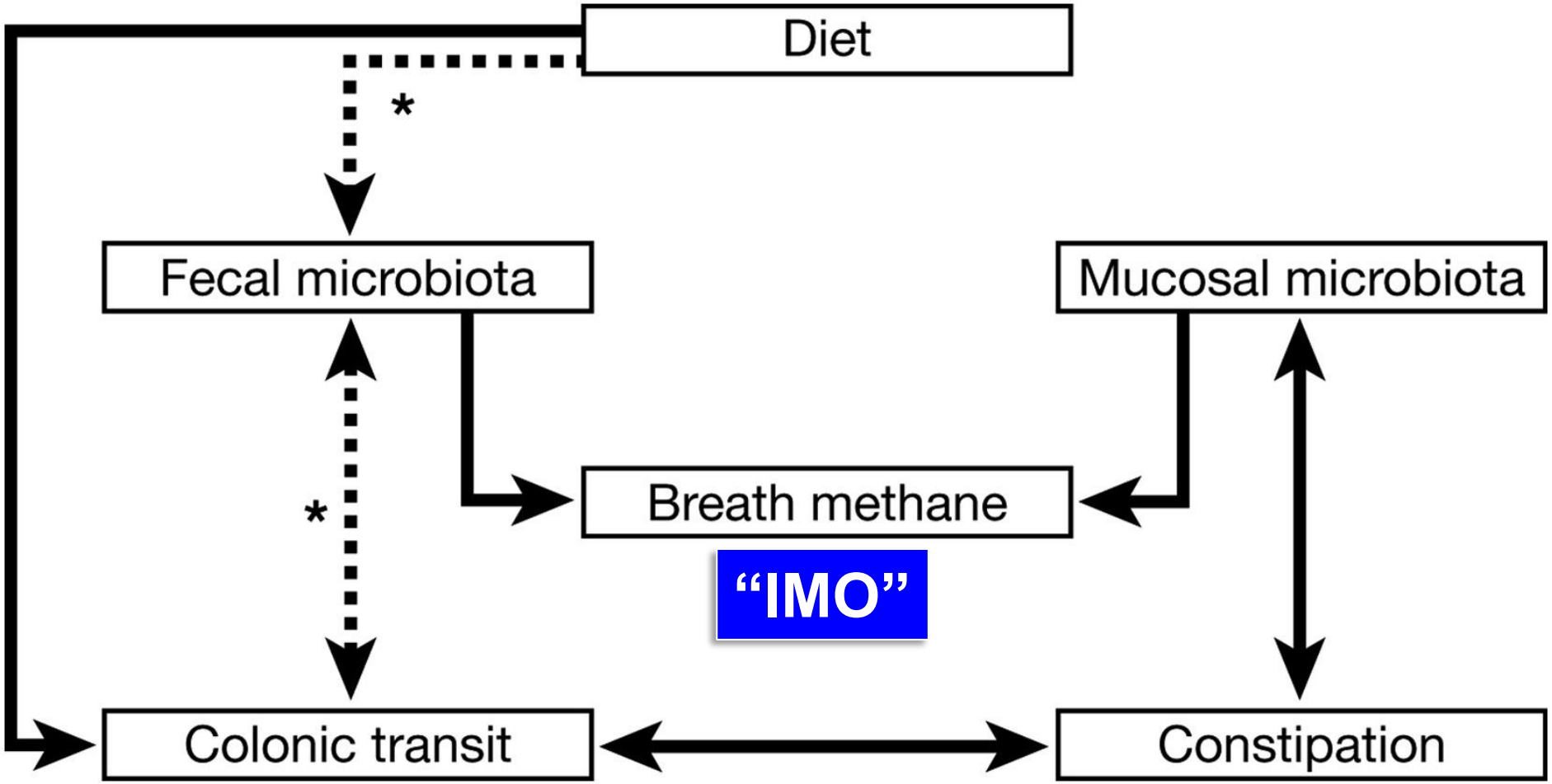
<<Firmicutes
>> Bacteroidetes
<< Ácidos Grasos Cadena corta

Cao H, Sci Rep 2017;7:10323
Ge X, Sci Rep 2017;7:441

Relationship Between Microbiota of the Colonic Mucosa vs Feces and Symptoms, Colonic Transit, and Methane Production in Female Patients With Chronic Constipation

Gopanandan Parthasarathy,[1] Jun Chen,[2,3] Xianfeng Chen,[2] Nicholas Chia,[2,3] Helen M. O'Connor,[4] Patricia G. Wolf,[5] H. Rex Gaskins,[5] and Adil E. Bharucha[1]

Gastroenterology 2016;150:367–379



Parthasarathy G, Gastroenterology 2016;150:367–379

microorganisms

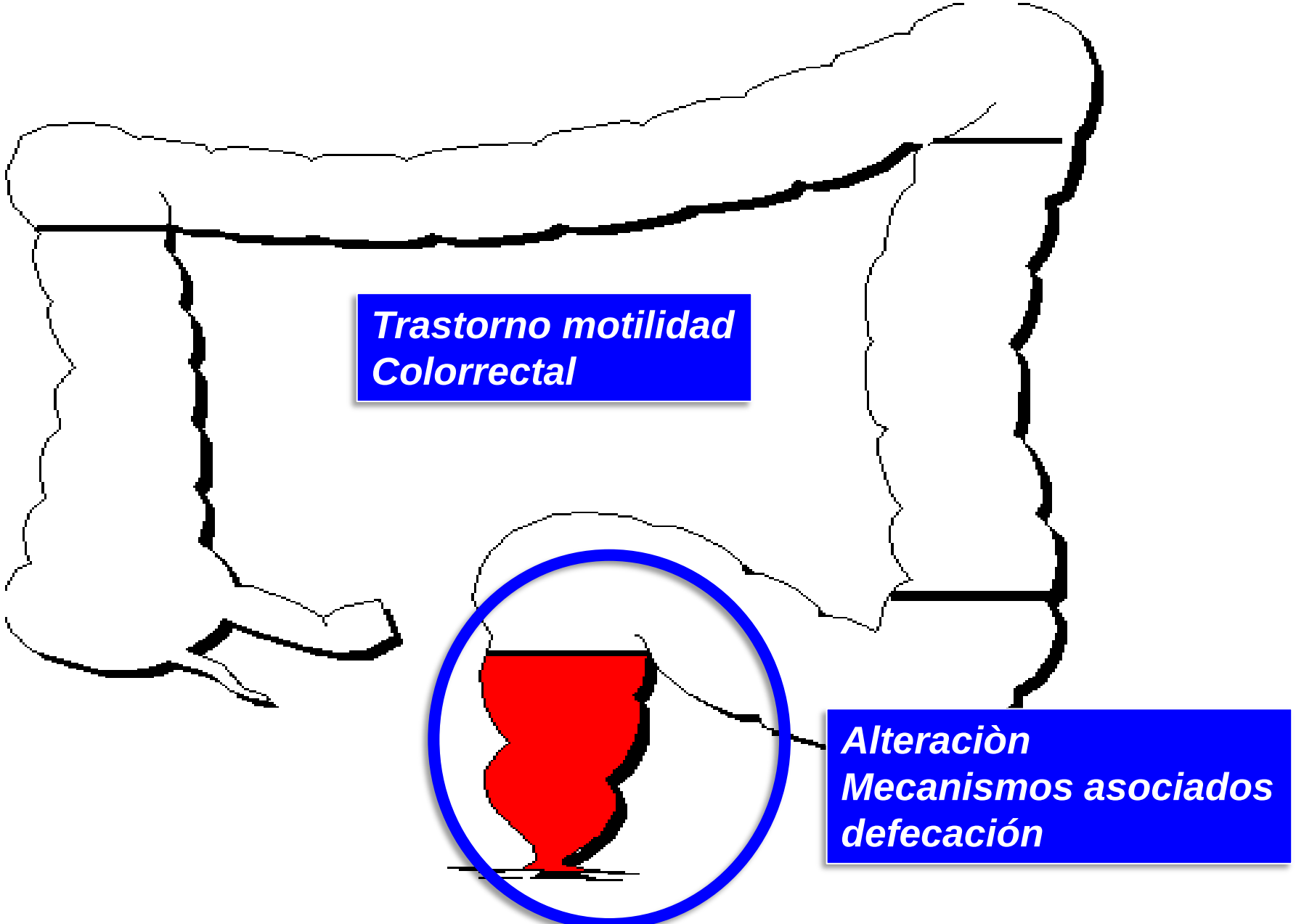
Review

Association between Gut Dysbiosis and the Occurrence of SIBO, LIBO, SIFO and IMO

Michalina Banaszak [1,2], Ilona Górna [1], Dagmara Woźniak [1,2], Juliusz Przysławski [1] and Sławomira Drzymała-Czyż [1,*]

Banaszak M, et al. Microorganisms 2023, 11, 573.

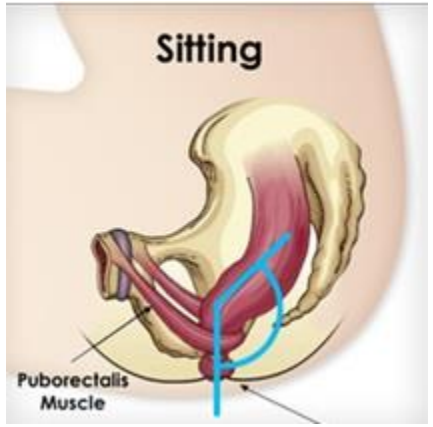
Estreñimiento Crónico Primario

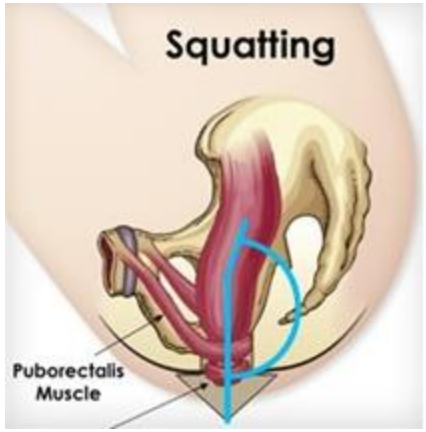


Posición en cuclillas relajada y natural


90°


35°


Sitting
Puborectalis
Muscle


Squatting
Puborectalis
Muscle

Diagnóstico

Historia clínica
Examen físico
Tacto rectal!

Todos los Expertos y Guías

Tacto rectal “Obligatorio”

Inspección anal
Orificio cerrado

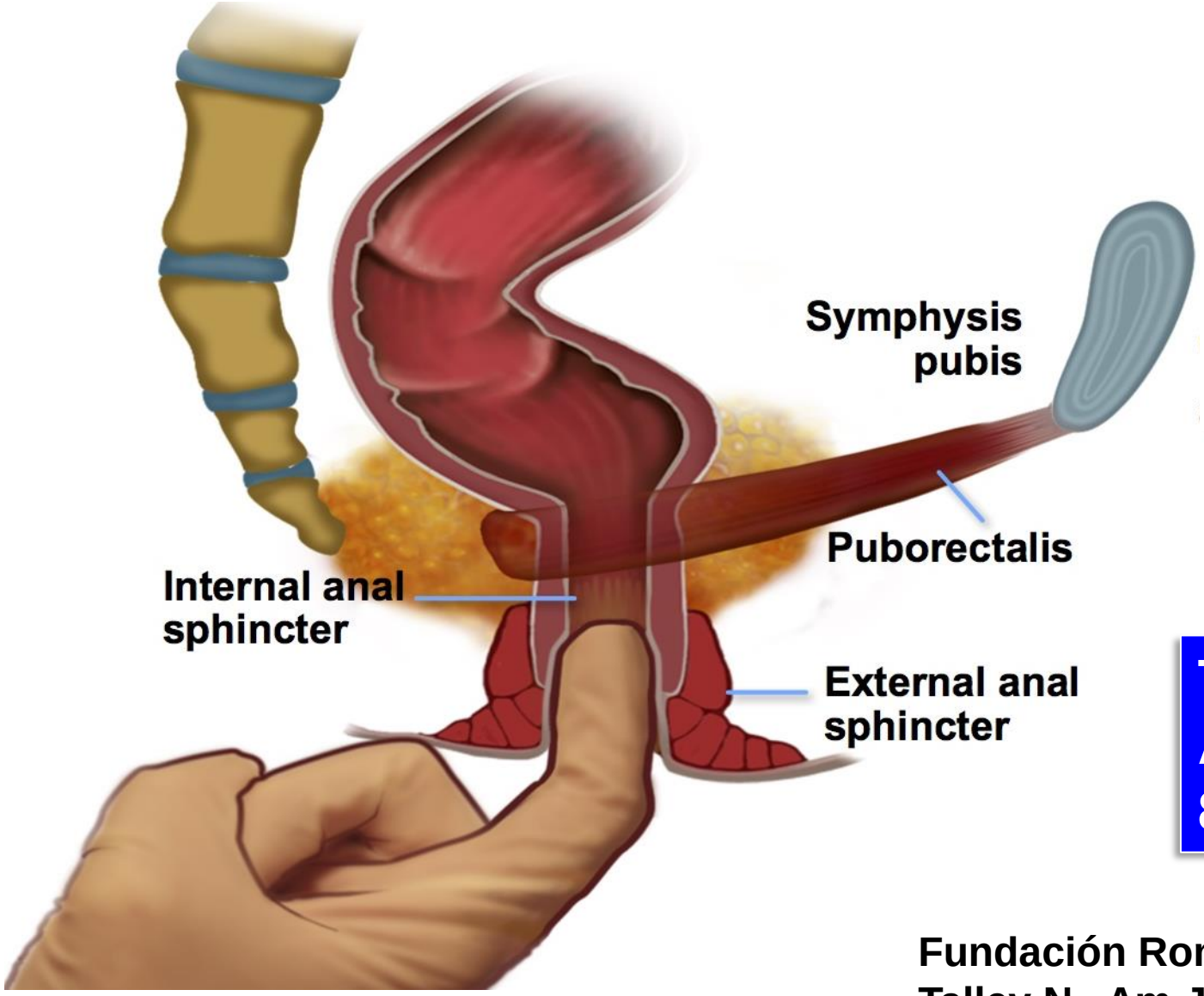
Estructuras Adyacentes

Fístulas, fisuras, Hemorroides

Pujo: descenso perineal <2 cm
No pasar las prominencias isquiáticas
Heces: hiposensibilidad ?, Tumores ?

Pineda LF . Temas Escogidos Gastroenterología
Asociación Colombiana Gastroenterología 2021

