GASTRO ENTEROLOGIA BELLUNO

Con il patrocinio di

PROGRESSI E NUOVE FRONTIERE IN
GASTROENTEROLOGIA ED ENDOSCOPIA DIGESTIVA
BELLUNO
15-16 GIUGNO 2023

La Malattia Diverticolare del Colon

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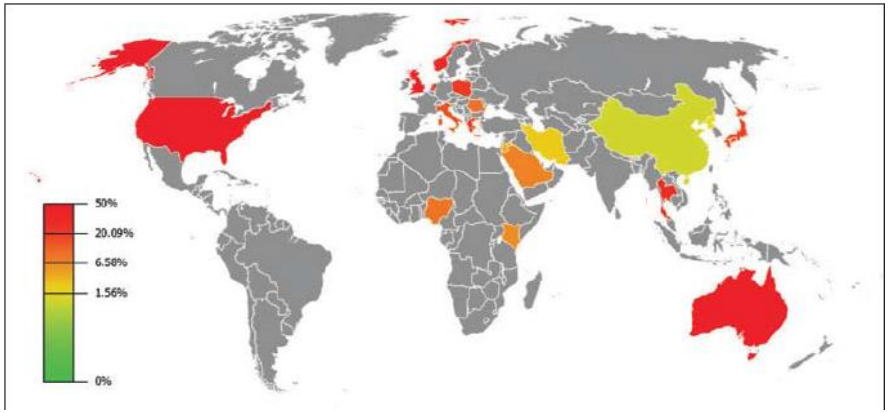
ASL BT
PugliaSalute

Gemelli
Fondazione Policlinico Universitario A. Gemelli
Università Cattolica del Sacro Cuore

Diverticulosis and Diverticular Disease are a global problem



EPIDEMIOLOGY OF DIVERTICULOSIS

High prevalence (stable): USA, Australia, Norther Eur.
Medium-High prevalence (increasing): Jpn, Thai, South.-East. Eur.
Medium prevalence (increasing): Kenia, Nigeria, Saudi Arabia
Low prevalence (increasing): China, Iran, Jordania, South Korea

Reichert M. UEGJ 2015,3: 409-18; Tursi A. Therap Adv Gastroenterol 2016;9: 213-28

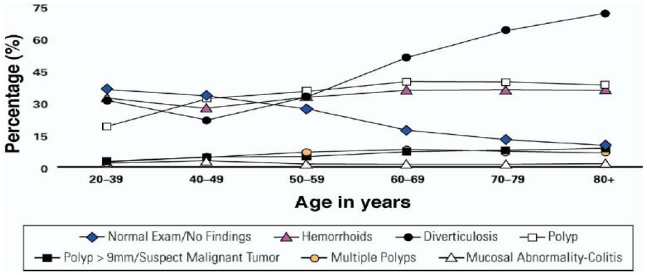


Figure 1. Colonoscopy findings in persons at routine risk by age, 2001–2005. *Source:* National Endoscopy Database/Clinical Outcomes Research Initiative.

Diverticulosis is the most frequent endoscopic diagnosis during routine colonoscopy

Everhart JE. Gastroenterology 2009;136: 741-754

Table 2. Leading Diagnoses in the Ambulatory Setting for Gastrointestinal, Liver and Pancreatic Disorders in the United States, 2010

Rank	Diagnosis	Estimated no. of visits: Office visits	ED	Hospital outpatient department	Total	ICD-9-CM codes
1	Abdominal pain	9,232,817	6,475,136	970,318	16,678,271	789.00
2	Gastroesophageal reflux and reflux esophagitis	6,222,275	294,942	549,992	7,067,209	530.11, 530.81
3	Hemorrhoids	3,592,943	120,128	226,505	3,939,576	455
4	Constipation	2,905,705	530,827	260,129	3,716,661	564.0
5	Nausea and vomiting	1,404,564	1,969,949	215,701	3,590,214	787.0
6	Abdominal wall and inguinal hernia	2,852,677	204,375	422,937	3,479,989	550, 553.0, 553.1, 553.2, 553.9
7	Malignant neoplasm of the colon or rectum	2,420,463	2,420	386,783	2,809,666	153, 154
8	Diverticular disease	2,275,438	262,910	195,771	2,734,119	562.1
9	Diarrhea	1,943,572	533,181	197,071	2,673,824	787.91
10	Gastritis and dyspepsia	1,902,993	472,165	234,836	2,609,994	535, 536.8
11	Irritable bowel syndrome	2,290,460	24,121	89,170	2,403,751	564.1
12	Crohn's disease	1,722,664	44,641	121,256	1,888,561	555
13	Cholelithiasis	872,040	355,504	119,166	1,346,710	574
14	Dysphagia	1,021,034	38,264	113,664	1,172,962	787.2
15	Rectal bleeding	648,827	176,160	61,772	886,759	569.3
16	Benign neoplasm of colon and rectum	726,675		144,775	871,450	211.3, 211.4
17	Pancreatitis	409,862	320,418	91,492	821,772	577, 577.1
18	Ulcerative colitis	633,445	17,166	72,763	723,374	556
19	Hepatitis C infection	563,442	19,496	90,334	673,272	070.41, 070.44, 070.51, 070.54, 070.7
20	Appendicitis	317,374	195,150	128,524	641,048	540, 541, 542
21	Hepatitis, unspecified	554,749	3212	9573	567,534	573.3
22	Chronic liver disease and cirrhosis	438,914	30,084	78,957	547,955	571
23	Barrett's esophagus	369,739		47,083	416,822	530.85
24	Celiac disease	23,521		4472	27,993	579.0

NOTE. Source: National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey (http://www.cdc.gov/nchs/ahcd.htm).

Table 3. Impact of diverticular disease on health in Europe (see assumptions in the text)

Total population in Europe (15 EU countries)	376 481 775
% population with colonic diverticula (median of available data in Table 2)	27.3%
Estimation population with colonic diverticula	102 779 524
Annual incidence of colonic perforation from diverticula	16/100 000
Number of perforation cases/year	60 237
Annual rate of hospital admissions for diverticular disease	209/100 000
Number of hospital admissions/year	786 846
Mortality rate of patients admitted for diverticular disease	3%
Number of deaths from diverticular disease/year	23 605

Diverticular disease in US

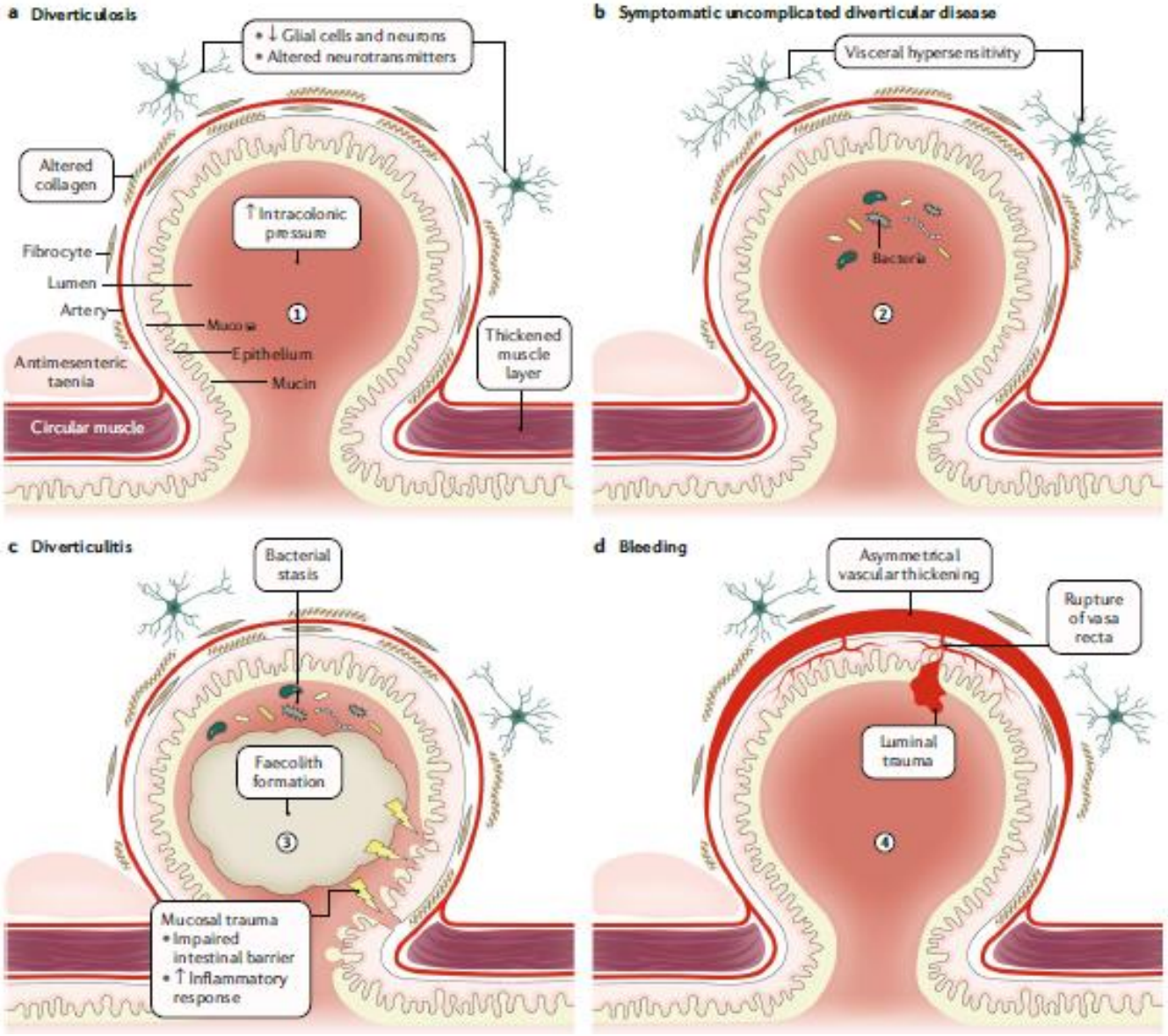
- 8th most frequent outpatient gastrointestinal diagnosis: 2.7 million clinic visits
- Diverticulitis without hemorrhage admissions are more than 200,000 with an aggregate cost of 2,2 billions of USD
- Diverticular hemorrhage (included in gastrointestinal hemorrhage diagnosis) have an adjunctive burden of admissions and costs

Peery AF. Gastroenterology 2015;149: 1731-1741

Diverticular disease in Europe

- 27.3% of people having diverticulosis
- 3% of mortality
- 23,605 deaths/year

Delvaux M. Aliment Pharmacol Ther 2003;18 Suppl 3:71-4



Tursi A. Nature Rev Dis Primers 2020;6: 20

Apart from the large epidemiological and economic impact, little is known about the clinical management of diverticular disease

The most important questions are about:

- ✓ **Classification**
- ✓ **Therapy**
- ✓ **Timing of surgery**

SPOTLIGHT ON:

Management in term of:

Symptomatic Uncomplicated Diverticular Disease

Prevention of acute diverticulitis

Treatment of acute diverticulitis

Prevention of acute diverticulitis recurrence

When to operate

Classification

SPOTLIGHT ON:

