

MILANO 2015
1 MAGGIO • 31 OTTOBRE

NUTRIRE IL PIANETA
ENERGIA PER LA VITA



Incontri AIGO in EXPO 2015



Alimentazione nelle Malattie Infiammatorie croniche dell'intestino :
una terapia e una prevenzione

MALATTIE INFIAMMATORIE CRONICHE DELL'INTESTINO o INFLAMMATORY BOWEL DISEASE (IBD)

- Rettocolite Ulcerosa**
- Malattia di Crohn**
- Colite indeterminata**



avrò
un'intolleranza
alimentare ?? !!!

perché mi è
venuta ???

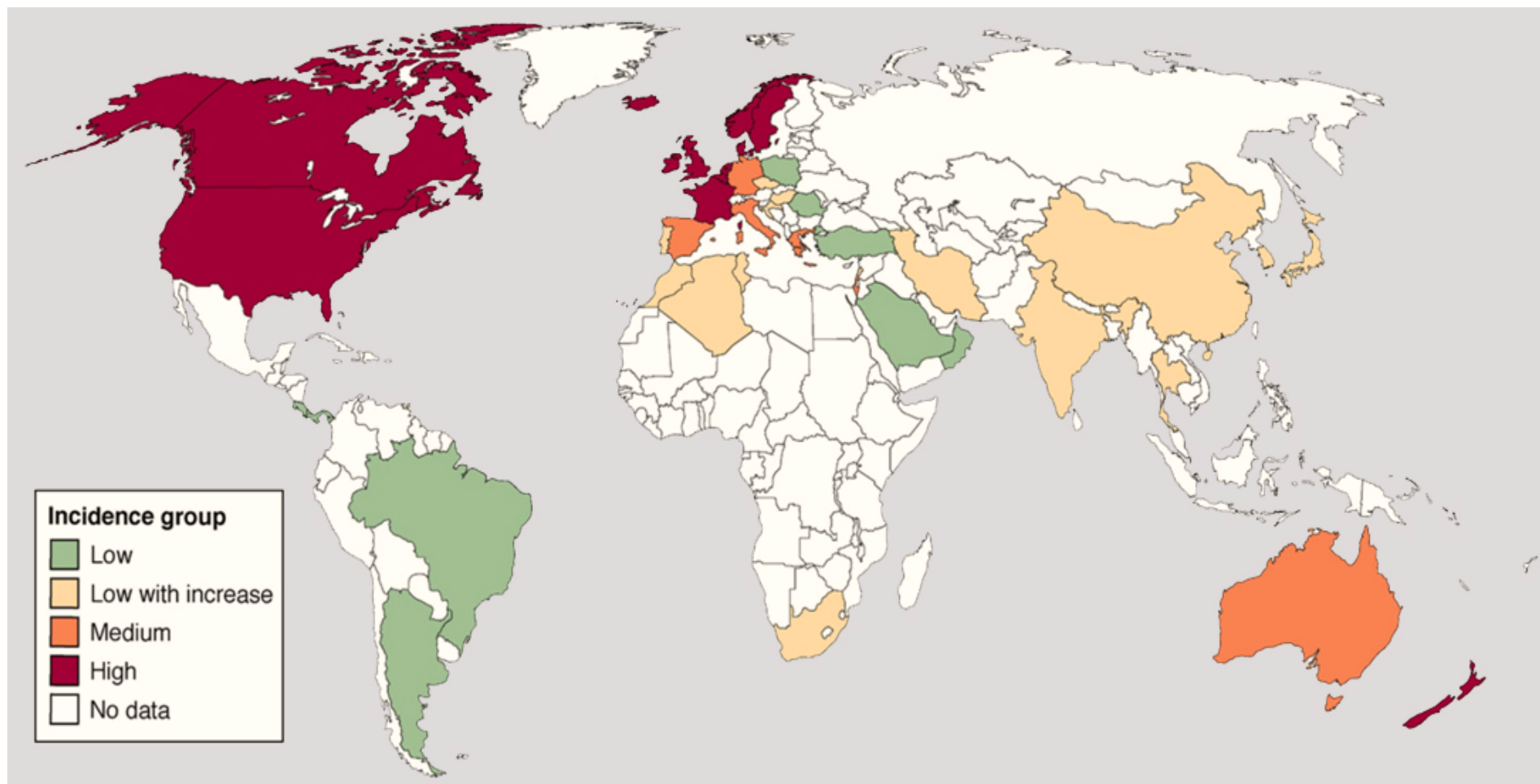
ed ora cosa
devo
mangiare ??

la dieta può
curare la malattia ?

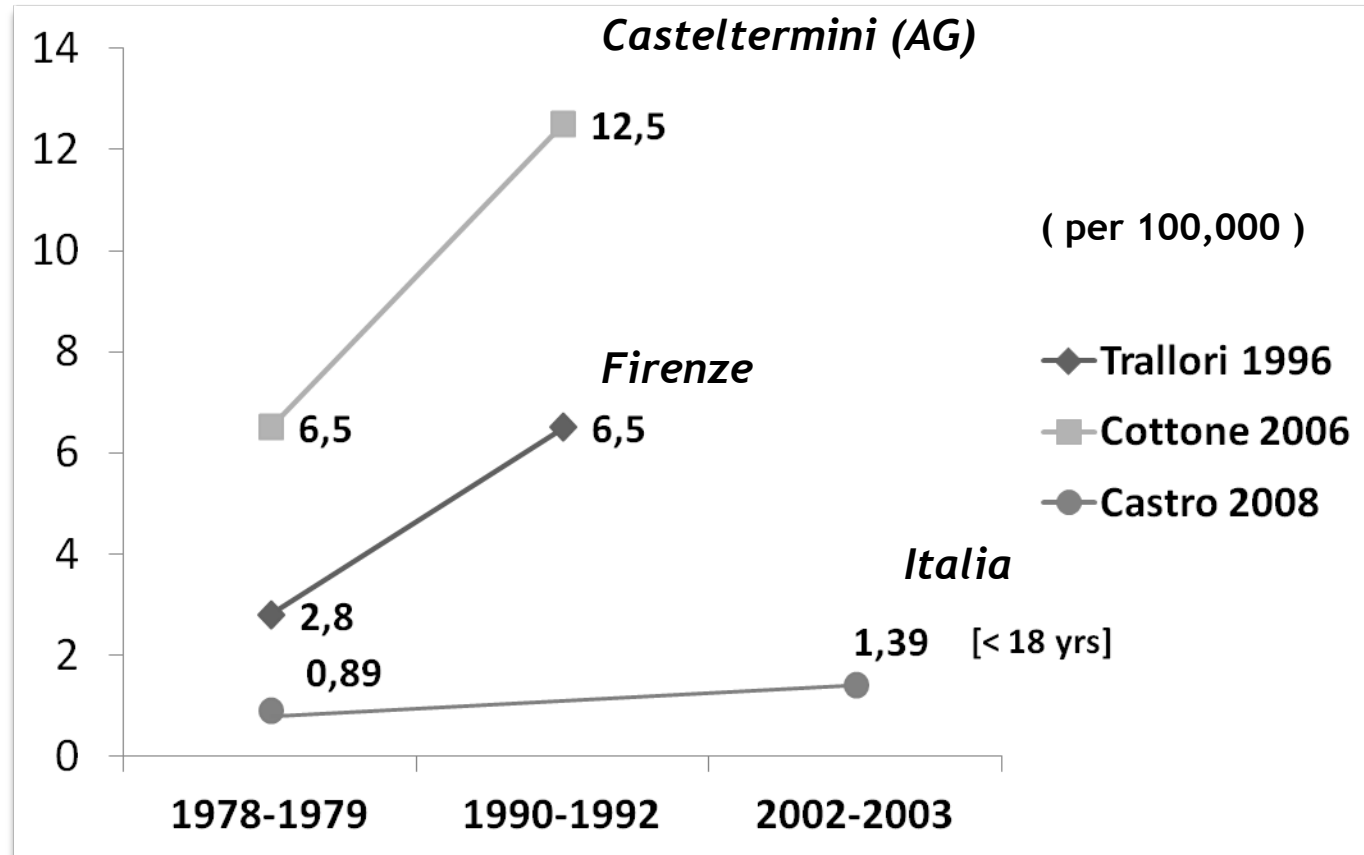


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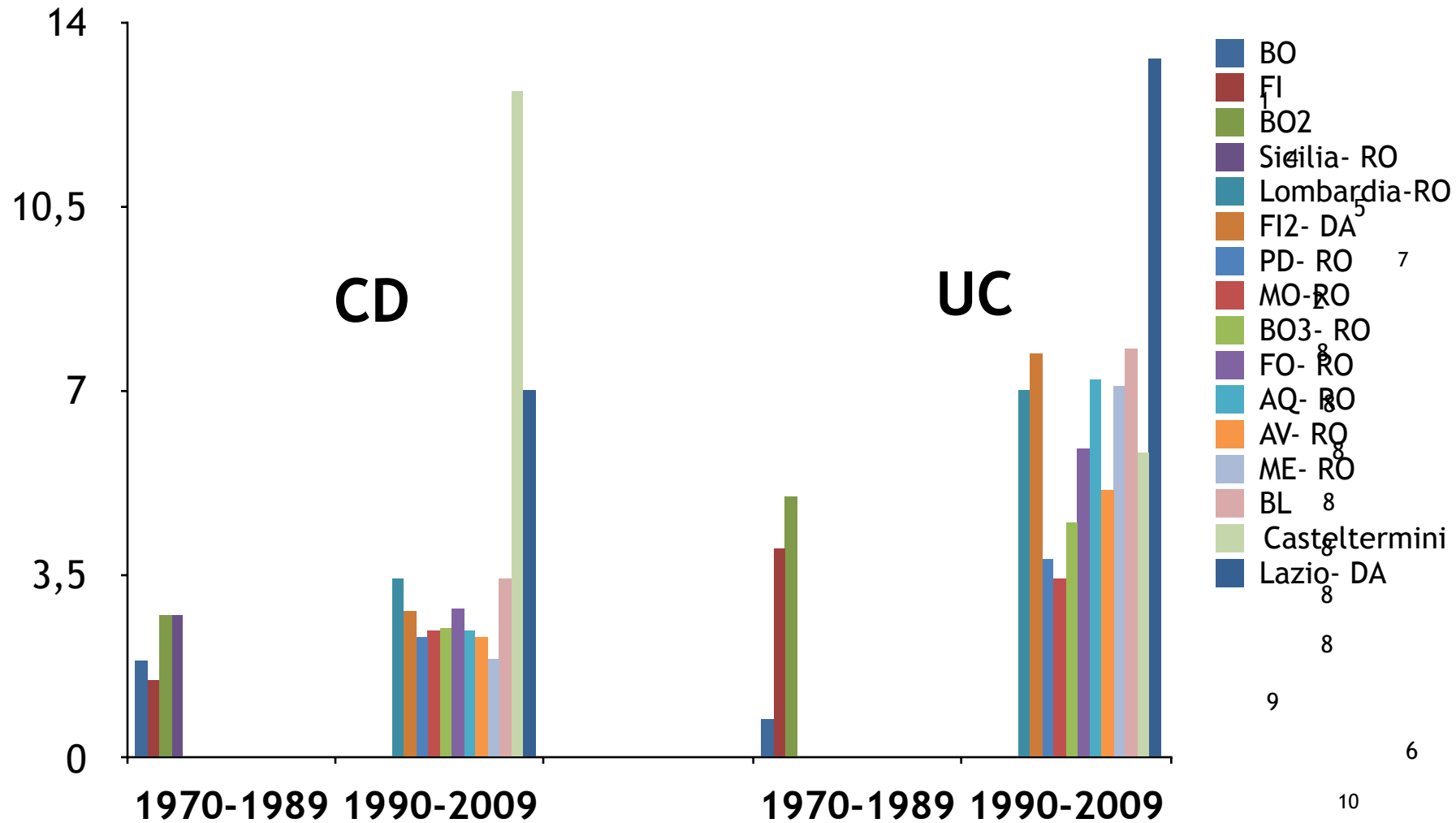
The global map of inflammatory bowel disease



Rise in IBD incidence rates in Italian districts



Incidence of Inflammatory Bowel Disease in Italy



Trallori G, 1991¹; Trallori G, 1996²; Lanfranchi GA, 1976³; Tragnone A, 1993⁴; Cottone M, 1991⁵; Cottone M, 2006⁶; Ranzi R, 1996⁷; Tragnone A, 1996⁸; Dal Pont E, 2010⁹; Di Domenicantonio R, 2013¹⁰.

