Bile Acid Malabsorption in Crohn's Disease: Worth looking for?

Dr. Jordi Guardiola

Hospital Universitari de Bellvitge-IDIBELL

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- How frequent is BAM in CD?
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Are clinical symptoms in CD explained by the underlying inflammation?

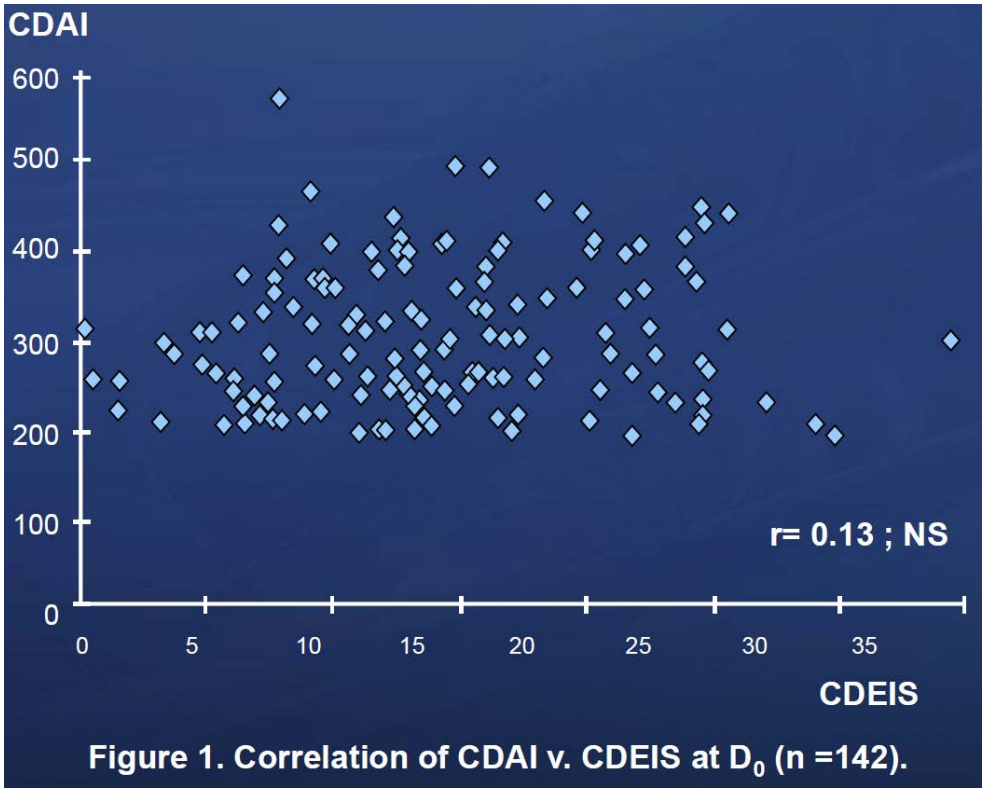

Figure 1. Correlation of CDAI v. CDEIS at D_0 (n =142).

Symptomps in CD:

- Underestimate endoscopic activity in 40% of patients in clinical remission.
- Overestimate endoscopic activity in 20% of symptomatic patients.

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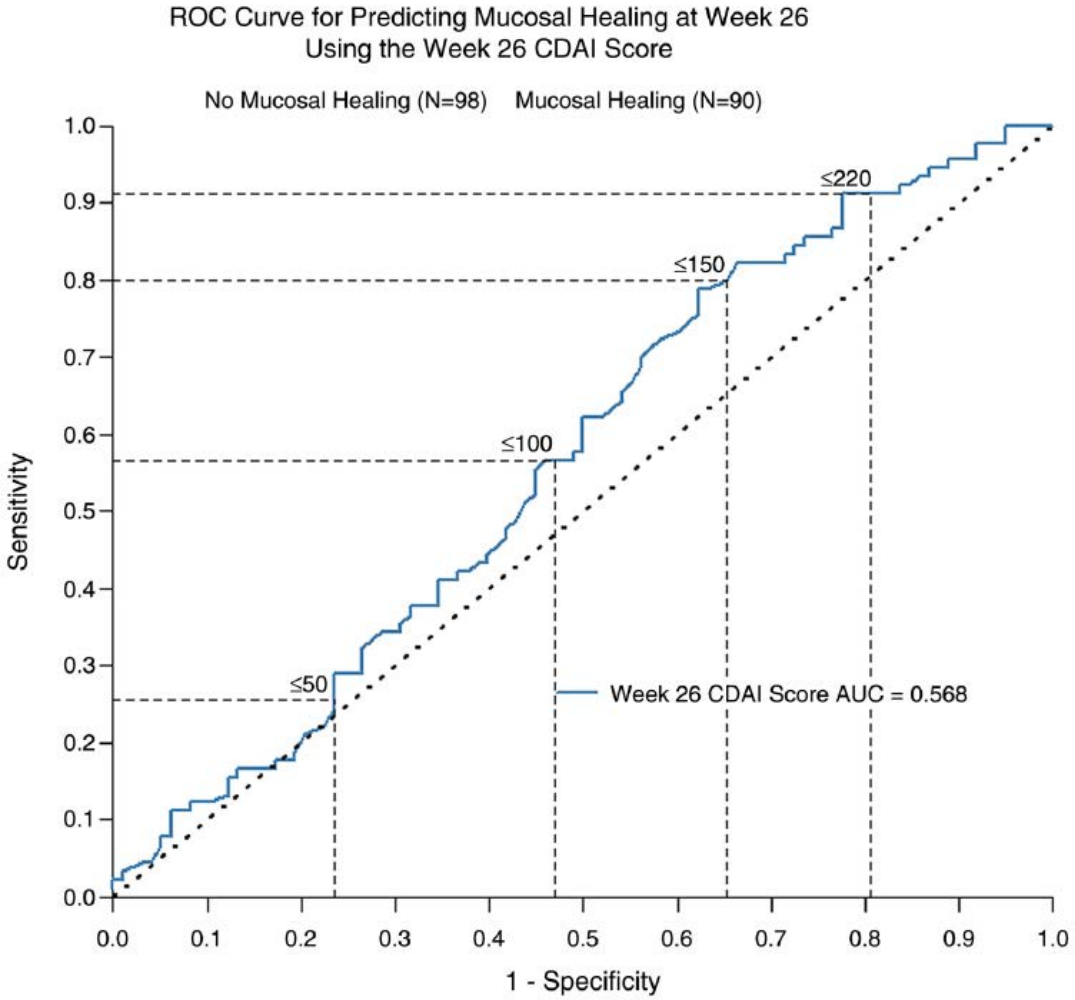
Modiglani et al. Gastroenterology. 1990 Apr;98(4):811-8.

Are clinical symptoms in CD explained by the underlying inflammation?



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Peyrin-Biroulet L et al. Gut Published Online: doi:10.1136/gutjnl-2013-304984.

IBS-Type Symptoms in IBD: Systematic Review and Meta-Analysis

Stephen J. Halpin and Alexander C. Ford

- **39 %** of CD patients meet criteria for IBS (8 studies including 616 patients).
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Odds ratios for IBS in IBD patients vs. controls without IBD, and according to disease activity and disease type

	Number of studies	Number of subjects	Pooled OR	95% confidence interval
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Am J Gastroenterol 2012; 107:1474– 1482

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Bile acid malabsorption in Crohn's disease and indications for its assessment using SeHCAT

H Nyhlin, M V Merrick, M A Eastwood

TABLE IV *Outcome of SeHCAT in Crohn's disease patients with and without bowel resection*

SeHCAT retention	*Bowel resection (n=26)*	*No resection (n=25)*
<5%	23	7
5–10%	3	1
>10%		17

TABLE V *Cholestyramine, effectiveness on symptoms in relation to SeHCAT results*