Tacto rectal para disinergia y continencia

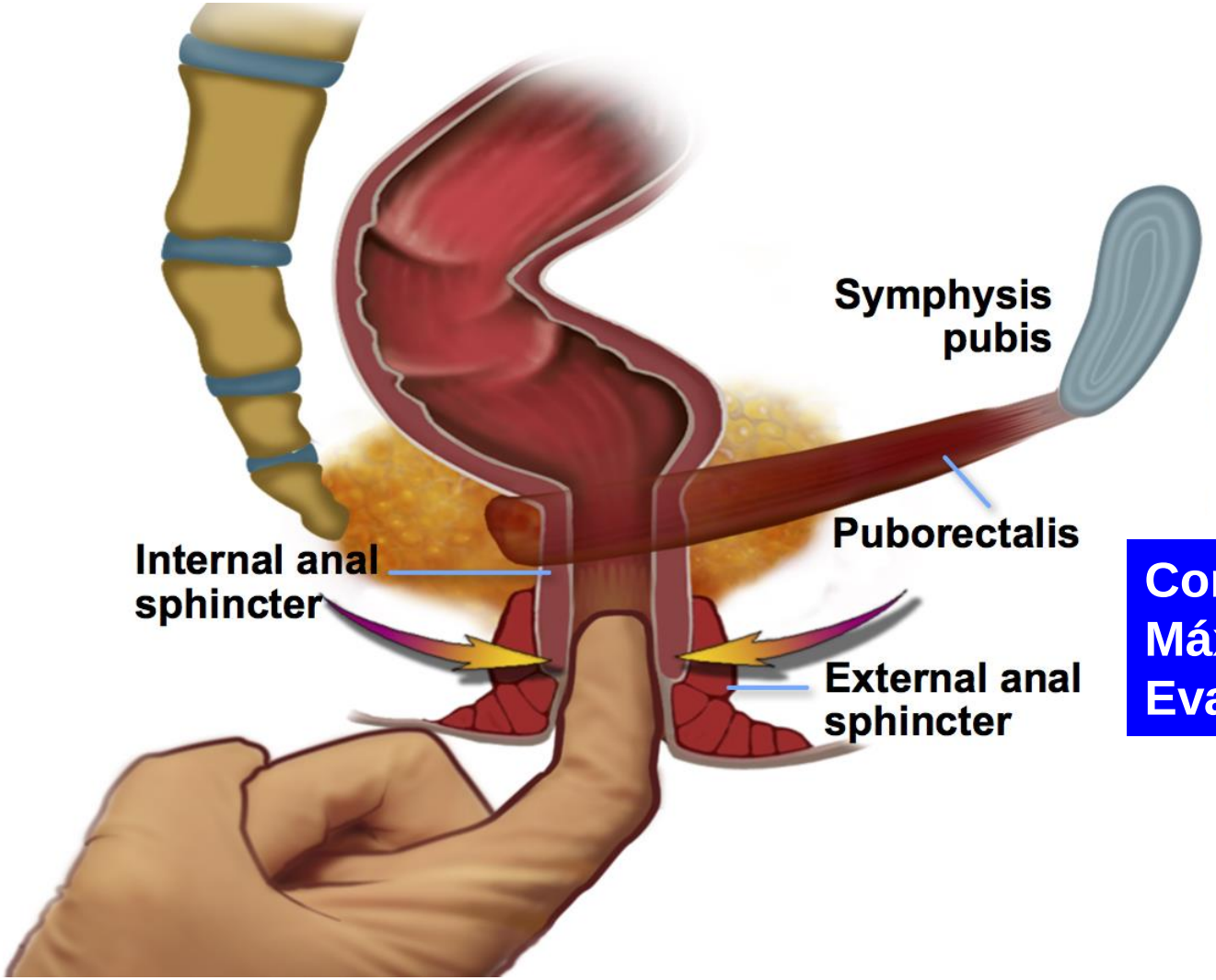


Posición 1

Tono esfínter Anal en reposo 80% EA Interno

Fundación Roma
Talley N, Am J Gastroenterol 2008;103:820-22

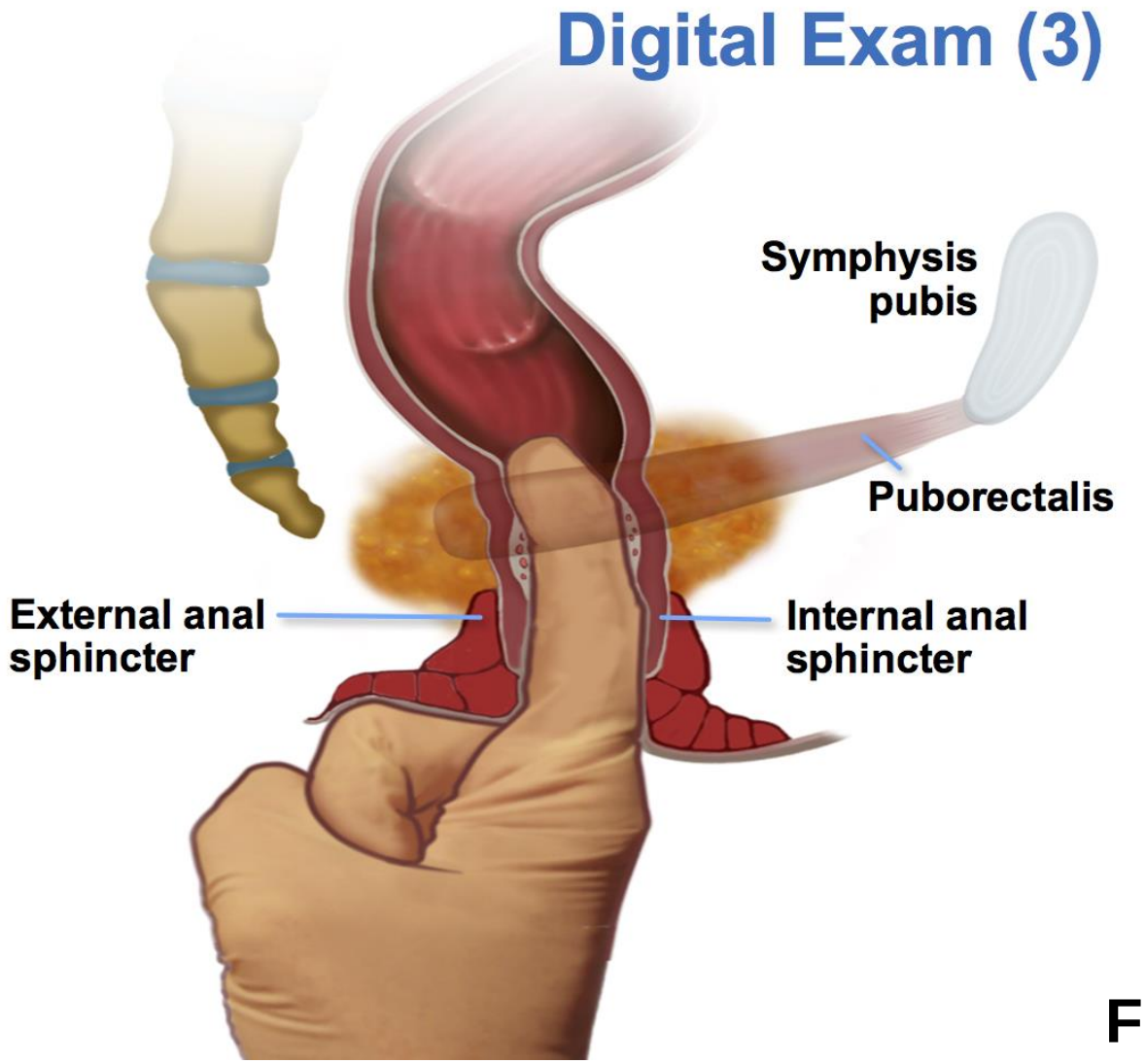
Tacto rectal para disinergia y continencia



Contraiga o aprete el ano
Máxima fuerza
Evalúa capacidad de continencia

Fundación Roma

Tacto rectal para disinergia y continencia

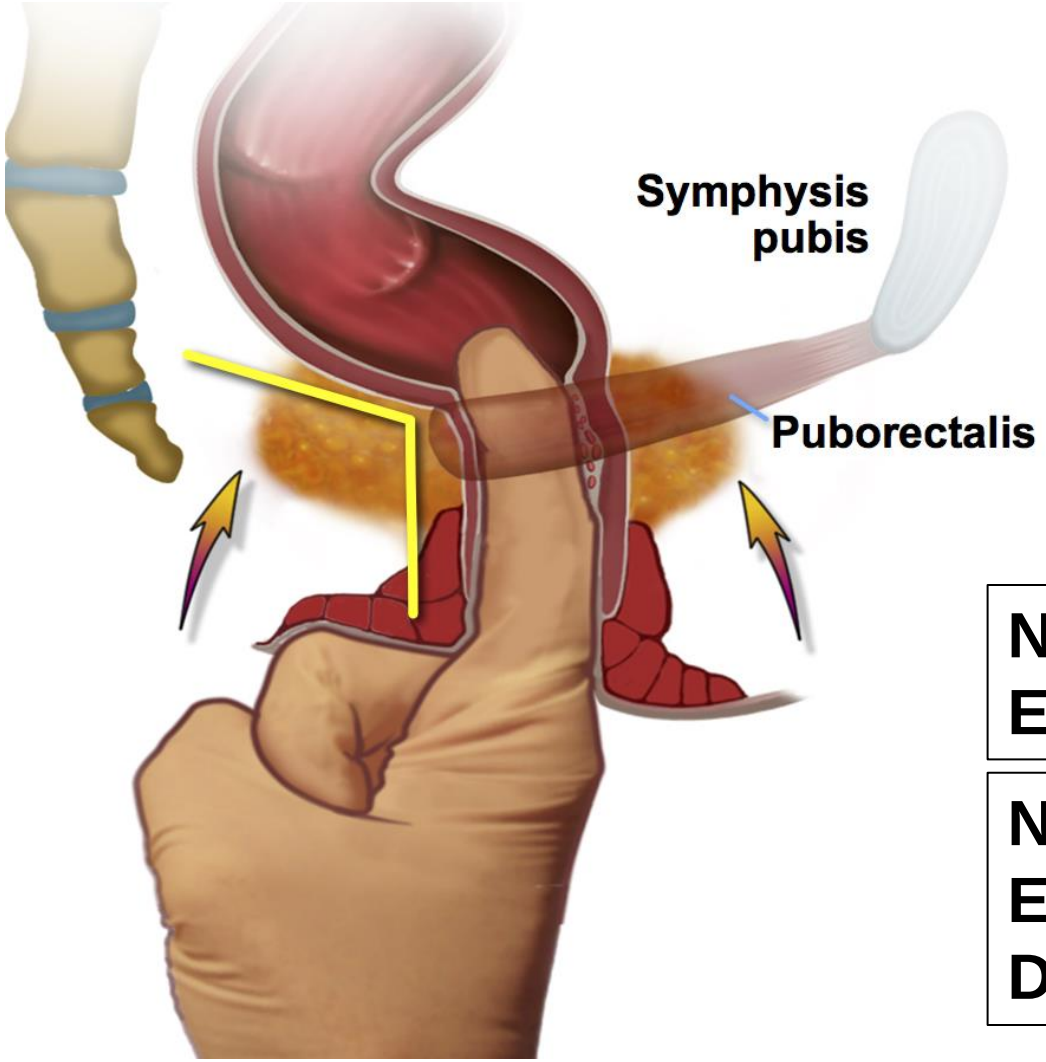


Position 2

Insert finger deeper and feel puborectalis muscle

Fundación Roma

Tacto rectal para disinergia y continencia



Examen digital 4

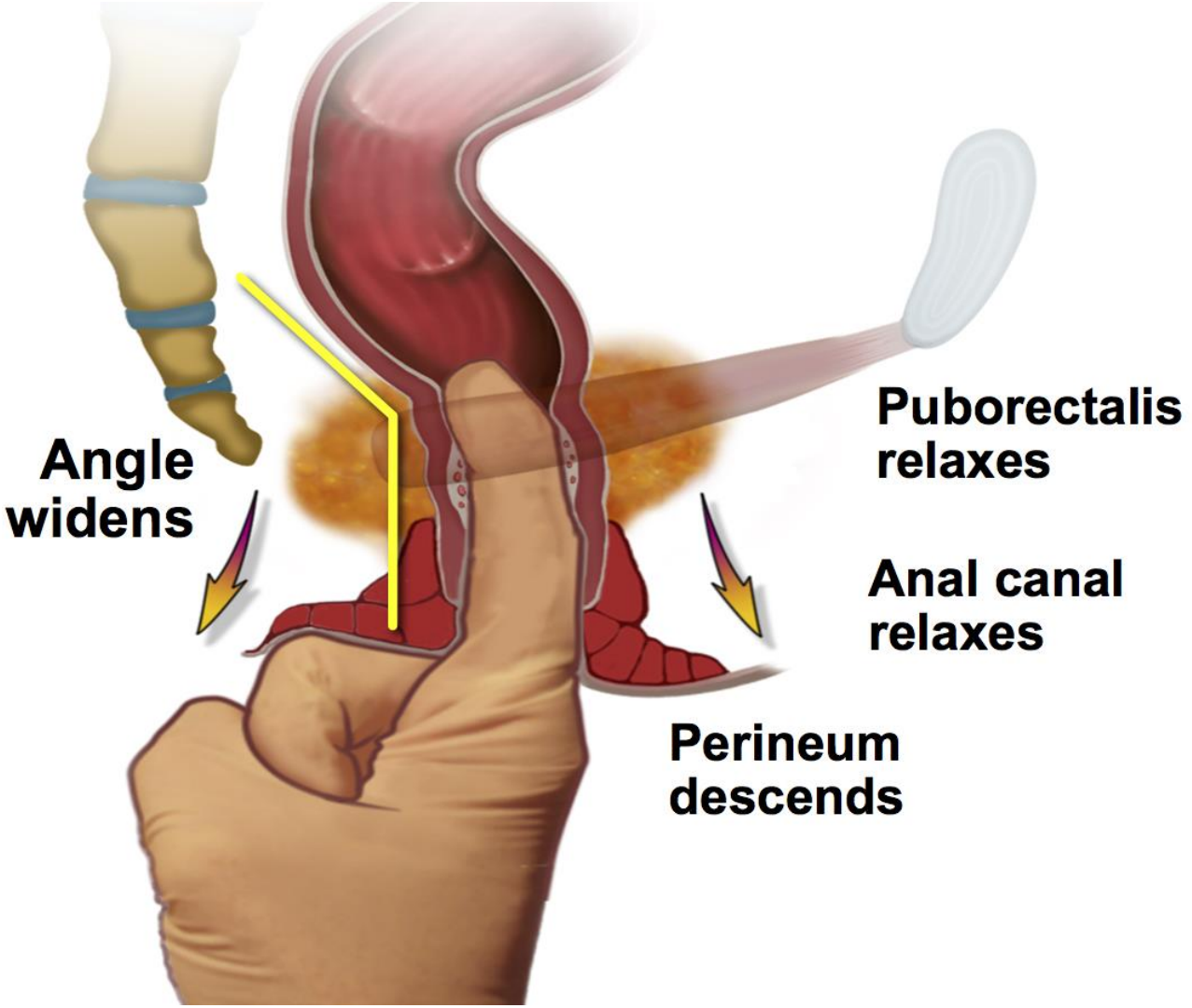
Puje simulando
Una defecación

Normalmente relajación
Esfínter anal y puborectalis

No hay relajación, el dedo
Empujado hacía adelante
Defecación disinérgica ?

Fundación Roma
Pineda LF, 2021 Colombia

Tacto rectal para disinergia y continencia



Examen digital 5

- Sen 75%
- Esp 87%

- Vpp 61%
- Vpn 91%

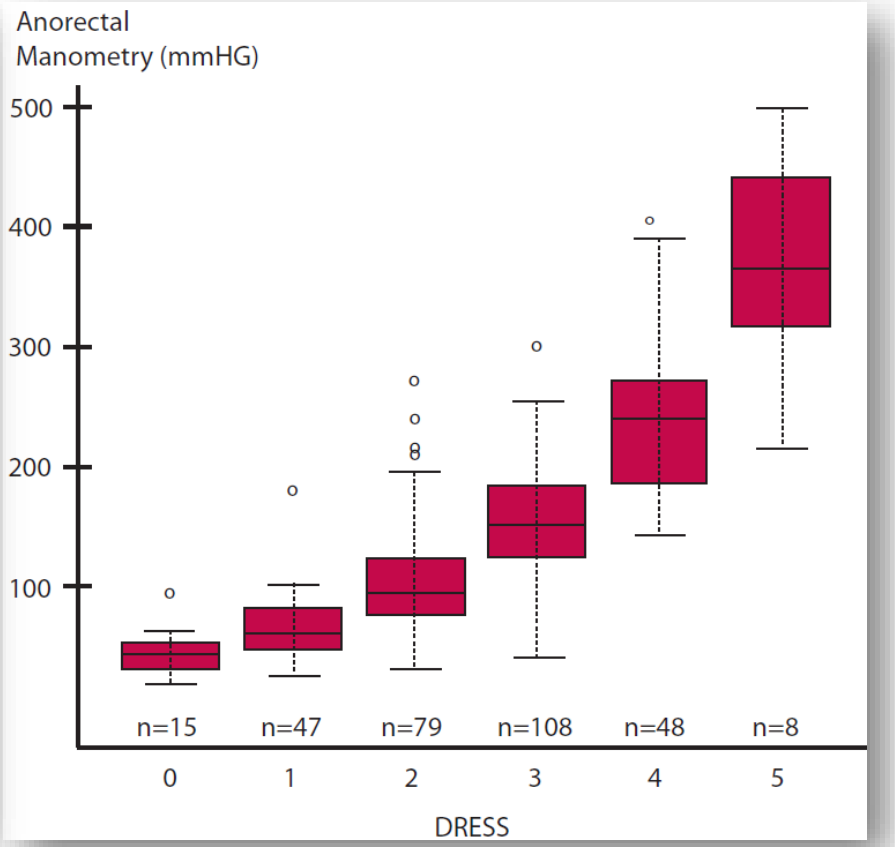
Fundación Roma

The Digital Rectal Examination Scoring System (DRESS)

Bruce A. Orkin, M.D.[1] • Svetlana B. Sinykin, B.A.[2] • Patricia C. Lloyd, Sc.M.[2]

TABLE 1. The Digital Rectal Exam Scoring System (DRESS)

Resting Score	
0	No discernable tone at rest, an open or patulous anal canal
1	Very low tone
2	Mildly decreased tone
3	*Normal*
4	Elevated tone, snug
5	Very high tone, a tight anal canal, difficult to insert a finger
Squeeze Score	
0	No discernable increase in tone with squeezing effort
1	Slight increase
2	Fair increase but below normal
3	*Normal*
4	Strong squeeze
5	Very strong squeeze, to the point of being painful to the examiner



Dis Colon Rectum 2010; 53: 1656–1660

Desórdenes defecatorios
"Obstrucción funcional tracto de salida"

Disminución
Fuerza rectal
Propulsiva

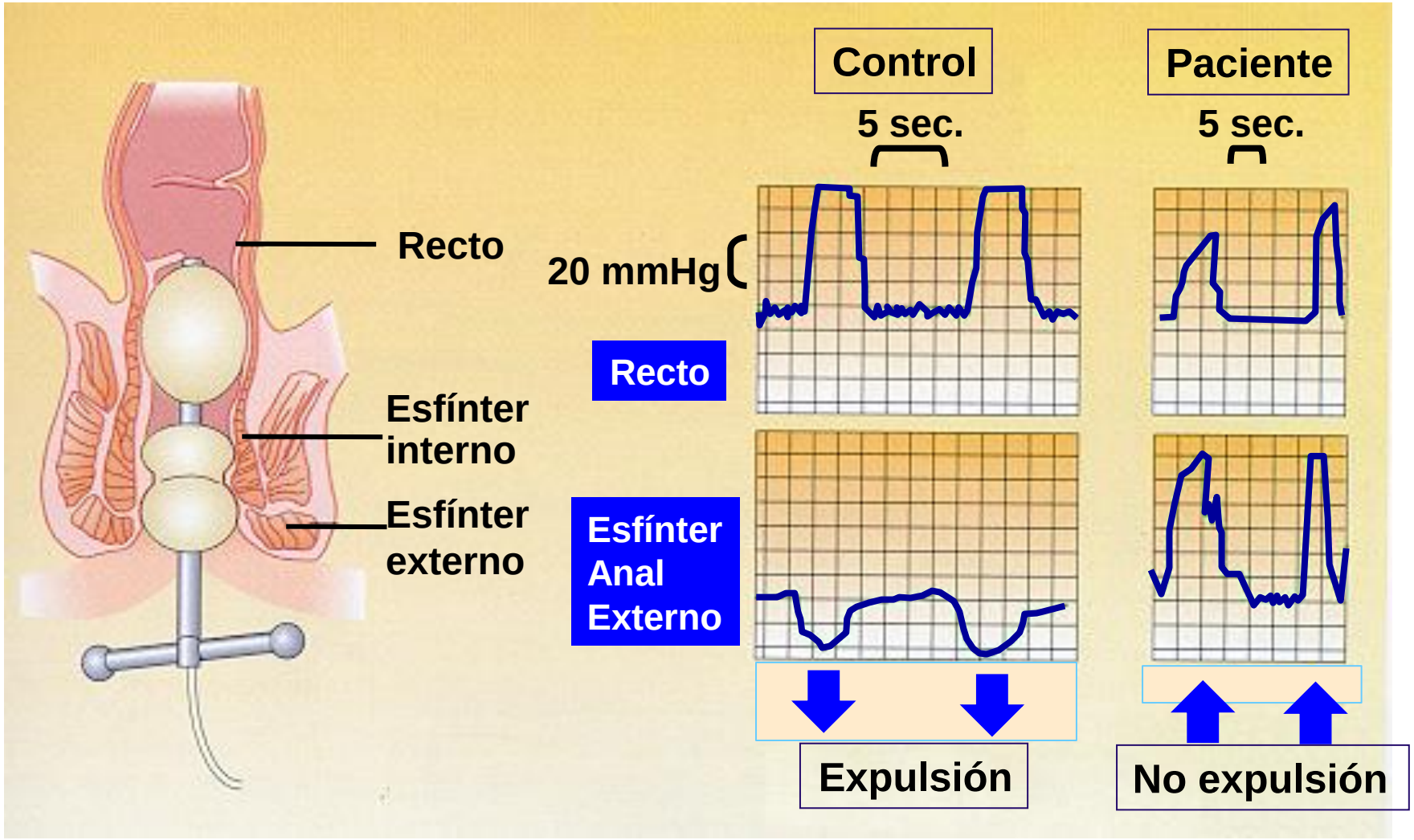
Aumento
Resistencia
Evacuación

Presión anal
Reposo aumentada

Relajación incompleta
Contracción paradójica
Piso pélvico
Esfínteres anales

Barucha AE, Gastroenteology 2020;158:1232-49

Disfunción del piso pélvico



Wald A. Clinical Perspectives, 1998; 1:106-15

Desórdenes defecatorios

SF3a. Inadecuada propulsion defecatoria

Inadecuda fuerza propulsiva, medida manometria conm o si inapropiada contracciòn del esfìnter anal y/o m mùsculos del piso pèlvico

F3b. Defecaciòn disinèrgica

Inadecuda cintracciòn muscular del piso pèlvico con EMG anal o manometrìa con adecuada fuerza propulsiva durante intentos de defecaciòn

RaonSS, Baruch AE, Gastroenterology2016;150:1430-42

Desórdenes defecatorios

Síntomas de estreñimiento

Estreñimiento

SII –Estreñimiento

2 de 3!