Copayment exemptions



resident population (2011): 60.626.442 (ISTAT)

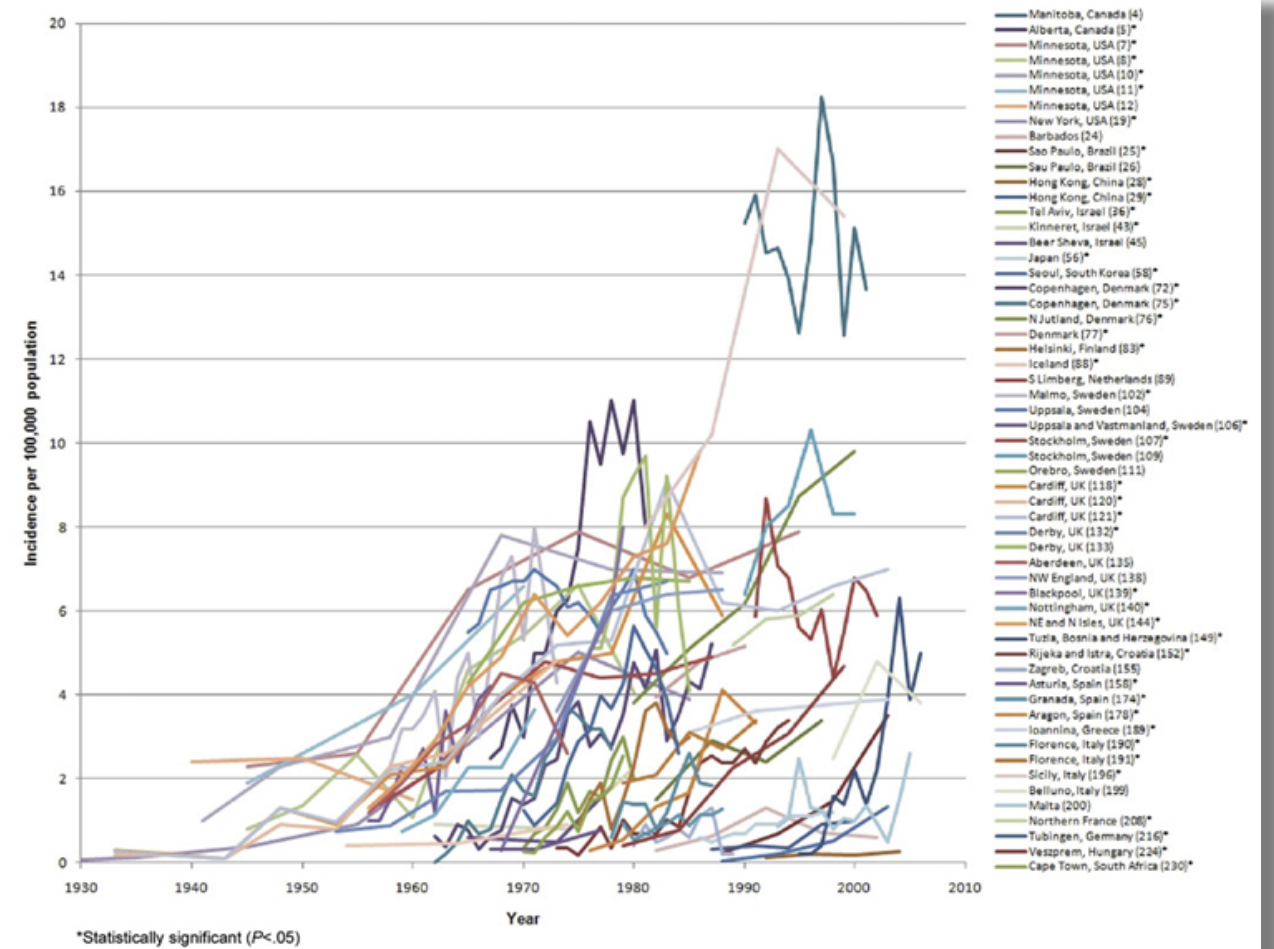
Agg. Febbraio 2014



Fonte: AMICI Onlus

ITALIA	152.821
Abruzzo	3.210
Basilicata	979
Calabria	3.620
Campania	10.033
Emilia Romagna	12.795
Friuli Venezia Giulia	3.654
Lazio	9.764
Liguria	4.665
Lombardia	26.452
Marche	3.150
Molise	658
Piemonte	19.206
Valle d'Aosta	334
Puglia	12.431
Sardegna	2.323
Sicilia	11.154
Toscana	11.189
Trentino Alto Adige	2.081
Umbria	2.848
Veneto	12.275

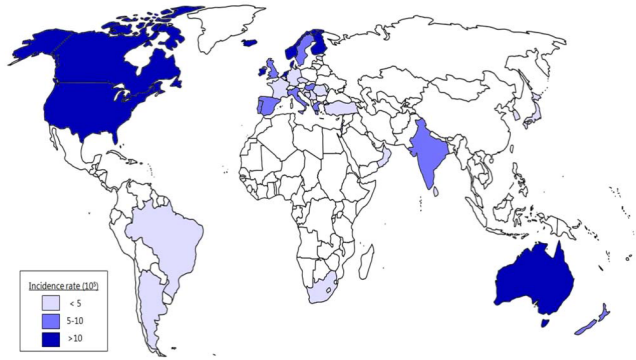
“invertire il trend epidemiologico”