SeHCAT retention	*Effective*	*Not effective*
<5%	18	1
5–10%	–	2
>10%	1	–

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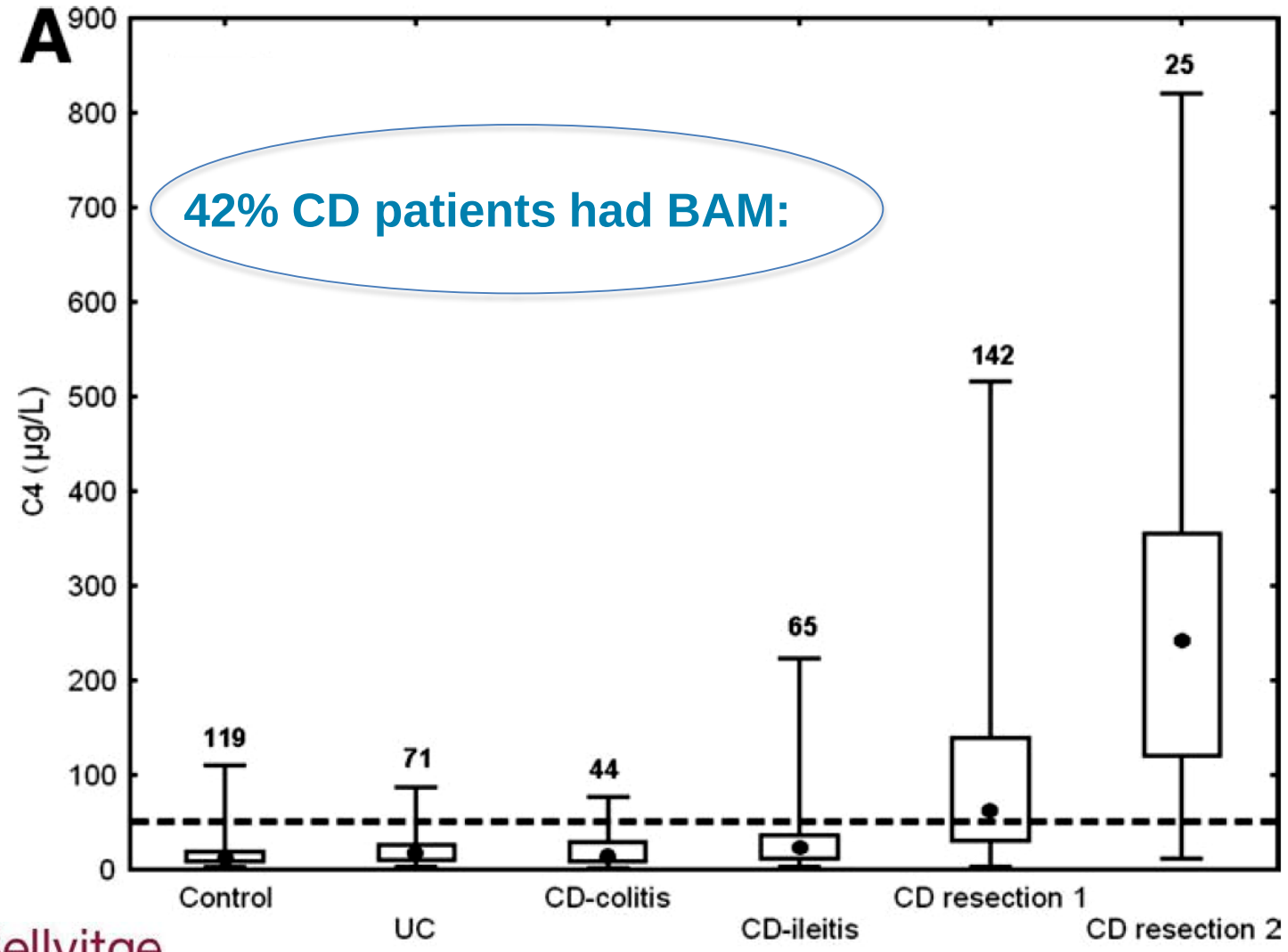
Gut 1994; 35: 90-93

Bile Acid Malabsorption in Inflammatory Bowel Disease: Assessment by Serum Markers

Martin Lenicek, *et al.*



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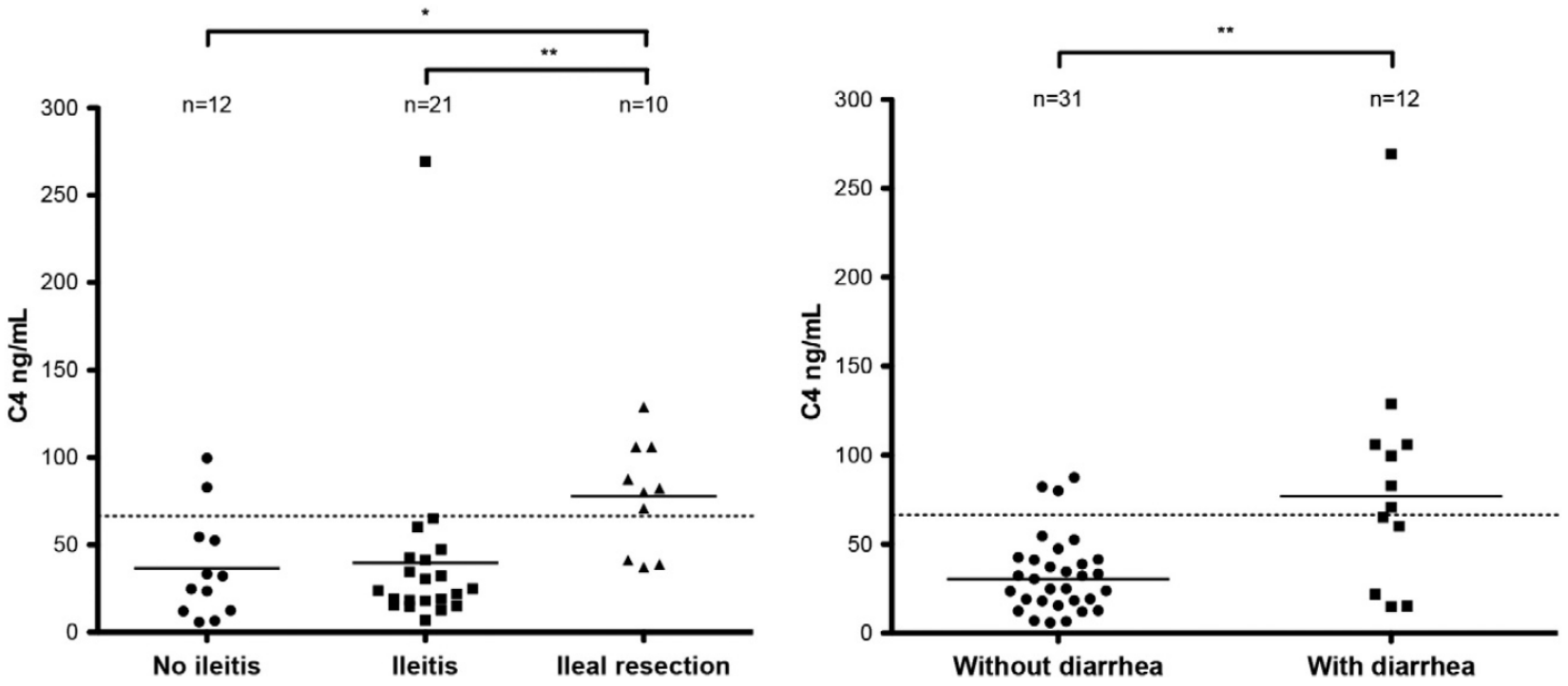
Inflamm Bowel Dis 2011;17:1322–1327

Bile acid malabsorption assessed by 7 alpha-hydroxy-4-cholesten-3-one in pediatric IBD: Correlation to clinical and laboratory findings.