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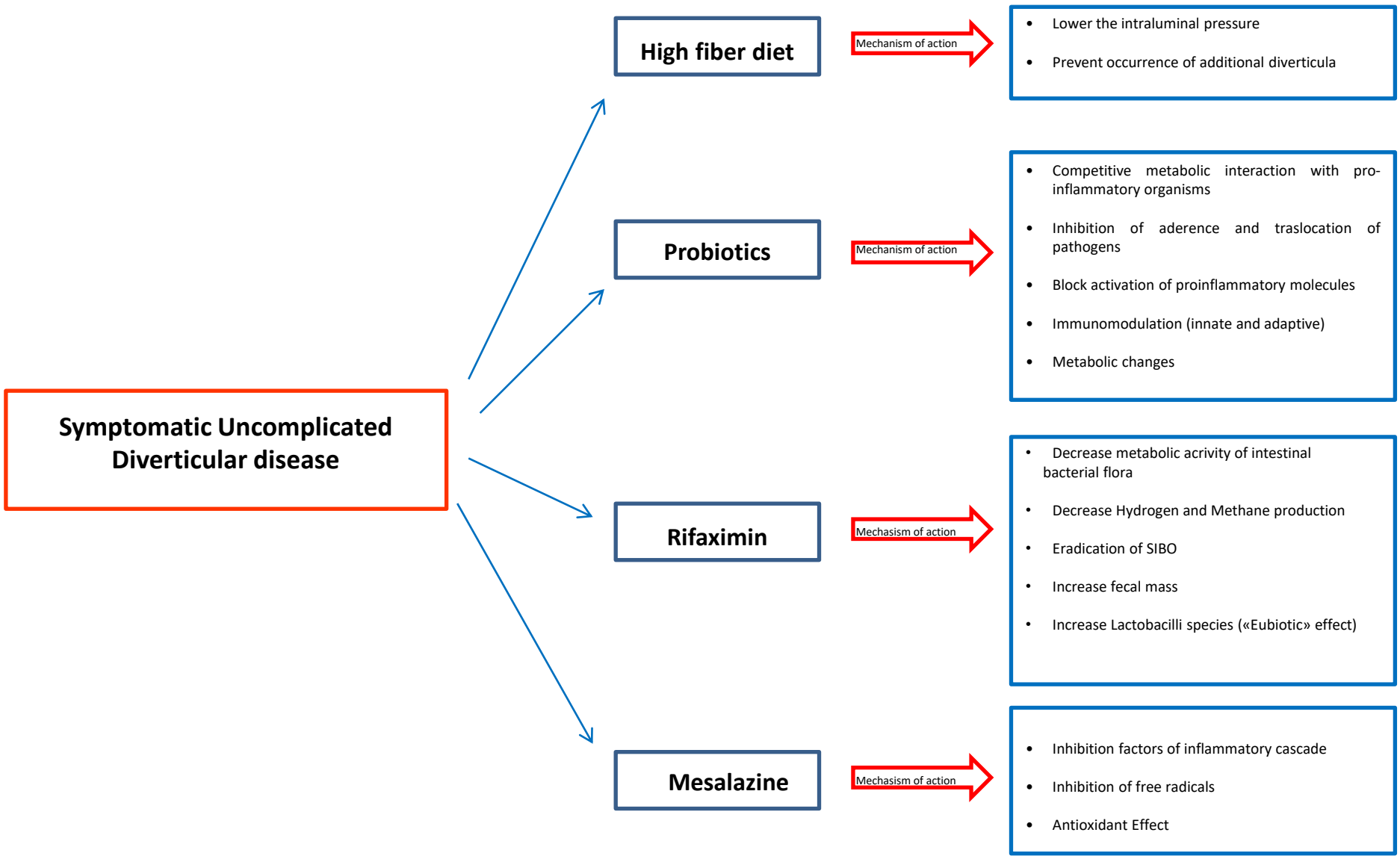
Classification



Sopeña F, Lanas A. Therap Adv Gastroenterol 2011;4: 365-74

Clin Gastroenterol Hepatol.2013 Dec;11(12):1622-7. doi: 10.1016/j.cgh.2013.06.033. Epub 2013 Jul 23.

Constipation and a low-fiber diet are not associated with diverticulosis.

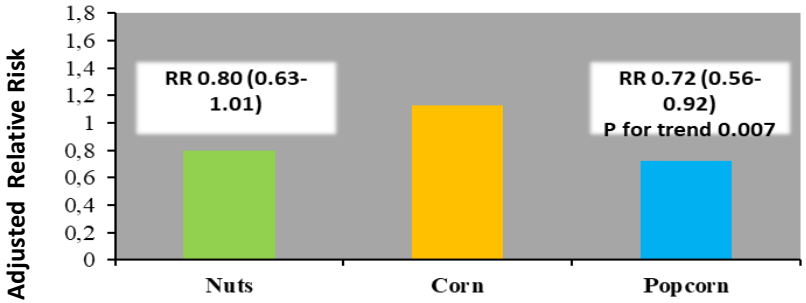
Peery AF, Sandler RS, Ahnen DJ, Galanko JA, Holm AN, Shaukat A, Mott LA, Barry EL, Fried DA, Baron JA.

Neither constipation nor a low-fiber diet was associated with an increased risk of diverticulosis.

JAMA. 2008 Aug 27;300(8):907-14. doi: 10.1001/jama.300.8.907.

Nut, corn, and popcorn consumption and the incidence of diverticular disease.

Strate LL, Liu YL, Syngal S, Aldoori WH, Giovannucci EL.



Western Dietary Pattern Increases, and Prudent Dietary Pattern Decreases, Risk of Incident Diverticulitis in a Prospective Cohort Study

Gastroenterology 2017;152:1023–1030

Lisa L. Strate,[1] Brieze R. Keeley,[2] Yin Cao,[3,4,5] Kana Wu,[5] Edward L. Giovannucci,[5,6,7] and Andrew T. Chan[3,4,7]

Higher association with western dietary pattern (HR 1.55; 95% CI, 1.20-1.99) than prudent pattern (HR 0.74; 95% CI, 0.60-0.91) and AHEI pattern (0.67;95% CI, 0.55-0.82)

Pol Arch Intern Med. 2020 Mar 27;130(3):232-239. doi: 10.20452/pamw.15199. Epub 2020 Feb 20.

Diet in colonic diverticulosis: is it useful?

Tursi A, Elisei W.

High-fiber diet does not prevent diverticulosis, and there are conflicting data on the prevention and treatment of DD and acute diverticulitis.

No data are currently available about FODMAP diet in SUDD patients

No association has been reported between nut, corn, or popcorn consumption and the development of diverticulosis, DD, and acute diverticulitis.

Western diet increases the risk of acute diverticulitis in patients with diverticulosis.

Digestive Diseases

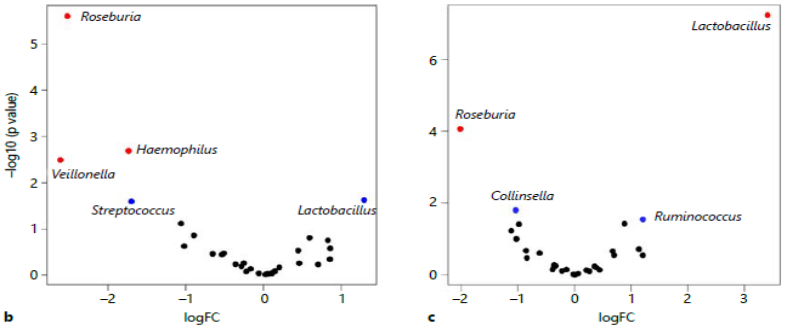
Review Article

Dig Dis 2016;34:269–278
DOI: 10.1159/000443361

The Role of Antibiotics in Gut Microbiota Modulation: The Eubiotic Effects of Rifaximin

Francesca Romana Ponziani[a] Franco Scaldaferri[a] Valentina Petito[a]
Francesco Paroni Sterbini[b] Silvia Pecere[a] Loris R. Lopetuso[a]
Alessandra Palladini[b] Viviana Gerardi[a] Luca Masucci[b] Maurizio Pompili[a]
Giovanni Cammarota[a] Maurizio Sanguinetti[b] Antonio Gasbarrini[a]

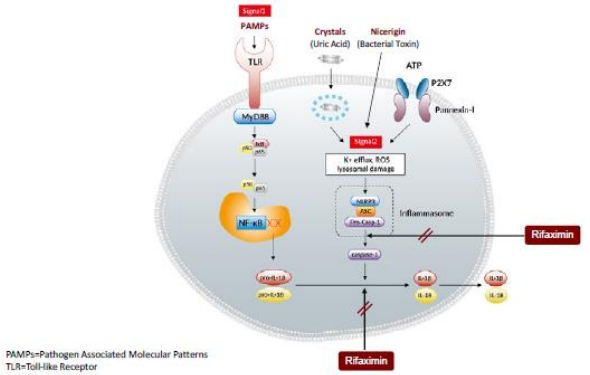
[a]Internal Medicine and Gastroenterology Division and [b]Institute of Microbiology, A. Gemelli Hospital, Rome, Italy



Rifaximin for the Management of Colonic Diverticular Disease: far Beyond a Simple Antibiotic

J Gastrointestin Liver Dis, December 2018 Vol. 27 No 4: 351-355

Antonio Tursi[1], Carmelo Scarpignato[2], Giovanni Brandimarte[3], Francesco Di Mario[4], Angel Lanas[5]



Meta-analysis: long-term therapy with rifaximin in the management of uncomplicated diverticular disease

M. Bianchi, V. Festa, A. Moretti, A. Ciaco, M. Mangone, V. Tornatore, A. Dezi, R. Luchetti, B. De Pascalis, C. Papi & M. Koch

Aliment Pharmacol Ther 2011; **33**: 902–910

Table 1 | Studies addressing rifaximin in the treatment of symptomatic diverticular disease

Author	No. patients	Study design	Jadad scale	Treatment	Study period (months)
Papi *et al.*[19]	217	Open	2	Glucomannan 2 g	12
				Glucomannan 2 g + Rifaximin*	
Latella *et al.*[21]	968	Open	3	Glucomannan 4 g	12
				Glucomannan 4 g + Rifaximin*	
Papi *et al.*[20]	168	RCT	4	Glucomannan 2 g + Placebo	12
				Glucomannan 2 g + Rifaximin*	
Colecchia *et al.*[22]	307	Open	3	Dietary fibre Supp†	24
				Dietary fibre Supp† + Rifaximin*	

* Rifaximin 400 mg b.d. for 7 days each month for 12 months.

† Dietary fibre Supplementation (20 g/die).

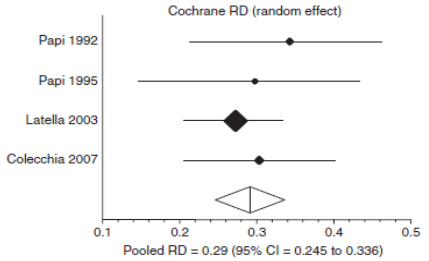
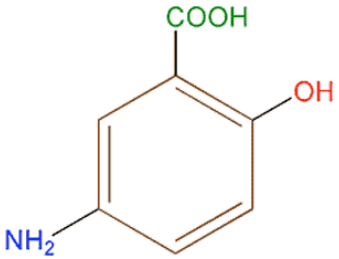


Figure 2 | Rate differences (RD) (95% CI) for complete symptom relief at the end the follow-up in prospective randomised trials addressing Rifaximin group vs. control group. Random effect model.