Evidencia objetiva evacuación rectal alterada

Test de expulsión del balón anormal >1 min

Patrón disinérgico: manometría, EMG anal superficie

Alteración de la evacuación por imágenes

***Defecografia RM*

***Tránsito con marcadores*

Barucha AE, Mayo Clin Proc. 2019;94:2340-57

Tránsito colónico: funciòn motora del colon

Gammagrafía del colon
Manometría del colon
Cápsula de motilidad inalámbrica
Marcadores radio-opacos

Saad RJ, Am J Gastroenterol 2010;105:403-11

Menos reproducible desórdenes defecatorios

Barucha AE,
Mayo Clin Proc. 2019;94:2340-2357

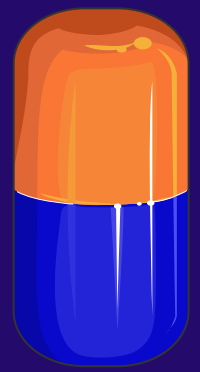
Técnica Hinton
1 cápsula 24 marcadores
Rx simple abdomen 5 día
5 o más marcadores en colon

Hinton JM,. Gut 1969;10:842-847

Técnica Metcalf
1 cápsula 24 marcadores
Días 1,2,3
Rx simple abdomen día 4, 7
> 68 marcadores

Metcalf AM, Gastroenterology. 1987;92:40-7

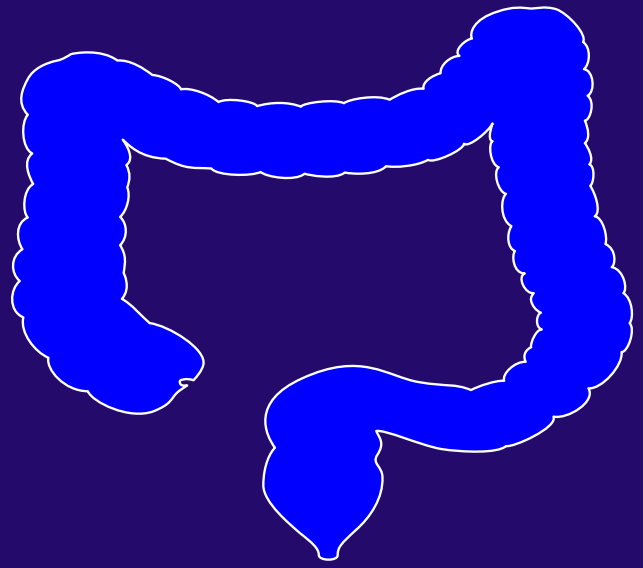
Bharucha AE, Neurogastroenterol Motil 2019;31:e13541



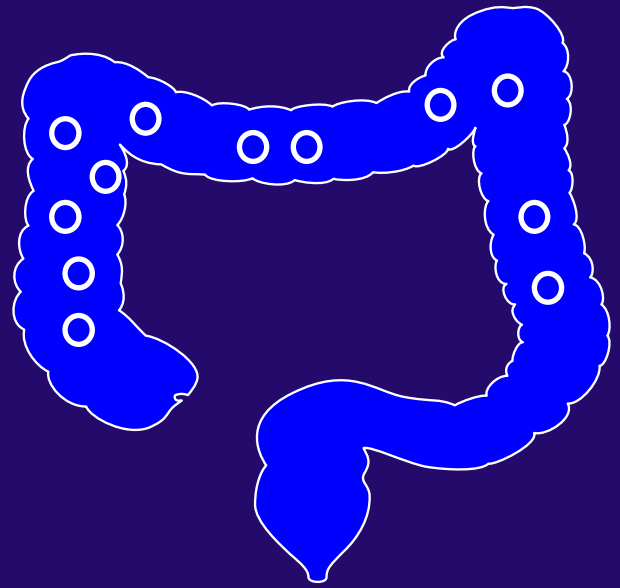
Sitzmarks ®
24 marcadores radiopacos

Sìntomas
Trànsito colònico
Pruebas ano-rectales

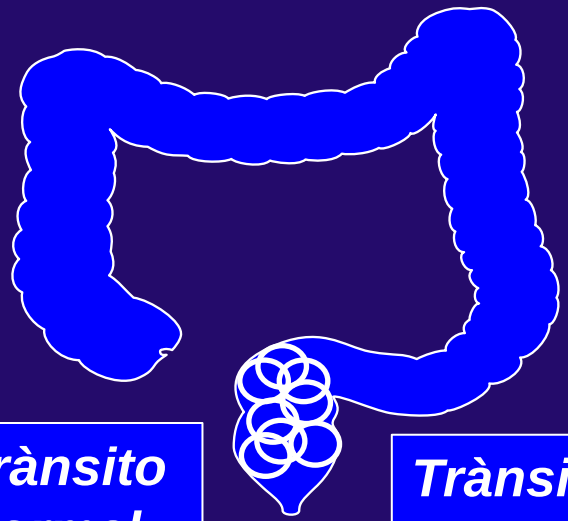
Trànsito Normal 20-72h < 5 marcadores



Trànsito Lento > 5 marcadores



Desòrdenes Defecatorios > 5 marcadores

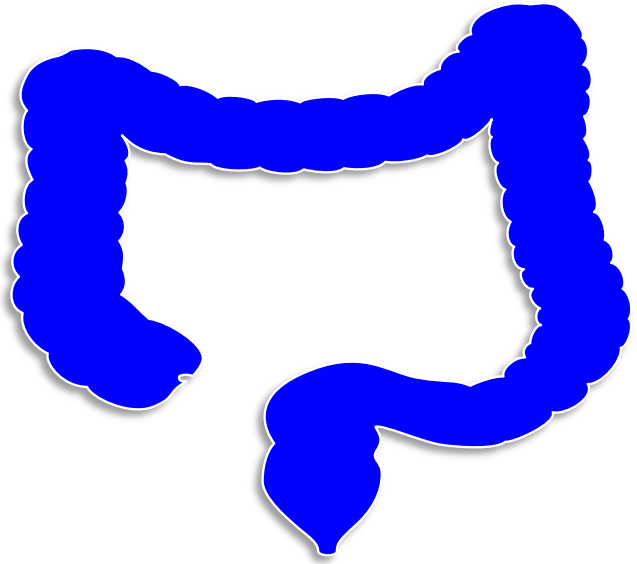


Trànsito Normal

Trànsito Lento

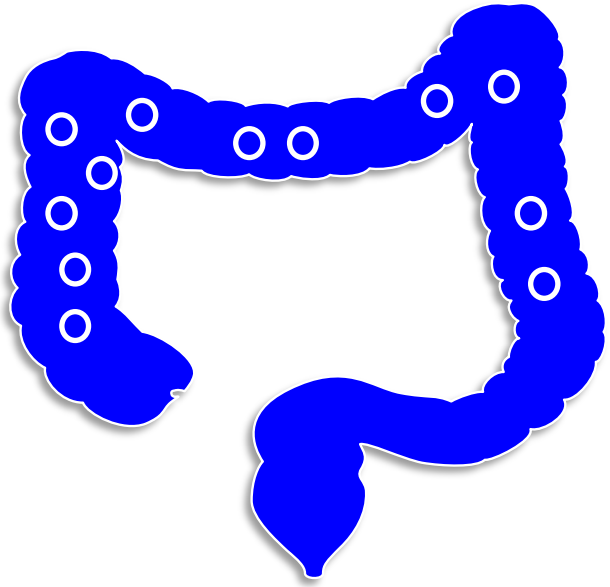
AGA 2020
Roma IV 2016

Trànsito Normal



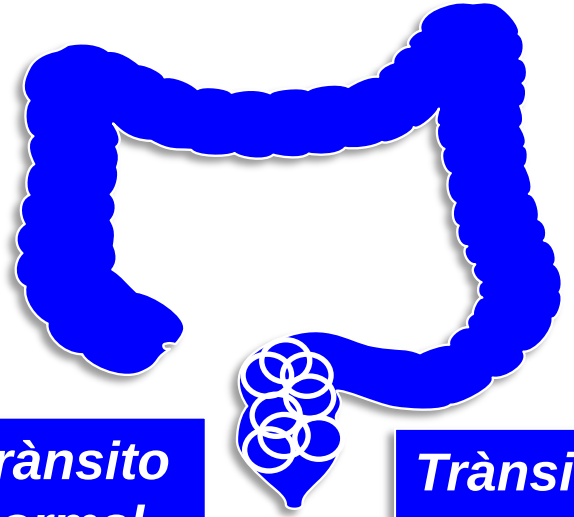
Hiposensibilidad Rectal
Alteración percepción
Frecuencia consistencia heces

Trànsito Lento



Menos contracciones Colónicas propagadas
Alta amplitud
< Neuronas sustancia “p”

Desòrdenes Defecatorios



Trànsito Normal

Trànsito Lento

Incoordinación entre Músculos abdominales Y del piso pélvico

Remes-Troche JM,et al. Rev Gastroenterol Mex 2018;83:168-89

Biofeedback therapy for constipation in adults

Satish S.C. Rao, M.D., Ph.D., FRCP (LON), AGAF *

Department of Gastroenterology-Hepatology, University of Iowa Carver College of Medicine, Iowa City, IA, USA

6 sesiones

Table 2
Summary of the randomized controlled trials of biofeedback therapy for dyssynergic defecation.

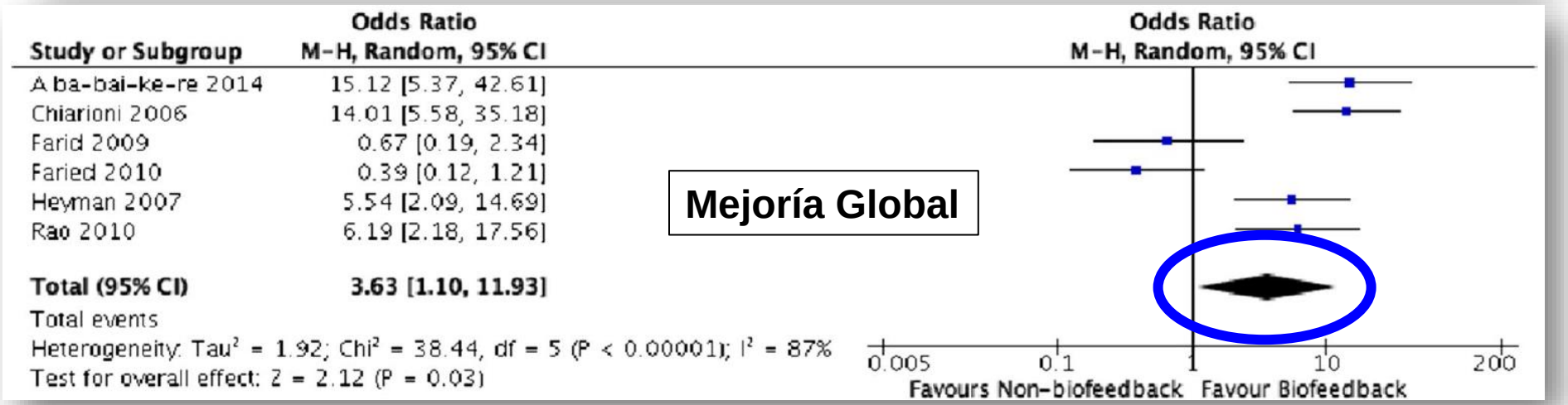
	Chaironi et al [18]	Rao et al [11]	Chaironi et al [10]	Heymen et al [13]	Rao et al [9,12]
Trial design	Biofeedback vs. PEG 14.6 g	Biofeedback vs. standard vs. sham biofeedback	Biofeedback for slow transit vs. dyssynergia	Biofeedback vs. diazepam five milligram vs. placebo	Biofeedback vs. standard therapy
Subjects and randomisation	104 women 54 biofeedback 55 polyethylene glycol	77 (69 women) 1:1:1 distribution	52 (49 women)	84 (71 women) 30 biofeedback diazepam bo	52; short term therapy 26 = long term study 12 = biofeedback 13 = standard therapy
Durationand number of biofeedback sessions	3 months and 1 year, 5 weekly, 30 min training sessions performed by physician investigator	3 months, bi-weel maximum of six three months, biofeedback nu		v, one hour	One year; 6 active therapy sessions and 3 reinforcement sessions at 3 month intervals
Primary outcomes	Global improvement of symptoms Worse = 0 No improvement = 1 Mild = 2 Fair = 3 Major improvement = 4	1. Presence of d 2. Balloon expuls 3. Number of comp spontaneous bowel m 4. Global satisfaction		om relief	Number of complete spontaneous bowel movements Secondary Outcome; Presence of dyssynergia Balloon expulsion time Global satisfaction
Dyssynergia corrected or symptoms improved	79.6% reported major improvement at 6 and 12 months 81.5% reported major improvement at 24 months	Dyssynergia corrected at 3 months in 79% with biofeedback vs 4% sham and 6% in standard group; CSBM = Biofeedback group vs Sham or standard, $p < 0.05$	71 % with dyssynergia and 8% with slow transit alone reported fair improvement in symptoms	70% improved with biofeedback compared to 38% with placebo and 30 % with diazepam	No of CSBM/week increased significantly in biofeedback $9p < 0.001$ Dyssynergia pattern normalised $9p < 0.0010$ Balloon expulsion improved ($p < 0.001$) Colonic transit normalised ($p < 0.01$)
Conclusions	Biofeedback was superior to laxatives	Biofeedback was superior to sham feedback and standard therapy	Biofeedback benefits dyssynergia and not slow transit constipation	Biofeedback is superior to placebo and diazepam	Biofeedback is superior to standard therapy

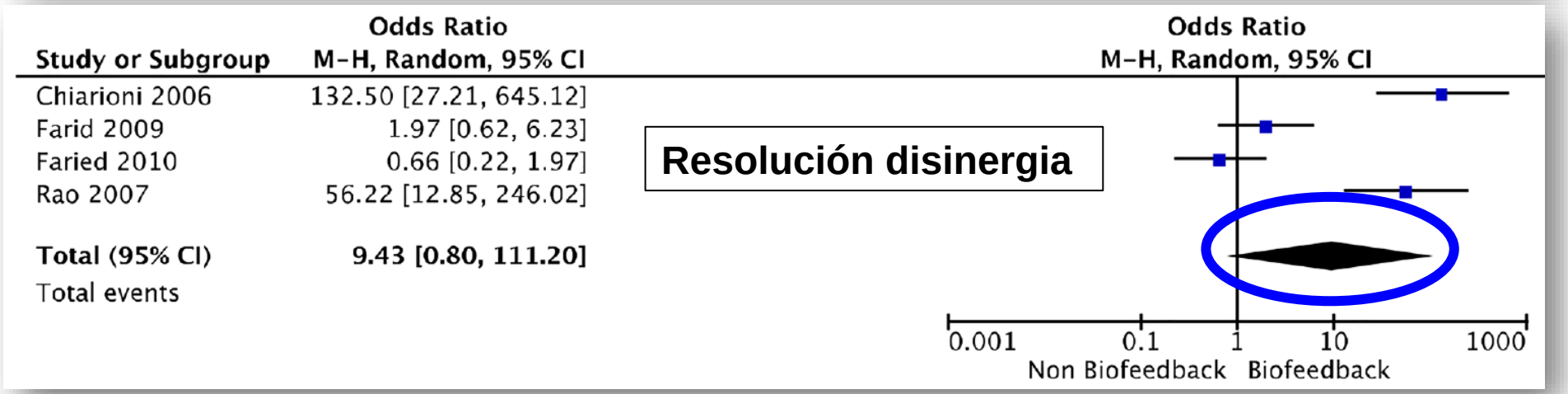
70-80%

Best Practice & Research Clinical Gastroenterology 2011;25 :159–166

A systematic review and meta-analysis of biofeedback therapy for dyssynergic defaecation in adults

D. Moore[1] · C. J. Young[1,2,3]





Moore D, Tech Coloproctol. 2020;24:909-918

Colonoscopia
NO está indicada
De rutina

Indicaciones colonoscopia

Pérdida de peso
Rectorragia
Anemia
Estreñimiento > 50 años
Familiar Ca de Colon o EII

Tack J, Neurogastroenterol Motil 2011;23:697-710

Tratamiento

Medidas generales ?
Fibra soluble ??
Psyllium 10 gr 2v/d
4 S 77 vs 44%

Estreñimiento

Laxantes osmóticos
Polietilen-Glicol ***17-34 gr***
Lactulosa

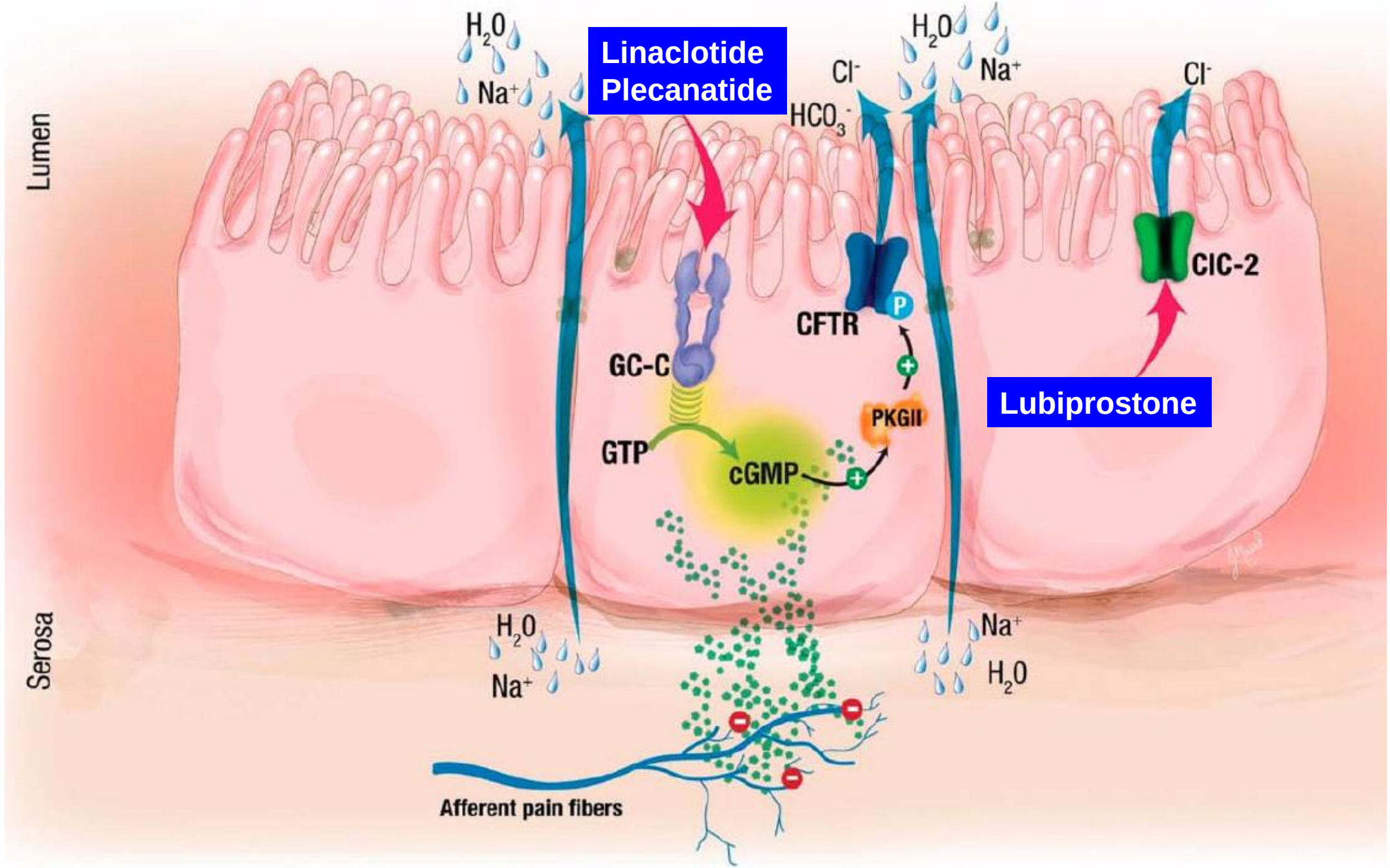
Laxantes Estimulantes
Bisacodilo/Picosulfato de sodio
Prodrogas, Deacetilasas mucosa/muicrobiota
BHPM, anti absorbente/Secreciòn,
Rescate 2- días

