

# Epidemiology & Environmental factors

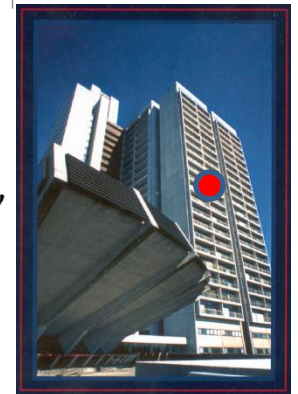
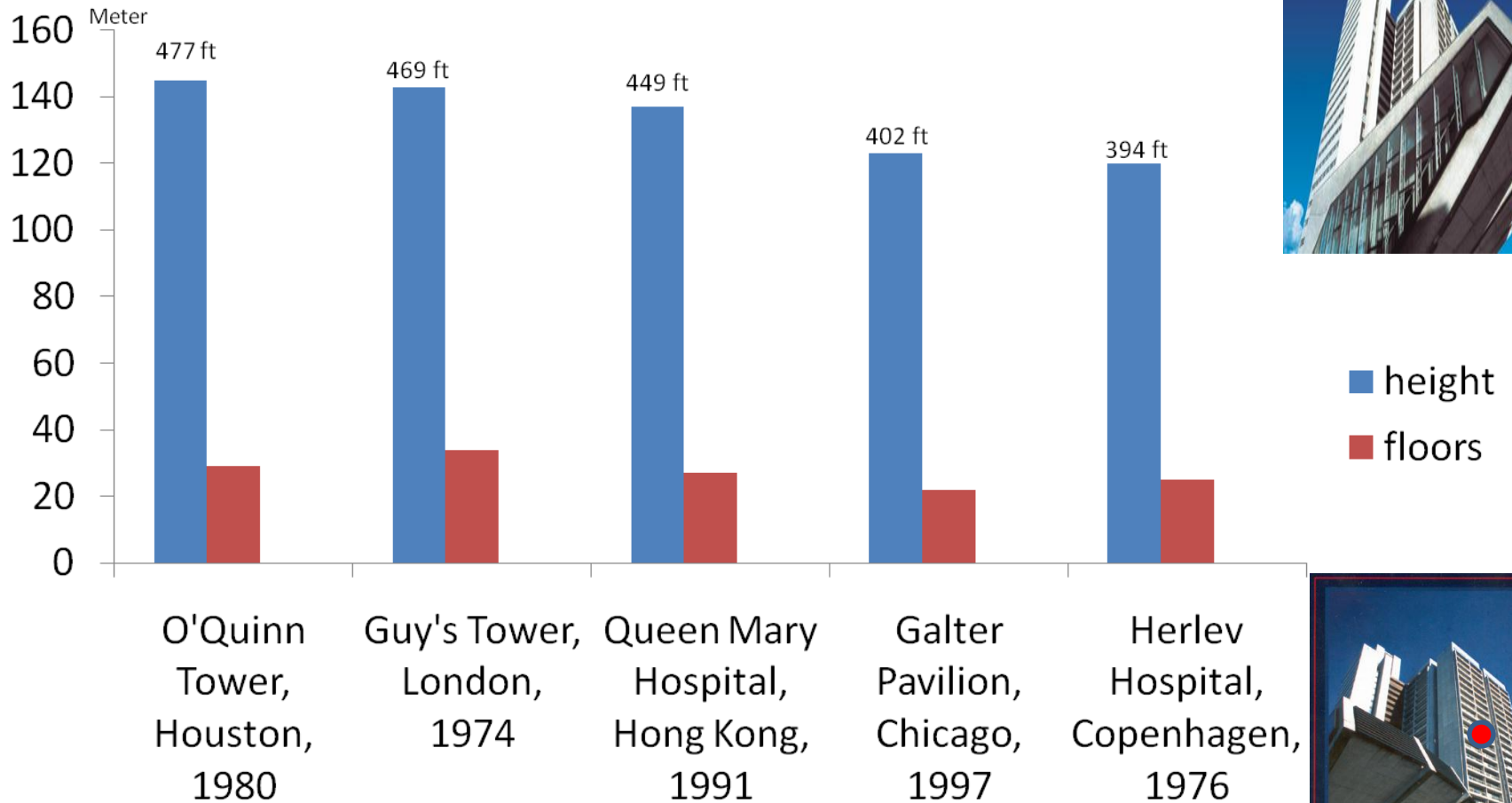
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# Environmental - Bad Luck!