5-AMINO SALICYLIC ACID

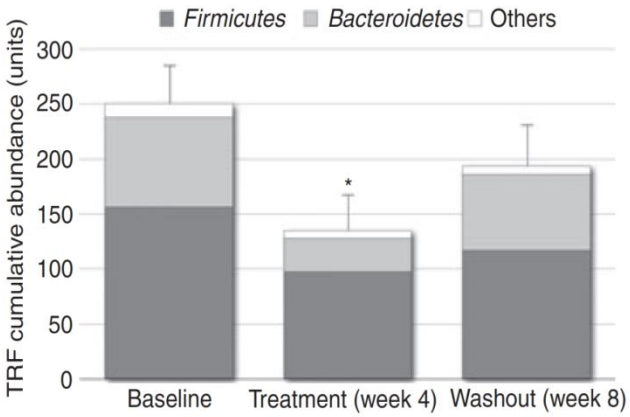
5-ASA Mechanism of action

- Blocking of prostaglandin and leukotrienes synthesis
- Inhibition of neutrophils chemotaxis
- Scavenger on the oxygen free radicals

Mesalazine (5-aminosalicylic acid) alters faecal bacterial profiles, but not mucosal proteolytic activity in diarrhoea-predominant irritable bowel syndrome

C. N. Andrews*, T. A. Griffiths*, J. Kaufman*, N. Vergnolle†, M. G. Surette‡ & K. P. Rioux*,‡

Aliment Pharmacol Ther 2011; **34**: 374–383



Mesalazine to Treat Symptomatic Uncomplicated Diverticular Disease and to Prevent Acute Diverticulitis Occurrence. A Systematic Review with Meta-Analysis of Randomized, Placebo-Controlled Trials

J Gastrointestin Liver Dis, September 2018 Vol. 27 No 3: 291-297

Marcello Picchio[1], Walter Elisei[2], Antonio Tursi[3]

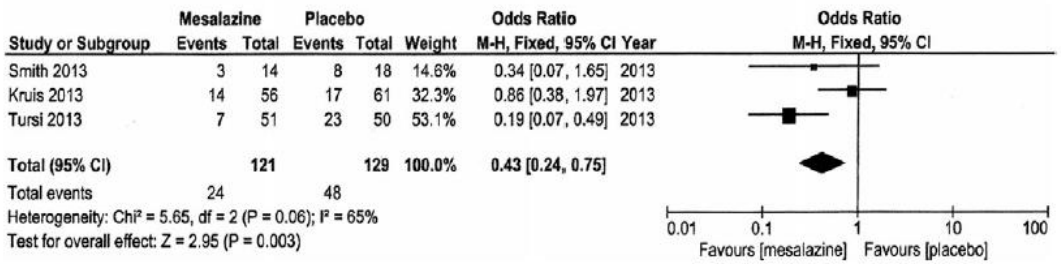


Fig. 2. Forest plot analysing the effect of mesalazine in obtaining symptoms relief.

Inflammopharmacol
DOI 10.1007/s10787-017-0363-y

Inflammopharmacology

ORIGINAL ARTICLE

A randomized double-blind placebo-controlled trial of a multi-strain probiotic in treatment of symptomatic uncomplicated diverticular disease

Charlotte L. Kvasnovsky[1,2,3] · Ingvar Bjarnason[3] · Ana Nora Donaldson[4] · Roy A. Sherwood[3] · Savvas Papagrigoriadis[3]

- Double-blind placebo-controlled RCT
- 143 SUDD Patients, 72 treated with probiotic mixture (Symprove™, containing *L. Rhamnosus, E. Faecium, L. Acidophilus, L. Plantarum*) and 71 with placebo
- Primary endpoint: abdominal pain
- Secondary outcomes: 8 symptoms + fecal caprotectin
- **Abdominal pain: No difference**
- **4 symptoms better** with probiotic: Constipation, Diarrhea, Mucorrhea, Back pain
- Symprove™ was associated with **decreased fecal calprotectin** in males

APT Alimentary Pharmacology and Therapeutics

Randomised clinical trial: mesalazine and/or probiotics in maintaining remission of symptomatic uncomplicated diverticular disease – a double-blind, randomised, placebo-controlled study

A. Tursi*, G. Brandimarte†, W. Elisei‡, M. Picchio§, G. Forti¶, G. Pianese¶, S. Rodino**, T. D'Amico**, N. Sacca**, P. Portincasa††, E. Capezzuto‡‡, R. Lattanzio§§, A. Spadaccini¶¶, S. Fiorella¶¶, F. Polimeni***, N. Polimeni***, V. Stoppino†††, G. Stoppino†††, G. M. Giorgetti‡‡‡, F. Aiello§§§ & S. Danese¶¶¶

- Double-blind placebo-controlled RCT
- 210 SUDD patients were randomly treated:
  Group M (active mesalazine 1.6 g/day plus *L. casei subsp. DG* placebo)
  Group L (active *L. casei subsp. DG* 24 billion/day plus mesalazine placebo)
  Group LM (active *L. casei subsp. DG* 24 billion/day plus active mesalazine)
  Group P (*L. casei subsp. DG* placebo plus mesalazine placebo).
  Patients received treatment for 10 days/month for 12 months.
- Recurrence of SUDD occurred in no (0%) in group LM, in 7 (13.7%) pts in group M, in 8 (14.5%) pts in group L and in 23 (46.0%) pts in group P (LM group vs. M group, P = 0.015; LM group vs. L group, P = 0.011; LM group vs. P group, P = 0.000; M group vs. P group, P = 0.000; L group vs. P group, P = 0.000).
- Acute diverticulitis occurred in six group P cases and in one group L case (P = 0.003).

International Journal of Colorectal Disease
https://doi.org/10.1007/s00384-019-03295-1

ORIGINAL ARTICLE

Supplementation with *Lactobacillus reuteri ATCC PTA 4659* in patients affected by acute uncomplicated diverticulitis: a randomized double-blind placebo controlled trial

Carmine Petruzziello[1] · Alessio Migneco[2] · Silvia Cardone[2] · Marcello Covino[2] · Angela Saviano[1] · Francesco Franceschi[1,2] · Veronica Ojetti[1,2]

- Double-blind placebo-controlled RCT
- 88 AUD Patients, 44 treated with ciprofloxacin 400 mg/bid and metronidazole 500 mg/tid for 1 week, plus *L. reuteri*/bid for 10 days; 44 treated with he same antibiotic therapy for 1 week, plus placebo/bid for 10 days
- Primary endpoint: reduction of abdominal pain and CRP
- Secondary outcomes: reduction of hours of hospitalization
- **Abdominal pain and CRP: significant decrease within 72 hours** ($p < 0.0001$)
- The *L. reuteri* group had a mean hospital stay of 93 ± 17 h (3, 8 days), while the placebo group had a mean hospital stay of 113 ± 20 h (4, 8 days) ($p < 0.0001$)

Rome 2016

a. Fiber supplementation alone provides controversial results in terms of symptoms relief.

b. There is insufficient evidence that probiotics are effective in reducing symptoms.

c. Fiber plus rifaximin provide a greater prevalence of symptom-free SUDD patients compared with fiber alone.

d. Mesalazine alone is effective in reducing symptoms in SUDD patients

Statement 3.5 (EL: 2b-RG: B)

Statement 3.12 (EL: 4-RG: C)

Statement 3.6 (EL: 2b-RG: B)

Statement 3.8 (EL: 2b-RG: B)

Madrid 2019

a.There are some evidences that probiotics could be effective in reducing symptoms in SUDD patients.

b.Rifaximin plus fibre is effective in reducing symptoms in SUDD patients compared to fibre alone.

c.Mesalazine is effective in reducing symptoms in SUDD patients.

Statement 4.3 (EL: 3a-RG: B)

Statement 4.1 (EL: 2b-RG: B)

Statement 4.2 (EL: 1b-RG: A)

SPOTLIGHT ON:

Management in term of:

- Symptomatic Uncomplicated Diverticular Disease
- Prevention of acute diverticulitis
- Treatment of acute diverticulitis
- Prevention of acute diverticulitis recurrence
- When to operate

Classification

Long-term Risk of Acute Diverticulitis Among Patients With Incidental Diverticulosis Found During Colonoscopy

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2013;11:1609–1613

KAMYAR SHAHEDI,[*] GARTH FULLER,[*] ROGER BOLUS,[*,‡] ERICA COHEN,[*] MICHELLE VU,[*] RENA SHAH,[‡] NIKHIL AGARWAL,[*,‡,§] MARC KANESHIRO,[‡,§] MARY ATIA,[§] VICTORIA SHEEN,[§] NICOLE KURZBARD,[‡] MARTIJN G. H. VAN OIJEN,[*,‡] LINNETTE YEN,[‖] PAUL HODGKINS,[‖] M. HAIM ERDER,[‖] and BRENNAN SPIEGEL[*,‡,§,¶]

During a 10-years follow-up, only 4% of patients with diverticulosis developed acute diverticulitis

Prospective, Five-Year Follow-up Study of Patients with Symptomatic Uncomplicated Diverticular Disease

Tarek A. Salem, F.R.C.S.Ed., F.R.C.S.I.,[1] Richard G. Molloy, F.R.C.S.I., M.D., F.R.C.S.,[2] Patrick J. O'Dwyer, F.R.C.S.I., M.Ch., F.R.C.S.(Glasg.)[3]

AP&T Alimentary Pharmacology and Therapeutics

Aliment Pharmacol Ther 2013; **38**: 741–751

Randomised clinical trial: mesalazine and/or probiotics in maintaining remission of symptomatic uncomplicated diverticular disease – a double-blind, randomised, placebo-controlled study

A. Tursi*, G. Brandimarte†, W. Elisei‡, M. Picchio§, G. Forti¶, G. Pianese¶, S. Rodino**, T. D'Amico**, N. Sacca**, P. Portincasa††, E. Capezzuto‡‡, R. Lattanzio§§, A. Spadaccini¶¶, S. Fiorella¶¶, F. Polimeni***, N. Polimeni***, V. Stoppino†††, G. Stoppino†††, G. M. Giorgetti‡‡‡, F. Aiello§§§ & S. Danese¶¶¶

Acute diverticulitis occurred in 1.7-3.1% of SUDD patients at 5 years

The natural history of symptomatic uncomplicated diverticular disease: a long-term follow-up study

Antonio Tursi[a], Marilisa Franceschi[b], Walter Elisei[c], Marcello Picchio[d], Francesco Di Mario[e], Giovanni Brandimarte[f]

Annals of Gastroenterology (2021) **34**, 208-213

During a 13-years follow-up, acute diverticulitis occurred in 7.6% of SUDD patients

Meta-analysis: long-term therapy with rifaximin in the management of uncomplicated diverticular disease

M. Bianchi, V. Festa, A. Moretti, A. Ciaco, M. Mangone, V. Tornatore, A. Dezi, R. Luchetti, B. De Pascalis, C. Papi & M. Koch

Aliment Pharmacol Ther 2011; **33**: 902–910

Rifaximin could be effective in reducing diverticular disease complication but….NNT: 57

Table

Author					
Papi *et al.*					
Latella *et al.*					
Papi *et al.*					
				Glucomannan 2 g + Rifaximin*	
Colecchia *et al.*[22]	307	Open	3	Dietary fibre Supp†	24
				Dietary fibre Supp† + Rifaximin*	

* Rifaximin 400 mg b.d. for 7 days each month for 12 months.