Molodecky NA et al, Gastroenterology 2012

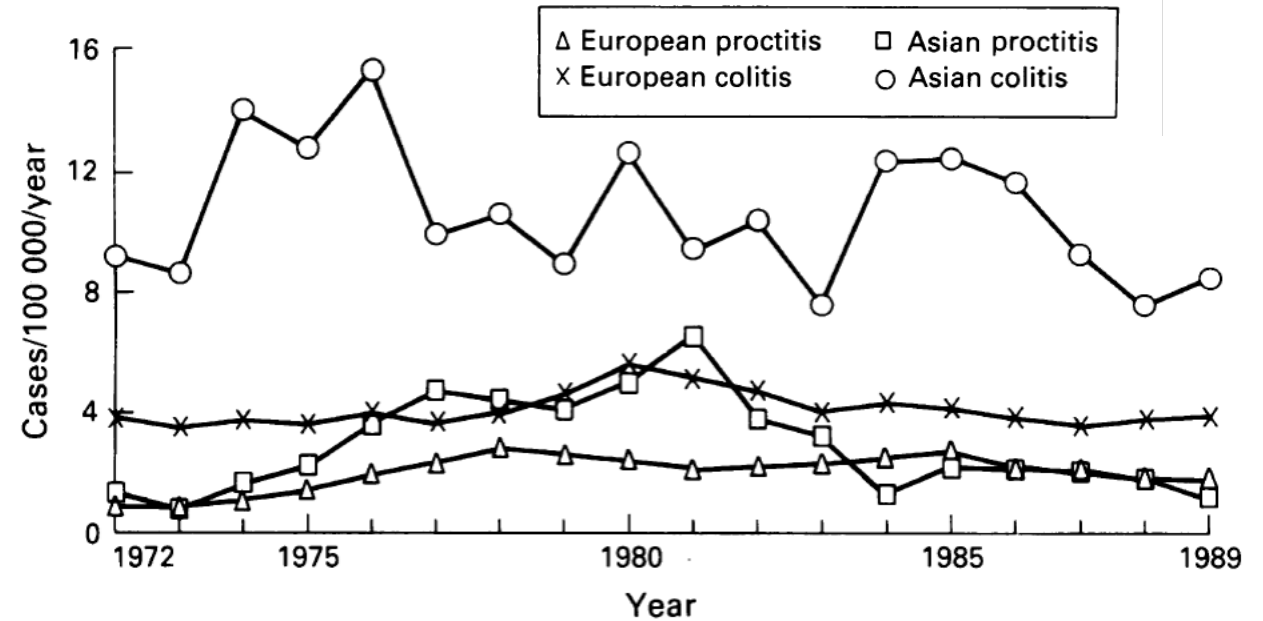


Epidemiological studies in Indian migrants



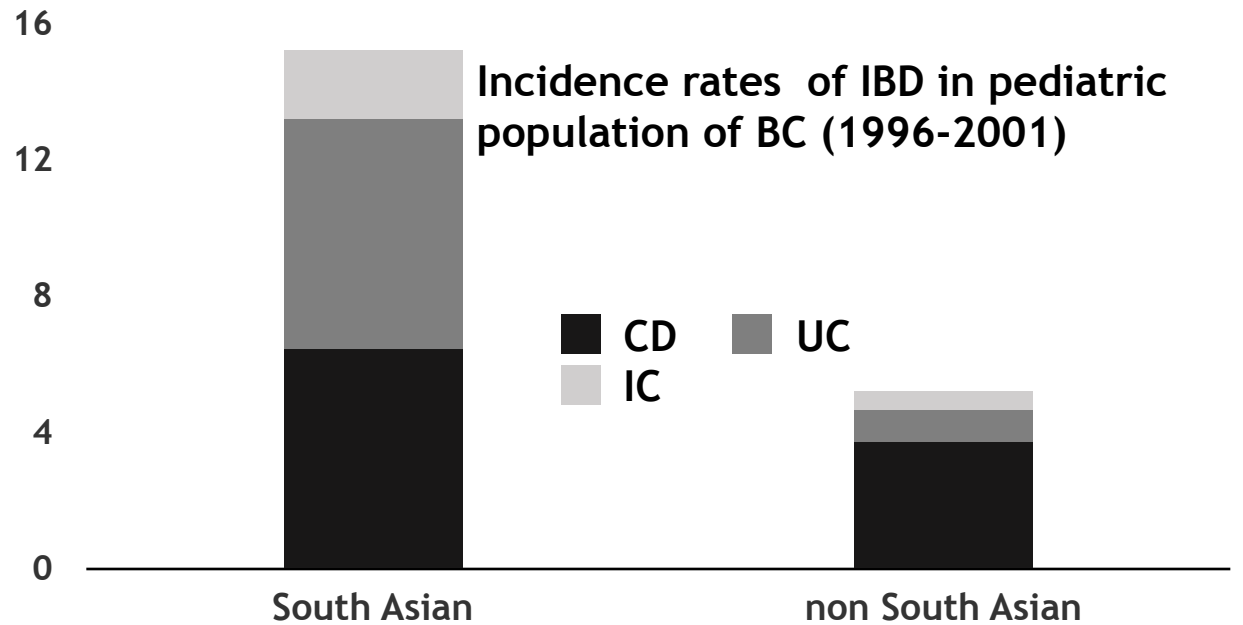
Leicestershire

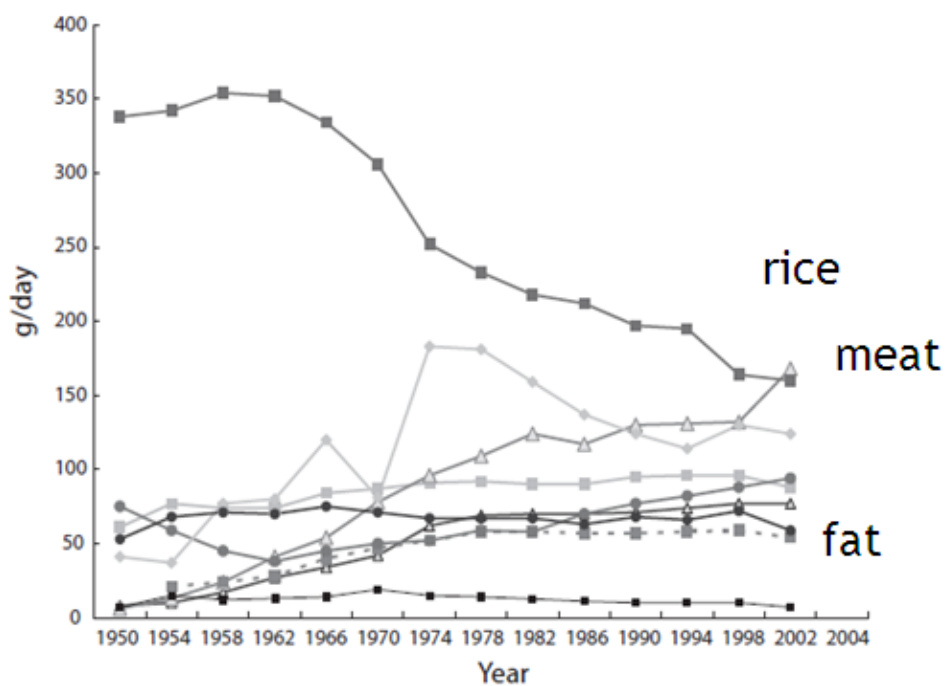
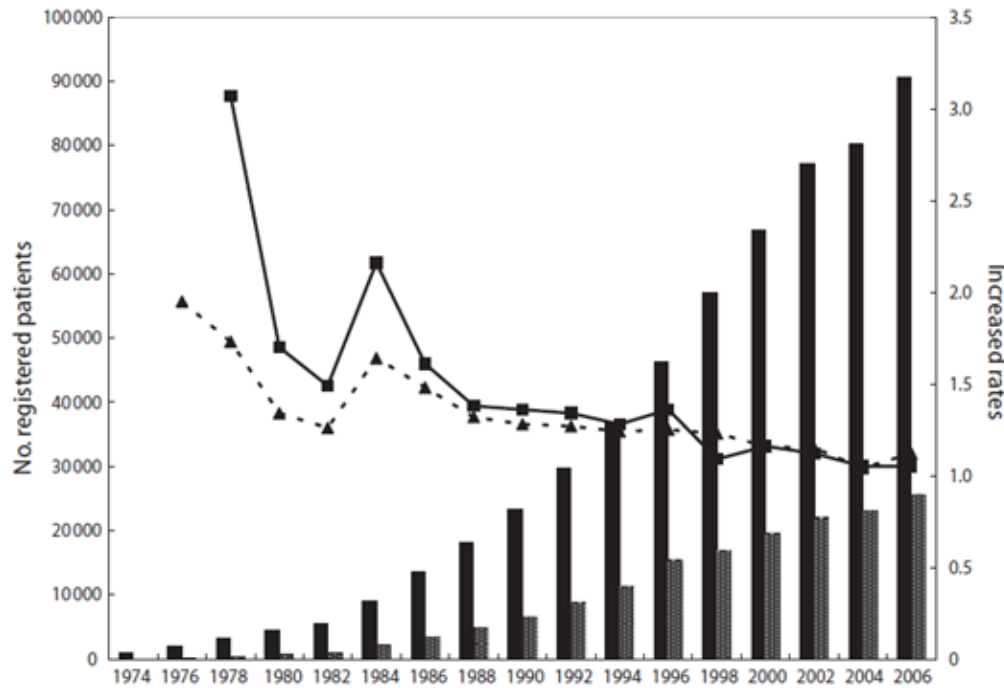
Probert CSJ et al., GUT 1992



British Columbia

Pinsk V et al., AJG 2007





diet

Is there a link
between food
and intestinal
microbes and
the occurrence of
CD and UC?

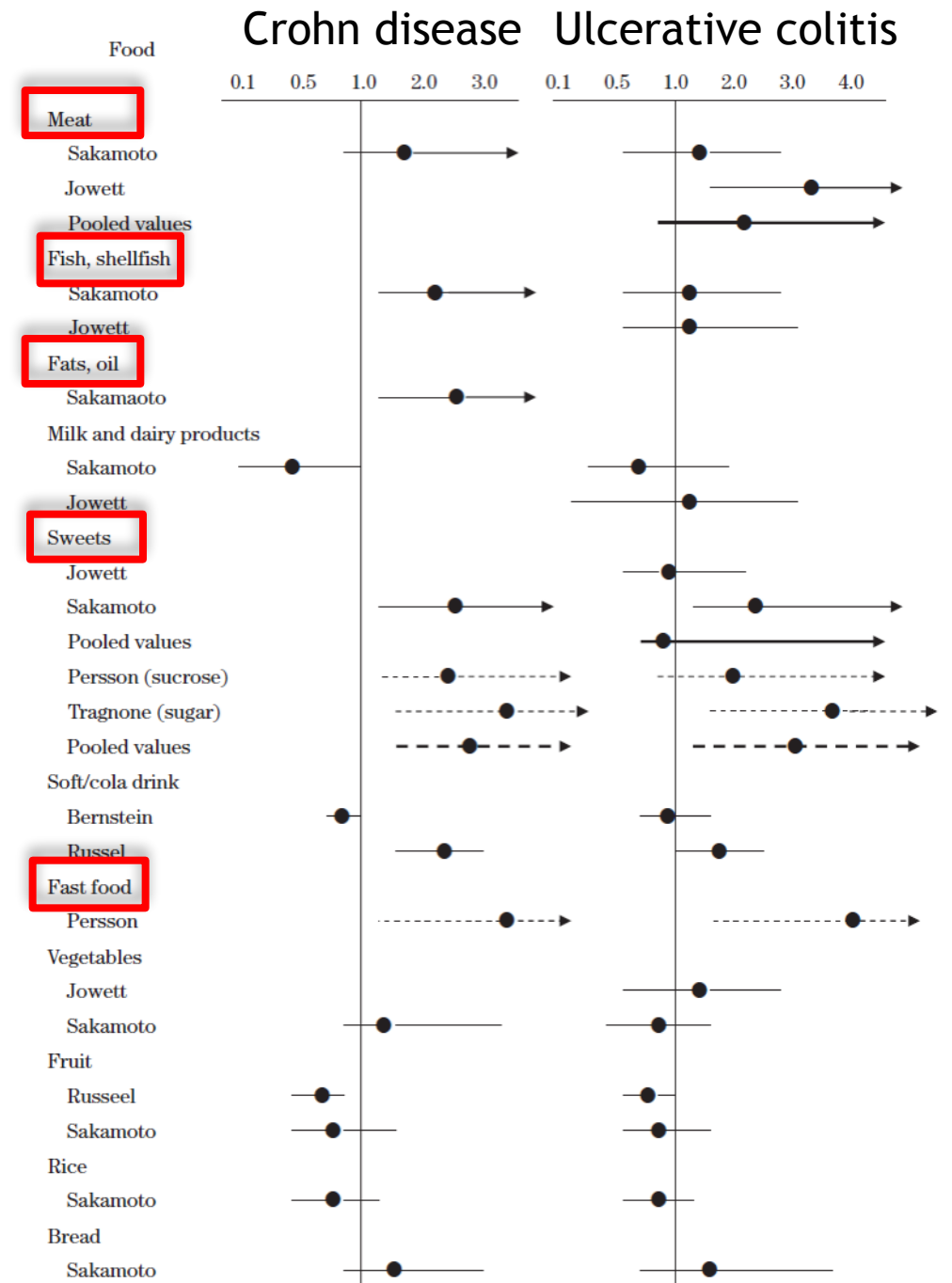
Asakura H et al J Gastroenterol Hepatol 2008

Food: An intestinal environmental factor

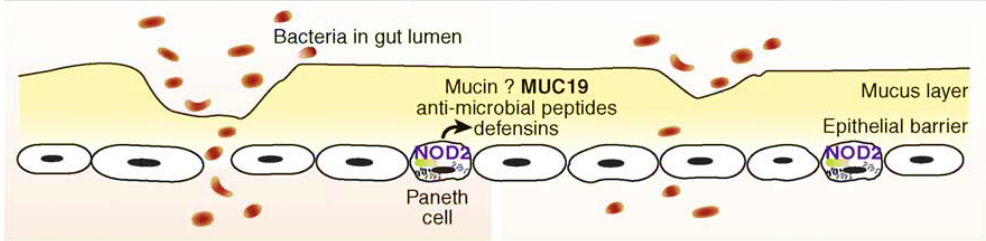
Animal-derived food

Case-control studies on the consumption of dairy food by IBD vs healthy controls

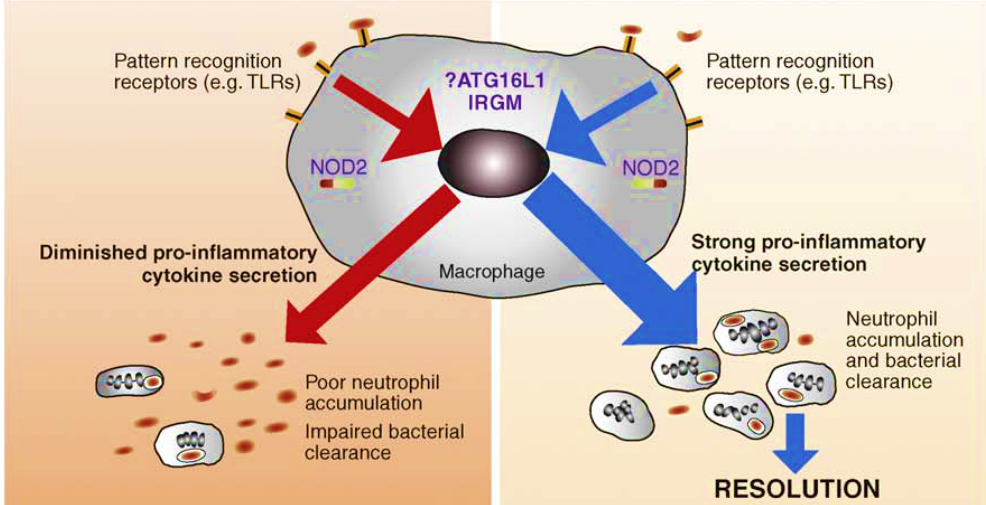
Animal meat, sweets and sugar / confectionery and fast food increased the OR of the occurrence of CD and UC