Secretagogos ClNa
Salida neta de iones y agua,
> tránsito intestinal, < dolor
Lubiprostone PG E1,canales Cl
Linaclotide: Guanilato ciclasa GMPc
Plecanatide Guanilato cicalsa GMPc

Proquinéticos 5HT4
Prucalopride

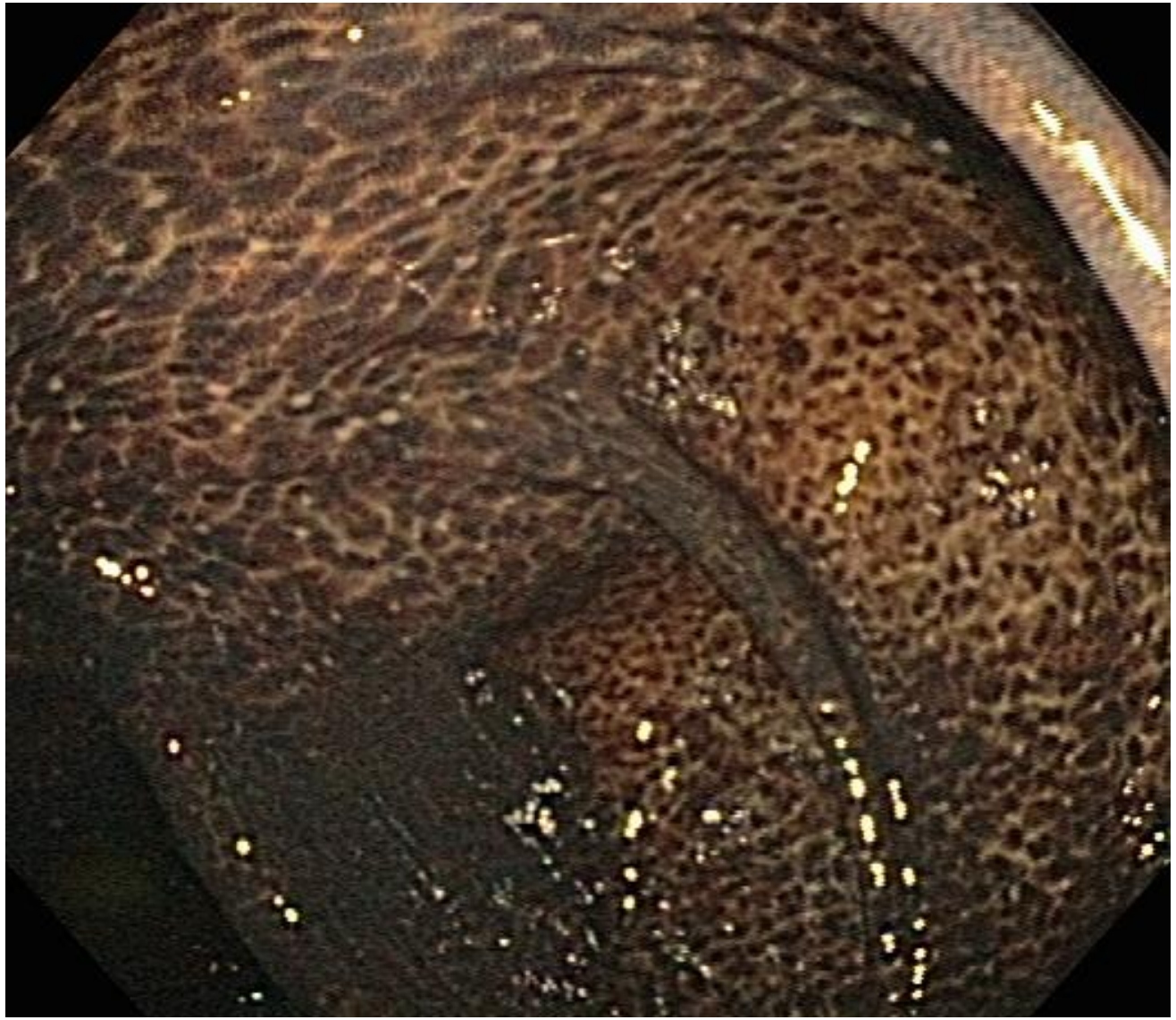
Antagonistas opioides
PAMORAs

AGA 2020, Roma IV 16



Sayuk GS, et al. Am J Gastroenterol 2022;117:S6–S13.

Laxantes estimulantes
Cáscara sagrada, Sen



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Sa1736 — 2020

AGA

PSEUDOMELANOSIS COLI CAUSES DISTURBED COLONIC MOTILITY FROM THE NREVOUS AND MUSCULAR SYSTEMS

Ask the Author

Laxantes antraquinona lesionan plejo Auerbach
Disminución del Tiempo Tránsito Colónico
Menos neuronas y engrosamiento muscular
Histología en colectomias

Author(s): Noriaki Manabe[1], Ken Haruma[1], Minoru Fujita[1], Tomo

[1] Kawasaki Medical School, Okayama, Japan

Background & Aims: *Pseudomelanosis coli* (*P. coli*) is most ofte
term use of anthracene cathartics. Anthraquinones induce apopto
nerves of the intestinal tract, causing disturbed colonic motility, but the mechanisms of this phenomenon are still unknown. The first aim of this study was to determine the association between *P. coli* and colonic motility. The second aim was to investigate whether *P. coli* histologically affects Auerbach's plexus. **[Study 1]** ***Methods:*** Thirty-seven consecutive constipated patients with *P. coli*, 17 constipated patients without *P. coli*, and 61 controls matched by age and sex at a 1:2 ratio were enrolled. The colonic transit time (CTT) was evaluated by an ultrasonographic (US) method, which has been validated previously. The constipation index (CI), as measured by the US method, was an indirect indicator of CTT. ***Results:*** The *P. coli* group had significantly higher CI values than did the control group, which indicated that the CTT in *P. coli* was significantly delayed. **[Study 2]** ***Methods:*** A total of 33 patients who had a resected colon due to colorectal cancer were enrolled. Normal areas that were su) [group A] and 20 patients: histological *P. coli* (−) [group B]). Th ss colonic wall fragment by two authors: (1) characteristics of gangl of nerve cells and (ii) the rate of normal or degenerative changes in rs could not reach a consensus on diagnosis resulted in exclusion of th than that that in group B (8.09 ± 5.07 vs. 13.37 ± 7.40 cells/cm, p < (to be lower than that in group B. The thickness of the mucosal musc m, p < 0.01). ***Conclusions:*** *P. coli* affects not only Auerbach's plexus, which controls colonic motility, but also the thickness of the muscularis mucosa. This situation may cause disturbed colonic motility

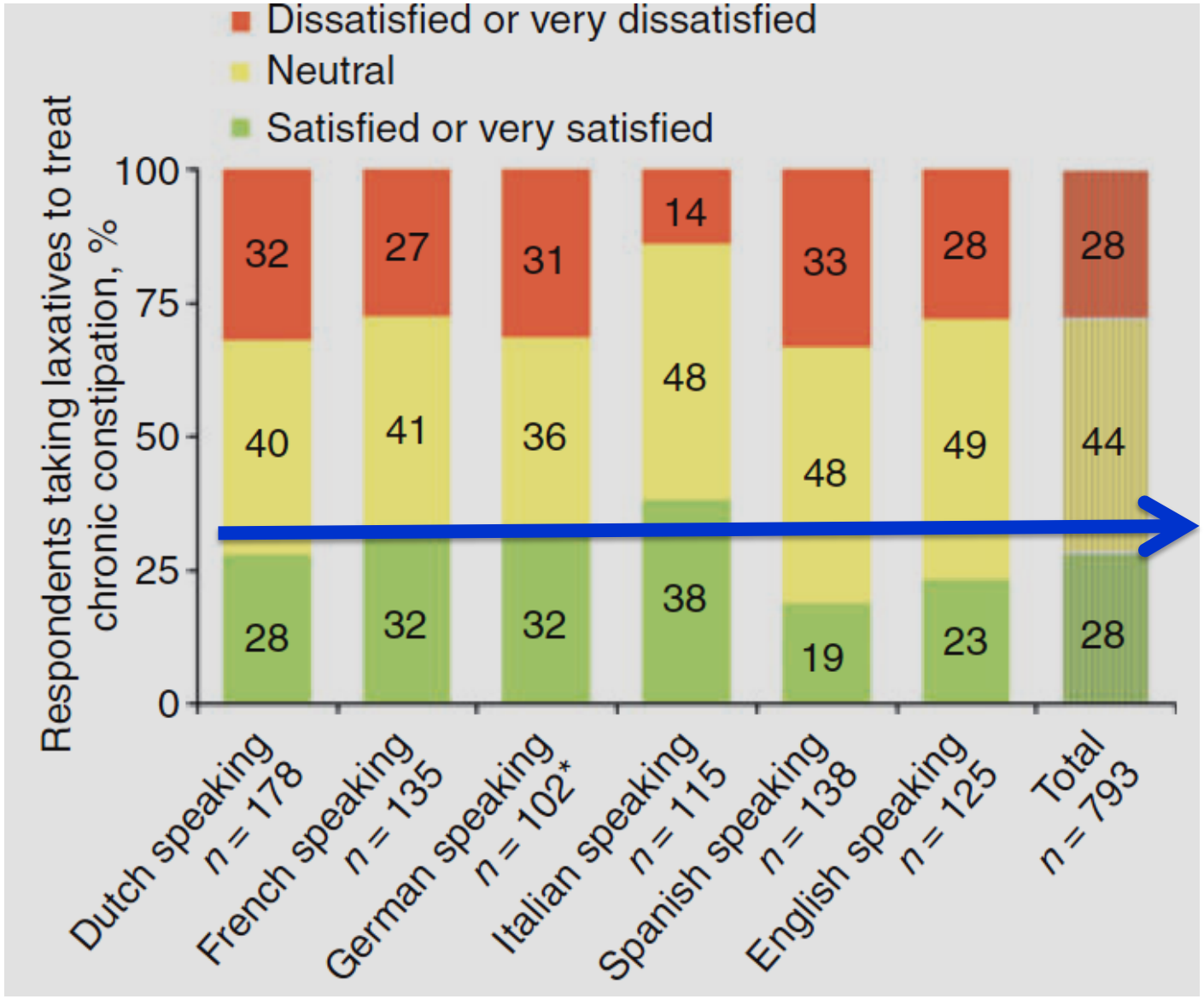
No los aconsejamos
Sólo si no hay nada mas!

Calidad de la evidencia

Levels of satisfaction with current chronic constipation treatment options in Europe – an internet survey

S. Müller-Lissner*, J. Tack†, Y. Feng‡, F. Schenck‡ & R. Specht Gryp§

Aliment Pharmacol Ther 2013;37:137-45



Open

Efficacy and Safety of Over-the-Counter Therapies for Chronic Constipation: An Updated Systematic Review

Satish S.C. Rao, MD, PhD[1] and Darren M. Brenner, MD[2]

	Grado de recomendación	Nivel de evidencia
PEG	A	I
Psyllium	B	II
Leche de Magnesia Docusato	C	III

GRADE

	Recommendation[b]	Quality of Evidence[c]
Bulk agents	Strong	Low
Psyllium, methylcelluose, calcium polycarbophil, wheat dextrin		
Nonabsorbed substances		
PEG 3350	Strong	High
Lactulose[d]	Strong	Low
Magnesium salts	NA	NA
Stimulants		
Bisacodyl	Strong	Moderate
Senna	NA	NA
Secretory drugs[d]		
Lubiprostone	Strong	High
Linaclotide	Strong	High

Wald A, *JAMA*. 2016;315:185-191

	American College of Gastroenterology		World Gastroenterology Organization	
	Grade of evidence	Level of recommendation	Grade of evidence	Level of recommendation
Lactulose	Low	Strong	B	2
PEG	High	Strong	A	1
Psyllium	Low	Strong	B	2
Bisacodil	Moderate	Strong	B	2
Senna	N/A	N/A	C	3
Prucalpride	Moderate	Strong	A	1

Sadeghi A, Turk J Gastroenterol. 2023;34):182-195.

Medicamento	Dosis/día	NNT
PEG	17 gr	2 (IC95% 1-3)
Lactulosa	20 gr	4 (IC95% ND)
Bisacodilo	10 mg	4 (IC 95% ND)
Lubiprostone	24µg 2v/día	4 (IC95% 3-6)
Linaclotide	145 µg 1v/día	5.6 (IC95% ND)
Prucalopride	2 mg/día	6 (IC 95%5-9)
Velusetrag	15 mg/día	3.4 (IC95% ND)
Elobixibat	10 mg/día	3 (IC95% ND)

Włodarczyk J, et al. J. Clin. Med. 2021:10:1738.

PEG debería ser el comparador

Ford A. Gastroenterology 2013:145:897-8

Comparaciones

Agonista 5HT4
Prucalopride

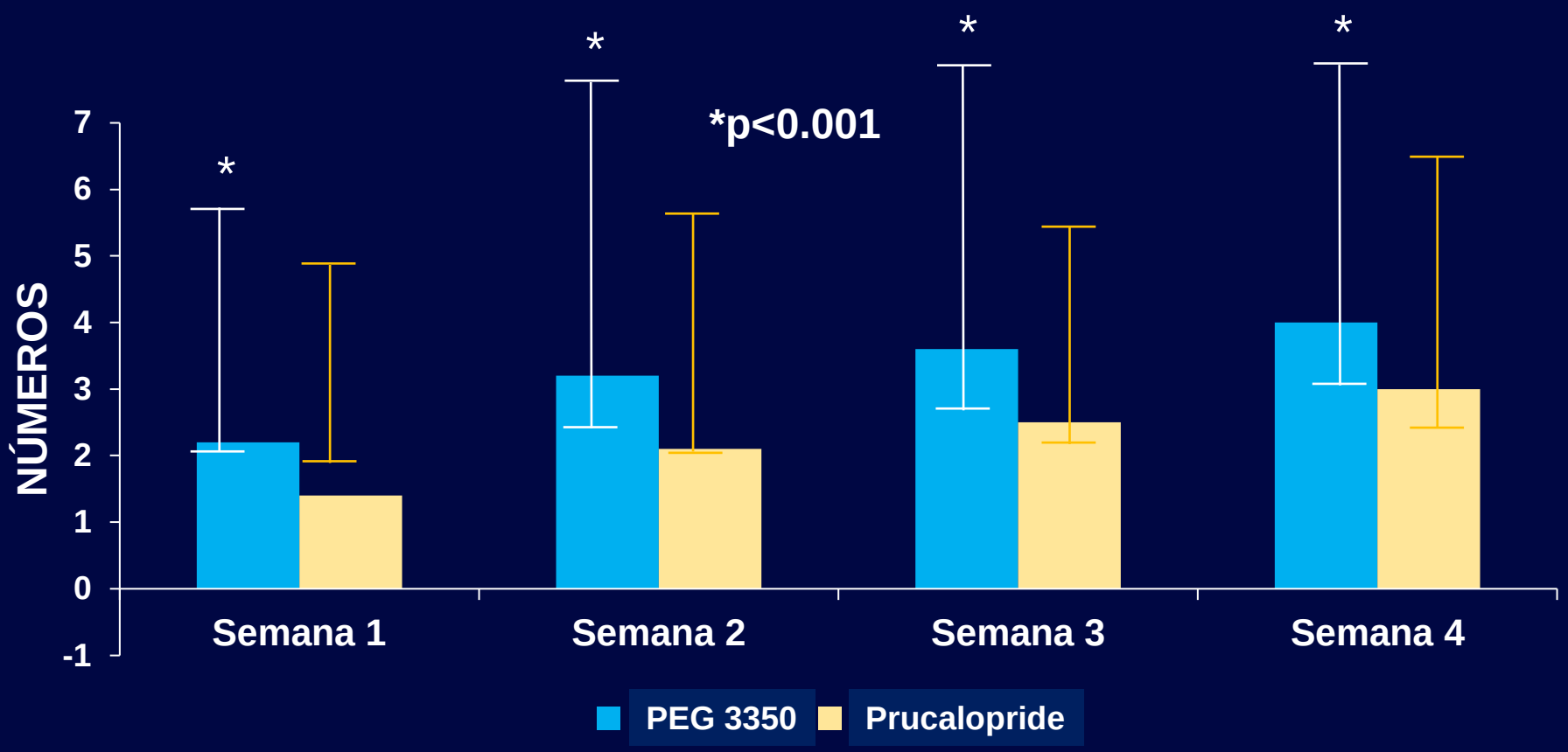
Table 1 | Receptor binding profile of 5-HT_4 agonists for GI disorders, at therapeutic concentrations

	Receptor binding profile at therapeutic concentrations					
Drug	5-HT_4	5-HT_3	5-HT_2	5-HT_1	D_2	hERG
Cisapride	+	+	+			+
Tegaserod	+	+	+	+		
Renzapride	+	+				
Clebopride	+	+			+	
Mosapride	+	+				
Prucalopride	+					
Velusetrag	+					
Naronapride	+					