† Dietary fibre Supplementation (20 g/die).

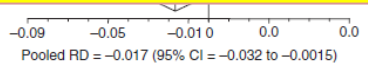


Figure 3 | Rate differences (RD) (95% CI) for complication rate in prospective randomised trials addressing Rifaximin group vs. control group. Random effect model.

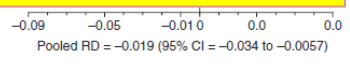


Figure 4 | Rate differences (RD) (95% CI) for complication rate (acute diverticulitis alone) in prospective randomised trials addressing Rifaximin group vs. control group. Random effect model.

Mesalazine to Treat Symptomatic Uncomplicated Diverticular

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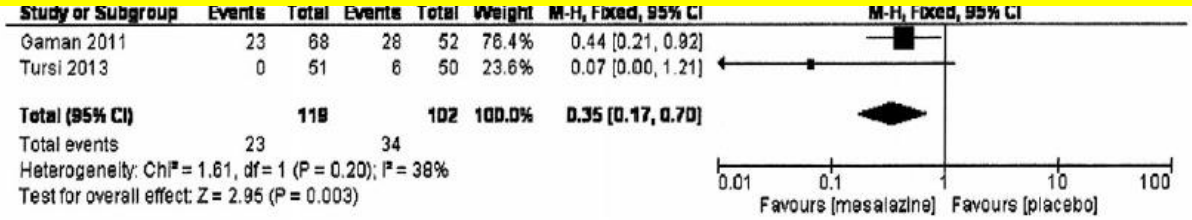
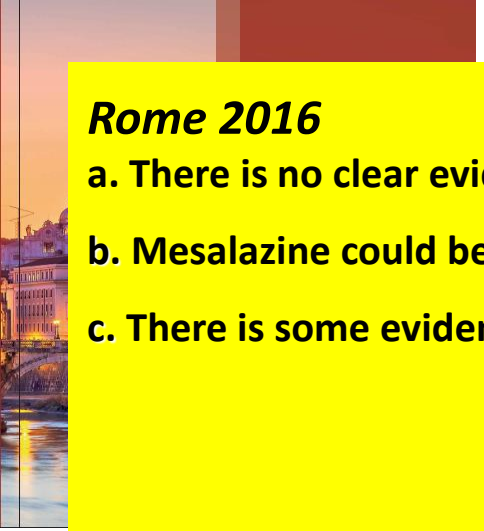
Mesalazine seems to be better than placebo in preventing the first episode of acute diverticulitis (but NNT is higher: 8)





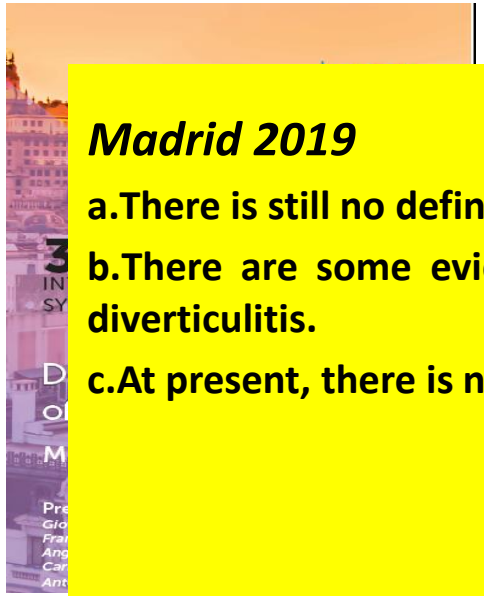
Rome 2016

a. There is no clear evidence that rifaximin reduces acute episodes of diverticulitis

b. Mesalazine could be effective in reducing AD occurrence.

c. There is some evidence that mesalazine reduces symptoms after acute episode of diverticulitis.

Statement 3.7 (EL: 2b-RG: C)
Statement 3.9 (EL: 2b-RG: B)
Statement 3.11 (EL: 2c-RG: C)



INTERNATIONAL CONSENSUS ON DIVERTICULOSIS AND

Madrid 2019

a.There is still no definite evidence that rifaximin reduces acute episodes of diverticulitis.

b.There are some evidences that mesalazine could reduce symptoms following acute episode of diverticulitis.

c.At present, there is no evidence that mesalazine reduces acute episodes of diverticulitis.

Statement 2.5 (EL: 4-RG: D)
Statement 2.6 (EL: 3a-RG: B)
Statement 2.7 (EL: 1c-RG: B)

*J Gastrointestin Liver Dis 2019 ;*28 (Suppl 4): 57-65

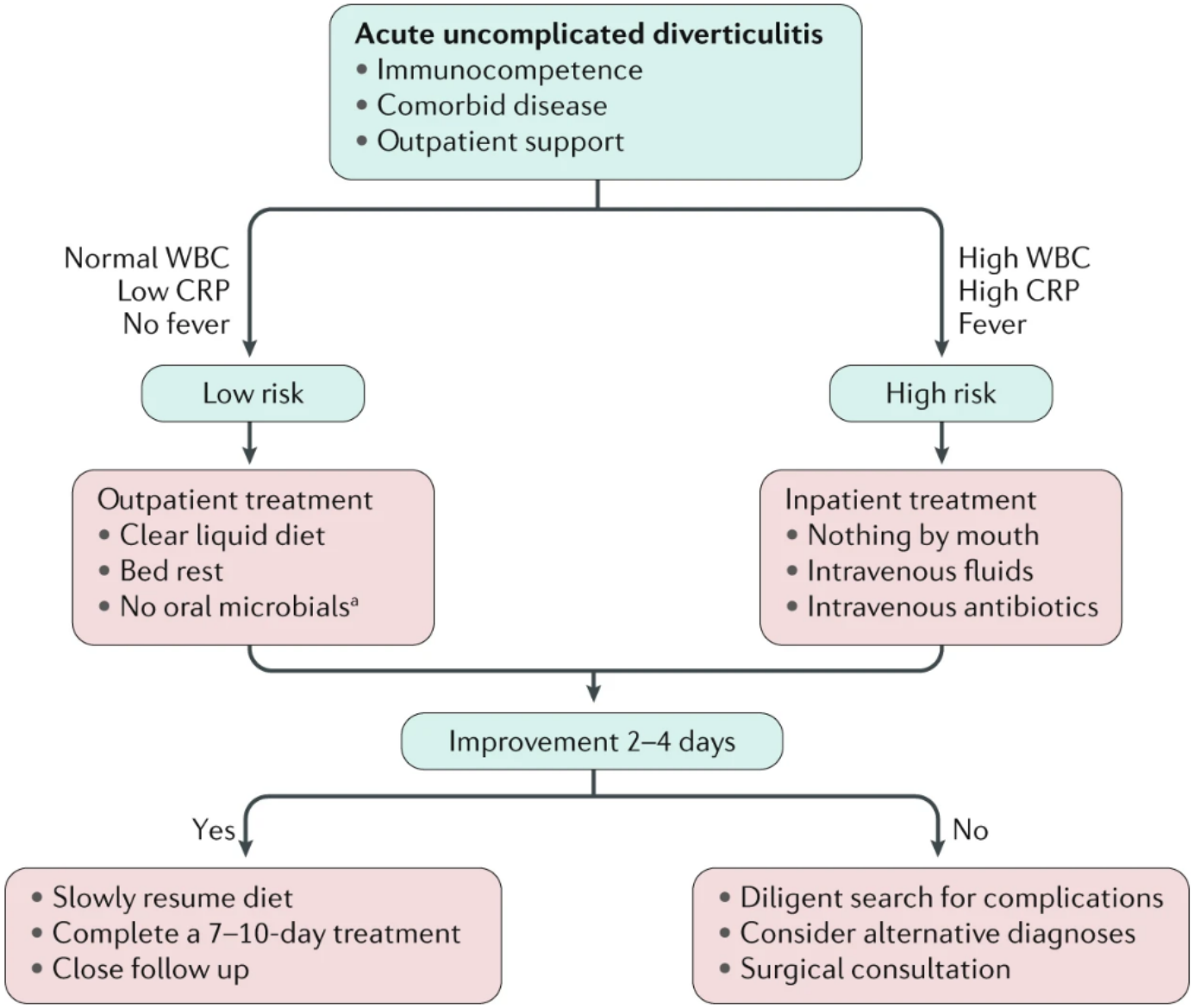
SPOTLIGHT ON:

Management in term of:

- Symptomatic Uncomplicated Diverticular Disease
- Prevention of acute diverticulitis
- Treatment of acute diverticulitis
- Prevention of acute diverticulitis recurrence
- When to operate

Classification

Algorithm for the management of uncomplicated acute diverticulitis



Tursi A. Nature Rev Dis Primers 2020;6: 20

Rifamycin vs placebo for the treatment of acute uncomplicated diverticulitis: A randomised, double-blind study

Wolfgang Kruis[1] | Tomas Poškus[2] | Günther Böhm[3] | Ivan Bunganic[4] | István Rácz[5] | Ovidiu Fratila[6] | Giovanni Barbara[7] | Sarah Wehrum[8] | Tanju Nacak[8] | Roland Greinwald[8]

GastroHep. 2020;2:295–308.