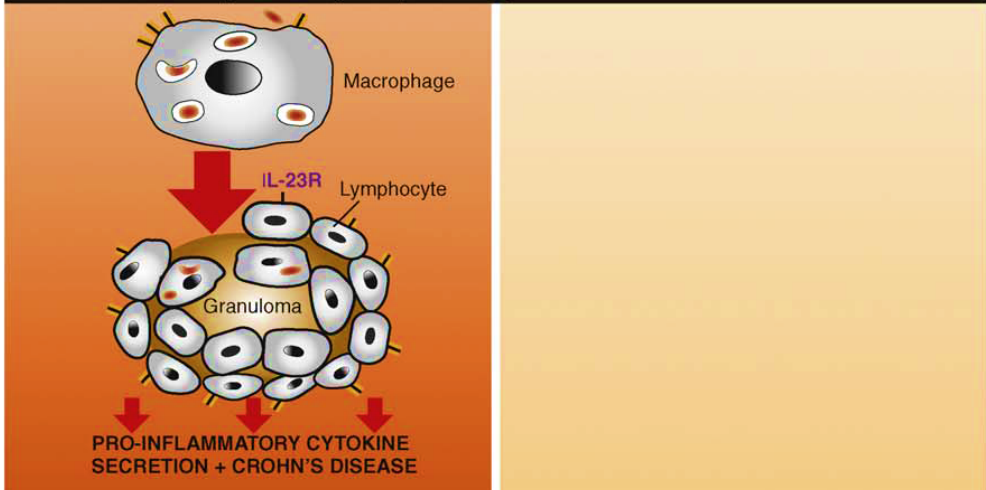
STAGE 1: Penetration of foreign material



STAGE 2: Impaired clearance of material



STAGE 3: Compensatory adaptive responses



‘three-stage mechanism for the development of CD lesions’

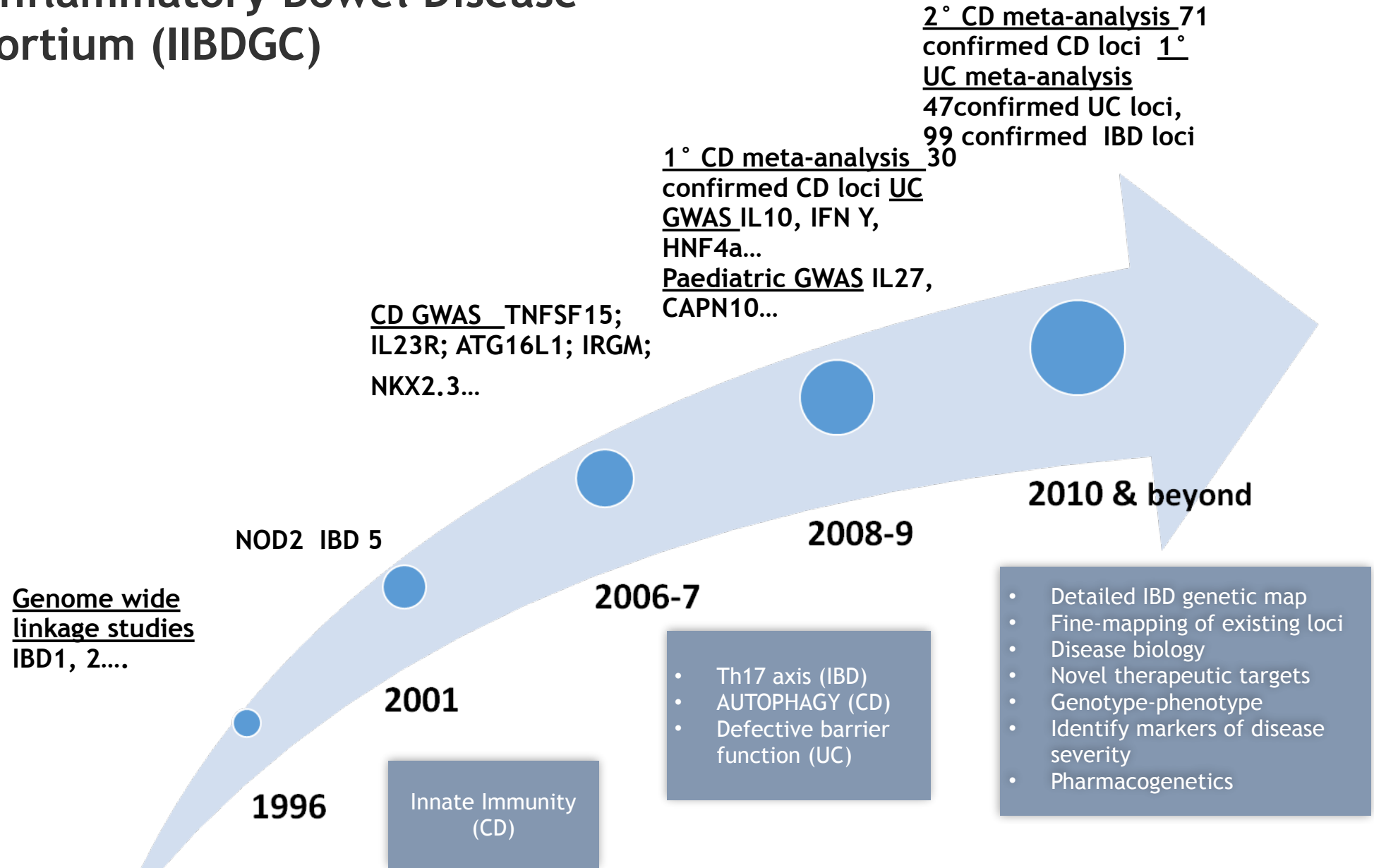
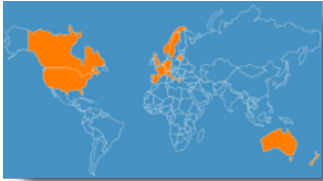
penetration of luminal contents into the bowel wall

impaired clearance of foreign material from the bowel wall

compensatory adaptive immune responses

International Inflammatory Bowel Disease Genetics Consortium (IIBDGC)

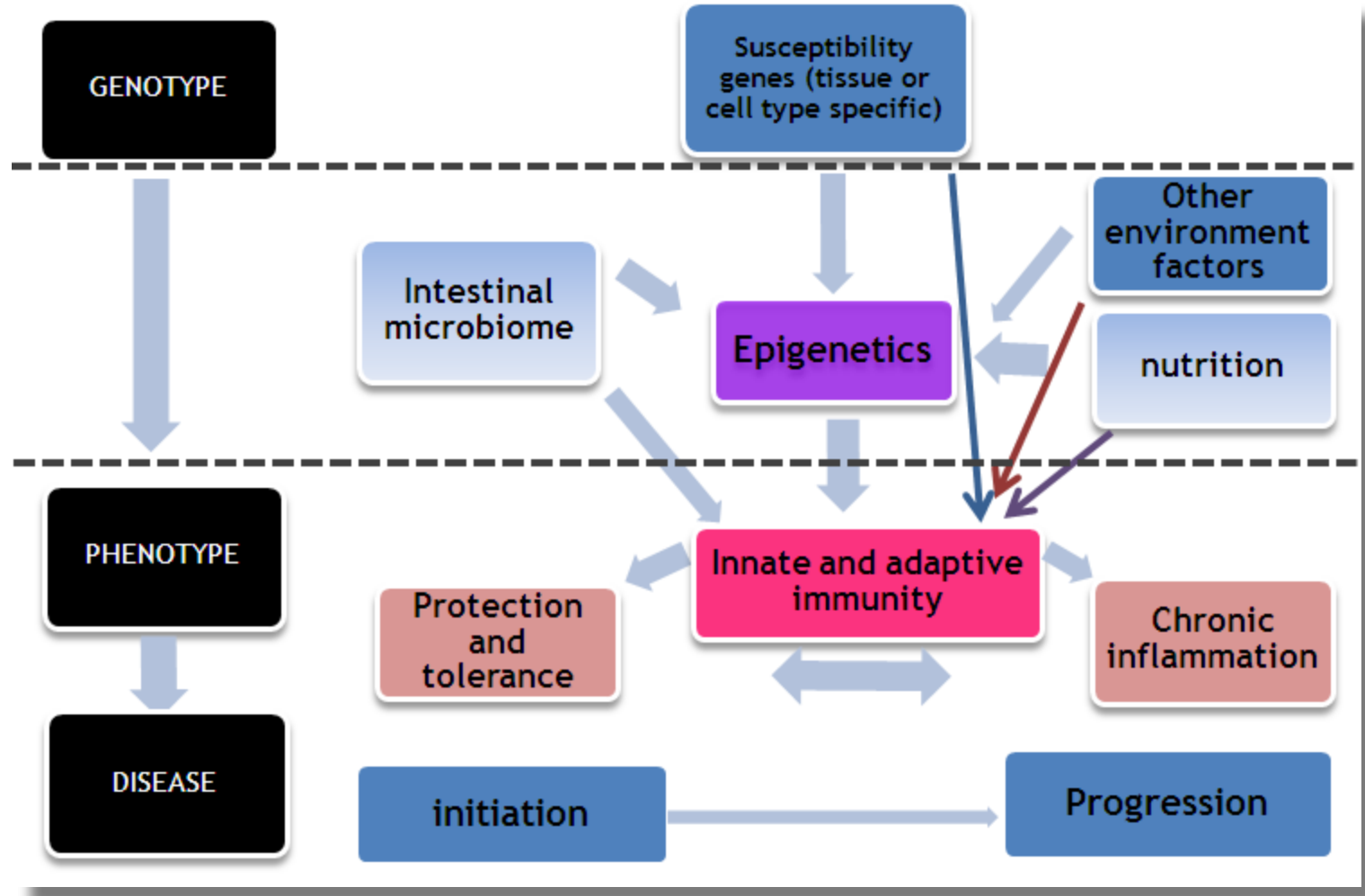
Oxford, 1997



From the Environment to Genetics via Epigenetics

epigenetics may partially account for the “hidden heritability” in IBD.

several environmental factors produce epimutations including smoking, the microbiota, and diet.





smoking

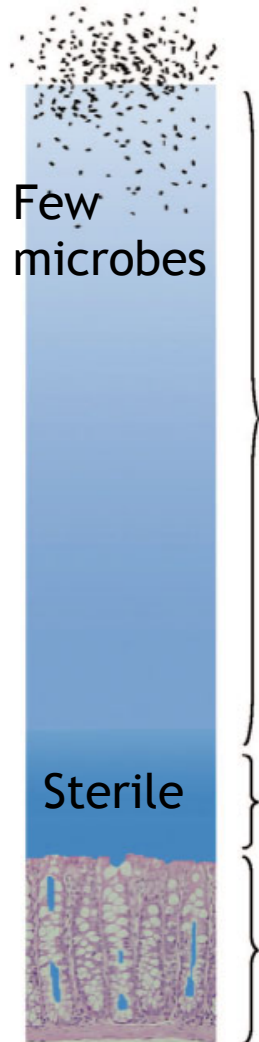
appendectomy

diet

environmental effects on microbiota

*infections
antibiotics early in life
socioeconomic factors
oral contraceptives
bottle feeding
vaccinations ...*