Tack J, et al. Aliment Pharmacol Ther 2012; 35: 745-767

PEG 3350 con electrolitos Vs Prucalopride

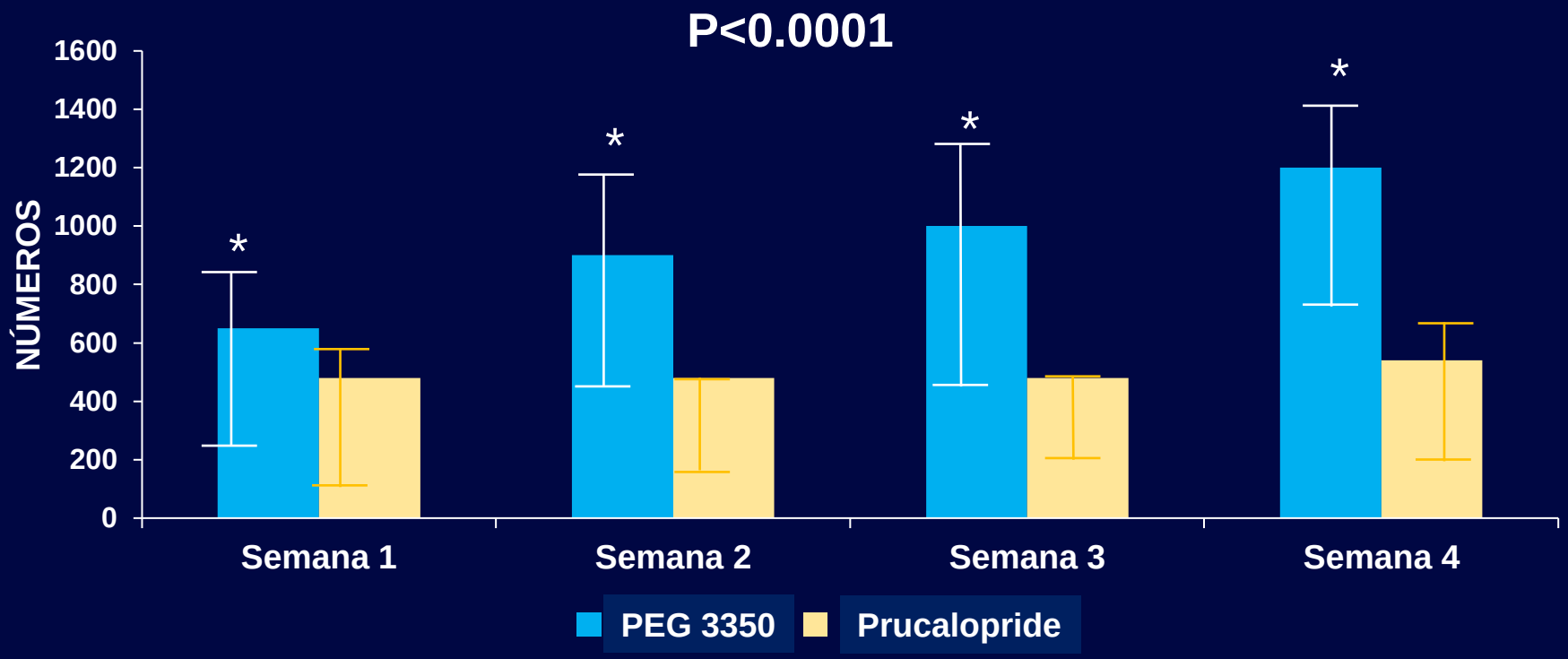
Movimientos intestinales espontáneos completos



Cinca R, et al. Aliment Pharmacol Ther 2013; 37: 876-886

PEG 3350 con electrolitos Vs Prucalopride

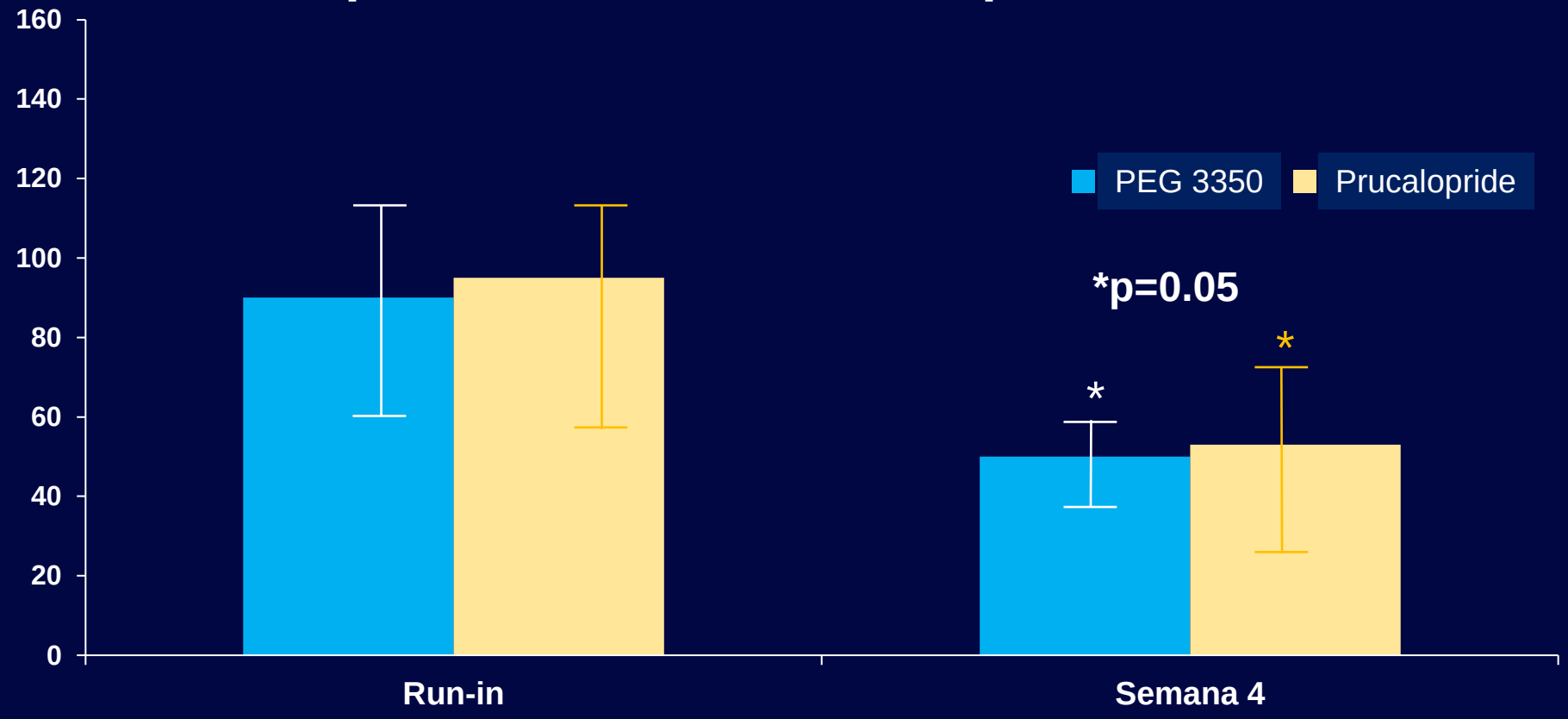
Peso promedio de materias fecales



Cinca R, et al. Aliment Pharmacol Ther 2013; 37: 876-886

PEG 3350 Vs Prucalopride

Tiempo de tránsito intestinal promedio horas



Cinca R, et al. Aliment Pharmacol Ther 2013; 37: 876-886

Comparison of the effectiveness of polyethylene glycol with and without electrolytes in constipation: a systematic review and network meta-analysis

Peter Katelaris[1*], Vasi Naganathan[2], Ken Liu[3], George Krassas[4] and John Gullotta[5]

No hay diferencias

BMC Gastroenterology (2016) 16:42

American Journal of Gastroenterology
© 2005 by Am. Coll. of Gastroenterology
Published by Blackwell Publishing

Vol. 100, No. S1, 2005
ISSN 0002-9270
doi: 10.1111/j.1572-0241.2005.50613.x

An Evidence-Based Approach to the Management of Chronic Constipation in North America

American College of Gastroenterology Chronic Constipation Task Force

THERAPY OF CHRONIC CONSTIPATION: OSMOTIC LAXATIVES (SEE SECTION 2.8)

Polyethylene glycol (PEG) is effective at improving stool frequency and stool consistency in patients with CC (Grade A recommendation). Lactulose is effective at improving stool frequency and stool consistency in patients with CC (Grade A recommendation). There are insufficient data to make a recommendation about the effectiveness of milk of magnesia (MOM) in patients with CC (Grade B recommendation).

Lactulose versus Polyethylene Glycol for Chronic Constipation (Review)

Lee-Robichaud H, Thomas K, Morgan J, Nelson RL

THE COCHRANE COLLABORATION®

2010, Issue7

PEG es superior a lactulosa en :
1. Frecuencia de deposiciones/semana
2. Forma de las heces
3. Necesidad de productos adicionales

Adultos
Niños

Comparative Efficacy of Drugs for the Treatment of Chronic Constipation

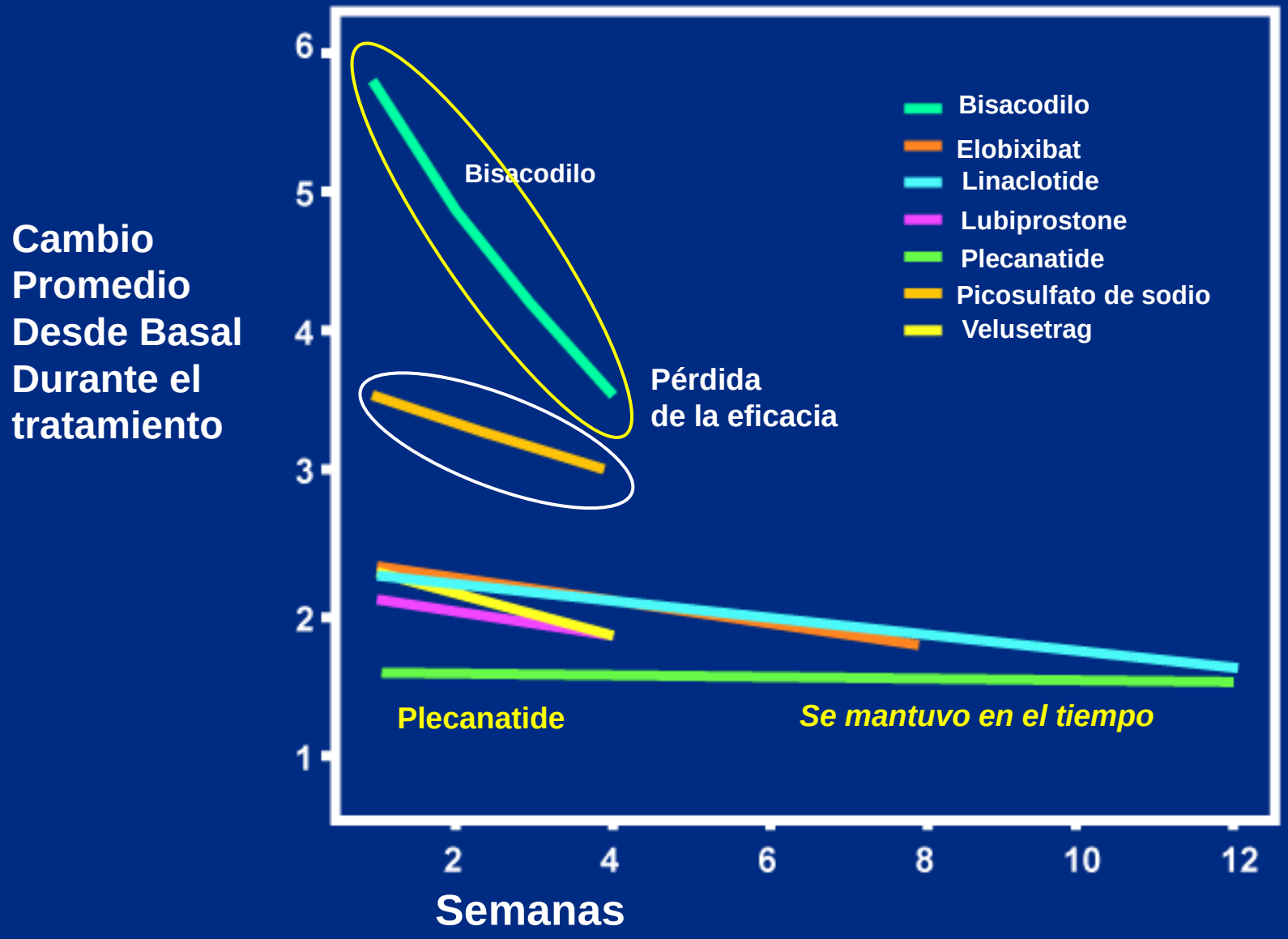
Quantitative Information for Medication Guidelines

Yi Zhang, MS, Fang Yin, PhD, Ling Xu, PhD, Yun-fei Li, PhD, Jun-chao Chen, PhD, Hong-xia Liu, PhD, Qing-shan Zheng, PhD, and Lu-jin Li, PhD

Meta-análisis basado en modelos
Técnica con resultados agrupados
Múltiples estudios, permite entendimiento global
Perfil de farmacodinamia
Características dosis-respuesta
Eficacia durante el tiempo
Explora influencias sobre el comportamiento

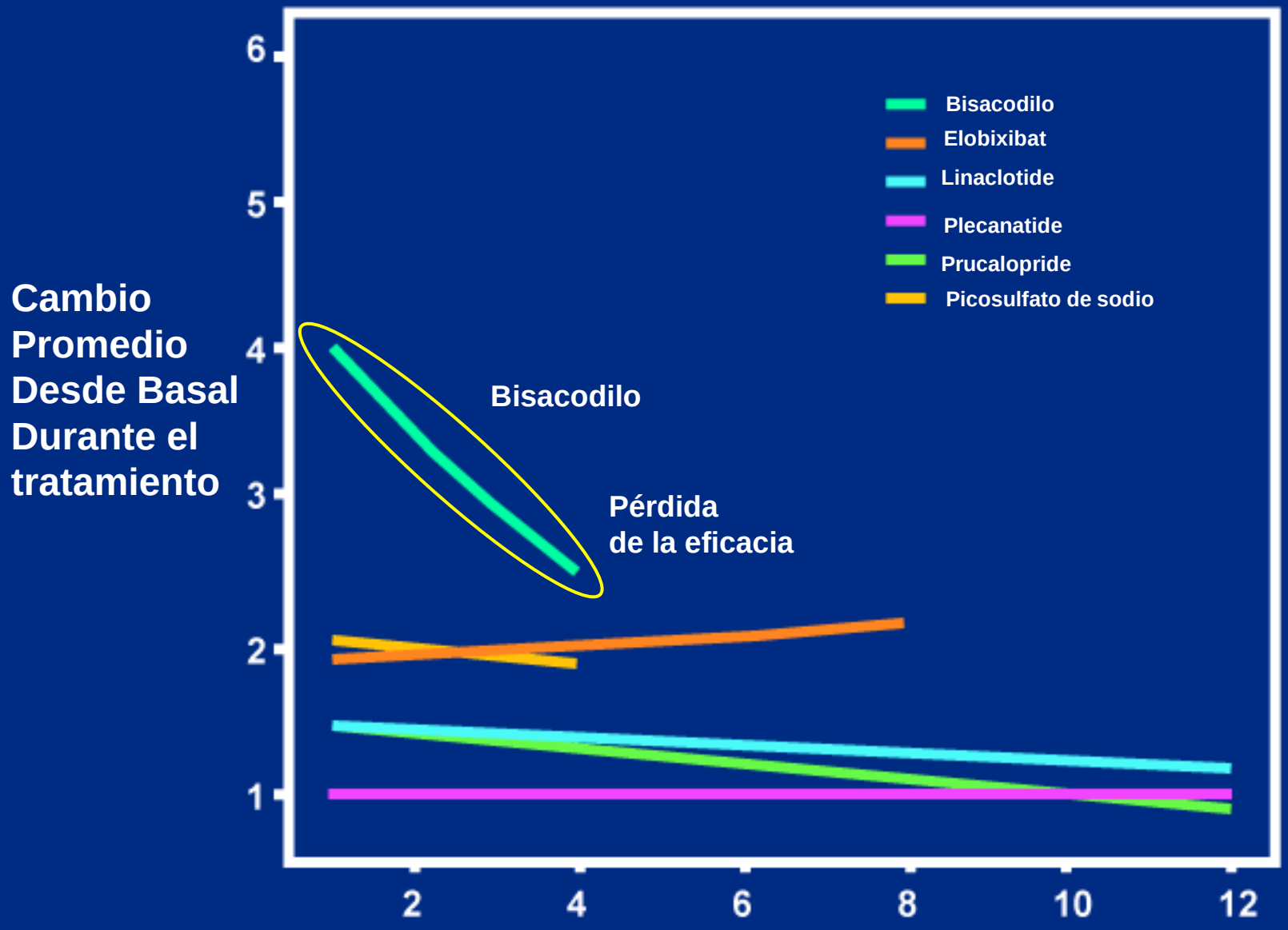
Zhang Y, J Clin Gastroenterol. 2020;54:e93-e102

Movimientos intestinales espontáneos



Zhang Y, J Clin Gastroenterol. 2020;54:e93-e102

Movimientos intestinales Completos espontáneos



Zhang Y, J Clin Gastroenterol. 2020;54:e93-e102

Treatments	Cost per Month, 2015 $	
Bulk agents		
Psyllium (10 g daily), range[b]	14.22	
Nonabsorbed substances		
Lactulose (20 g daily)	144.00	
PEG 3350 (17 g daily)[b]	18.25	***
Stimulants		
Senna (2 tabs daily)	0.34	
Bisacodyl (2 tabs daily)	0.75	
Secretory drugs		
Lubiprostone (24 µg twice daily)	293.02	
Linaclotide (145 µg daily)	283.70	

Wald A, *JAMA*. 2016;315:185-191

American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation

Lin Chang,[1,*] **William D. Chey**,[2,*] **Aamer Imdad**,[3,*] Christopher V. Almario,[4] Adil E. Bharucha,[5] Susan Diem,[6,7] Katarina B. Greer,[8,9] Brian Hanson,[6,10] Lucinda A. Harris,[11] Cynthia Ko,[12] M. Hassan Murad,[13] Amit Patel,[14] Eric D. Shah,[2,15] **Anthony J. Lembo**,[16,§] and **Shahnaz Sultan**[6,17,§]

Recommendations	Strength of recommendation	Certainty of evidence
Fiber		
Recommendation 1: In adults with CIC, the panel suggests the use of fiber supplementation over management without fiber supplements	Conditional	Low
Implementation considerations		

- Dietary assessment is important to determine total fiber intake from diet and supplements
- Fiber supplements can be used as first-line therapy for CIC, particularly for individuals with low dietary fiber intake
- Among the evaluated fiber supplements, only psyllium appears to be effective (with very limited and uncertain data on bran and inulin)
- Adequate hydration should be encouraged with the use of fiber
- Flatulence is a commonly observed side effect with the use of fiber

Chan L, et al. Gastroenterology 2023;164:1086-1106

Sales Mg

Lactulosa

	Fuerza recomendación	Certeza Evidencia
Recommendation 3: In adults with CIC, the panel suggests the use of magnesium oxide over management without magnesium oxide	Conditional	Very low
Implementation considerations • The trials were conducted for 4 wk, although longer term use is probably appropriate • The panel suggests starting at a lower dose, which may be increased if necessary • Avoid use in patients with renal insufficiency due to risk of hypermagnesemia		
Recommendation 4: In adults with CIC who fail or are intolerant to OTC therapies, the panel suggests the use of lactulose over management without lactulose	Conditional	Very low
Implementation considerations • Bloating and flatulence are dose-dependent and common side effects, which may limit its use in clinical practice		