# The Highest Hospitals in the World



# Epidemiology

## epicom-ECCO

Thursday 16 February: Epidemiology Course 8 am & EpiCom group meeting 11.30 am

## Highest evidence in epidemiology

### **A. Inception cohorts**

Unselected (any phenotype indolent-aggressive)

Defined area

Defined background populations, age, sex 5 years

### **B. Register cohorts**

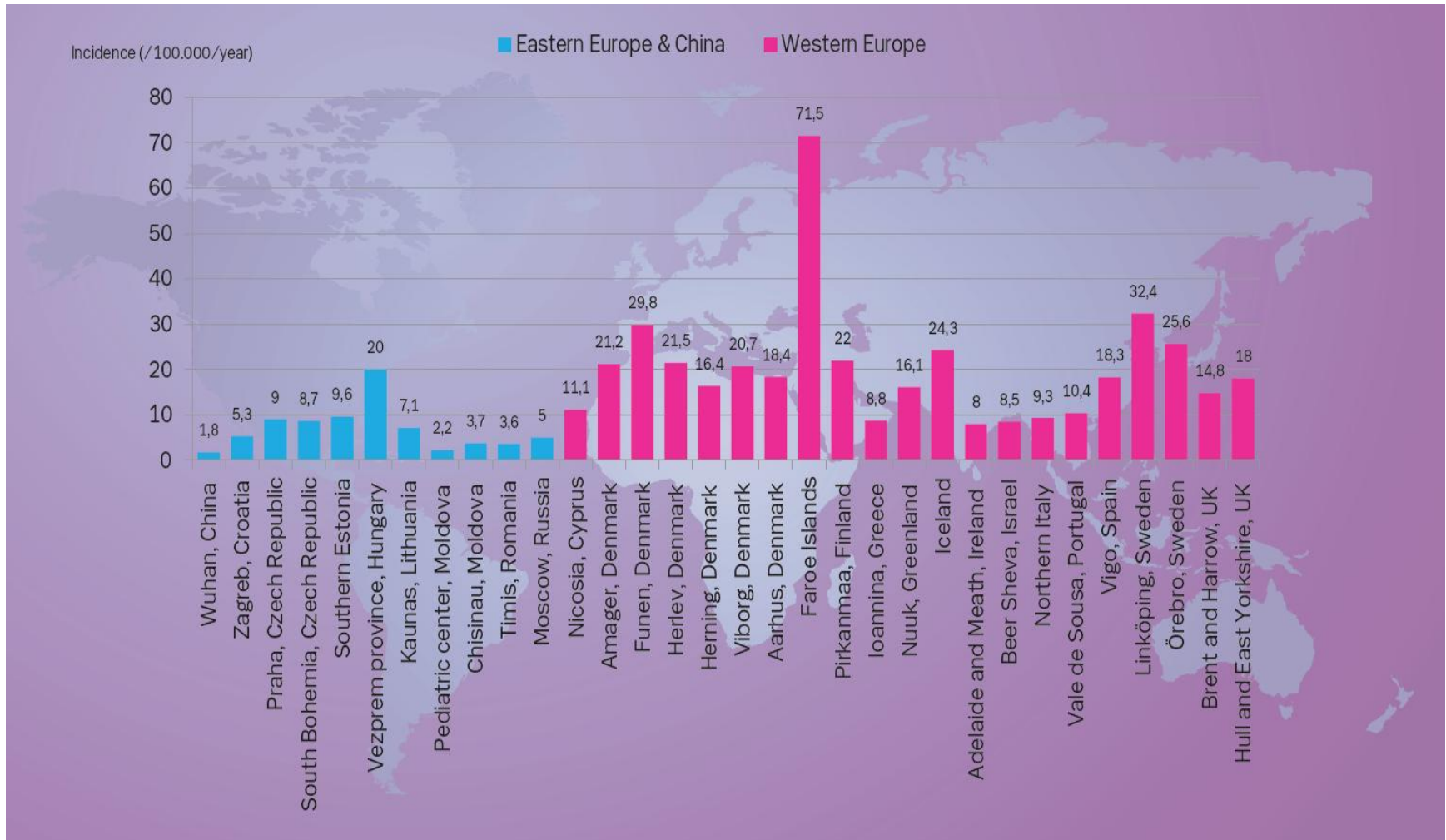
Bias: correct diagnosis not always true

### **C. Referral Centre cohorts**

Bias: often most aggressive

# Incidences IBD

Is there an East-West gradient in Europe. [www.epicom-ecco.eu](http://www.epicom-ecco.eu)



# How to do an incidence cohort

The Copenhagen diagnostic criteria

## Crohns (2 out of 4)

1. History of abdominal pain, weight loss, and/or diarrhea for more than 3 months.
2. Characteristic endoscopic findings of ulceration (aphthous lesions, snail track ulceration), or cobble stoning, or radiological features of stricture.
3. Histopathology consistent with CD (epithelioid granuloma of Langerhans type or transmural, discontinuous focal or patchy inflammation) (12).
4. Fistula and/or abscess in addition to affected bowel segments.