Mucosal flora in IBD: a barrier defect

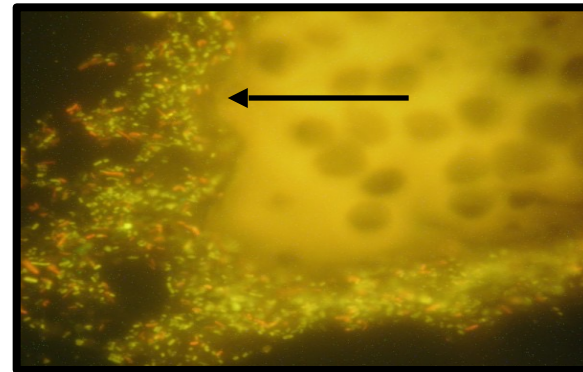


Intestinal Lumen

10^{14} (an)aerobic bacteria

Outer mucus layer (700 μm)

mucins ⁽⁻⁾ and
antibacterial peptides ⁽⁺⁾
(defensins, cathelicidines)

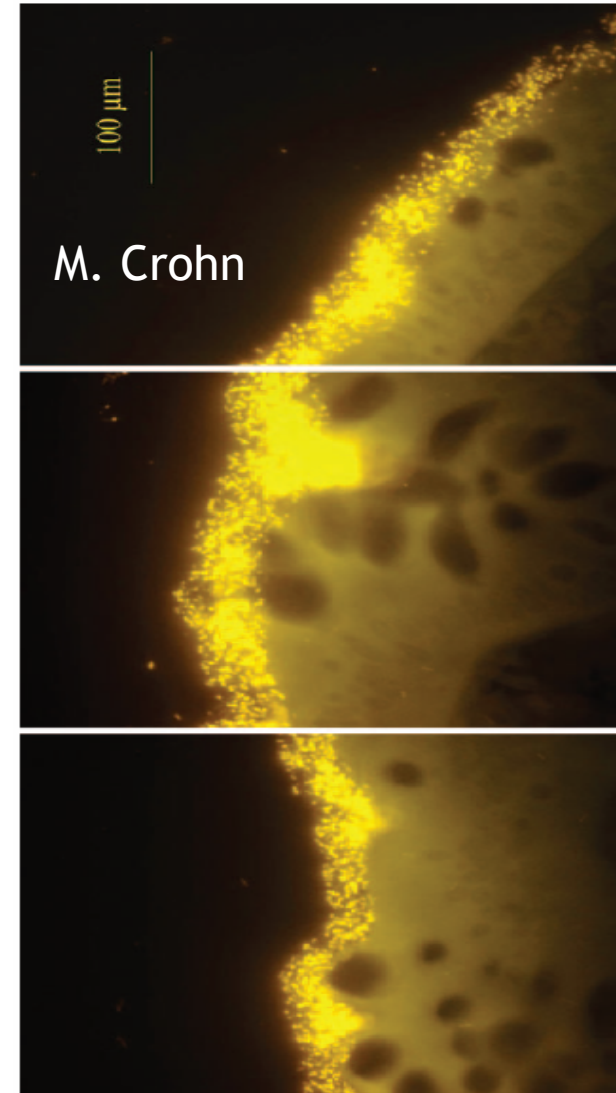


Inner mucus layer (100 μm)

adherent, rich in
antibacterial peptides

Crypts (200 μm)

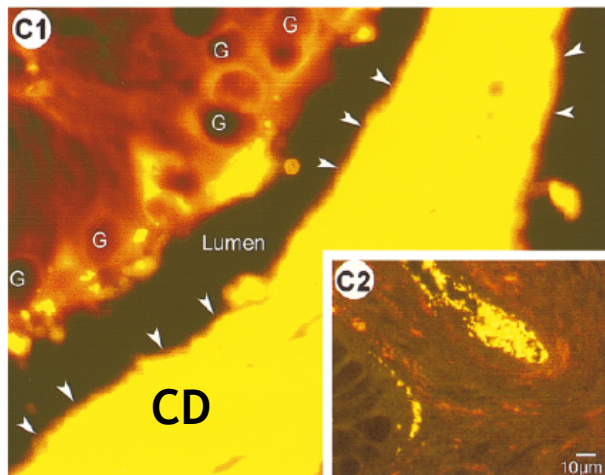
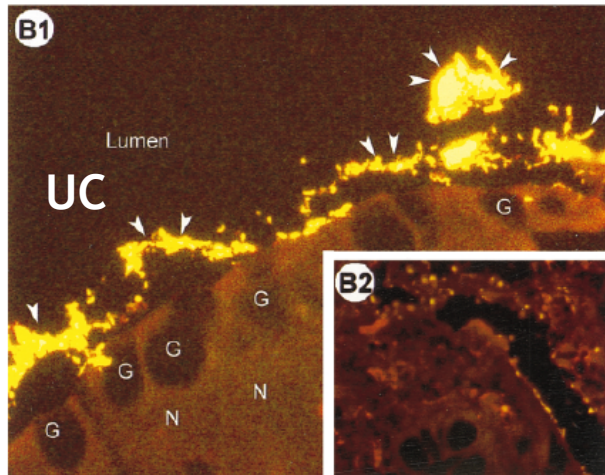
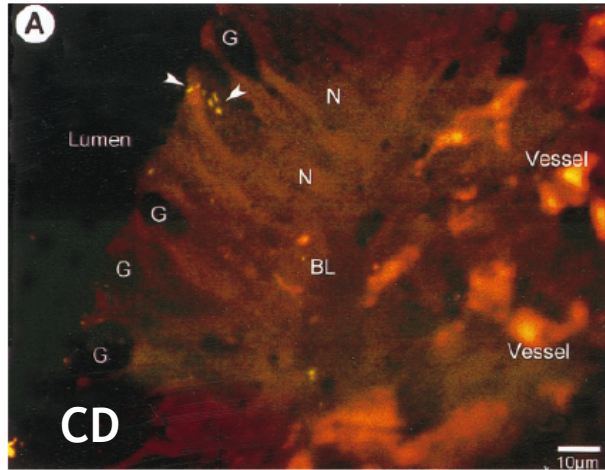
epithelial cell barrier
secretion of mucus
and defensins etc.



A. Swidsinski

Mucosal Flora in Inflammatory Bowel Disease

Swidsinski A et al, Gastroenterology 2002



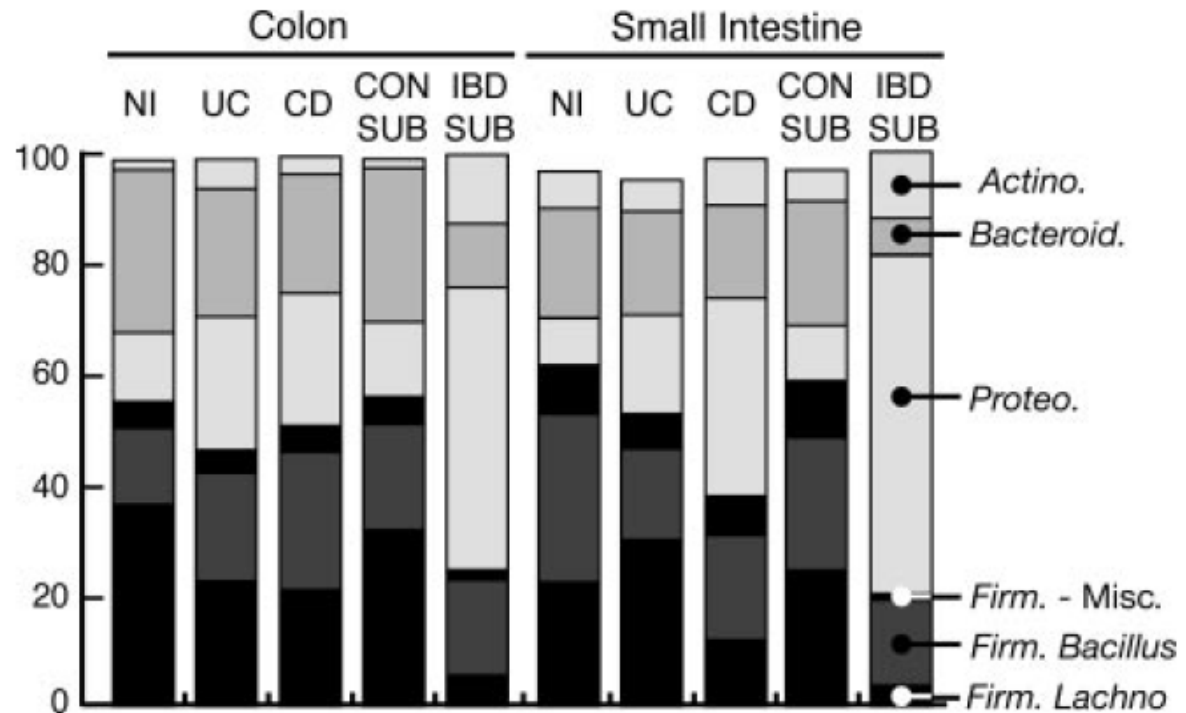
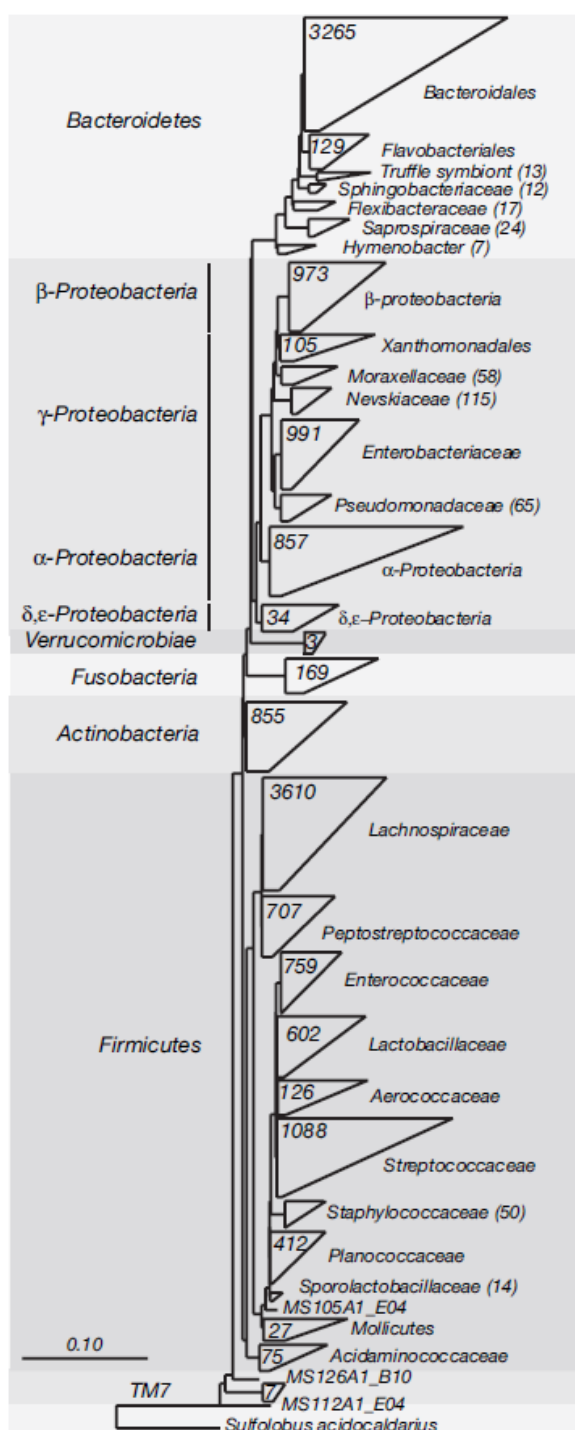
high concentrations of mucosal bacteria
in patients with bowel inflammation

concentrations of mucosal bacteria higher
in non-inflamed than inflamed mucosa

The main anaerobic microorganism
isolated from the mucosa was *Bacteroides*.
The main aerobes were
Enterobacteriaceae (primarily *E. coli*).