Chan L, et al. Guís AGA, ACG, Gastroenterology 2023;164:1086-1106

Stimulant laxatives

	Fuerza recomendación	Certeza Evidencia
Recommendation 5: In adults with CIC, the panel recommends the use of bisacodyl or sodium picosulphate short term or as rescue therapy over management without bisacodyl or sodium picosulphate	Strong	Moderate

Implementation considerations

- Short-term use is defined as daily use for 4 wk or less. While long-term use is probably appropriate, data are needed to better understand tolerance and side effects
- This is a good option for occasional use or rescue therapy in combination with other pharmacological agents for CIC
- The most common side effects are abdominal pain, cramping and diarrhea. The panel suggests starting at a lower dose and increasing the dose as tolerated

Chan L, et al. Guís AGA, ACG, Gastroenterology 2023;164:1086-1106

Secretagogues

Lubiprostone

Recommendation 7: In adults with CIC who do not respond to OTC agents, the panel suggests the use of lubiprostone over management without lubiprostone	Conditional	Low

Implementation considerations

- Can be used as a replacement or as an adjunct to OTC agents
- Duration of treatment in trials was 4 wk, but the drug label does not provide a limit
- Nausea may occur; however, the risk of nausea is dose-dependent and seems to be lower when taken with food and water

Linaclotide

Recommendation 8: In adults with CIC who do not respond to OTC agents, the panel recommends the use of linaclotide over management without linaclotide	Strong	Moderate

Implementation considerations

- Can be used as a replacement or as an adjunct to OTC agents
- Duration of treatment in trials was 12 wk but the drug label does not provide a limit
- May be associated with side effects of diarrhea leading to discontinuation of treatment

Plecanatide

Recommendation 9: In adults with CIC who do not respond to OTC agents, the panel recommends the use of plecanatide over management without plecanatide	Strong	Moderate

Implementation considerations

- Can be used as a replacement or as an adjunct to OTC agents
- Duration of treatment in trials was 12 wk, but the drug label does not provide a limit
- May be associated with side effects of diarrhea leading to discontinuation of treatment

5-HT_4 agonist

Prucalopride

Recommendation 10: In adults with CIC who do not respond to OTC agents, the panel recommends the use of prucalopride over management without prucalopride	Strong	Moderate

American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation

Lin Chang,[1,*] **William D. Chey**,[2,*] **Aamer Imdad**,[3,*] Christopher V. Almario,[4] Adil E. Bharucha,[5] Susan Diem,[6,7] Katarina B. Greer,[8,9] Brian Hanson,[6,10] Lucinda A. Harris,[11] Cynthia Ko,[12] M. Hassan Murad,[13] Amit Patel,[14] Eric D. Shah,[2,15] **Anthony J. Lembo**,[16,§] and **Shahnaz Sultan**[6,17,§]

Osmotic Laxatives

Recommendation 2: In adults with CIC, the panel recommends the use of PEG compared with management without PEG (strong recommendation, moderate certainty of evidence).

Implementation considerations

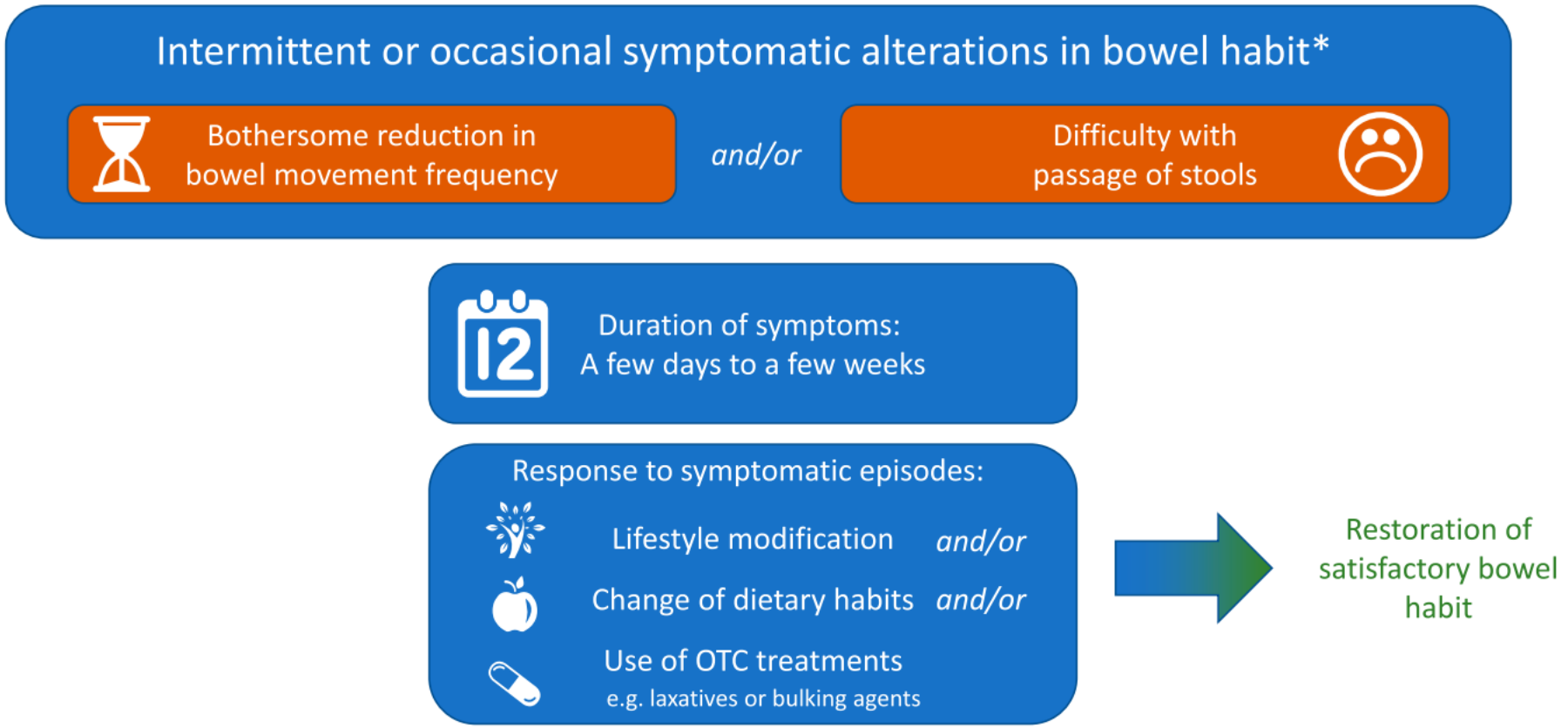
- A trial of fiber supplement can be considered for mild constipation before PEG use or in combination with PEG.
- Response to PEG has been shown to be durable over 6 months.
- Side effects include abdominal distension, loose stool, flatulence, and nausea.

	Fuerza recomendación	Calidad Evidencia
Osmotic laxatives		
Recommendation 2: In adults with CIC, the panel recommends the use of PEG compared with management without PEG	Strong	Moderate

Chan L, et al. Gastroenterology 2023;164:1086-1106

Recognizing and Defining Occasional Constipation: Expert Consensus Recommendations

Satish S.C. Rao, MD, PhD[1], Brian E. Lacy, MD, PhD[2], Anton Emmanuel, MD[3], Stefan Müller-Lissner, MD[4], Daniel Pohl, MD[5], Eamonn M.M. Quigley, MD[6] and Peter Whorwell, MD, PhD[7]

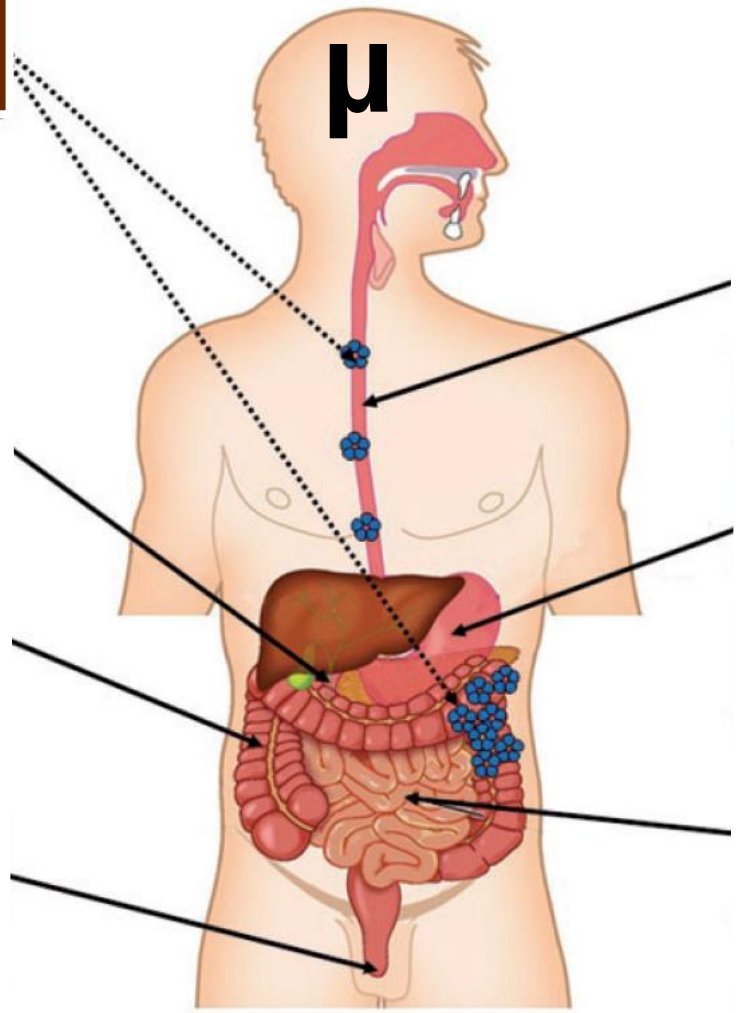


Rao SSC, et al. Am J Gastroenterol 2022;117:1753-8

Estreñimiento y opioides

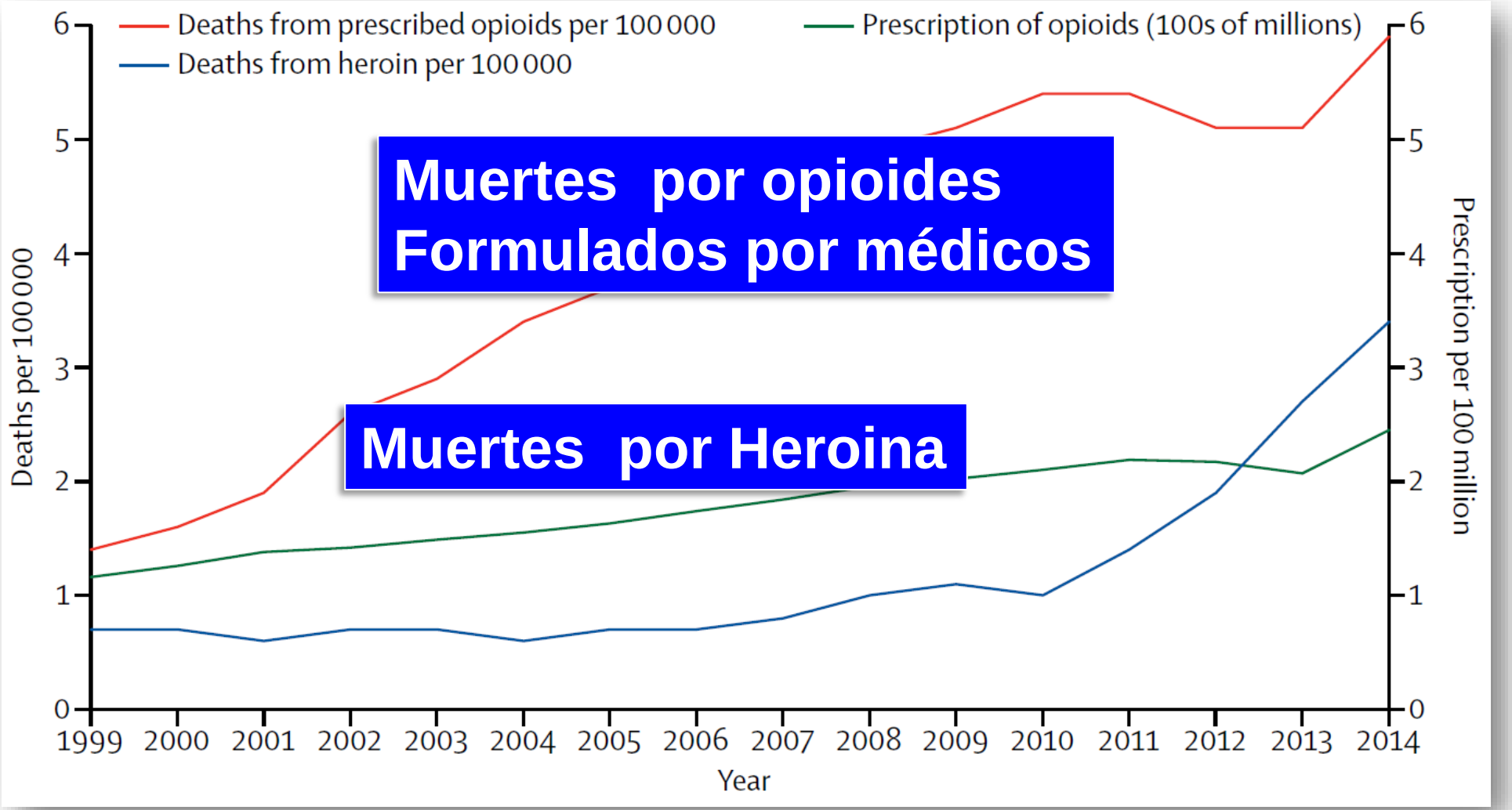
Intestino narcótico

μ



Farmer AD, United Eur Gastroenterol J 2019;7:7–20

Muertes por opioides USA

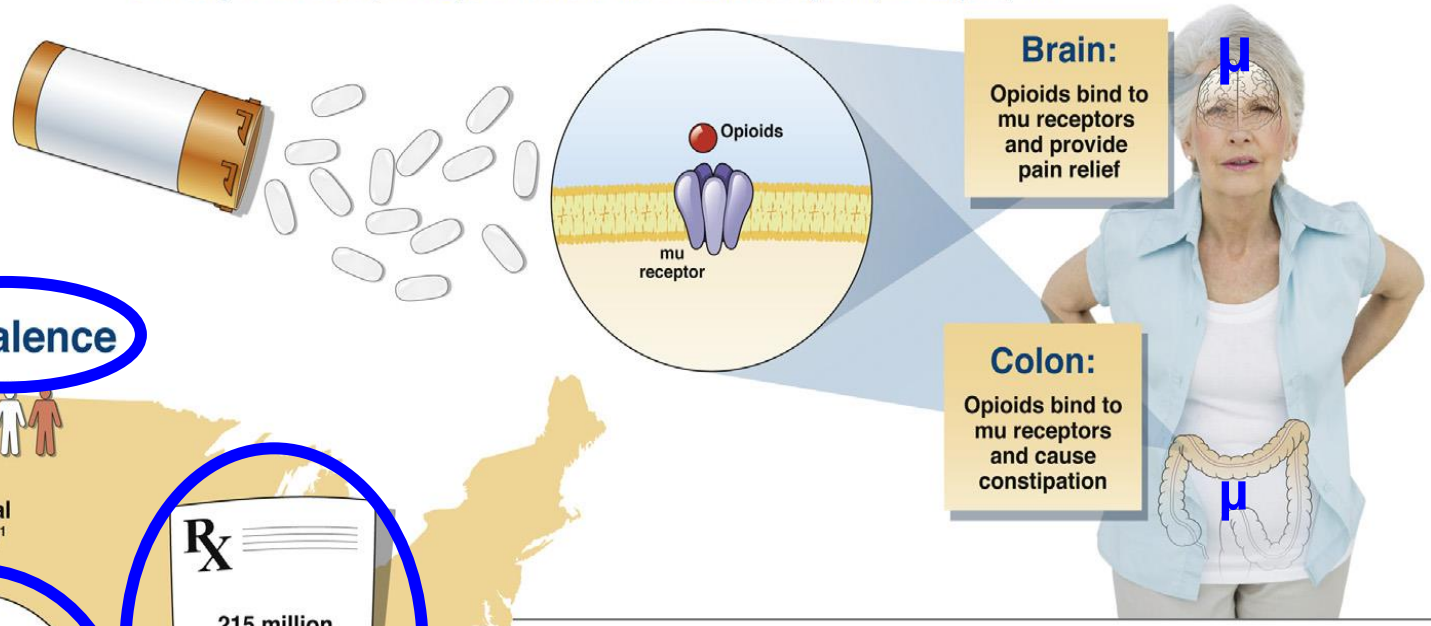


Fatmer AD, *Lancet Gastroenterol Hepatol* 2017; 2: 361–68

Opioid-Induced Constipation (OIC) Guideline

Seth Crockett, MD, MPH[1]; Katarina B. Greer, MD, MS[2]; Shahnaz Sultan, MD, MHSc[3]

[1]University of North Carolina School of Medicine, Chapel Hill, NC; [2]Division of Gastroenterology and Liver Disease, Department of Medicine, University Hospitals Cleveland Medical Center, Cleveland, OH; Department of Medicine, Louis Stokes Cleveland VA Medical Center, Cleveland, OH; [3]University of Minnesota, Minneapolis Veterans Affairs Healthcare System, Minneapolis, MN



Prevalence

Chronic pain affects 10%-15% of the general population (or 1 in 10)[1]

OIC affects up to 80% of patients taking chronic opioid therapy[3]

80%

215 million prescriptions for opioids are written in the US each year[2]

1. Mansfield et al. Pain 2016;157(1):55-64
2. CDC data, 2016
3. Bell et al. Pain Med. 2009; 10(1):35-42

The Rome IV criteria for OIC[4]