F. Gothe , *et al.*

Crohn's Disease



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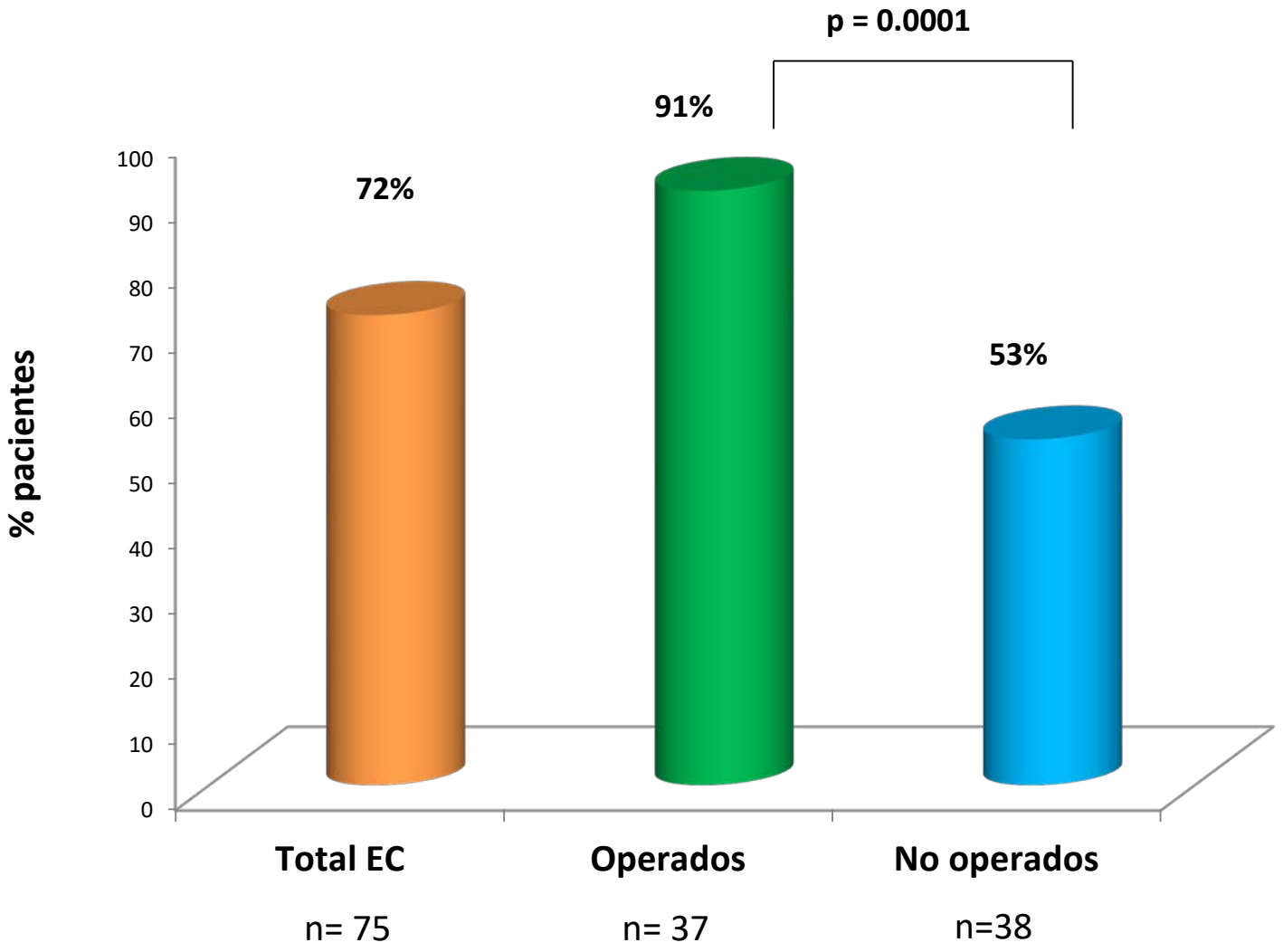
J Crohns Colitis (2014), http://dx.doi.org/10.1016/j.crohns.2014.02.027

Prevalence of BAM in Crohn's disease patients



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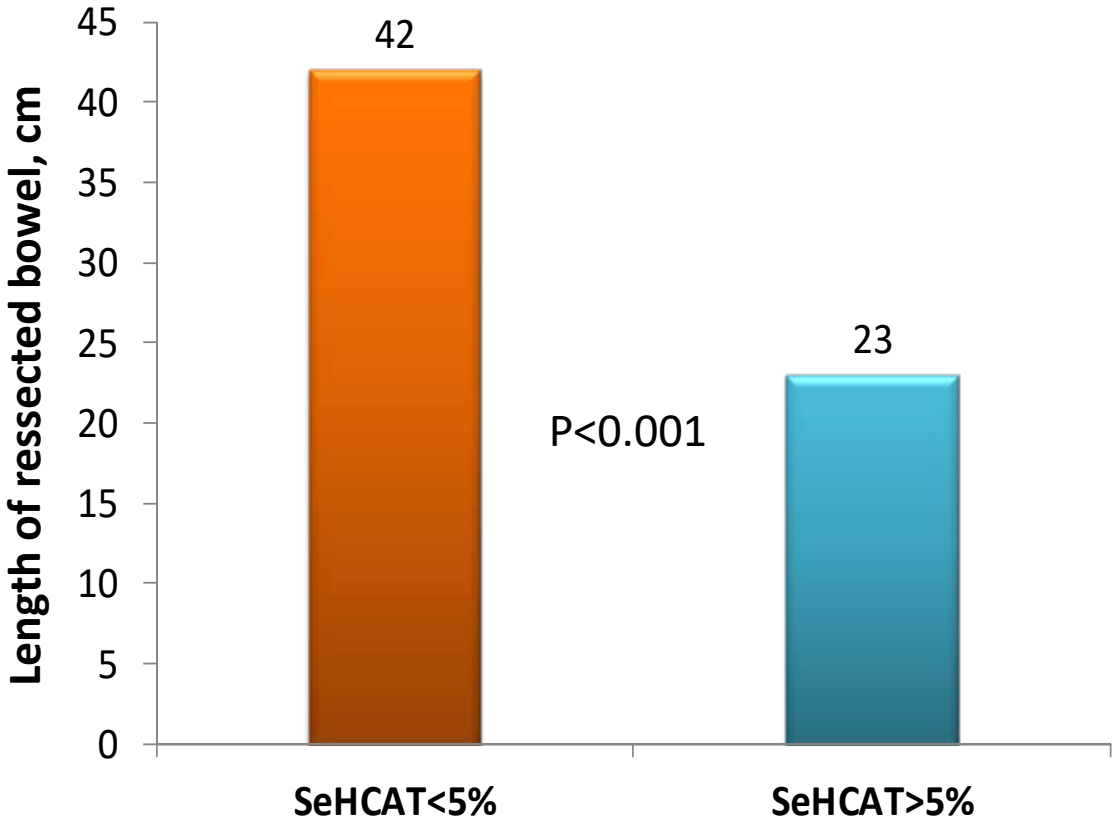
Ruiz-Cerulla et al. ECCO 2014

Length of ressected bowel according to the presence Severe BAM



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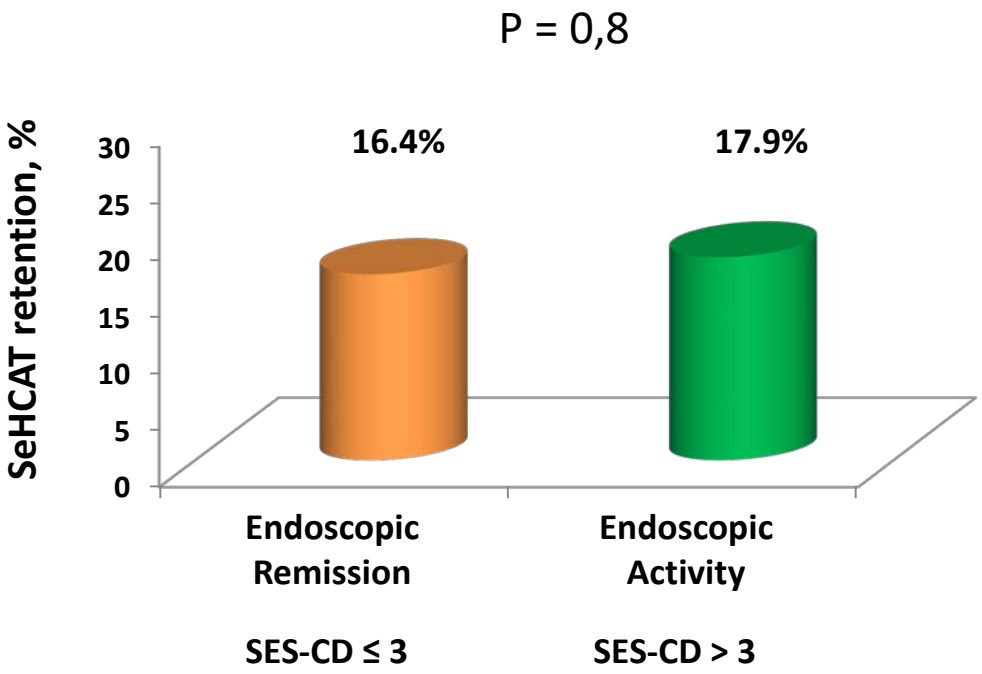
Ruiz-Cerulla et al. ECCO 2014