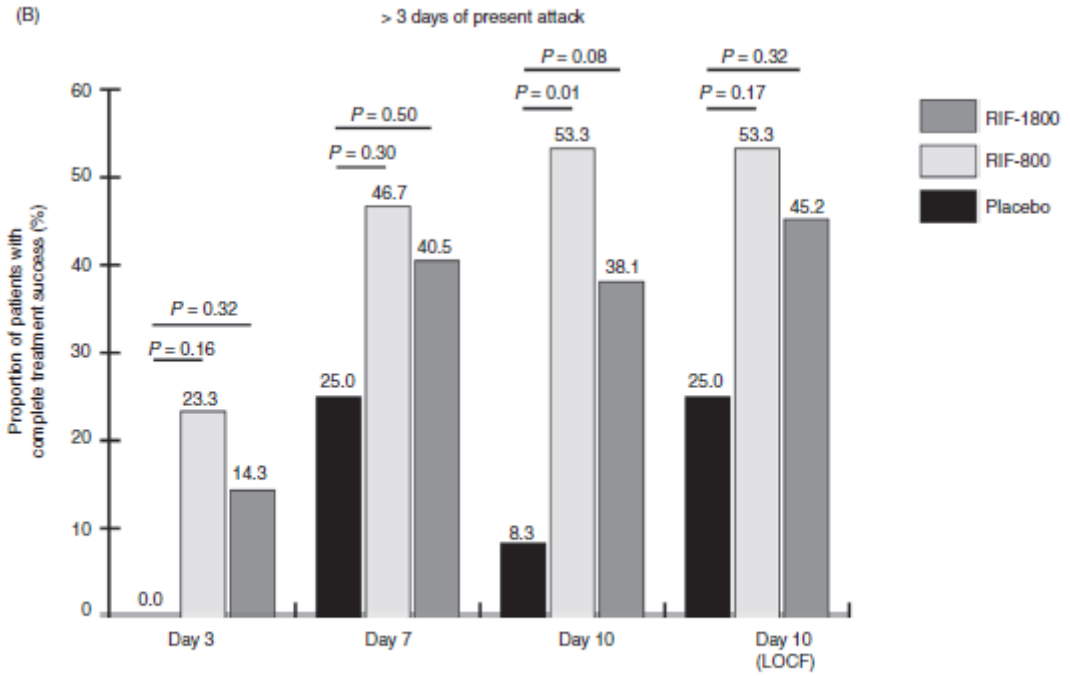
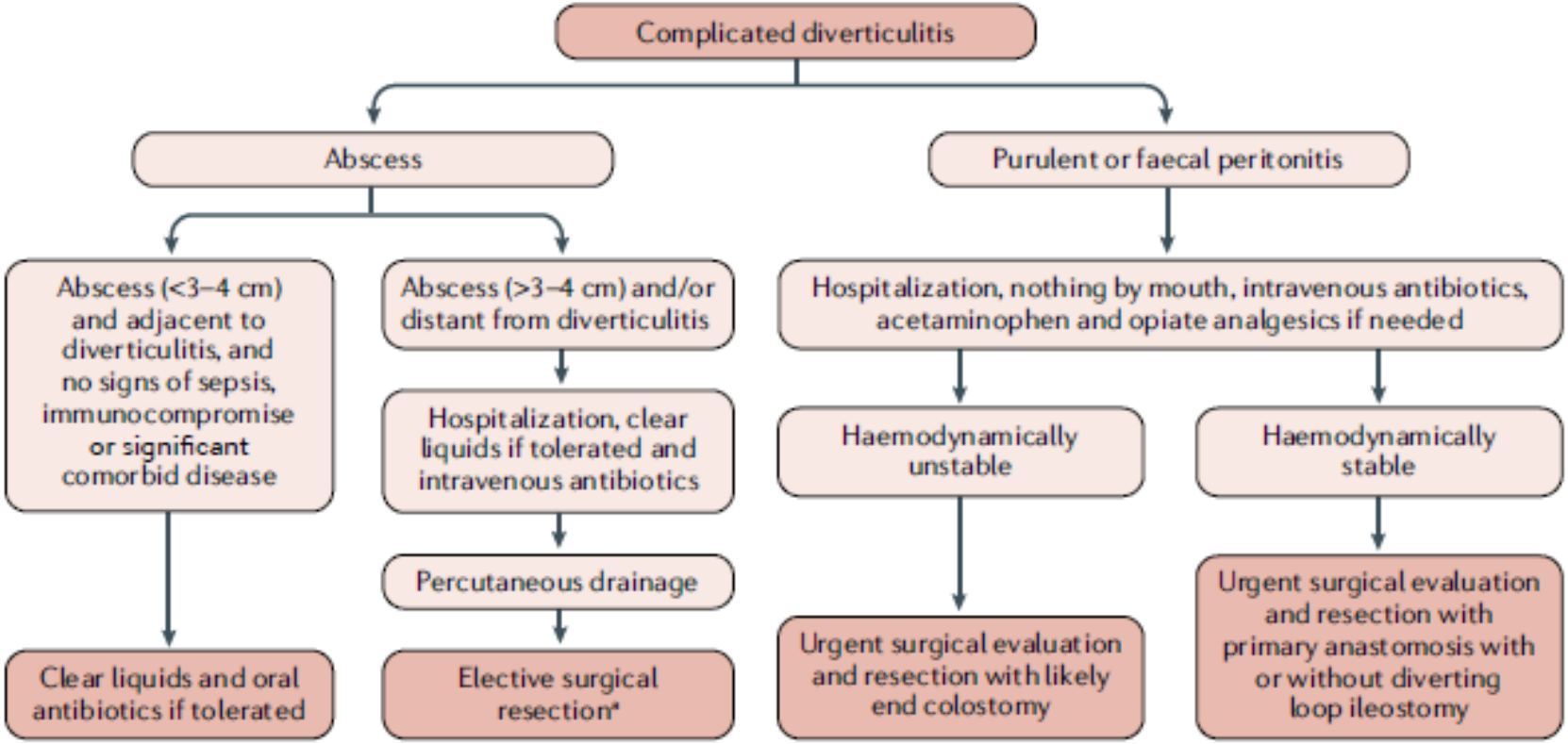


FIGURE 3 Rate of patients with treatment success (A) or complete treatment success (B) with symptom duration of present attack longer than 3 days on Day 3/7/10 and Day 10 (LOCF). All P-values are compared with placebo. RIF-800, RIF-MMX 400 mg twice daily; RIF-1800, RIF-MMX 600 mg three times daily. LOCF, last observation carried forward; RIF-MMX, Rifamycin SV multi-matrix

Algorithm for the management of complicated acute diverticulitis



Tursi A. Nature Rev Dis Primers 2020;6: 20

Rome 2016

a. Management and treatment approaches to AD depend on severity (uncomplicated and complicated) and complexity (ie, abscess, fistula, etc.) of the condition.

b. Antibiotics may not improve outcome in acute uncomplicated diverticulitis and are used on a case-by-case basis.

6. In severe/complicated acute diverticulitis (AD), hospitalization, bowel rest, and broad spectrum antibiotics are needed.

Statement 3.13 (EL: 3b-RG: C)
Statement 3.14 (EL: 3b-RG: C)
Statement 3.15 (EL: 3b-RG: C)

INTERNATIONAL CONSENSUS ON DIVERTICULOSIS AND DIVERTICULAR DISEASE. STATEMENTS FROM THE 3rd

Madrid 2019

a.Treatment of acute uncomplicated diverticulitis (AUD) without antibiotics is safe and effective and it is not associated with worse outcomes, including need for surgery, complications, recurrence and lenght of hospital stay.

b.In Uncomplicated Acute Diverticulitis antibiotic therapy is still considered in patients immunocompromised, with severe comorbidities (ASA>2) and with sign of sepsis.

Statement 5.1 (EL: 2b-RG: B)

Statement 5.2 (EL: 3b-RG: C)

*J Gastrointestin Liver Dis 2019 ;*28 (Suppl 4): 57-65

SPOTLIGHT ON:

Management in term of:

- Symptomatic Uncomplicated Diverticular Disease
- Prevention of acute diverticulitis
- Treatment of acute diverticulitis
- Prevention of acute diverticulitis recurrence
- When to operate

Classification

Original article

Br J Surg 2010;97(6):952-7

Patterns of recurrence in patients with acute diverticulitis

T. Eglinton, T. Nguyen, S. Raniga, L. Dixon, B. Dobbs and F. A. Frizelle

Colorectal Unit, Department of Surgery, Christchurch Hospital, Riccarton Avenue, Christchurch, New Zealand
Correspondence to: Professor F. A. Frizelle (e-mail: frank.frizelle@cdhb.govt.nz)

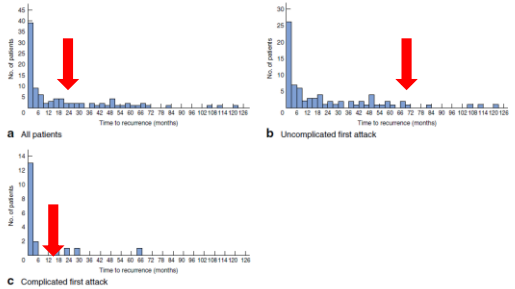


Fig. 1 Timing of first recurrent attack of acute diverticulitis: a all patients, b patients with an uncomplicated first attack, c patients with a complicated first attack

Retrospective study
502 pts: 337 UD and 165 CD
Median Follow-up: 101 mo. (60-124)
UD recurred in 23.4%
CD recurred in 24% (p=0.622)
Recurrence usually occurred within 12 mo.
From the initial episode

Temporal Trends in the Incidence and Natural History of Diverticulitis: A Population-Based Study

Adil E. Bharucha, MBBS, MD[1], Gopanandan Parthasarathy, MBBS[1], Ivo Ditah, MD[1], J.G. Fletcher, MD[2], Ofor Ewelukwa, MBBS[1,7], Rajesh Pendlimari, MD[3,8], Barbara P. Yawn, MD[4], L. Joseph Melton III, MD[5], Cathy Schleck, MS[6] and Alan R. Zinsmeister, PhD[6]

Am J Gastroenterol 2015;110(11):1589-96

	1y	5y	10y
RD1	8%	17%	22%
RD2	19%	44%	55%
RD3	24%	40% (3y)	

RD1 1st , RD2 2nd, RD3 3th episode

3222 pts with AD from 1980 to 2007.
Over the 27-year study period, 635 people had 1, 280 had 2, and 127 had 3 episodes of RD.
Incidence of RD is greater than currently recognized, and particularly so after RD1.
The risk of RD1 is greater in men, people who were younger (30-69 years), or had diverticulitis more recently in time.

ORIGINAL CONTRIBUTION

Long-Term Follow-up After an Initial Episode of Diverticulitis: What Are the Predictors of Recurrence?

Jason F. Hall, M.D., M.P.H.[1] • Patricia L. Roberts, M.D.[1]
Rocco Ricciardi, M.D., M.P.H.[1] • Thomas Read, M.D.[1] • Christopher Scheirey, M.D.[2]
Christoph Wald, M.D.[2] • Peter W. Marcello, M.D.[1] • David J. Schoetz, M.D.[1]

1 Department of Colon and Rectal Surgery, Lahey Clinic, Burlington, Massachusetts
2 Department of Radiology, Lahey Clinic, Burlington, Massachusetts

Dis Colon Rectum 2011; 54: 283-288

TABLE 3. Multivariate model

	HR (95% CI)
Retroperitoneal abscess	4.5 (1.1–18.4)
Family history of diverticulitis	2.2 (1.4–3.2)
Segment >5 cm	1.7 (1.3–2.3)
Right colonic disease	0.27 (0.09–0.86)

- 5-year recurrence: 36%
- Complicated recurrence: 3.9%
- Although recurrence is common following an initial attack managed medically, complicated recurrence is uncommon

Management of Patients With Diverticulosis and Diverticular Disease

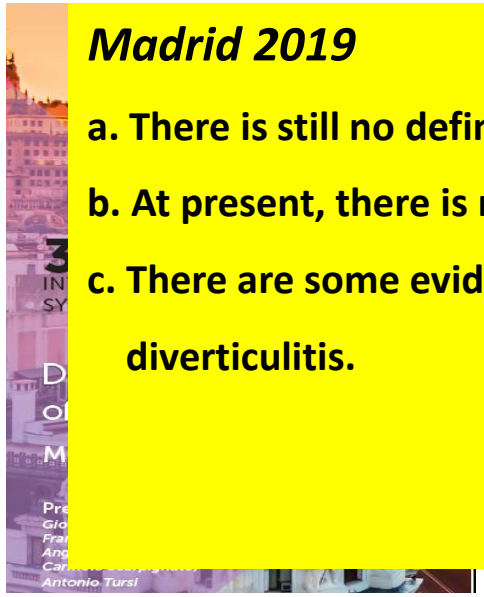
Rome 2016

At present, any drug was found significantly effective in preventing diverticulitis recurrence

Statement 3.7 (EL: 2b-RG: C)

Statement 3.10 (EL: 2b-RG: C)

Statement 3.12 (EL: 4-RG: C)



Madrid 2019

a. There is still no definite evidence that rifaximin reduces acute episodes of diverticulitis.

b. At present, there is no evidence that mesalazine reduces acute episodes of diverticulitis.

c. There are some evidences that mesalazine could reduce symptoms following acute episode of diverticulitis.