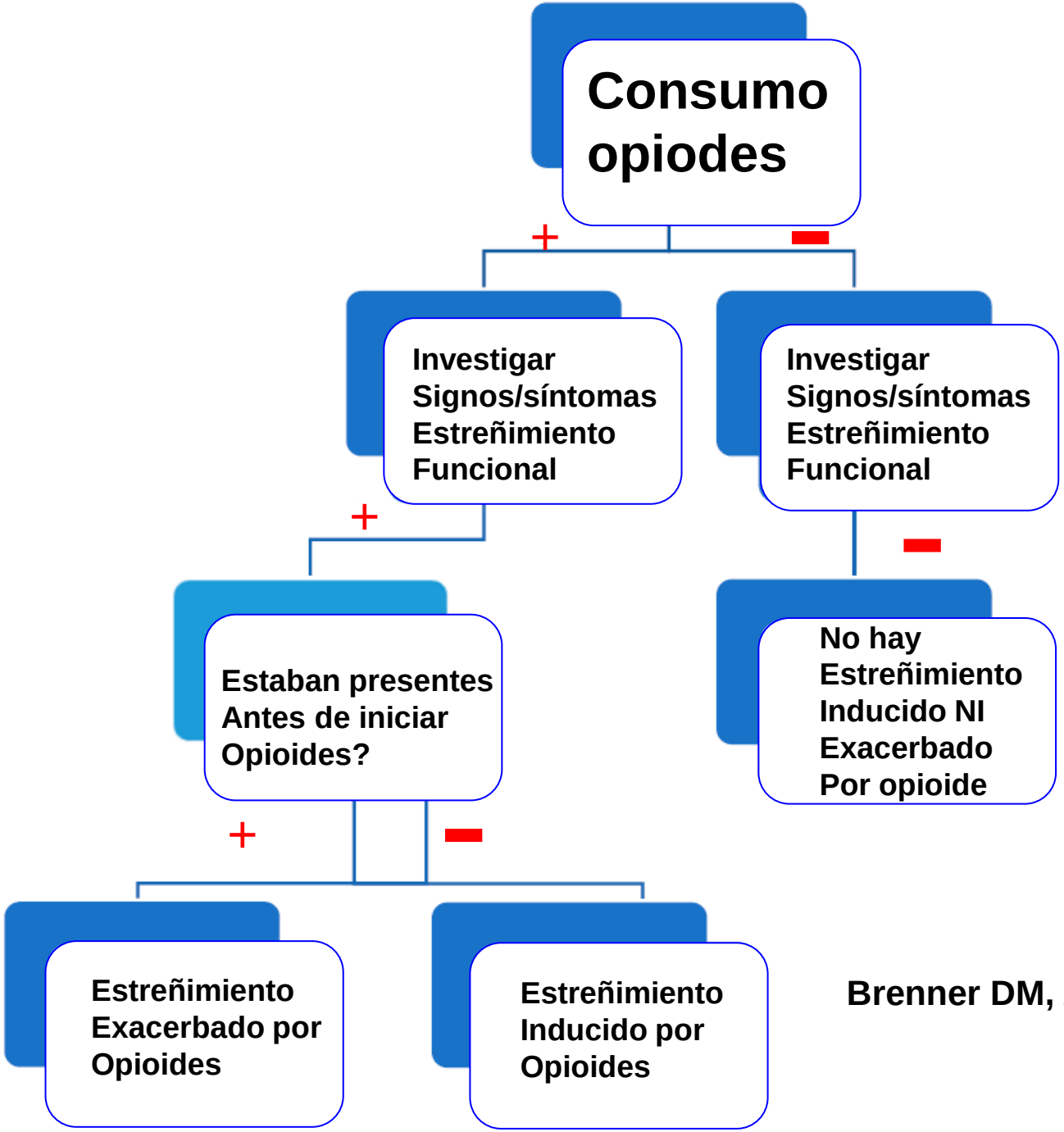
New, or worsening, symptoms of constipation when initiating, changing, or increasing opioid therapy, that must include 2 or more of the following > 25% of the time:

- Straining
- Lumpy/hard stools
- Sensation of incomplete evacuation
- Sensation of anorectal obstruction/blockage
- Manual maneuvers to facilitate defecations
- Reduced stool frequency (fewer than 3 spontaneous bowel movements per week)**

**With loose stools rarely present without the use of laxatives

[4]Lacy BE, Mearin F, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R. Bowel Disorders. *Gastroenterology*, 2016. 150(16) 1393-1407.

Crocket S, Gastroenterology 2019;156:229–253



Brenner DM, Am J Gastroenterol 2020;115:307-10.

Gastroenterology 2019;156:229–253

American Gastroenterological Association Institute Technical Review on the Medical Management of Opioid-Induced Constipation

Brian Hanson,[1,*] **Shazia Mehmood Siddique**,[2,*] Yolanda Scarlett,[3] and Shahnaz Sultan,[1] on behalf of American Gastroenterological Association Institute Clinical Guidelines Committee

UNITED EUROPEAN GASTROENTEROLOGY ueg journal

Review Article

United European Gastroenterology Journal
2019, Vol. 7(1) 7–20

DOI: 10.1177/2050640618818305
journals.sagepub.com/home/ueg
SAGE

Pathophysiology and management of opioid-induced constipation: European expert consensus statement

Adam D Farmer[1,2,3], Asbjørn M Drewes[2], Giuseppe Chiarioni[4,5], Roberto De Giorgio[6], Tony O'Brien[7,8], Bart Morlion[9] and Jan Tack[10]

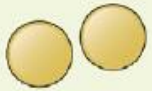
Adv Ther (2021) 38:3589–3621
https://doi.org/10.1007/s12325-021-01766-y

REVIEW

Management of Opioid-Induced Constipation and Bowel Dysfunction: Expert Opinion of an Italian Multidisciplinary Panel

Roberto De Giorgio · Furio Massimino Zucco · Giuseppe Chiarioni · Sebastiano Mercadante · Enrico Stefano Corazziari · Augusto Caraceni · Patrizio Odetti · Raffaele Giusti · Franco Marinangeli · Carmine Pinto

PAMORAs Antagonistas Periféricos Receptor μ

	Polyethylene glycol (Miralax)	Bisacodyl (Dulcolax)	Naldemedine (Symproic)	Naloxegol (Movantik)	Methylnaltrexone (Relistor)	Lubiprostone (Amitiza)	Prucalopride
							
Mechanism of action	**Osmotic laxative** *Draws water into intestine to hydrate and soften stool*	**Stimulant laxative** *Irritates sensory nerve endings to stimulate colonic motility*	**Peripherally acting mu opioid receptor antagonist (PAMORA)** *Blocks opioid receptors in the gut*	**Peripherally acting mu opioid receptor antagonist (PAMORA)** *Blocks opioid receptors in the gut*	**Peripherally acting mu opioid receptor antagonist (PAMORA)** *Blocks opioid receptors in the gut*	**Intestinal secretagogue** *Acts on chloride channels in the gut to stimulate fluid secretion*	**Selective 5-HT agonist** *Activates 5-HT4 receptor, leading to increased colonic motility and accelerated transit*
Route of administration	• Oral	• Oral • Suppository	• Oral	• Oral	• Oral • Subcutaneous injection	• Oral	• Oral
Recommended dose	17–34 g/day	5–15 mg/day	0.2 mg/day	12.5–25 mg/day	Oral: 450 mg/day SubQ: 12 mg/day	24 mcg twice daily	2 mg/day
Estimated monthly cost (USD)*	$	$	$$$	$$$	$$$$	$$$	Unknown: currently not FDA approved
AGA recommendation	In patients with OIC, the AGA recommends use of laxatives as first-line agents (strong recommendation, moderate quality evidence)	In patients with OIC, the AGA recommends use of laxatives as first-line agents (strong recommendation, moderate quality evidence)	In patients with laxative-refractory OIC, the AGA recommends naldemedine over no treatment (strong recommendation, moderate quality evidence)	In patients with laxative-refractory OIC, the AGA recommends naloxegol over no treatment (strong recommendation, moderate quality evidence)	In patients with laxative-refractory OIC, the AGA suggests methylnatrexone over no treatment (conditional recommendation, low quality evidence)	In patients with OIC, the AGA makes no recommendation for the use of lubiprostone (no recommendation, evidence gap)	In patients with OIC, the AGA makes no recommendation for the use of prucalopride (no recommendation, evidence gap)

Crocket S, Gastroenterology 2019;156:228

A Randomized, Multicenter, Prospective, Crossover, Open-Label Study of Factors Associated With Patient Preferences for Naloxegol or PEG 3350 for Opioid-Induced Constipation

Darren M. Brenner, MD[1], Yiqun Hu, MD, PhD[2], Catherine Datto, MD, MS[2], Dana Creanga, PhD[2] and Michael Camilleri, MD[3]

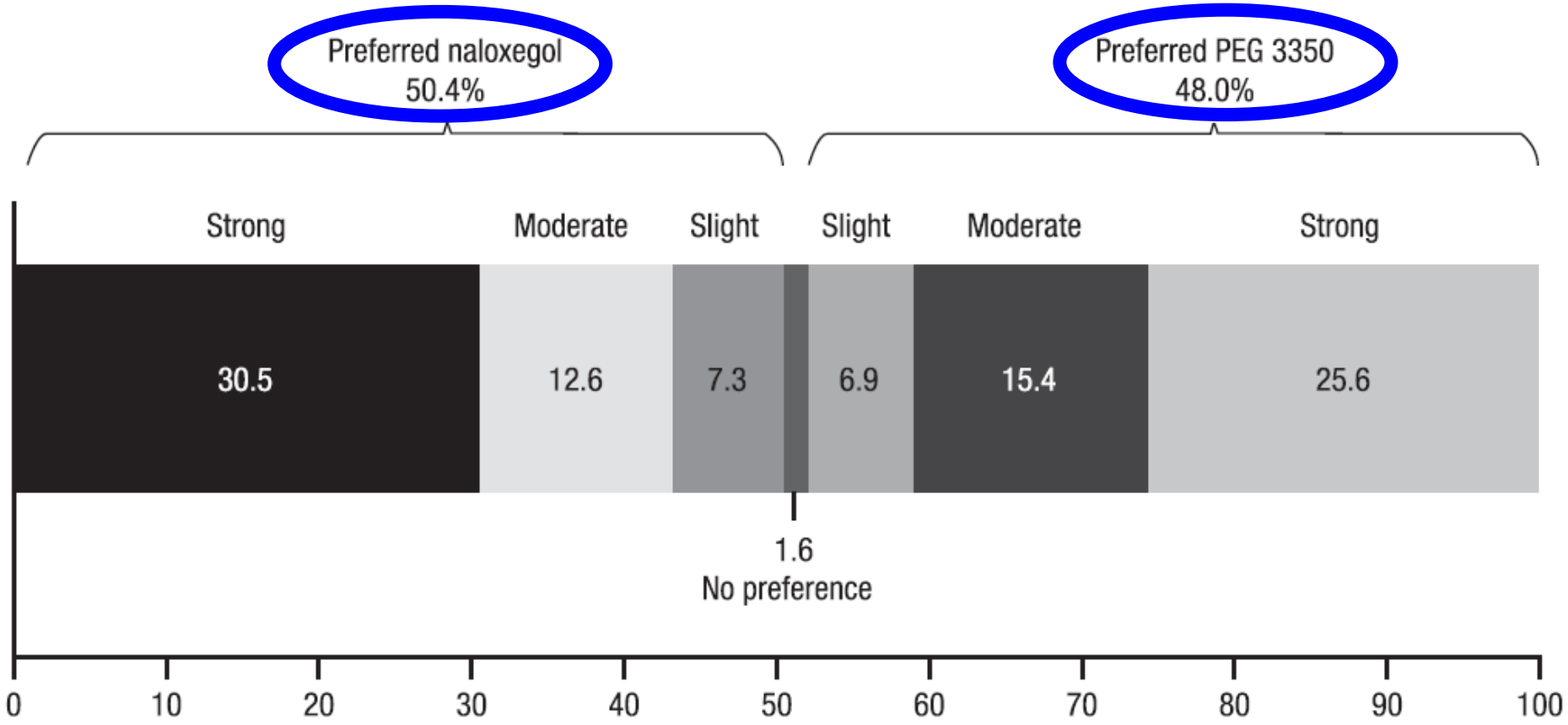
Brenner DM, Am J Gastroenterol 2019;114:954–63.

Table 3. TEAEs with an incidence ≥2% in either treatment group (safety-analysis population)

System organ class Preferred term	Naloxegol (n = 271)	PEG 3350 (n = 268)
Gastrointestinal disorders	44 (16.2)	29 (10.8)
Abdominal pain	15 (5.5)	6 (2.2)
Upper abdominal pain	10 (3.7)	4 (1.5)
Diarrhea	11 (4.1)	4 (1.5)
Flatulence	9 (3.3)	9 (3.4)
Nervous system disorders	12 (4.4)	0 (0.0)
Headache	6 (2.2)	0 (0.0)

PEG, polyethylene glycol; TEAE, treatment-emergent adverse event.

Brenner DM, Am J Gastroenterol 2019;114:954–63.



Similar mejoría del estreñimiento

Brenner DC, Am J Gastroenterol 2019;114:954–96

A randomized double-blind placebo-controlled trial showing to improve constipation by reducing methane production and accelerating colon transit: A pilot study

Uday C. Ghoshal [1] · Deepakshi Srivastava [1] · Asha Misra [1]

Estreñimiento crónico >> CH4 controles
Rifaximina 400 g 3v/d 14 días << CH4 vs placebo
TT colónico Mejoró Rifaximina vs placebo
> Deposiciones Rifaximina vs placebo

Ind J Gastroenterol Nov 18, 2018

DDW2020
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SIBO en estreñimiento refractario

Previous Next

Sa1708 — 2020

Poster of Distinction AGA

SMALL INTESTINAL BACTERIAL OVERGROWTH IN REFRACTORY CONSTIPATION IS ASSOCIATED WITH DELAYED COLONIC TRANSIT, BUT NOT DYSSYNERGIC DEFECATION

Estreñimiento refractario tránsito lento
61% IMO ➡ CH4,
Defecación disinérgica NO IMO

Colorectal Diseases
Constipation and Other Functional Colonic Syndromes
Presented on Saturday, May 2, 2020 12:30 PM

Author(s): Samuel Tanner[1], Ahson Chaudhry[1], Navneet Goraya[1], Rohan Badlani[1], Asad

[1] Temple University Hospital, Philadelphia, Pennsylvania, United States

Introduction: Small intestinal bacterial overgrowth (SIBO) is known to cause symptoms such as abdominal bloating, distension, and gas. SIBO has also been associated with diarrhea and constipation, although the exact pathophysiology is less clear. In this study, we correlate both the presence and subtypes of SIBO to whole gut transit (gastric emptying (GE), small bowel transit (SBT), and colonic transit (CT)) and anorectal function in patients referred to a tertiary motility center with refractory constipation. **Methods:** Lactulose breath testing (LBT), whole gut transit scintigraphy (WGTS), and high resolution anorectal manometry (HR-ARM) of consecutive patients being evaluated for refractory constipation between 6/2016 and 11/2019 were included. LBT was performed using the BreathTracker Analyzer (QuinTron Instruments). SIBO by hydrogen (H-SIBO) was defined as a rise of 20 ppm in hydrogen from baseline within the first 90 minutes of testing. SIBO by methane (M-SIBO) was defined as a peak value of >10ppm. CT was assessed by WGTS using the geometric center of radioactivity from cecum/ascending colon (region 1) to rectosigmoid (region 6) and excreted stool (region 7). HR-ARM was performed using ManoScan™ and analyzed using ManoView™ software (Medtronic). **Results:** 222 patients with refractory constipation completed LBT and WGTS. Of these patients, 201 also completed HR-ARM. SIBO was diagnosed in 137 patients (61%). This comprised of 53 patients with H-SIBO, 47 with M-SIBO, and 37 with both H-SIBO & M-SIBO. ***Colonic Transit:*** Patients with SIBO had slower CT at 48 h and 72 h (Table 1, both $p<0.01$), but no significant difference in GE, SBT, or CT at 24 h. M-SIBO, in particular, had slower CT at 48 h and 72 h compared to H-SIBO and H-SIBO & M-SIBO ($p=0.02$ and $p=0.01$, respectively). Baseline methane level was negatively correlated to CT at 72 h ($r=-0.36$, $p<0.001$). This correlation was stronger in patients with M-SIBO vs. M-SIBO & H-SIBO ($r=-0.49$, $p<0.01$ vs. $r=-0.12$, $p=0.48$). ***Anorectal Function:*** Patients with SIBO had a lower mean anal sphincter pressure (62.5±2.3 vs. 73.7±2.2 mm Hg, $p<0.001$). Lower mean anal sphincter pressure was seen in H-SIBO and M-SIBO, but not combined M-SIBO and H-SIBO ($p=0.03$). Otherwise, the presence of SIBO was not associated with differences in dyssynergic defecation or abnormal balloon expulsion testing and there were no statistically significant differences among SIBO subtypes (although sample size is small). **Conclusions:** SIBO is common in patients with refractory constipation. It was found in 61% of patients referred to our center. SIBO, and in particular M-SIBO, is associated with delayed CT, but not dyssynergic defecation. Baseline methane level correlates with CT. This suggests that methane in particular may play a role in the pathophysiology of delayed CT.

SIBO asociado a CH4

Methanosphaera stadtmaniae
Methanobrevibacter smithii

Estreñimiento

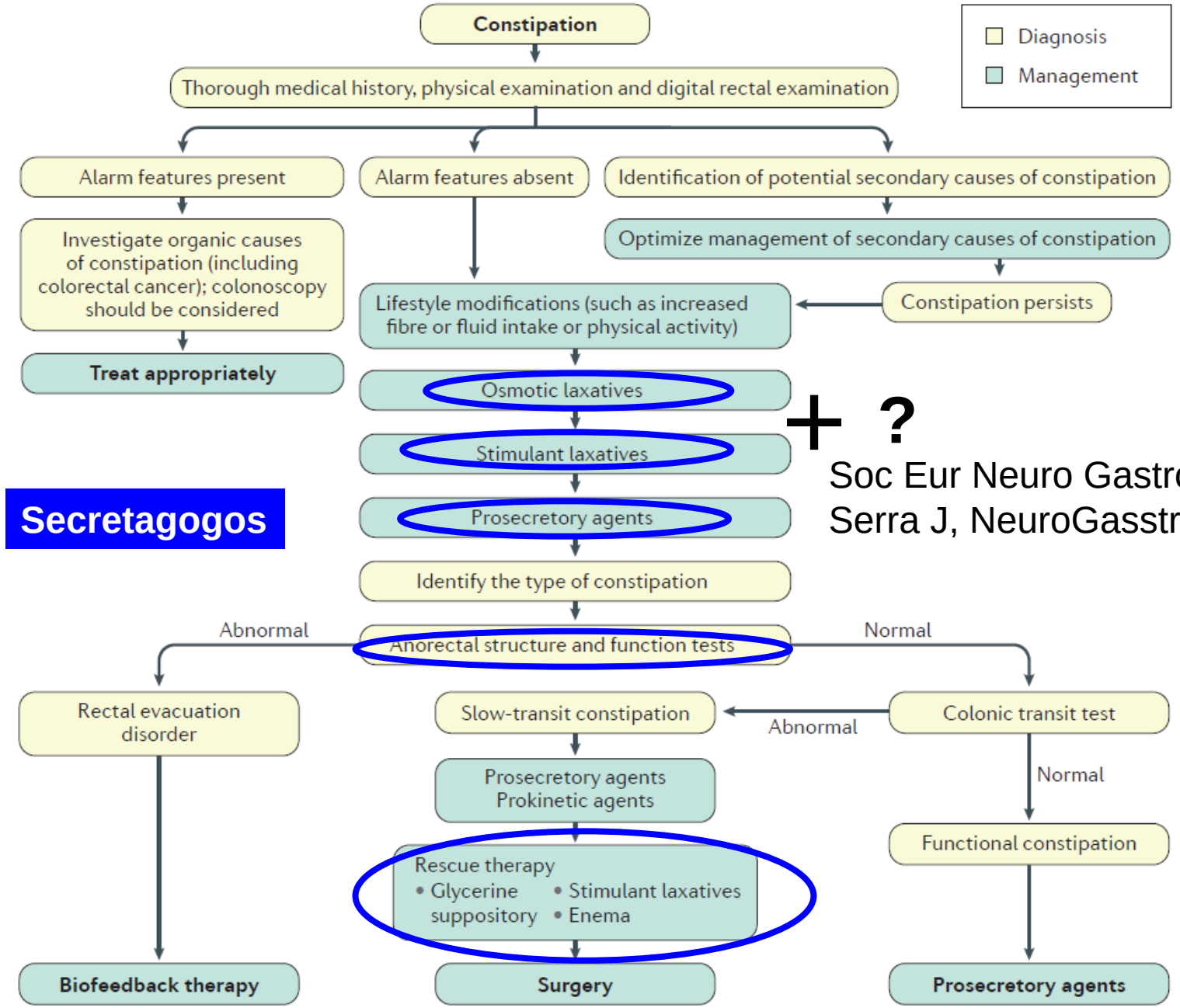
Neurotransmisor anticolinérgico Sistema nerviosos entérico

Pimentel M, Am J Physiol Gastrointest Liver Physiol 2006;290:G1089-95
Park YM, Neurogastroenterol Motil 2017;29:e113077
Suri J, Med (Baltimore) 2018;97:10554

Cómo maneja el médico General y el especialista de muchos sitios LATAM el Estreñimiento ?