Molecular-phylogenetic characterization of microbial community imbalances in human IBD

Frank DN et al, PNAS 2007



Therapeutic Manipulation of the Enteric Microflora in Inflammatory Bowel Diseases:

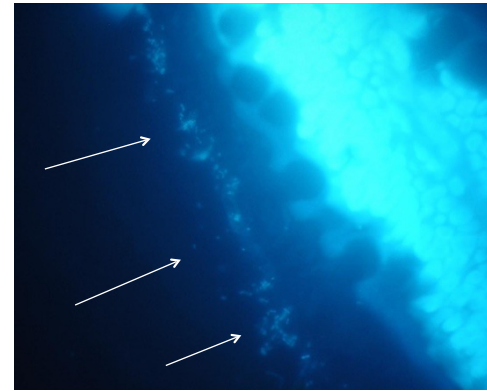
Diet

Probiotics

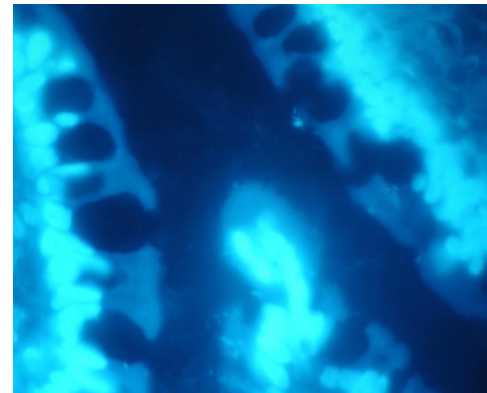
Prebiotics

Antibiotics

Fecal transplantation??



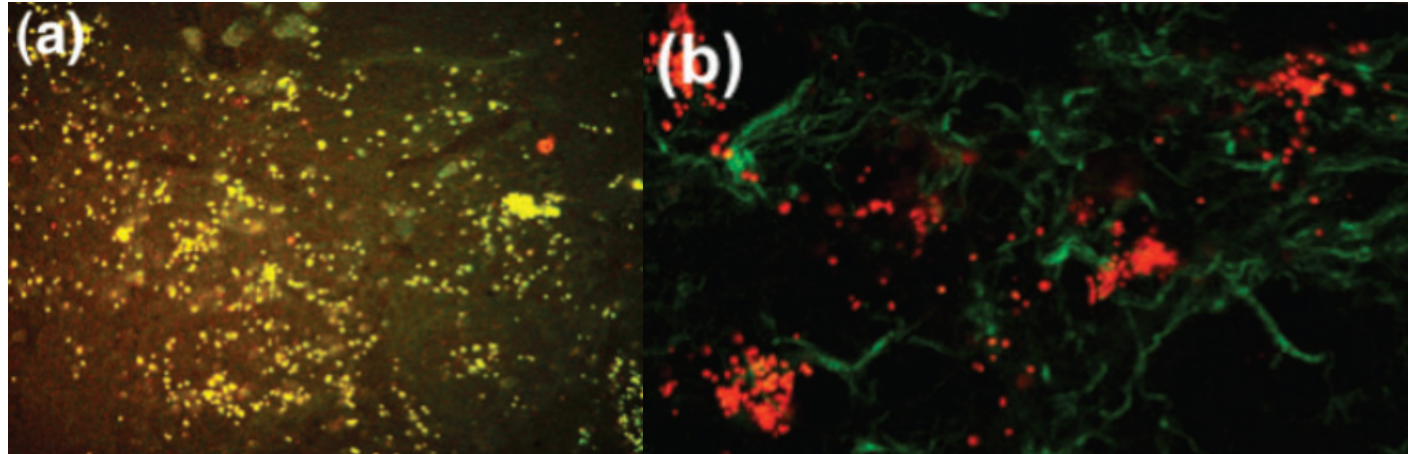
Day 0: CDAI 314



Day 84: CDAI 181

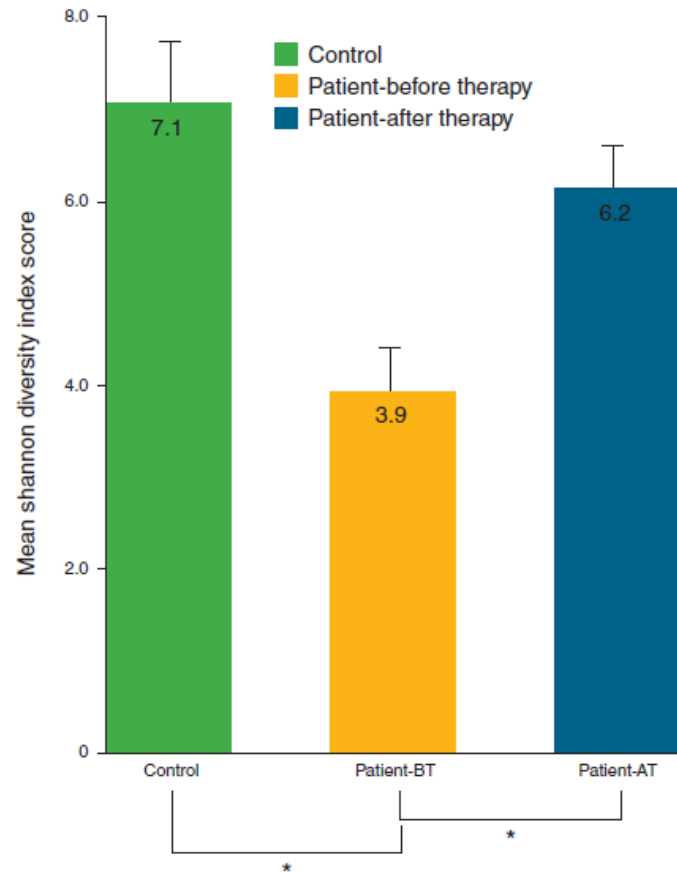
Microbiological and immunological effects of enteral feeding on the upper gastrointestinal tract

Smith AR et al, J Med Microbiol 2011

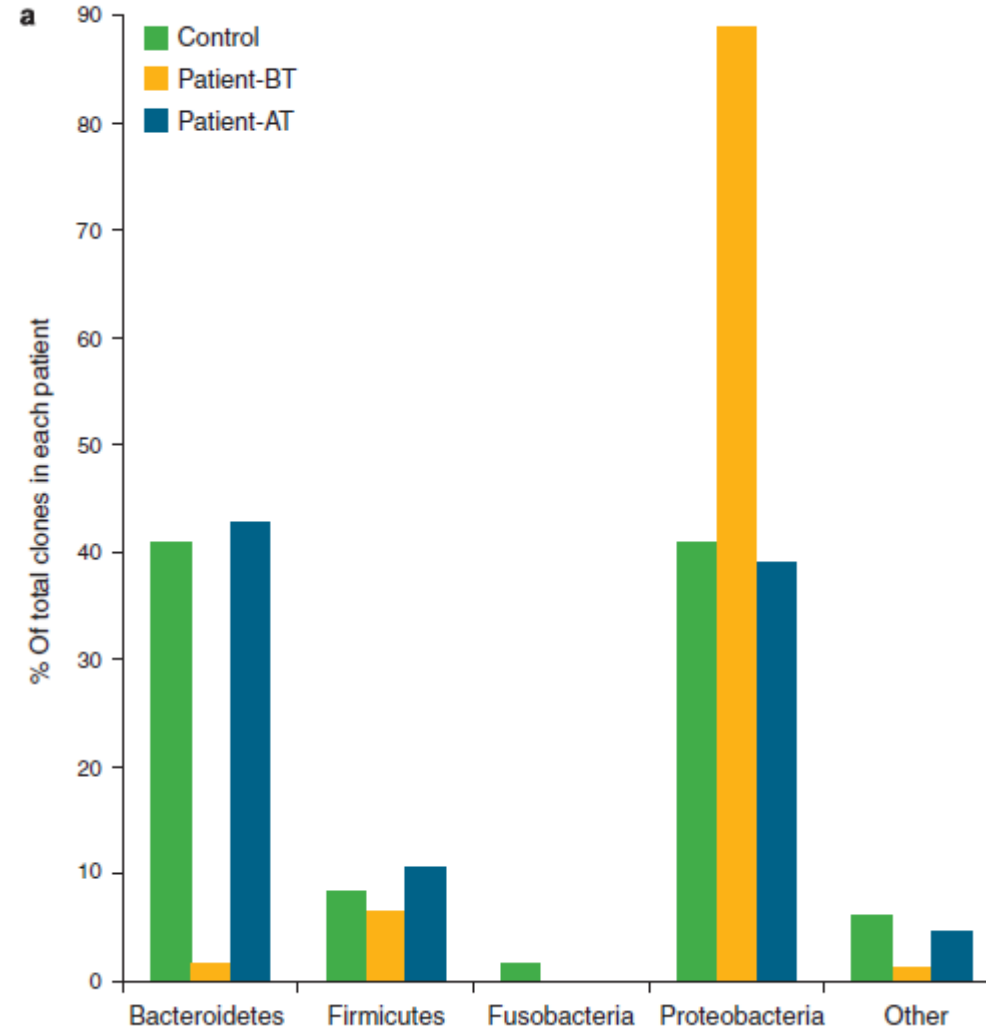


Organisms	Normal diet (<i>n</i> =10)		EN (<i>n</i> =8)	
	Stomach	Duodenum	Stomach	Duodenum
Enterobacteria	0.25 ± 0.14	1.10 ± 0.16	5.01 ± 2.62	5.41 ± 2.59
Bifidobacteria	0.90 ± 0.31	0.53 ± 0.18	1.63 ± 0.35	1.63 ± 0.20
Staphylococci	1.12 ± 0.15	0.56 ± 0.19	2.20 ± 0.19	1.83 ± 0.35
<i>C. albicans</i>	1.11 ± 0.26	1.21 ± 0.36	1.47*	ND