SeHCAT retention according to the presence of endoscopic lesions



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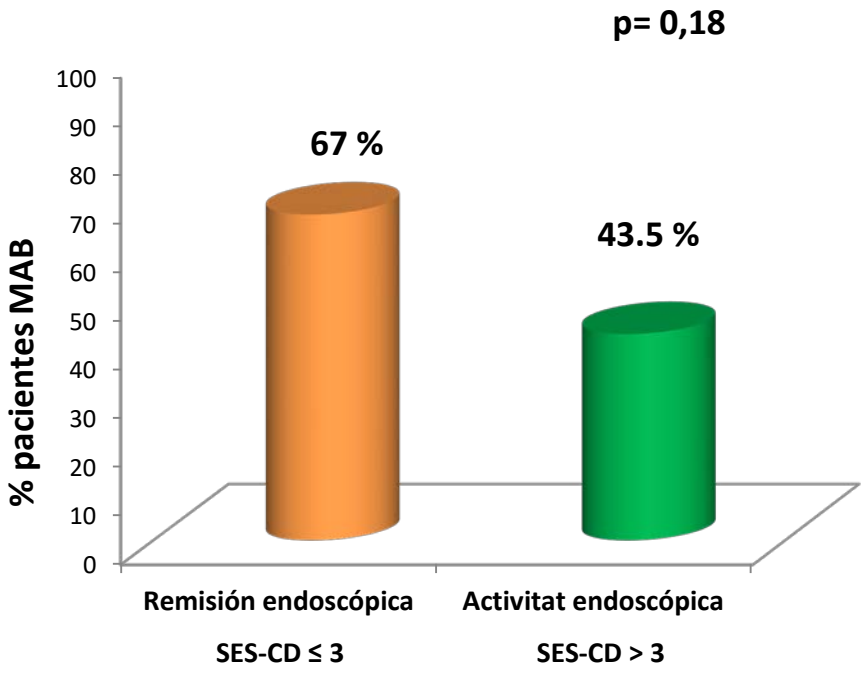
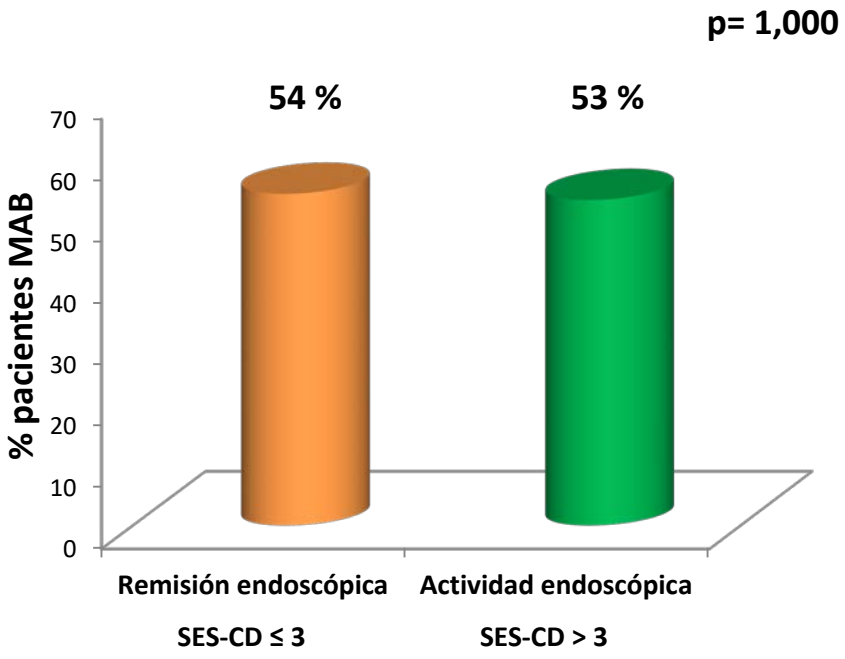
MAB en función de la actividad endoscópica en EC no operada



MAB en función de la actividad endoscópica en EC ILEAL no operada



Gut, **1979, 20,** 1072-1077

Bile acid studies in patients with Crohn's colitis

P. RUTGEERTS, Y. GHOOS, AND G. VANTRAPPEN
From the Department of Medical Research, University of Leuven, Leuven, Belgium

Br J Surg. **1994** Feb;81(2):289-90.

Ileal bile acid malabsorption in colonic Crohn's disease.

Davie RJ, Hosie KB, Grobler SP, Newbury-Ecob RA, Keighley MR, Birch NJ.

J. R. Coll. Physicians Lond, 2000; 34(5), 448–451.

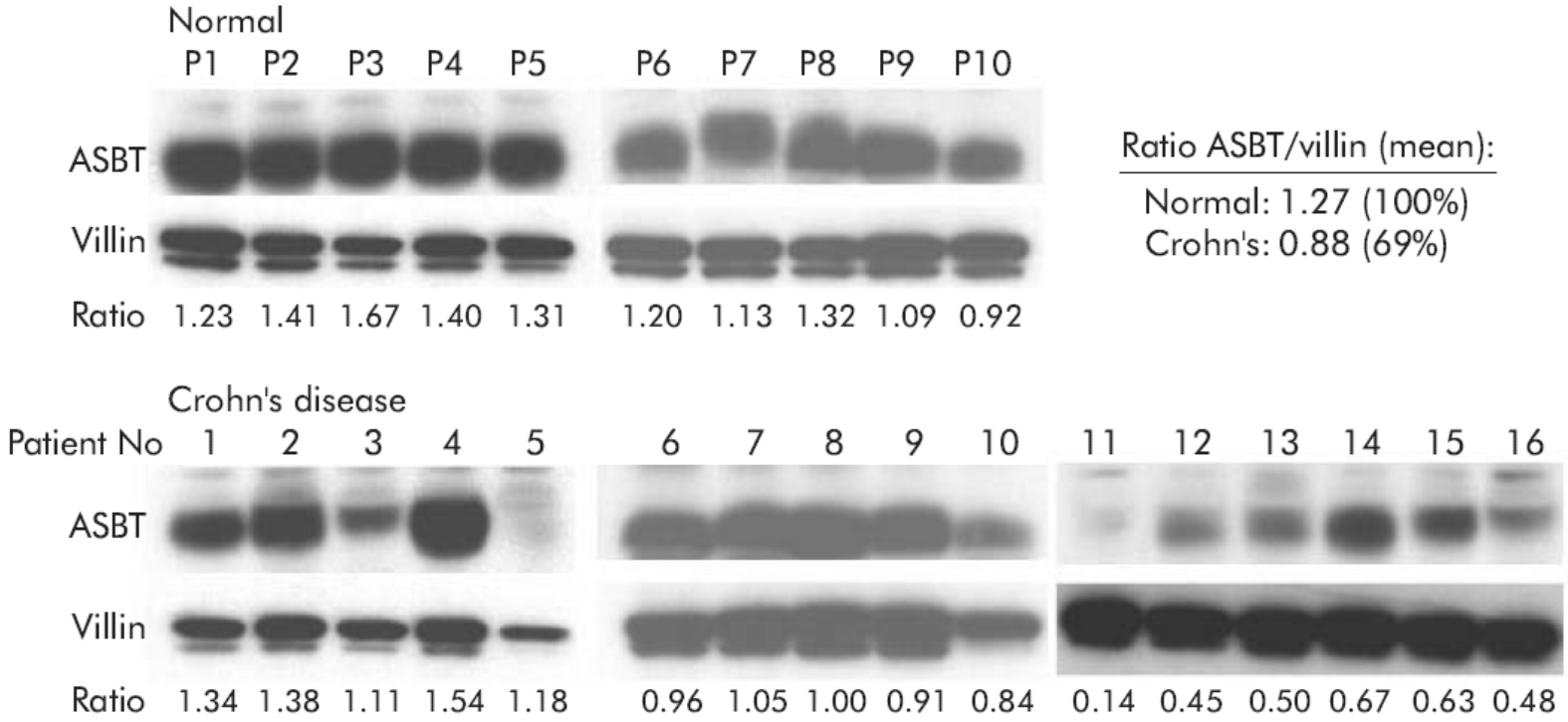
Bile acid malabsorption in persistent diarrhoea.