30%

En el 2023 hay más Conocimiento



Secretagogos

\+ ?

Soc Eur Neuro Gastro Motill
Serra J, NeuroGasstroenterol Motil 2021

Camilleri M, Nat Revi Dis Prim 2017;3:Art 1709

40-50% insatisfechos Con el tratamiento farmacológico

Tratamiento no farmacológico

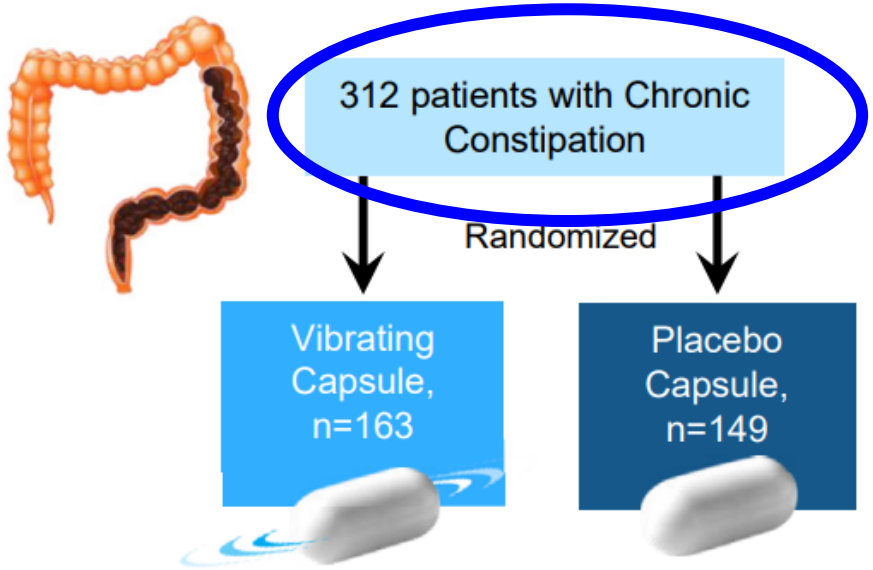
Oh SJ, Am J Gastroenterol 2020;115:895-905
Basilisco G, Aliment Pharmacol Ther 2020;51:629-36

Randomized Placebo-Controlled Phase 3 Trial of Vibrating Capsule for Chronic Constipation

Satish S. C. Rao,[1] Eamonn M. M. Quigley,[2] William D. Chey,[3] Amol Sharma,[1] and Anthony J. Lembo[4]

Vibrating Capsule Treatment for Chronic Constipation

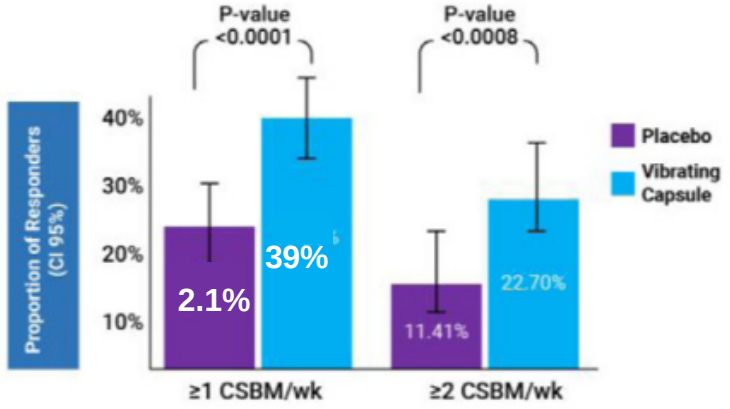
Phase 3, Double Blind, Multicenter, Placebo controlled trial



- Patients ingested one capsule at bedtime daily for 5 days a week
- Duration of study= 8 weeks

Primary Outcome Measures:
Increase in one or more or two or more complete spontaneous bowel movements (CSBM) per week over baseline in 6 out of 8 weeks

Effect of Vibrating Capsule on CSBM, Primary Outcomes



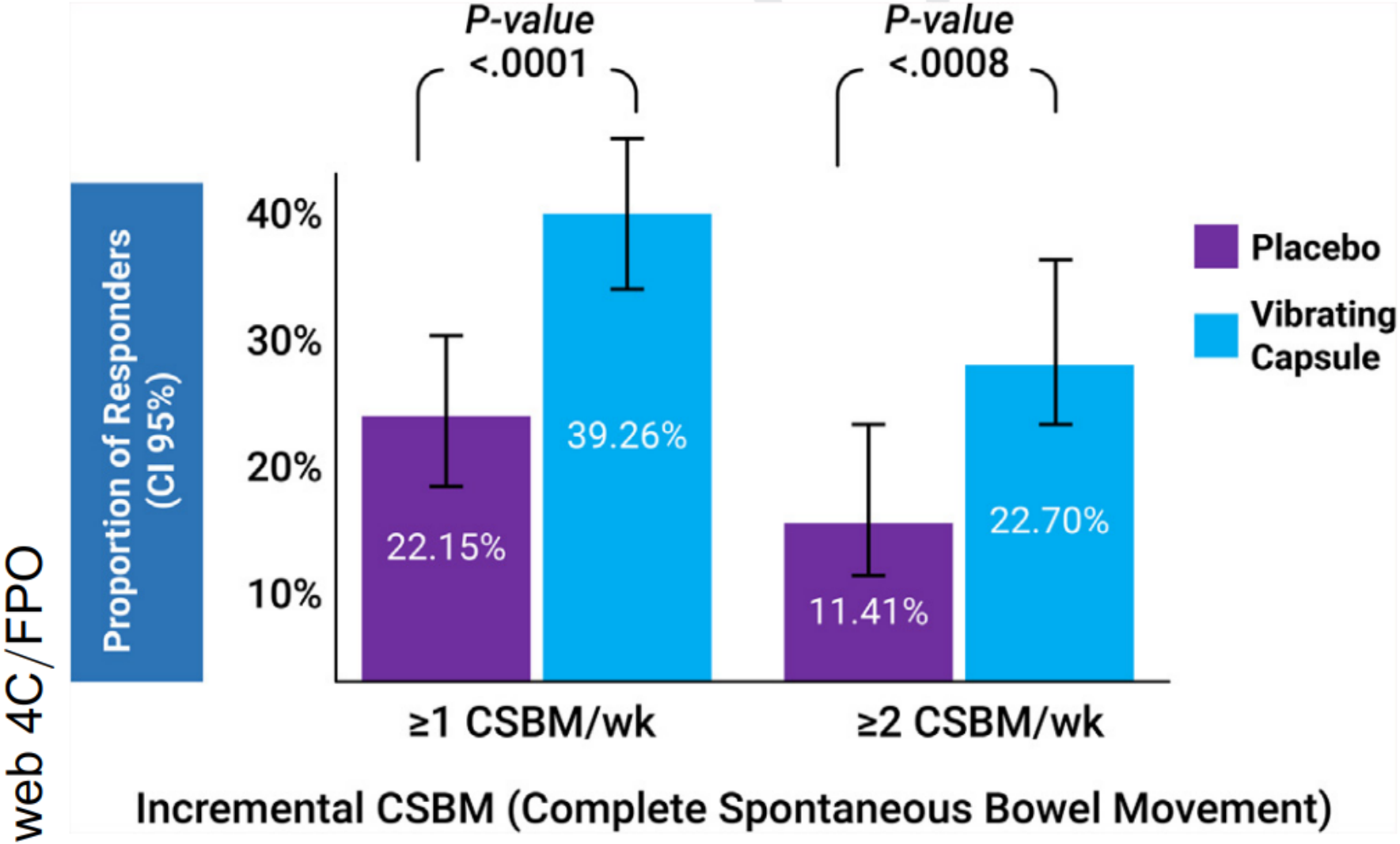
Incremental CSBM (Complete Spontaneous Bowel Movement)

Vibrating Capsule was superior to Placebo capsule in improving constipation symptoms and quality of life, and was safe and well tolerated

Rao SSC Gastroenterology 2023; Febrero 20

Randomized Placebo-Controlled Phase 3 Trial of Vibrating Capsule for Chronic Constipation

Satish S. C. Rao,[1] Eamonn M. M. Quigley,[2] William D. Chey,[3] Amol Sharma,[1] and Anthony J. Lembo[4]



Rao SSC Gastroenterology 2023; Febrero 20

Randomized Placebo-Controlled Phase 3 Trial of Vibrating Capsule for Chronic Constipation

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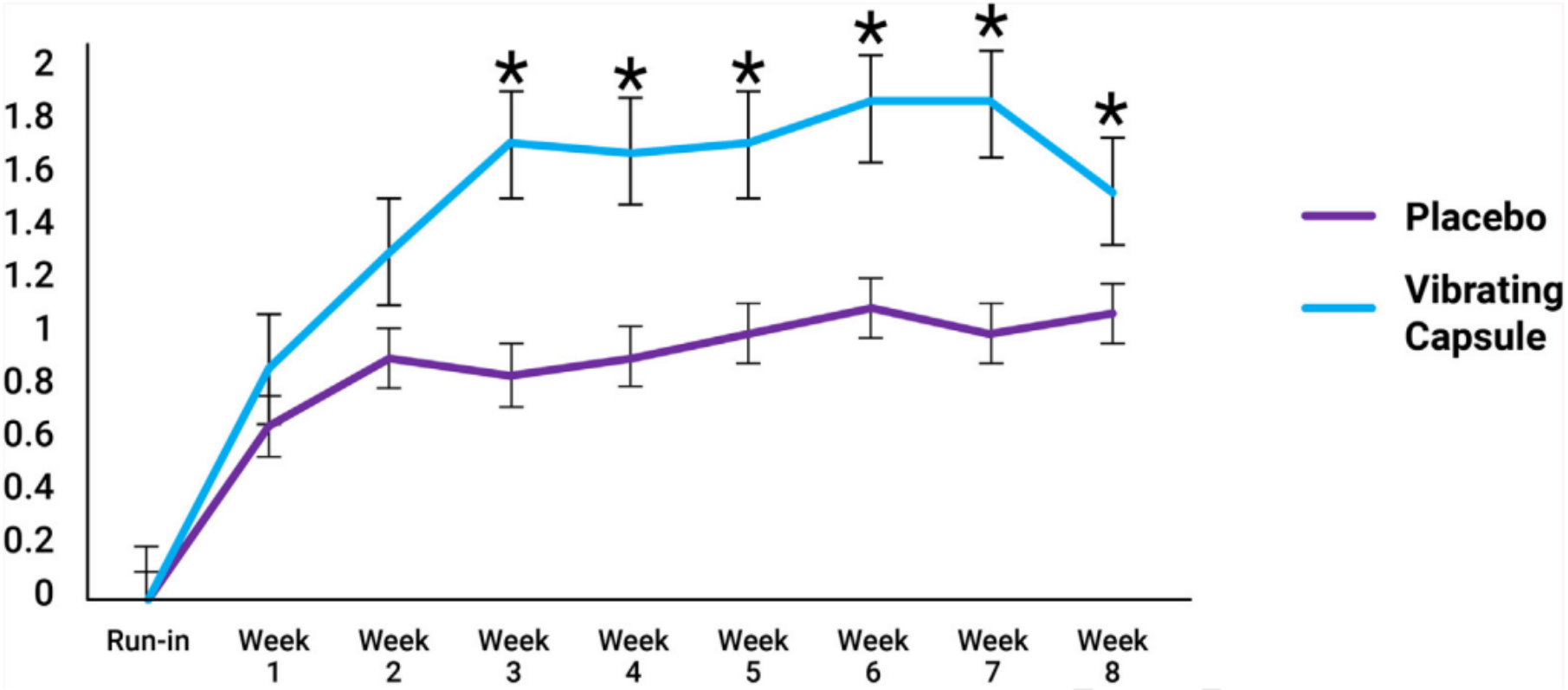


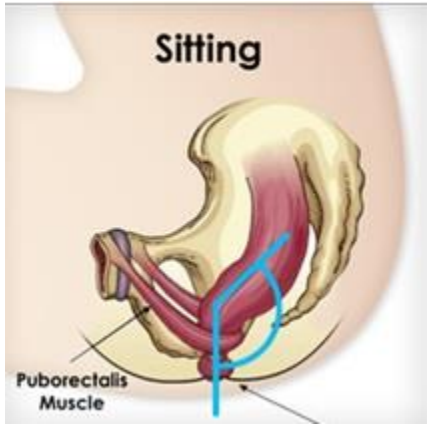
Figure 4. The change from baseline in the mean weekly $CSBM_1$ rate during the entire trial period.

Rao SSC Gastroenterology 2023; Febrero 20

Mensajes para la casa

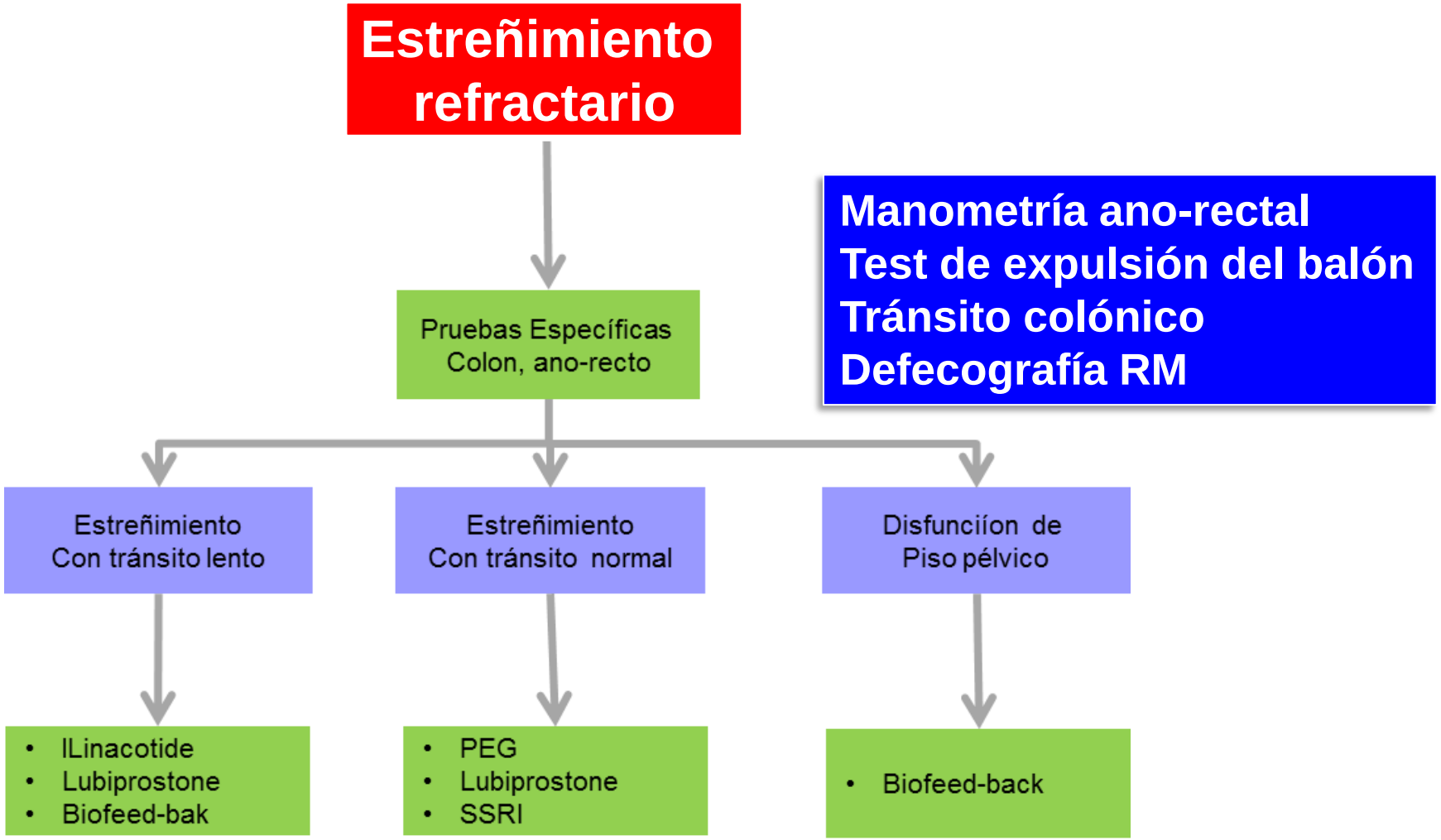
La “fibra y el agua” no es el único tratamiento
PEG primera línea 17-34 g, niños, útil opioides
PEG eficaz, seguro más económico
Prucalopride 1-2 mg/día
Lubiprostone 24 mcg/2v/dìa
Linaclotide 290 mcg/día
Colonoscopia tiene indicaciones
Defecación obstructiva exámenes biofeedback
SII-E no es diferente al EC primario
En la práctica tratamiento es similar

Así es más fisiológico



Siempre tacto rectal

Muchas gracias!



Manometría ano-rectal
Test de expulsión del balón
Tránsito colónico
Defecografía RM

Cirugía

Colectomia subtotal
Ileo-recto-anastomosis
Colostomia, ileostomìa

Estreñimiento-Síntoma

Estreñimiento Funcional

Disminución tránsito colónico
< Contracciones alta amplitud
Tránsito lento
Disinergia piso pélvico

Microbiota Metanogénica
Responden similar
Defecación Disinérgica

SII Estreñimiento

Hipersensibilidad visceral
Alodinia, hiperalgesia
> Permeabilidad
SIBO
Disinergia piso pélvico

Whitehead WE, Neurogastroenterol Motil 2016;28:783-92
Takakura W, Pimentel M. Front Psych 2020;11:Art 664

SII con Estreñimiento ?

Estreñimiento Funcional ?

Tranquilo:
Mientras la ciencia lo descubre

Los remedios son similares

El dolor requiere otros medicamentos

Anti espasmódicos, Rifaximina, SII