Statement 2.5 (EL: 4-RG: D)

Statement 2.7 (EL: 1c-RG: B)

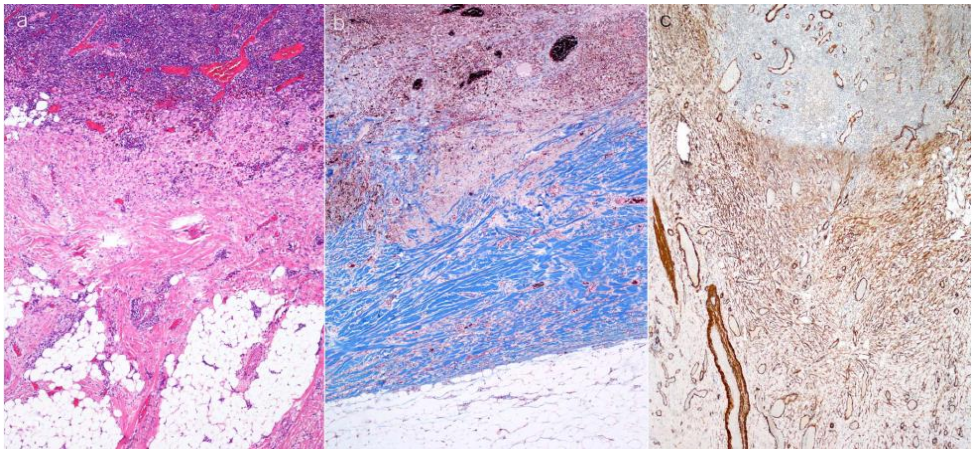
Statement 2.6 (EL: 3a-RG: B)

*J Gastrointestin Liver Dis 2019 ;*28 (Suppl 4): 57-65

Why Do We Have to Look Deep to Understand Diverticulitis?

Nina Zidar, MD, PhD[1]

Am J Gastroenterol 2019;00:1–2. https://doi.org/10.14309/ajg.0000000000000297



Prolonged Recurrent Abdominal Pain is Associated With Ongoing Underlying Mucosal Inflammation in Patients who had an Episode of Acute Complicated Diverticulitis

Adi Lahat, MD,† Daniela Necula, MD,‡ Miri Yavzori, MSc,*† Orit Picard, PhD,*† Sharon Halperin, MSc,§ Rami Eliakim, MD,*† and Shomron Ben-Horin, MD*†*

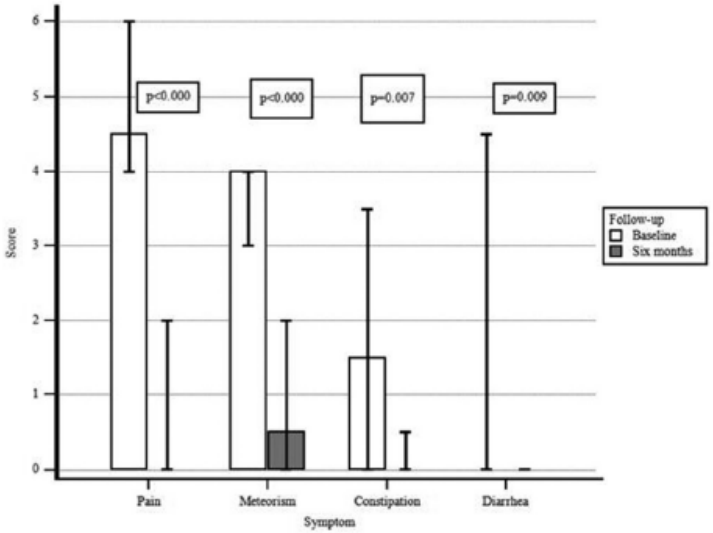
TABLE 2. Cytokine Expression in Affected Versus Uninvolved Colonic Tissue in Patients After severe AD Versus Nonsevere AD

Cytokine	Uninvolved Severe	Involved Severe	Uninvolved Nonsevere	Involved Nonsevere	*P* for Involved vs. Uninvolved Severe*	*P* for Involved vs. Uninvolved Nonsevere#	*P* for Involved Severe vs. Nonsevere+	*P* for Uninvolved Severe vs. Nonsevere^
TNFα	1.06 ± 1.57	5.4 ± 4.4	0.45 ± 0.35	0.19 ± 0.11	0.0127	0.4647	0.0045	0.5698
IL-6	1.56 ± 2.1	5.14 ± 10	0.34 ± 0.34	0.13 ± 0.07	0.05	0.2506	0.0084	0.4642
IL-1β	0.35 ± 0.5	0.8 ± 0.82	0.12 ± 0.05	0.13 ± 0.13	0.14	0.7728	0.5224	0.6698

Budesonide MMX™ Is Effective in Patients Having Persistent Symptoms and Raised Fecal Calprotectin Following Treatments for Diverticular Disease

Antonio Tursi[1], Claudio Cassieri[2], Raffaele Colucci[3], Walter Elisei[4], Marcello Picchio[5], Giovanni Brandimarte[2]

J Gastrointestin Liver Dis, 2019 Vol. 28 Suppl 4: 45-47



SPOTLIGHT ON:

Management in term of:

- Symptomatic Uncomplicated Diverticular Disease
- Prevention of acute diverticulitis
- Treatment of acute diverticulitis
- Prevention of acute diverticulitis recurrence
- When to operate

Classification

Indications for Elective Sigmoid Resection in Diverticular Disease

Bastiaan R. Klarenbeek, MD, Michelle Samuels, MD,* Maarten A. van der Wal, MD,†*
Donald L. van der Peet, MD, PhD, Wilhelmus J. Meijerink, MD, PhD,* and Miguel A. Cuesta, MD, PhD**

*Ann Surg 2010;*251:670-674

BRIEF ARTICLE

Colonic diverticulitis with comorbid diseases may require elective colectomy

World J Gastroenterol 2013 October 21; 19(39): 6613-6617

Kevin CW Hsiao, Joseph G Wann, Chien-Sheng Lin, Chang-Chieh Wu, Shu-Wen Jao, Ming-Hsin Yang

- Chronic renal failure
- Diabetes
- Smoking
- Obesity
- NSAIDs
- Immunosuppressive therapies

- Elective sigmoidectomy is associated with significant mortality and definite colostomy (2.3% and 11.4% respectively)[1]
- The risk of acute diverticulitis after surgery is 2.6-10.4%[2]
- 78% of pts with perforated diverticulitis did not have histopy of prior diverticulitis[3]

1. Netri G. Ann Ital Chir 2000;71: 209-214;
2. Thörn M. Am J Surg 2002;183: 7-11
3. Chapman J. Ann Surg 2005;242: 576-581

CLINICAL PRACTICE GUIDELINES

Dis Colon Rectum 2020; 63: 728–747
DOI: 10.1097/DCR.0000000000001679

The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Treatment of Left-Sided Colonic Diverticulitis

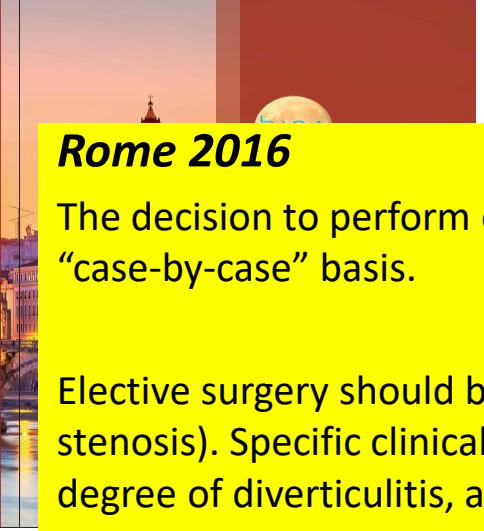
Jason Hall, M.D., M.P.H.[1] • Karin Hardiman, M.D., Ph.D.[2] • Sang Lee, M.D.[3]
Amy Lightner, M.D.[4] • Luca Stocchi, M.D.[5] • Ian M. Paquette, M.D.[6]
Scott R. Steele, M.D., M.B.A.[4] • Daniel L. Feingold, M.D.[7] • Prepared on behalf of the Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons

1. After successful nonoperative treatment of a diverticular abscess, elective resection should typically be considered. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.

2. Elective colectomy should typically be recommended for patients with diverticulitis complicated by fistula, obstruction, or stricture. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.

3. Elective resection based on young age at presentation is not recommended. Grade of Recommendation: Strong recommendation based on low-quality evidence, 1C.

4. The decision to recommend elective sigmoid colectomy after recovery from uncomplicated acute diverticulitis should be individualized. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.



Management of Patients With Diverticulosis

Rome 2016

The decision to perform elective resection after one or more episodes of AD should be undertaken on a "case-by-case" basis.

Statement 4.1 (EL: 3a-RG: B)

Elective surgery should be recommended in patients with symptomatic complicated DD (eg, fistula and stenosis). Specific clinical situations should be carefully evaluated (persisting symptoms and signs, age, degree of diverticulitis, and immunocompromised patients).

Statement 4.2 (EL: 3a-RG: B)

Elective resection in a patient with an episode of AD is safer when performed in an inflammation-free interval.

Statement 4.3 (EL: 2a-RG: B)

INTERNATIONAL SYMPOSIUM ON DIVERTICULAR DISEASE

Antonio TURSI[1], Giovanni BRANDIMARTE[2], Francesco DI MARIO[3], Angel LANAS[4], Carmelo SCARPIGNATO[5], Marco BALDUTTO[6], Giovanni BARBARA[7], Gabrio BASSOTTI[8], Gian Andrea PINDA[9], Alessandra VIOLI[2], Marjorie M.D. WALKER[10].

Madrid 2019

The decision to perform elective resection after one or more episodes of AD should be undertaken on a "case-by-case" basis.