Infection and cancer have to be ruled out.

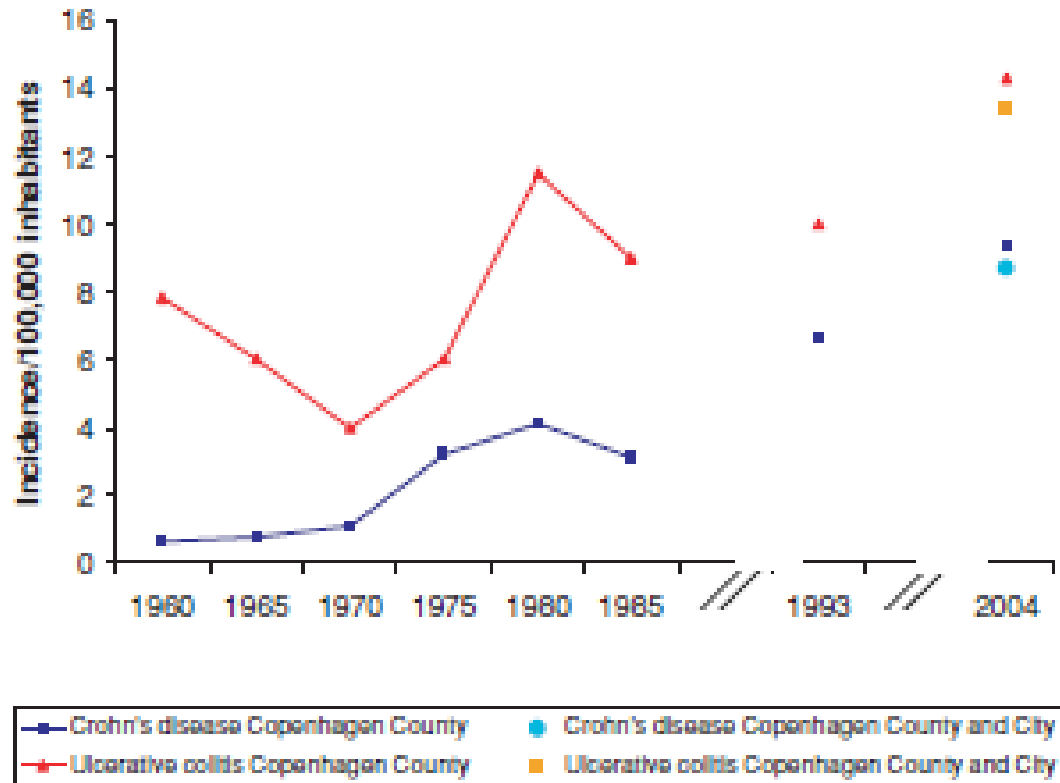
## Ulcerative colitis(3 out of 3)

1. History of diarrhea and/or rectal bleeding and pus for more than 1 wk or repeated episodes.
2. Characteristic endoscopic findings of continuous ulceration, vulnerability, or granulated mucosa.
3. Histopathology consistent with UC (neutrophils within epithelial structures, cryptitis, crypt distortion, crypt abscesses) (12).

Infection and cancer have to be ruled out.

# Steep increase in incidence

Copenhagen County and Community 1,2 mio background



**Figure 4.** Incidences of CD and UC 1962-1987 and 1991-1993 in Copenhagen County compared with 2003-2005 in Copenhagen County and combined Copenhagen County and City.