An Altered Gut Microbiome Profile in a Child Affected by Crohn's Disease Normalized After Nutritional Therapy



diet-EN

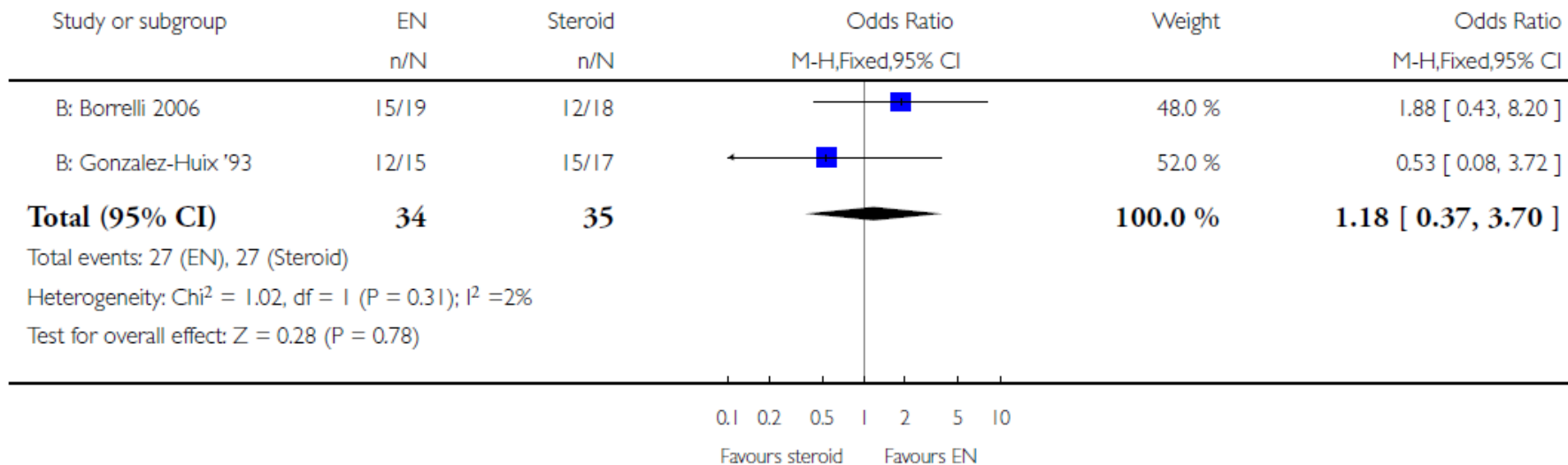


D'Argenio V et al, AJG 2013



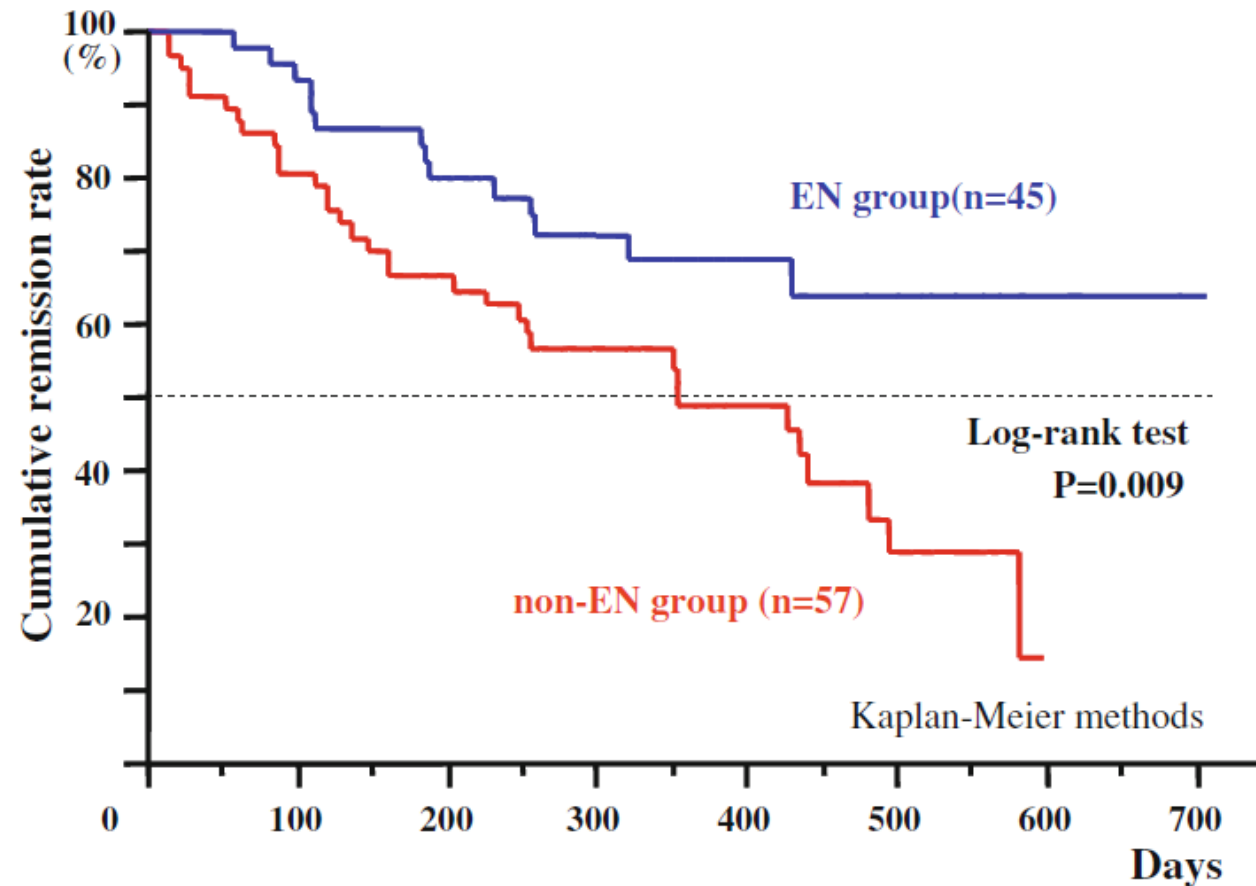
Enteral nutritional therapy for induction of remission in Crohn's disease

EN vs steroid: sensitivity analysis including only high quality studies



Effectiveness of Concomitant Enteral Nutrition Therapy and Infliximab for Maintenance Treatment of CD in Adults

Hirai F et L, Dig Dis Sci 2013



Observation time (days, mean±S.D.): 544.1±26.5

diet-EN

Impact of long-term enteral nutrition on clinical and endoscopic recurrence after resection for Crohn's disease: a prospective, non-randomized, parallel, controlled study

Table 2. Clinical and endoscopic recurrence rates after operation

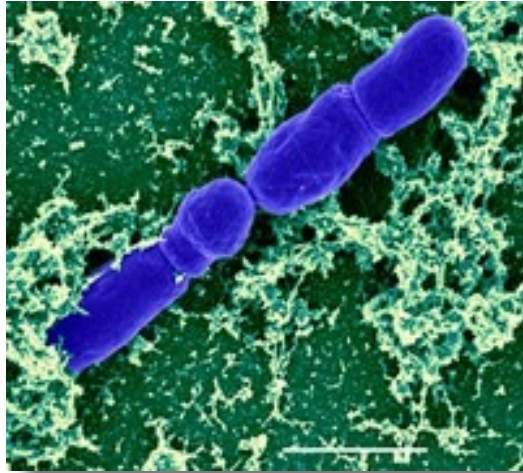
	EN group [<i>n</i> = 20; <i>n</i> (%)]	Non-EN group [<i>n</i> = 20; <i>n</i> (%)]	<i>P</i> -value
Clinical recurrence during 1-year follow-up	1 (5)	7 (35)	0.048
Endoscopic recurrence			
6 months after operation	5 (25)	8 (40)	0.50
12 months after operation	6 (30)	14 (70)	0.027

EN + low fat diet
≈ 2000-2500 kcal

Non-EN free diet

Pentasa 3 gr/die

probiotics for treatment of human IBD



probiotics

Protective role of certain bacterial strains of Lactobacillus sp and Bifidobacteria

Adherence inhibition of potentially pathogens bacteria to the intestinal wall

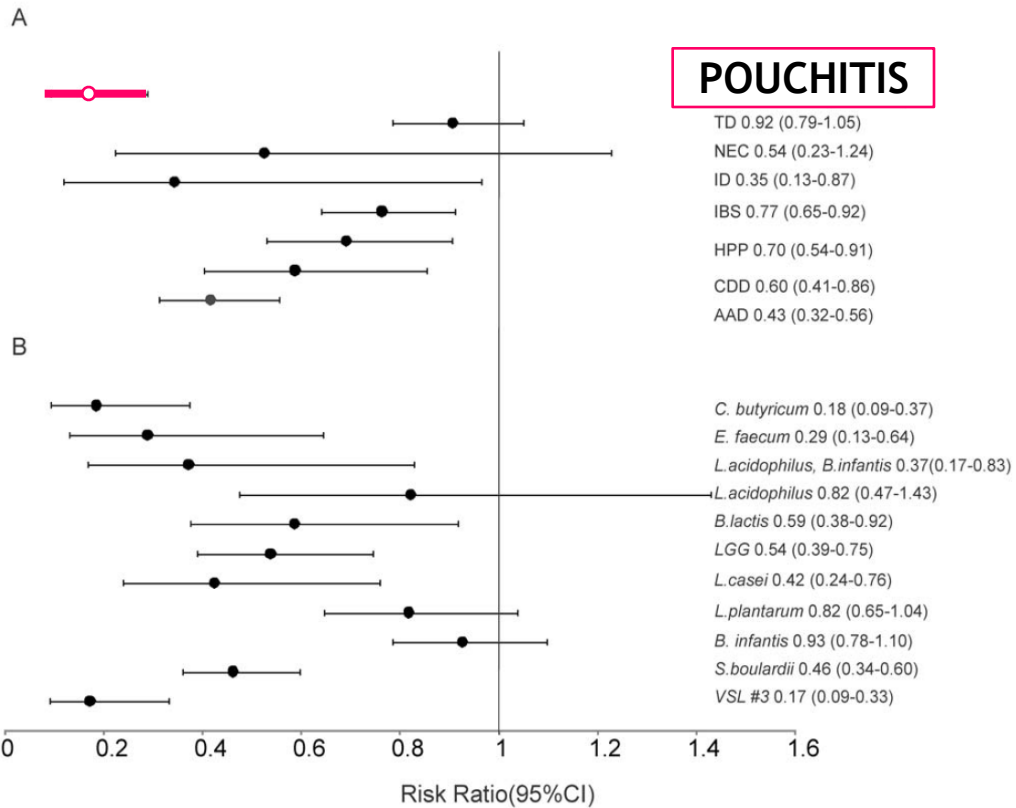
Upregulation of mucin-encoding genes

Stimulation of both cellular and humoral immune response

Restore permeability defect

Probiotics for IBD

probiotics



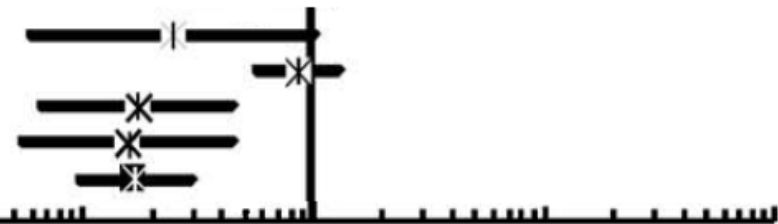
probiotics added to standard therapy may provide benefits in terms of reduction of disease activity and maintaining remission in mild to moderate UC

Mallo P et al., Cochrane Database Syst Rev 2007

ECCO statement 8E
VSL#3 for 9 or 12 months has shown efficacy for maintaining antibiotic-induced remission [EL1b, RG B] and for preventing pouchitis [EL2b, RG C]