Smith MJ, Cherian P, Raju GS, Dawson BF, Mahon S, Bardhan KD.

Human ileal bile acid transporter gene ASBT (SLC10A2) is transactivated by the glucocorticoid receptor

D Jung, A C Fantin, U Scheurer, M Fried, G A Kullak-Ublickile

- In 16 patients with Crohn's disease and histologically intact ileal mucosa with no inflammatory infiltrate , ASBT expression was reduced compared with healthy controls.



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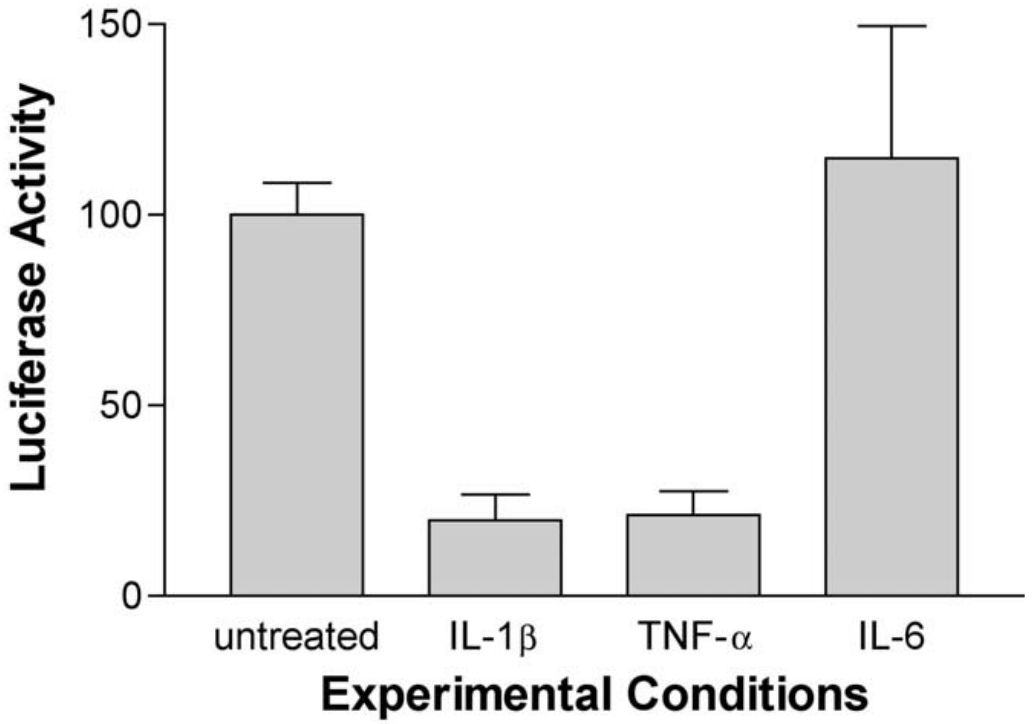
Gut 2004; 53: 78-84

c-Fos Is a Critical Mediator of Inflammatory-Mediated Repression of the Apical Sodium-Dependent Bile Acid Transporter

E Neimark et al. (Mount Sinai, NY)



Cytokine-induced repression of ASBT promoter activity. Caco-2 cells were cotransfected and treated for 40 hours with the human ASBT promoter plus 20 pg/mL of IL-1, 100 ng/mL of TNF-α, or 2 ng/mL of IL-6. The activity of the promoter was reduced with IL-1 and TNF- α .