# Age related incidence

Copenhagen County and Community 1,2 mio background

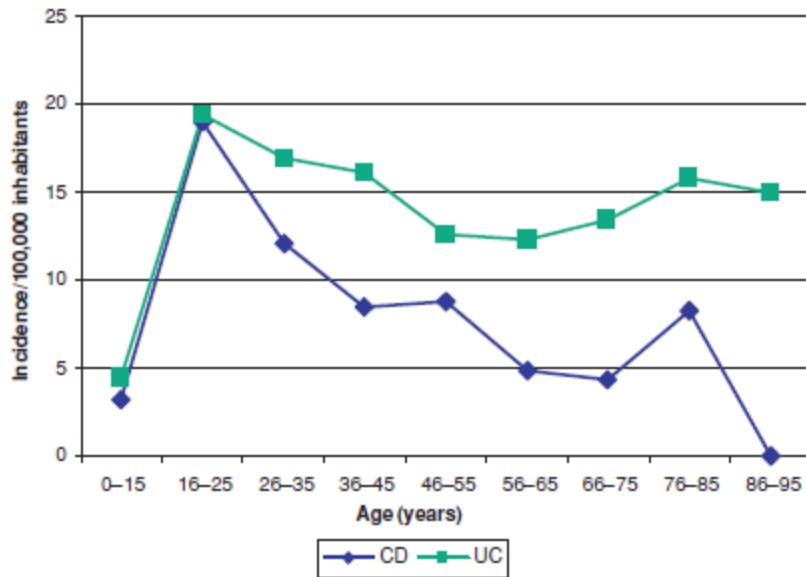


Figure 1. Age-related incidence of Crohn's disease and ulcerative colitis.

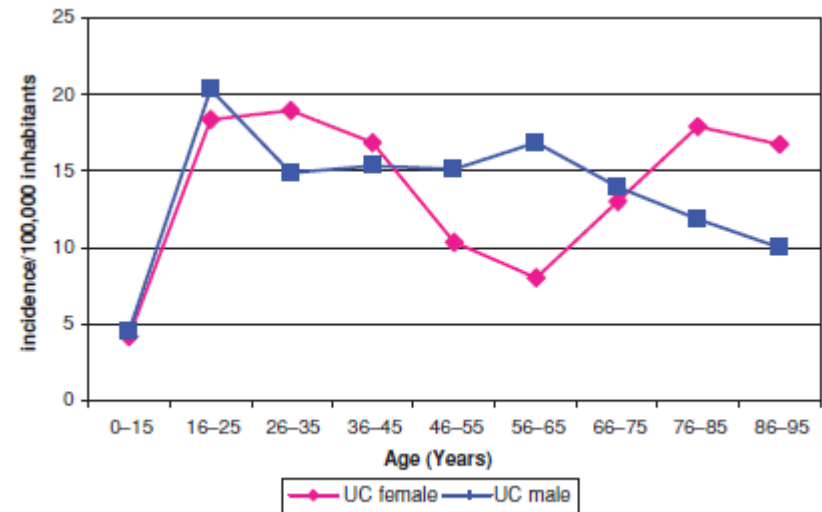
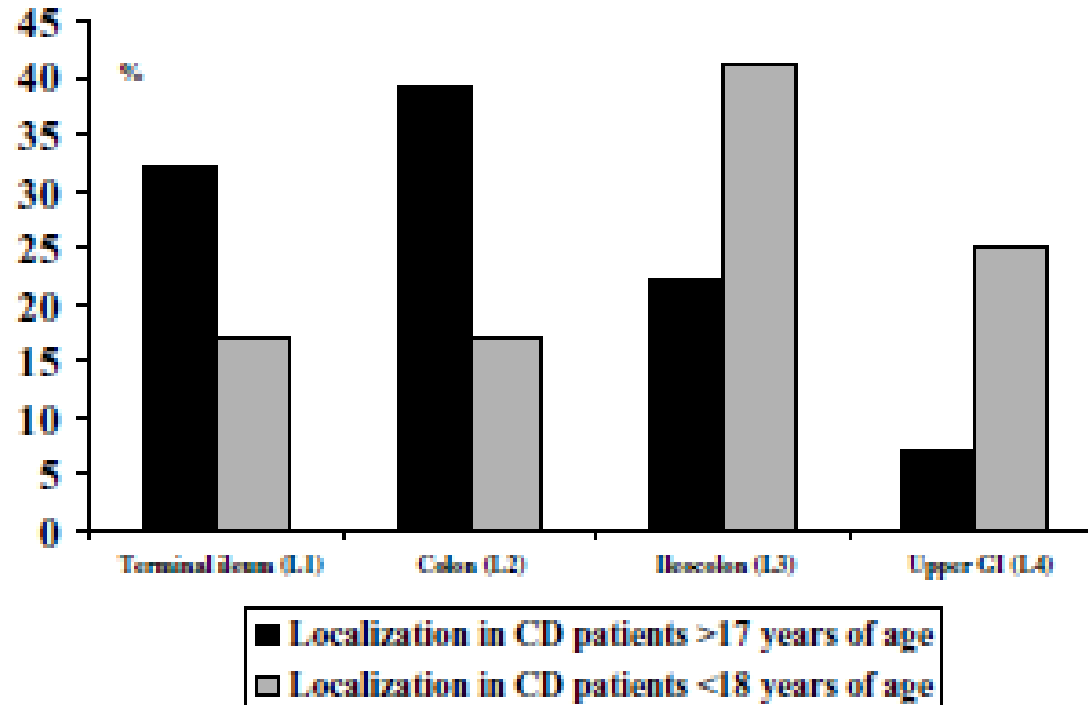