Statement 5.7 (EL: 2b; GR: B)

*J Gastrointestin Liver Dis 2019 ;*28 (Suppl 4): 57-65

SPOTLIGHT ON:

Management in term of:

- Symptomatic Uncomplicated Diverticular Disease
- Prevention of acute diverticulitis
- Treatment of acute diverticulitis
- Prevention of acute diverticulitis recurrence
- When to operate

Classification

CLASSIFICATION

TABLE 1. Hinchey Classification and Modified Hinchey Classification for Acute Diverticulitis

Hinchey Classification[12]		Modified Hinchey Classification[13]	
Stage		Stage	
		0	Mild clinical diverticulitis
I	Pericolic abscess or phlegmon	Ia	Confined pericolic inflammation–phlegmon
		Ib	Confined pericolic abscess
II	Pelvic, intra-abdominal, or retroperitoneal abscesses	II	Pelvic, intra-abdominal, or retroperitoneal abscesses
III	Generalized purulent peritonitis	III	Generalized purulent peritonitis
IV	Generalized fecal peritonitis	IV	Generalized fecal peritonitis

Hansen & Stock Classification of Colonic Diverticular Disease

Stage	Description	CT Scan
0	Diverticulosis	Gas- or contrast-filled diverticulum
I	Acute uncomplicated diverticulitis	+ Intestinal wall thickening
II	Complicated diverticulitis	
IIa	Peridiverticulitis, phlegmonous diverticulitis	+ Inflammatory reaction in pericolic fatty tissue
IIb	Abscess diverticulitis, covered perforation, fistulization	+ Mesocolic or retroperitoneal abscess, lower pelvis abscess
IIc	Free perforation	Free air, free fluid, abscesses where applicable
III	Chronic recurrent diverticulitis	Intestinal wall thickening, stenosis or fistula where applicable

International Consensus on Diverticulosis and Diverticular Disease. Statements from the 3rd International Symposium on Diverticular Disease.
J Gastrointestin Liver Dis 2019;28(suppl. 4): 57-66

tabella 1: score di Forrest - rischio di risanguinamento, di ricorso alla chirurgia e di morte (10)

Grado	Tipo di lesione	Risanguinamento entro 72 ore	Chirurgia	Mortalità
Sanguinamento attivo				
Ia	Emorragia a getto	90-100%	35%	11%
Ib	Emorragia a nappo	80%	35%	11%
Segni di emorragia recente				
IIa	Vaso visibile	40-60%	34%	11%
IIb	Coagulo adeso	20-25%	10%	7%
IIc	Chiazza di ematina	13%	6%	3%
Nessun segno di emorragia				
III	Ulcera a fondo deterso	5%	0.5%	2%

SCORE ENDOSCOPICI

CDEIS
CROHN'S DISEASE INDEX OF SEVERITY

SES-CD
SIMPLE ENDOSCOPIC SCORE FOR CROHN'S DISEASE

CDEIS & SES-CD

MAYO
ENDOSCOPIC

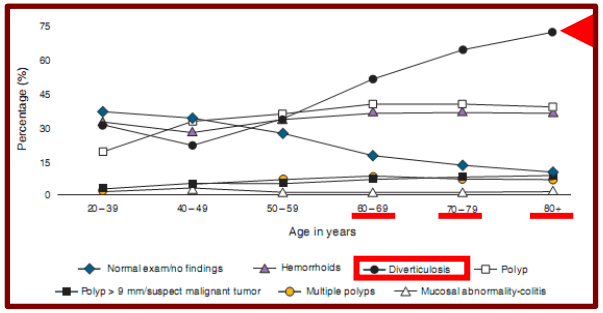
RUTGEERTS

Diverticular Disease?

Los Angeles Classification of Oesophagitis

Grade A	One (or more) mucosal break no longer than 5 mm that does not extend between the tops of two mucosal folds
Grade B	One (or more) mucosal break more than 5 mm long that does not extend between the tops of two mucosal folds
Grade C	One (or more) mucosal break that is continuous between the tops of two or more mucosal folds but which involve less than 75% of the circumference
Grade D	One (or more) mucosal break which involves at least 75% of the esophageal circumference

Why to develop an endoscopic classification for diverticulosis and diverticular disease?



Diverticulosis is the most frequent endoscopic finding at colonoscopy

Everhart JA, Ruhl JE. Gastroenterology 2009;136: 741-754

Signs of diverticular inflammation may be detected in 0.8-2% at colonoscopy

Ghorai S, Ulbright TM, Rex DK. Am J Gastroenterol 2003;98: 802-6

Tursi A. Aliment Pharmacol Ther 2011;33: 358-65

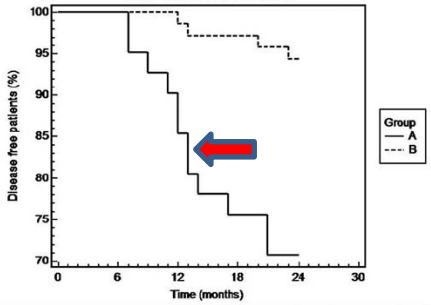


Fig. 2. Kaplan-Meier curve showing recurrence of diverticulis in patients with persistence of endoscopic/histological inflammation (Group A) and in patients without persistence of endoscopic/histological inflammation (Group B). Log rank test, p = 0.0004.

Extension of diverticular segment may be at risk of acute diverticulitis occurrence
Persistence of diverticular inflammation may be at risk of acute diverticulitis recurrence

Tursi A. Aliment Pharmacol Ther 2013;38: 741-51
Tursi A. J Gastrointestin Liver Dis 2013;22: 13-9

Until 2012, an endoscopic classification of diverticulosis and diverticular disease was absent

From February to December 2012, 32 Italian endoscopists developed and validated the first endoscopic classification of diverticulosis and diverticular disease, called

DICA

(Diverticular Inflammation and Complication Assessment)

1° STEP

IDENTIFICATION OF THE ENDOSCOPIC FINDINGS AND SCORING THEM

2° STEP

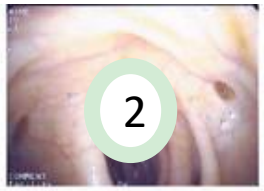
ASSESSMENT OF REPRODUCIBILITY

3° STEP

ASSESSMENT OF THE AGREEMENT

Diverticulosis extension:

- Left Colon
- Right Colon

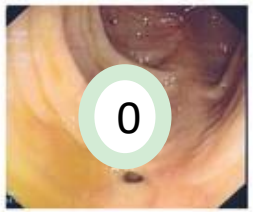


Left diverticulosis

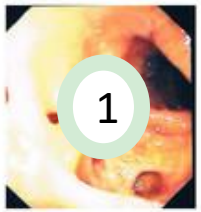
Right diverticulosis

Number of diverticula per colonic district:

- Less than 15;
- More than 15.



<15 diverticula



>15 diverticula

Presence and type of inflammatory findings:

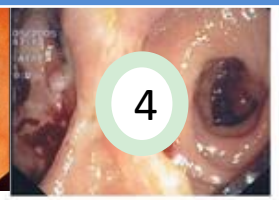
- Oedema/Hyperaemia;
- Erosions;
- SCAD.

DICA SCORE	Numeric values
DICA1	1-3 points
DICA 2	4-7 points
DICA 3	>7 points

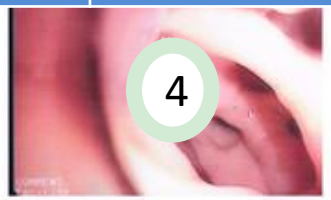
Presence of endoscopic complications:

- Rigidity;
- Pus;
- Stenosis;
- Diverticular bleeding.

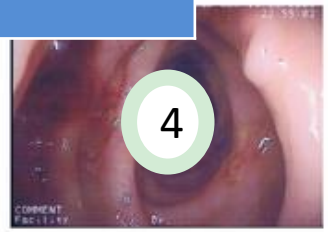
Rigidity



Pus



Stenosis



Bleeding

Tursi A, Brandimarte G, Di Mario F et al. Development and Validation of an Endoscopic Classification of Diverticular Disease of the Colon: The DICA Classification. Dig Dis 2015;33:68-76

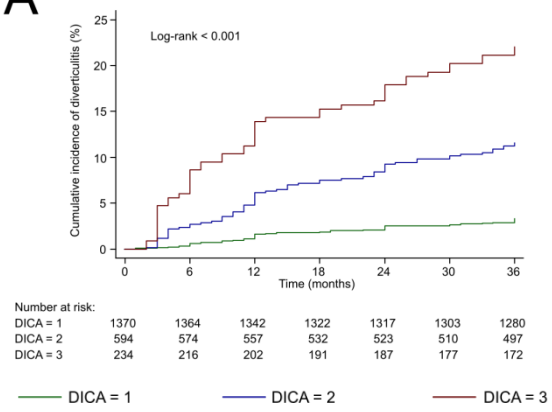
Original research

Prognostic performance of the 'DICA' endoscopic classification and the 'CODA' score in predicting clinical outcomes of diverticular disease: an international, multicentre, prospective cohort study

Antonio Tursi ,[1,2] Giovanni Brandimarte,[3] Francesco Di Mario,[4] Walter Elisei,[5] Marcello Picchio,[6] Leonardo Allegretta,[7] Maria Laura Annunziata,[8] Mauro Bafutto,[9] Gabrio Bassotti,[10] Maria Antonietta Bianco,[11] Raffaele Colucci,[12] Rita Conigliaro,[13] Dan Dumitrascu,[14] Ricardo Escalante,[15] Luciano Ferrini,[16] Giacomo Forti,[17] Marilisa Franceschi,[18] Maria Giovanna Graziani,[19] Frank Lammert,[20] Giovanni Latella,[21] Giovanni Maconi ,[22] Gerardo Nardone ,[23] Lucia Camara de Castro Oliveira,[24] Enio Chaves Oliveira,[25] Alfredo Papa,[26] Savvas Papagrigoriadis,[27] Anna Pietrzak,[28] Stefano Pontone ,[29] Tomas Poskus,[30] Giuseppe Pranzo,[31] Matthias Christian Reichert ,[20] Stefano Rodinò,[32] Jaroslaw Regula,[33,34] Giuseppe Scaccianoce,[35] Franco Scaldaferri,[36] Roberto Vassallo,[37] Costantino Zampaletta,[38] Angelo Zullo,[39] Daniele Piovani,[40,41] Stefanos Bonovas ,[40,41] Silvio Danese ,[42] DICA International Group

PRIMARY END POINTS

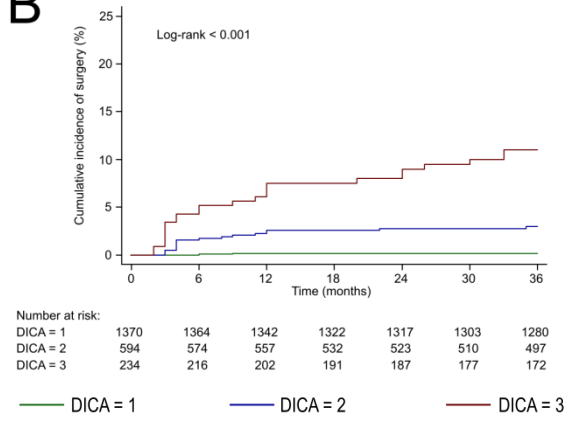
A



Acute Diverticulitis Occurrence/Recurrence

AD occurred in 130 patients. The stratified risk was:
3.3% (95% CI, 2.5–4.5) in DICA 1
11.6% (95% CI,9.2–14.5) in DICA 2
22.0% (95% CI,17·2–28·0) in DICA 3 (p<0·001)

B



Surgery

Surgery occurred in 37 patients. The stratified risk was:
0.15% (95% CI, 0.04–0.59) in DICA 1
3.0% (95% CI, 1.9–4.7) in DICA 2
11.0% (95% CI, 7.5–16.0) in DICA 3 (p<0·001)