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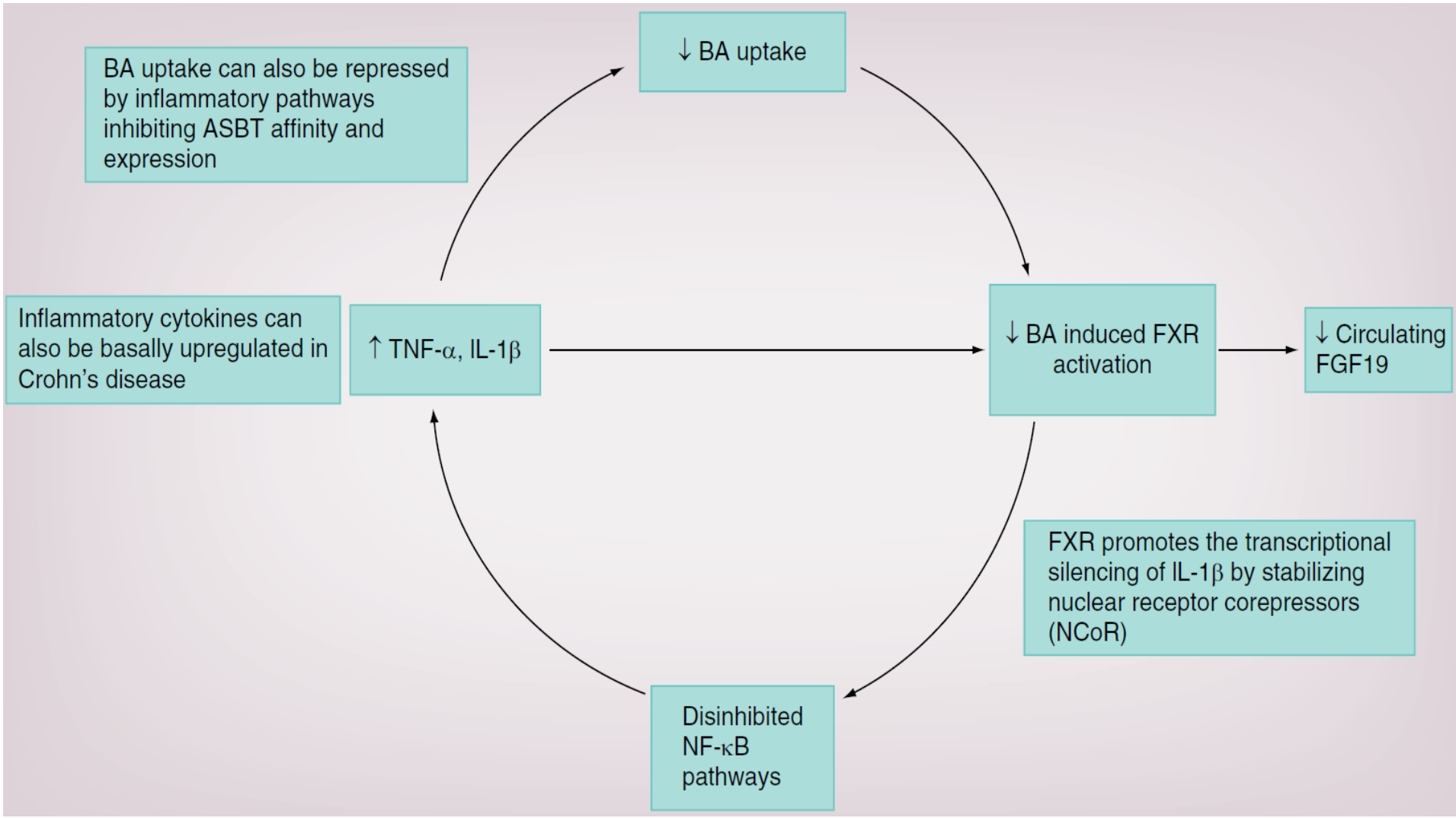
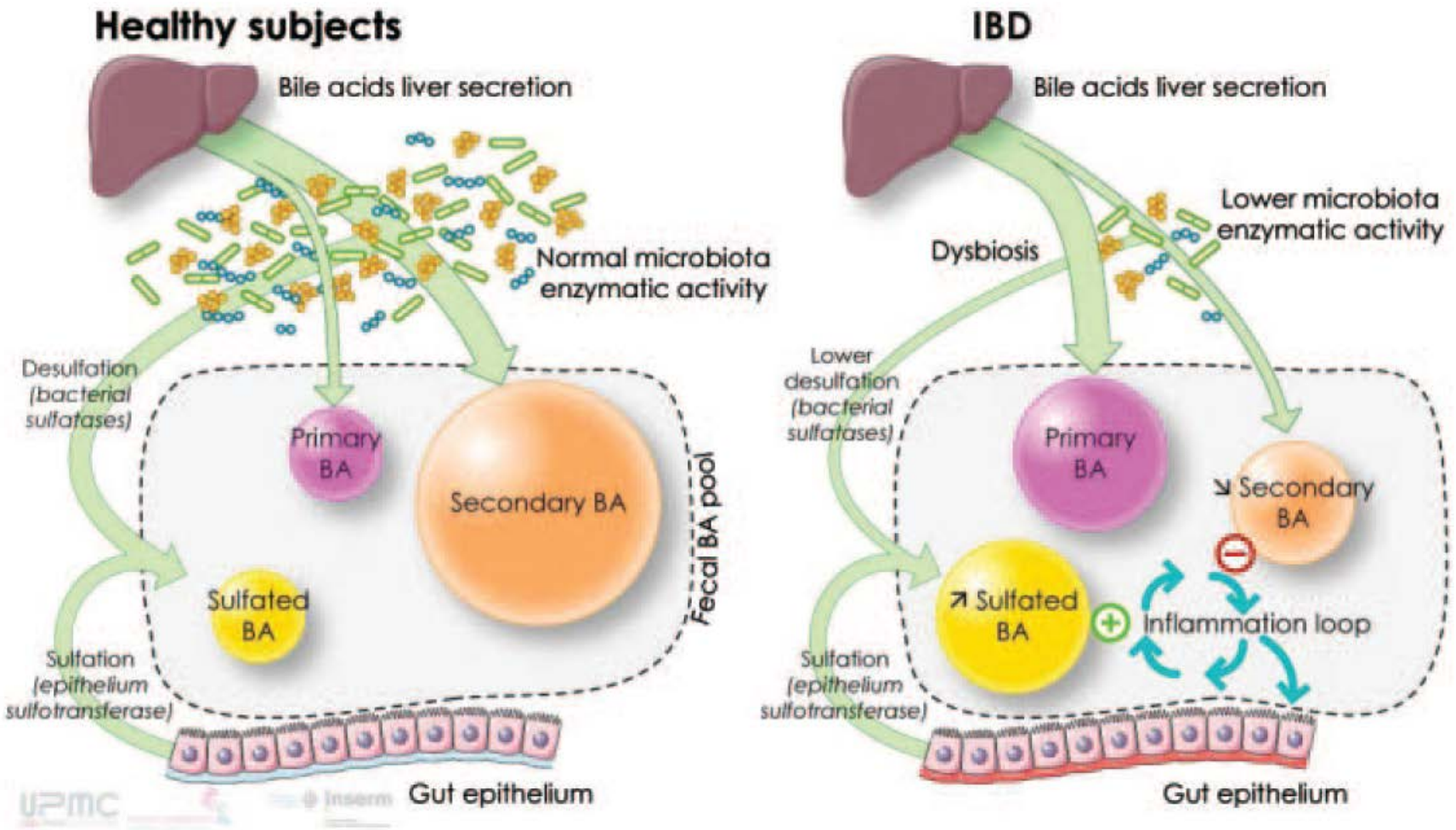
GASTROENTEROLOGY 2006;131:554–567



Nolan et al. Expert Rev. Gastroenterol. Hepatol. 7(1), 49–56 (2013)

Connecting dysbiosis, bile-acid dysmetabolism and gut inflammation in inflammatory bowel diseases

Henri Duboc *et al.*



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H. Duboc *et al.* Gut 2012

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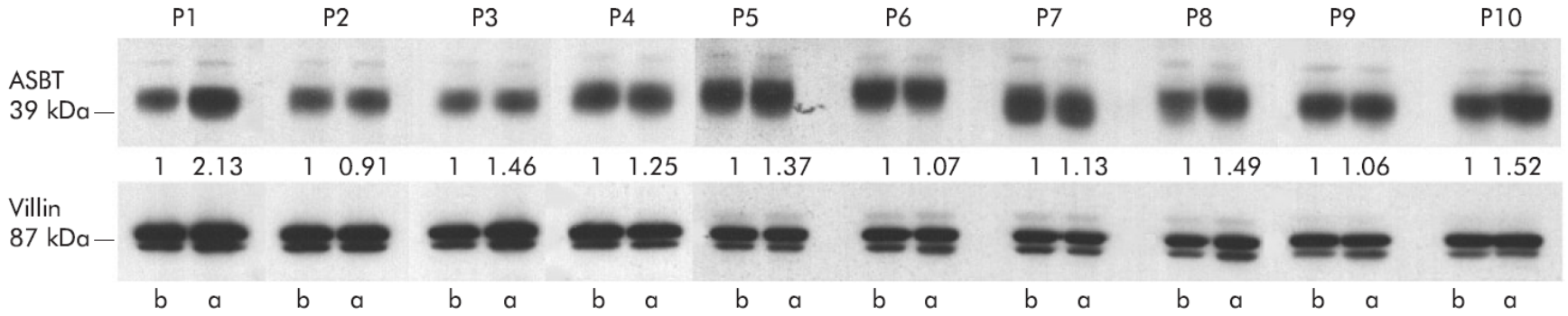
- In 10 healthy male volunteers, ASBT protein expression was increased after 21 days' intake of budesonide (9 mg/day)



(Ileal biopsies were taken from 10 male volunteers (P1–P10) before (b) and after (a) treatment with budesonide (9 mg/day) for 21 days.)

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Gut 2004; 53: 78-84

Budesonide treatment is associated with increased bile acid absorption in collagenous colitis