Figure 3. Age-related incidence of ulcerative colitis by gender.



# Epidemiology: Extent at diagnosis



**Figure 5.** Extent of disease at diagnosis in adults and children with Crohn's disease, 2003–2005.

# Epidemiology: Surgery at diagnosis

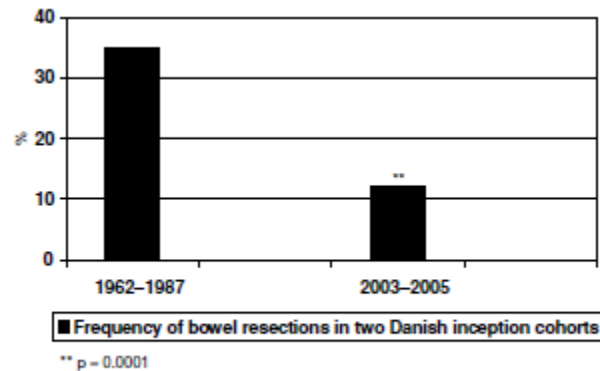


Figure 8. Surgical resections in CD patients within 1 yr after diagnosis in two Danish inception cohorts.

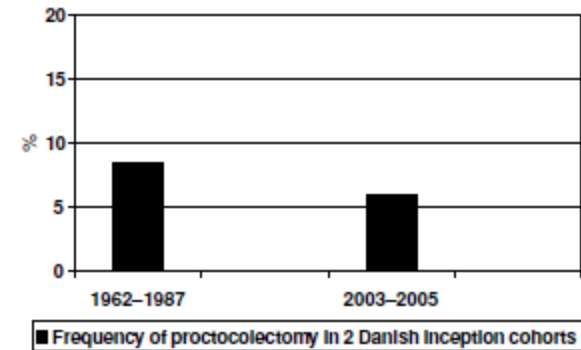
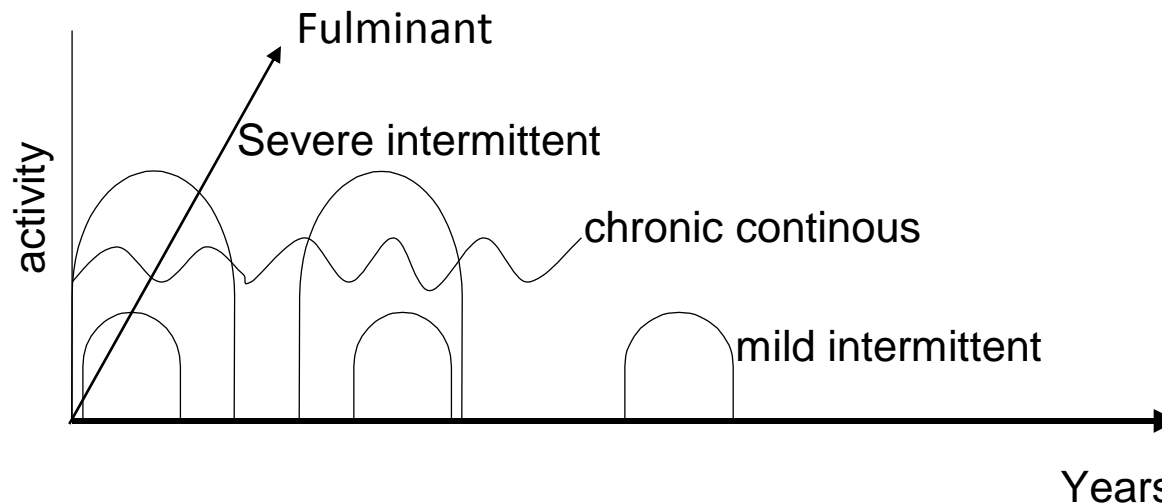


Figure 9. Proctocolectomy in UC patients within 1 yr after diagnosis in two Danish inception cohorts.