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DICA

DIVERTICULAR INFLAMMATION COMPLICATION ASSESSMENT

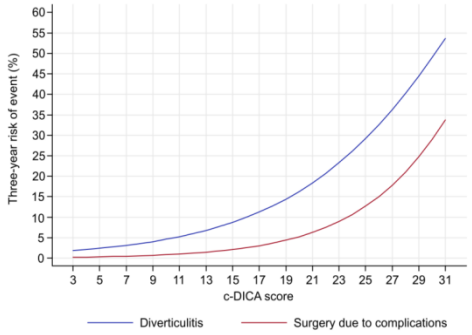
Data from prospective study

CODA

Combined Overview on Diverticular Assessment

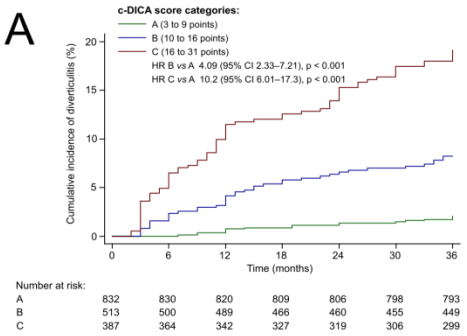
Baseline patient's characteristics	Points
Endoscopic score	
DICA 1	7
DICA 2	14
DICA 3	21
Abdominal pain score	
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10
Patient age	
<65 years	0
≥65 years	-4

	Score
CODA A	From 3 to 9
CODA B	From 10 to 16
CODA C	> 16

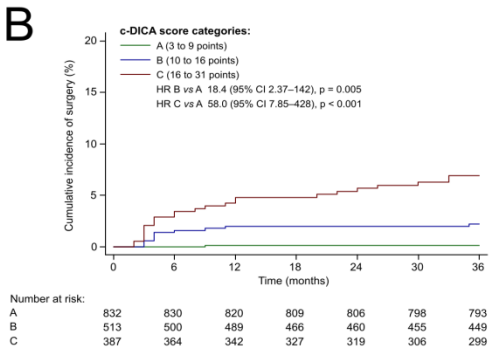


CODA score: scoring system.

A



B



The cumulative probability of diverticulitis was: ≤4% in CODA A
<10% in CODA B
>10% in CODA C

The cumulative probability of surgery was: ≤0·7% in CODA A
<2·5% in CODA B
>2·5% in CODA C

The CODA score showed optimal discrimination capacity in predicting the risk of surgery in the development (c-statistic: 0·829; 95% CI 0·811–0·846) and validation cohort (c-statistic: 0·943; 0·905–0·981).

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ORIGINAL ARTICLE

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Diverticular Inflammation and Complication Assessment classification, coda score and fecal calprotectin in clinical assessment of patients with diverticular disease: A decision curve analysis

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DICA International Group

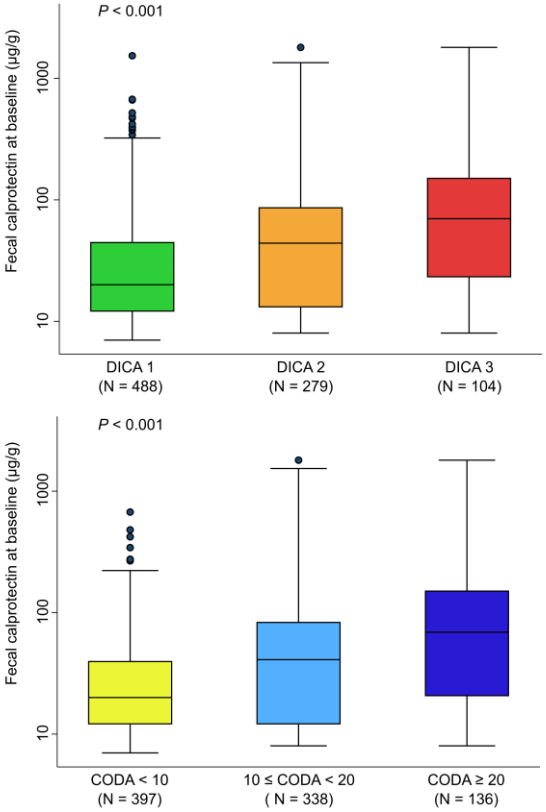
Key findings

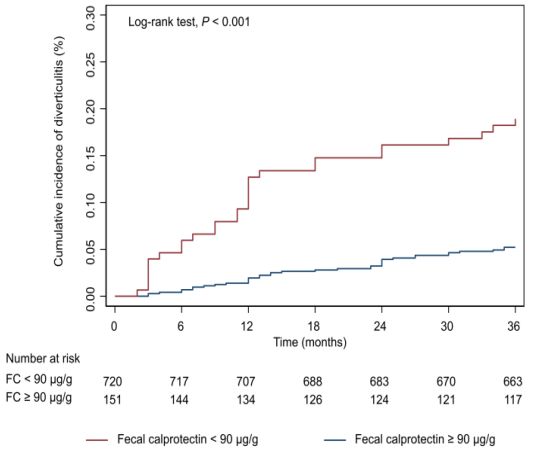
This large (871 patients), prospective, cohort study collected patients in 43 centres located in Europe and South America, followed up for three years patients with fecal calprotectin (FC) assessment. We compared the role FC with DICA endoscopic classification and CODA score in managing diverticular disease.

FC was significantly associated with DICA classification (A) and CODA score (B).

The estimated 3-year cumulative probability of diverticulitis was 5.2% (95% CI, 3.8−7.1%) in patients with basal FC<90 µg/g, and 18.9% (95% CI, 13.5−26.2%) in patients with basal FC≥90 µg/g, which significantly differed across strata (C)

FC was associated with the risk of AD at 3 years (HR per each base 10 logarithm increase: 3.29; 95% CI, 2.13−5.10) and showed moderate discrimination (c-statistic: 0.685; 0.614−0.756). DICA and CODA were more accurate predictors of AD than FC. However, FC showed high discrimination capacity to predict AD at 3 months, which was not maintained at longer follow-up times. The decision curve analysis comparing the combination of FC and CODA with CODA alone did not clearly indicate a larger net benefit of one strategy over the other.





CODA score provided the best predictive accuracy and net benefit in predicting acute diverticulitis in the long-term (3-years). FC showed a comparative short-term prognostic value with CODA (3 months) and enhanced the prognostic value of the DICA endoscopic classification.
FC measurement, together to DICA classification and CODA score, may be a possible tool to gauge the short-term risk of acute-diverticulitis.

Tursi A. United Eur Gastroenterol J 2023 (in press)

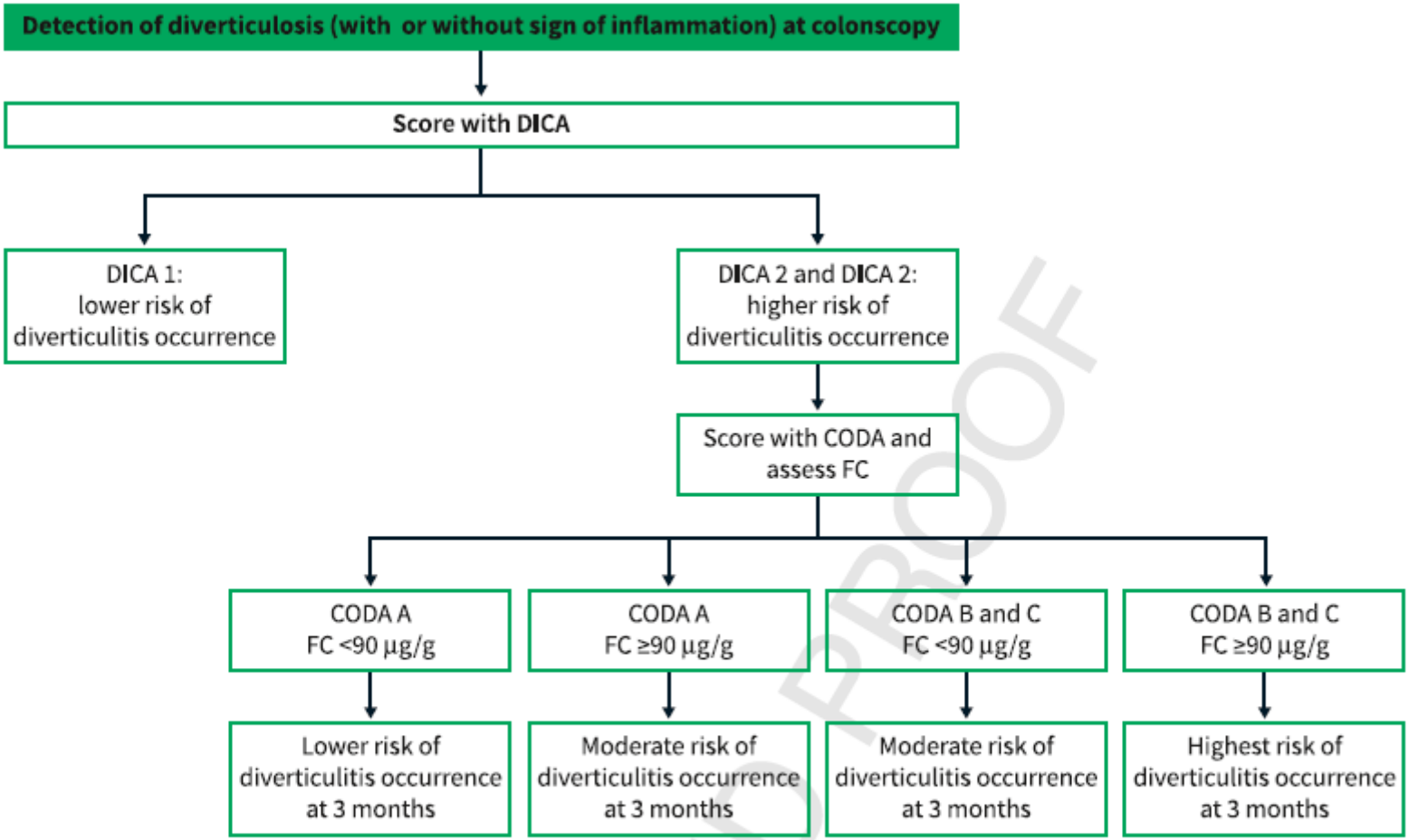


FIGURE 4 Flow-chart suggesting the possible short-term (3-month) risk stratification of patients with newly diagnosed colonic diverticulosis detected on endoscopy. CODA, Combined Overview on Diverticular Assessment; DICA, Inflammation and Complication Assessment; FC, fecal calprotectin.

TAKE HOME MESSAGES

- The epidemiology and costs of the diverticular disease of the colon impact significantly the real life
- Acute diverticulitis is the most umportant (but quite rare…) complication (it affects about 4- 5% of patients with diverticulosis and SUDD), but in the large majority of cases it is uncomplicated and can be medically managed
- At present, rifaximin and mesalazine seems to be the only drugs able to control SUDD
- Systemic antibiotics are still advised in the treatment of acute diverticulitis, even if their use in uncomplicated diverticulitis should be case by case
- At present, there are no drugs really effective in preventing acute diverticulitis recurrence
- Today, the elective surgery for diverticular disease should be case by case
- The DICA endoscopic classification, and its clinical evolution CODA, seem to be a good tool to predict the clinical outcome of the patients with diverticular disease. Further studies have to use this classification in order to select patients who can benefit from medical or surgical treatment according to the DICA/CODA score.