A. Bajor, A. Kilander, C. Gälman, M. Rudling & K.-A. Ung

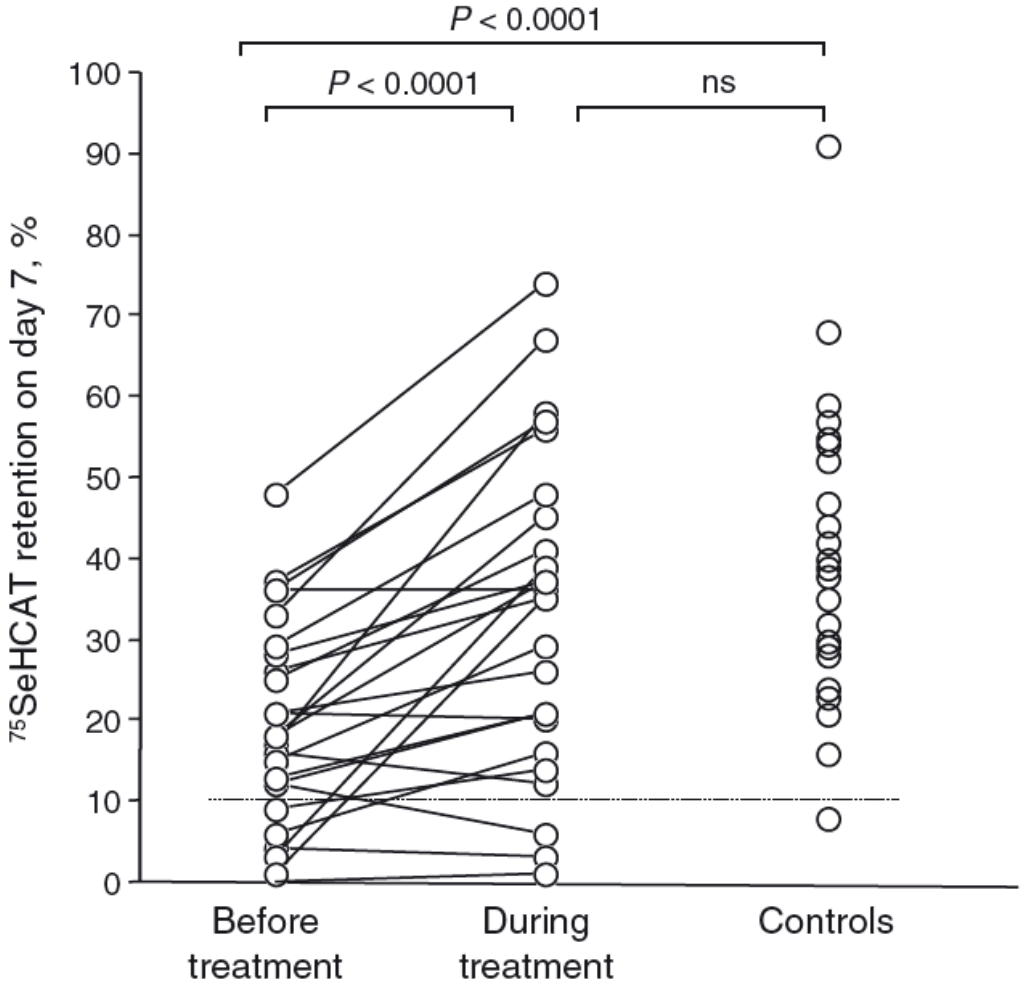

Figure 1. ^{75}Se-labelled homocholic acid-taurine (^{75}SeHCAT) retention values in patients with collagenous colitis on day 7 (%), before treatment and after 8 weeks of oral budesonide treatment (9 mg daily, $n = 25$). For comparison, ^{75}SeHCAT retention values from 29 healthy controls are shown. The horizontal bar represents the limit for abnormal values.

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Aliment Pharmacol Ther 24, 1643–1649

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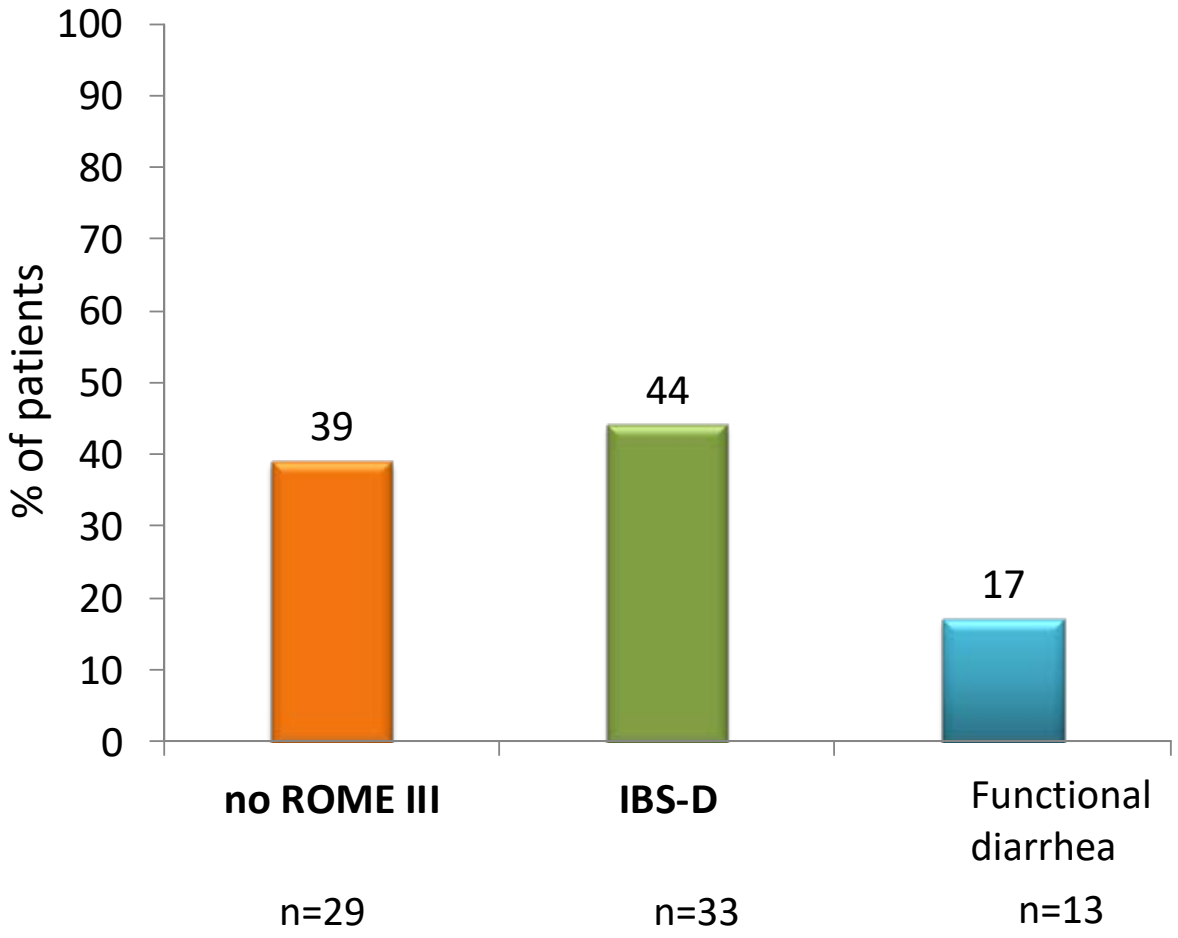
Rome III criteria in Crohn's disease patients



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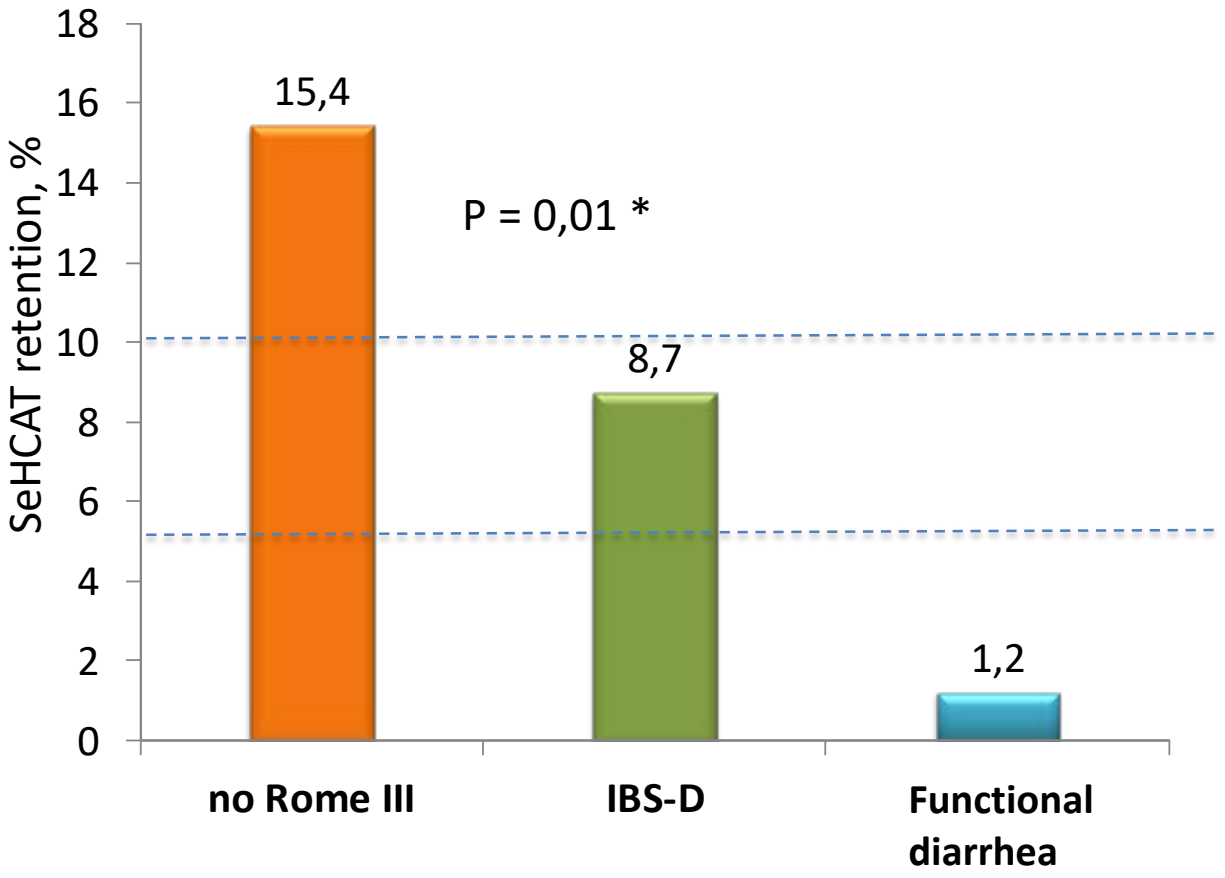
Ruiz-Cerulla et al. ECCO 2014