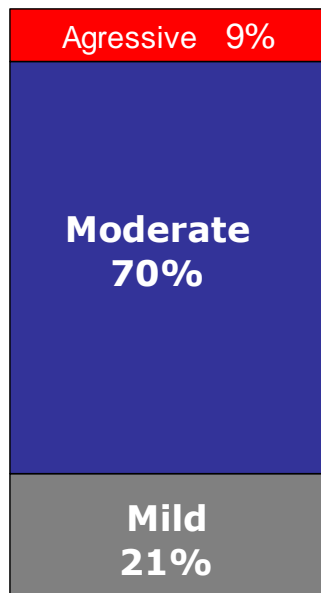
# Disease courses in IBD



About 50% of all IBD out-patient population is running an inactive disease course



# Disease course 8 years after diagnosis in inception cohorts UC(1161) and CD(373), 1962-87

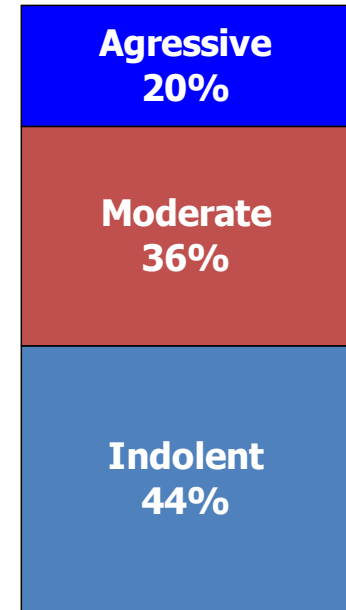


UC

**Aggressive:** relapse every year

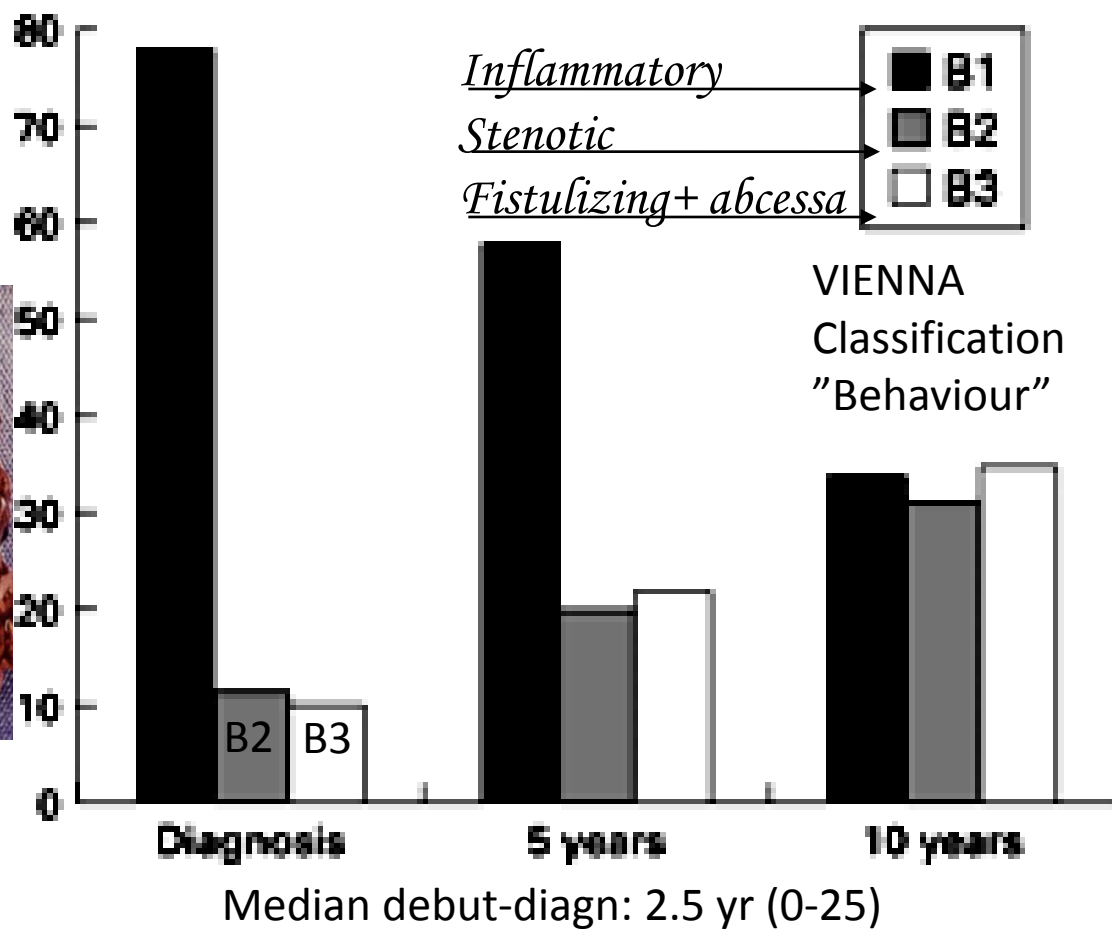
**Moderate:** Half of the years in inactive stage