Biancone L et al JCC 2007

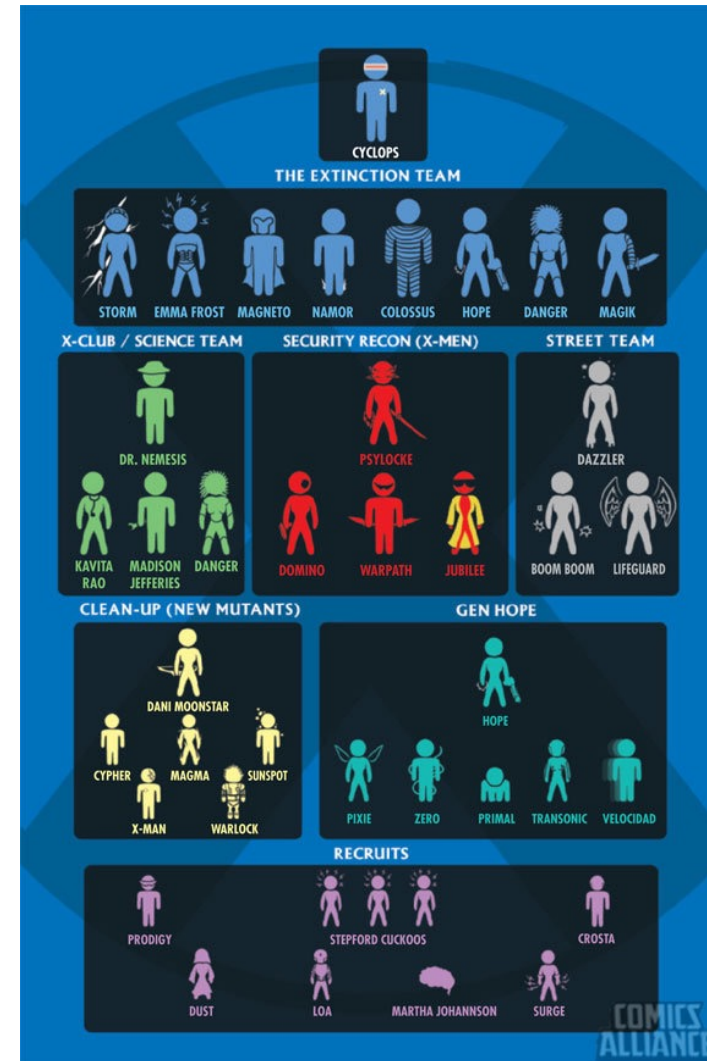
Disease	Author (year)	Measure (CI)	P value
Pouch	Gionchetti (2000)	0.25 (0.06-1.03)	0.06
Pouch	Gionchetti (2003)	0.87 (0.58-1.32)	0.52
Pouch	Martijn (2004)	0.18 (0.07-0.46)	0.00
Pouch	Mimura (2006)	0.16 (0.06-0.46)	0.00
Pouch Mean		0.17 (0.10-0.30)	



Ritchie ML et al , PLOS 2012

0.001 0.01 0.1 1 10 100

Although the vast therapeutic potential of manipulating the microbial milieu is quickly evident, proper application of diet, probiotics, and prebiotic treatments most likely will need to be done in a individualized manner to defined patient subsets rather than by the current random application



DIETA E RISCHIO DI INFIAMMAZIONE INTESTINALE

- **zucchero, carboidrati raffinati**
- **acidi grassi**
- **proteine**



rischio

Miller B, Verh Dtsch Inn Med, 1976
James AH, BMJ, 1978
Mayberry JF, Digestion, 1980



DIETA E RISCHIO DI INFIAMMAZIONE INTESTINALE

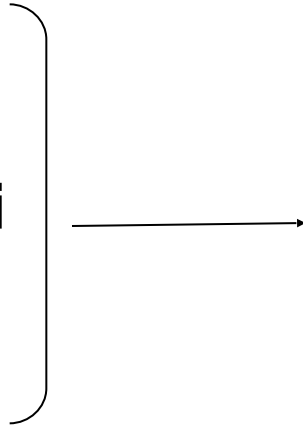
- **dieta ad alto
contenuto in grassi**

- ↑ **permeabilità intestinale**
Cani PD, Gut 2009
- **peggiora la colite sperimentale del topo**
Ma X, Clin Exp Immunol 2008
- **induce flora batterica produttrice di H₂S**
Devkota S, Nature 2012



DIETA E RISCHIO DI INFIAMMAZIONE INTESTINALE

- carne
- ac. grassi poli-insaturi
- ac. grassi omega-6



rischio

Hou JK, Am J Gastr 2011



Linoleic acid, a dietary n-6 polyunsaturated fatty acid, and the aetiology of ulcerative colitis: a nested case-control study within a European prospective cohort study

The IBD in EPIC Study Investigators

Gut 2009

↑ rischio di RCU OR 2.49

ORIGINAL ARTICLE

Long-term intake of dietary fat and risk of ulcerative colitis and Crohn's disease

Ashwin N Ananthakrishnan,¹ Hamed Khalili,¹ Gauree G Konijeti,¹ Leslie M Higuchi,² Punyanganie de Silva,¹ Charles S Fuchs,^{3,4} Walter C Willett,^{4,5} James M Richter,¹ Andrew T Chan^{1,4}

Gut 2014

ac. grassi poli-insaturi a lunga catena n-3

↓ rischio RCU HR 0.72

CLINICAL—ALIMENTARY TRACT

A Prospective Study of Long-term Intake of Dietary Fiber and Risk of Crohn's Disease and Ulcerative Colitis

ASHWIN N. ANANTHAKRISHNAN,¹ HAMED KHALILI,¹ GAUREE G. KONIJETI,¹ LESLIE M. HIGUCHI,² PUNYANGANIE DE SILVA,¹ JOSHUA R. KORZENIK,³ CHARLES S. FUCHS,^{2,4} WALTER C. WILLETT,^{5,6} JAMES M. RICHTER,¹ and ANDREW T. CHAN^{1,4}

fibre, frutta, verdura

↓ rischio Crohn HR 0.59

DIETA E STORIA NATURALE DELLE I.B.D.

Studi Osservazionali

INFLAMMATORY BOWEL DISEASE

Influence of dietary factors on the clinical course of ulcerative colitis: a prospective cohort study

S L Jowett, C J Seal, M S Pearce, E Phillips, W Gregory, J R Barton, M R Welfare

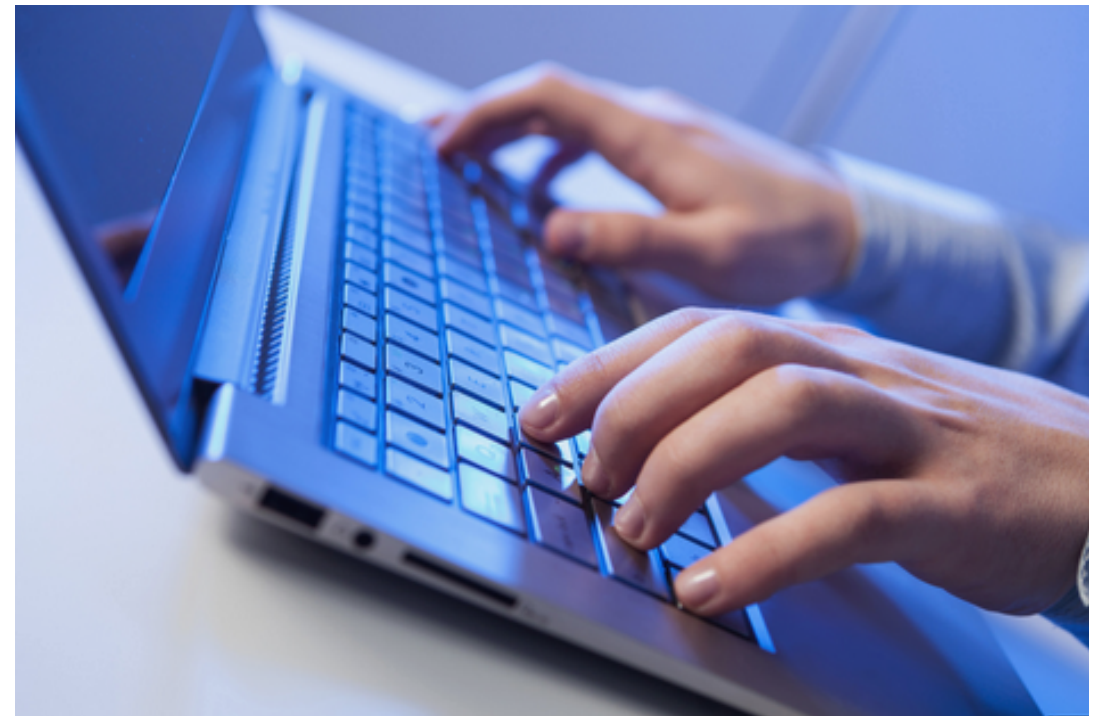
Gut 2004;53:1479-1484. doi: 10.1136/gut.2003.024828

↑ rischio di recidiva di RCU se elevato consumo di

- *carni rosse* (OR 5.19)
- *proteine* (OR 3.00)
- *alcol* (OR 2.71)



INTERNET



Grouping	Food category	No. of sites w/rec	Include (%)	Avoid (%)	Conflicting ^a (%)
Fruits/Vegetables	Any fruit	41	24	44	32
	Any vegetables	28	57	22	21
	Raw vegetables	22	8	92	—
	Cruciferous vegetables	21	—	100	—
	Cooked vegetables	12	100	—	—
	Citrus fruit	10	20	80	—
Proteins	Bean/legume/lentils	32	16	78	6
	Fish	25	96	4	—
	Nuts	24	4	79	17
	Poultry	17	100	—	—
	Eggs	16	69	31	—
	High protein	13	92	8	—
	Soy/tofu	12	83	17	—
	Lean protein	11	100	—	—
	Red meat	10	20	80	—
Fiber	Whole grain	34	26	56	18
	High fiber	32	19	72	9
	Seeds/popcorn	30	—	93	7
	Low fiber	15	87	13	—
	Refined grain	10	40	60	—
Beverages/dairy	Any dairy	42	17	69	14
	Alcohol	35	—	100	—
	Coffee/tea	34	3	91	6
	Carbonated beverages	21	—	100	—
Other	Fatty/fried food	41	5	88	7
	Spicy food	29	3	97	—
	Sugars	25	—	100	—
	Healthy oil	18	89	11	—



DIETE 'DEFINITE'

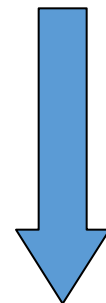
- *Specific Carbohydrate diet (SCD)*
- *FODMAP diet*
- *Paleolithic Diet*



DIETE 'DEFINITE'

- *Specific Carbohydrate diet (SCD)*
- *FODMAP diet*
- *Paleolithic Diet*

• presupposto di partenza: **LIMITARE OVERGROWTH BATTERICO**



↑ permeabilità intestinale

INFIAMMAZIONE INTESTINALE



DIETE 'DEFINITE'

- *Specific Carbohydrate diet (SCD)*
- *Paleolithic Diet*

nessuna pubblicazione scientifica formale riguardante le IBD



Dieta FODMAP e IBD

2 studi retrospettivi

Gerry RB, J Crohn Colitis 2009

Croagh C, Infl Bowel Dis 2007

miglioramento dei sintomi (dolore, gonfiore, diarrea) $p < 0.02$

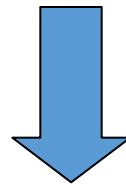
ma.....

- bias metodologici
- possibili componenti 'funzionali'
- possibile 'gluten sensitivity'



DIETE 'DEFINITE'

- *Specific Carbohydrate diet (SCD)*
- *FODMAP diet*
- *Paleolithic Diet*



- **nessuna evidenza scientifica**
- **poco pratiche**
- **impegno economico**
- **rischio di malnutrizione**



ALIMENTAZIONE E IBD

Conclusioni

- **esistono evidenze scientifiche su fattori alimentari che potrebbero influenzare il rischio di IBD**
- **dimostrata efficacia solo di diete ‘enterali’ (età pediatrica, poco palatabili, poco praticabili nel lungo termine)**



Consigli alimentari al paziente con IBD

....quelli del buon senso.....



- esperienza personale, non generalizzabile, in base ad esacerbazione o miglioramento dei sintomi
- evitare, nei periodi di malattia attiva, alimenti che possano peggiorare la diarrea
- evitare, se tratti intestinali stenotici, fibre formanti massa non frammentabili