SeHCAT retention according to the presence of Rome III criteria for IBS



(* After adjunsting according previous bowell ressection)

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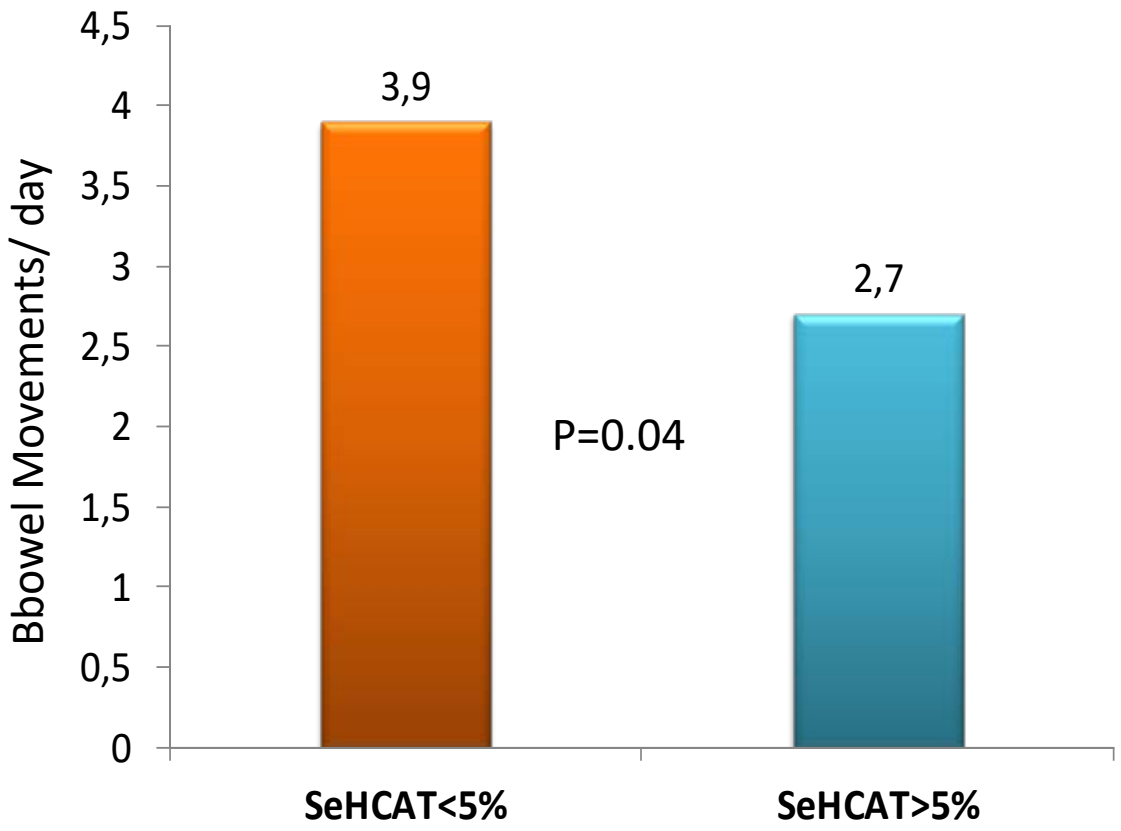
Diaorrhea according to the presence Severe BAM



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Multivariate predictors of IBS-D or FD

	β	OR	IC 95% OR	p
Surgery	-0,372	0,689	0,228-2,086	0,510
Endoscopic Activity	0,12	1,013	0,371-2,765	0,981
SeHCAT (%)	-0,046	0,955	0,917-0,995	0,027

SeHCAT value was the only independent predictor of IBS-D or FD after adjusting for the presence endoscopic lesions and previous resection

Ruiz-Cerulla et al. ECCO 2014

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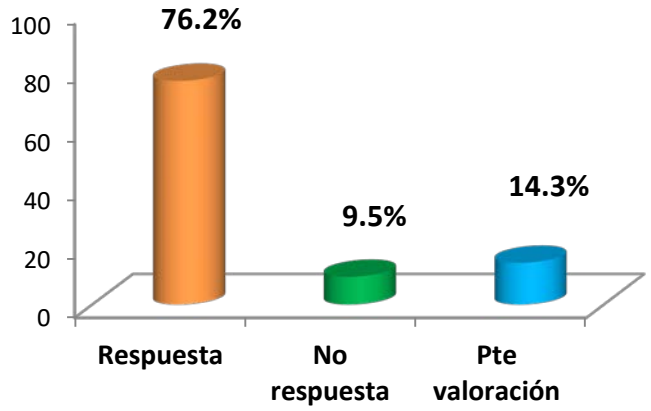
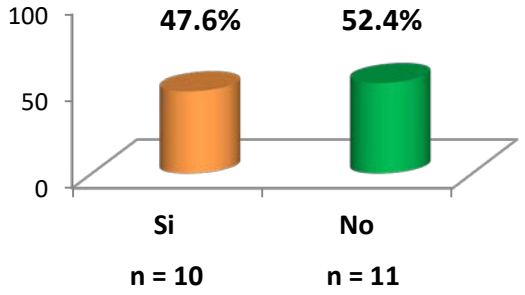
Gut 1994; 35: 90-93

Tratamiento con Resincolestiramina (n = 21)

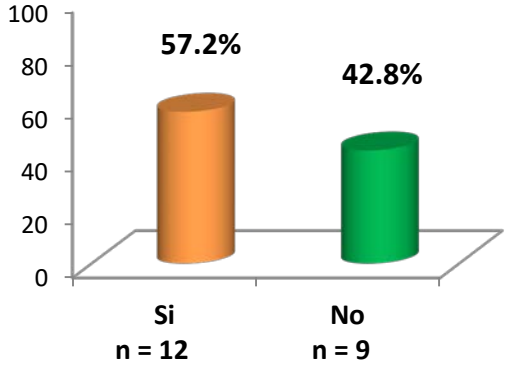
Respuesta a resincolestiramina



Efecto adverso



Continuan con Resincol.



Bile Acid Malabsorption in Crohn's Disease:
Drawbacks of a therapeutic trial of BA binders

- Poor palatability and frequent side effects (borborygmi, flatulence, bloating, nausea, abdominal cramps, constipation) .
- Poor compliance: over 50% of patients given bile acid sequestrants for hyperlipidaemia discontinued them within a year [Hiatt et al. 1999].
- Titration of the dose needed (sometimes high dose needed) and tips for improving palatability important.

Low ability to empirically diagnose BAM

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Bile Acid Malabsorption in Crohn's Disease: Worth looking for? Concluding remarks.

- In CD clinical symptoms are often not related to the underlying inflammation.
- BAM is common in CD, particularly in patients who have had a bowel resection.
- The presence of IBS-D and Functional Diarrhoea type symptoms in CD can be explained, at least in part, by BAM.
- Looking for BAM can be useful in CD patients, particularly in those without evidence of active inflammation.


THE END
IS NEAR
HERE