**Mild-indolent:** Inactive since diagnosis or the majority of the years



CD

# <sup>1</sup>Vienna & <sup>2</sup>Montreal: Crohn's disease is a transmural disease & panenteric: "Behaviour"

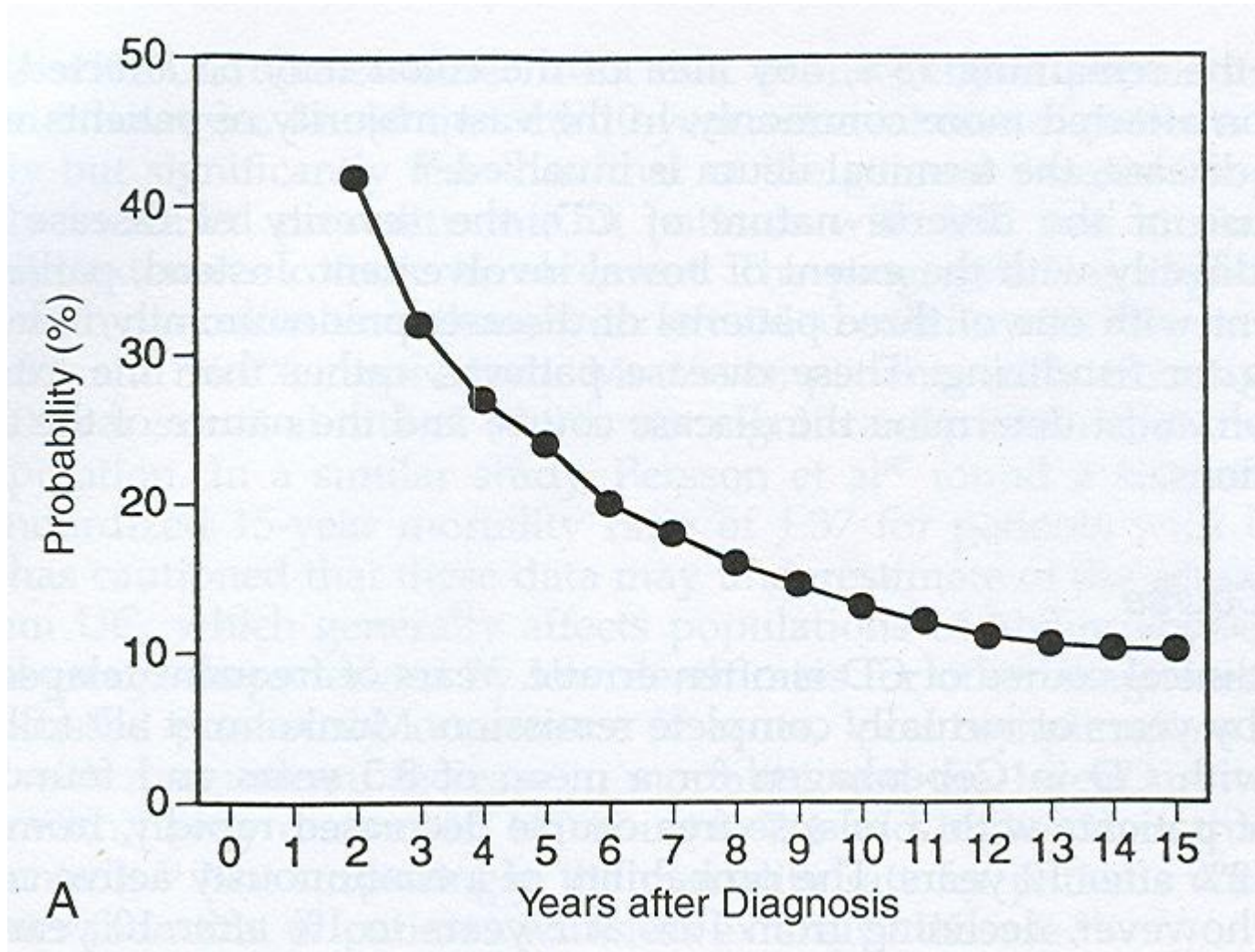


<sup>1</sup>Gasche C. IBD 2000;6(1):8-15

<sup>2</sup>Satsangi J. GUT 2006;55:749

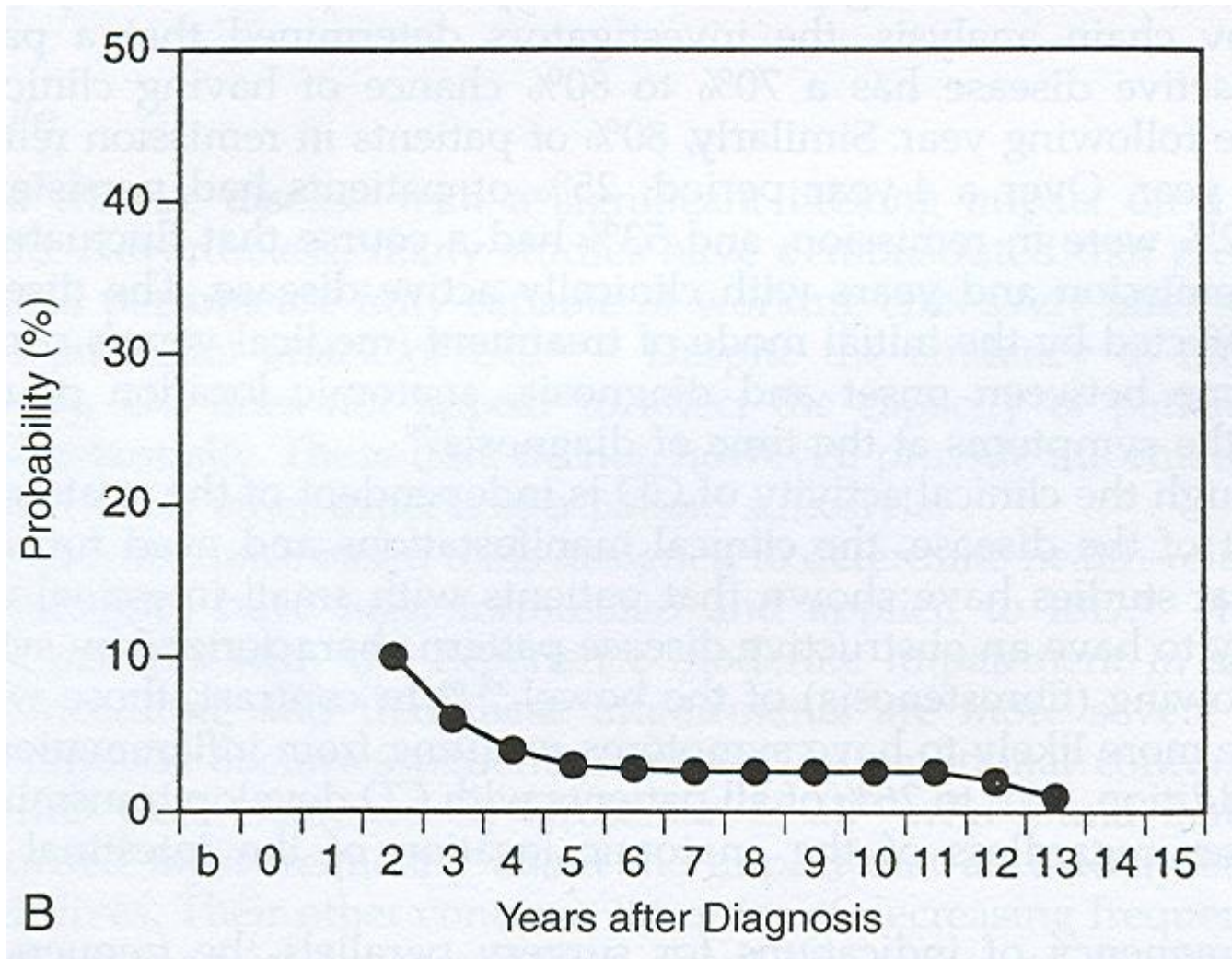
# Cumulative probability of CD patients experiecing: "A Chronic persistent course"

Munkholm P. SJG 1995;30:699 & DanMed Bull 1997;44(3):287-302



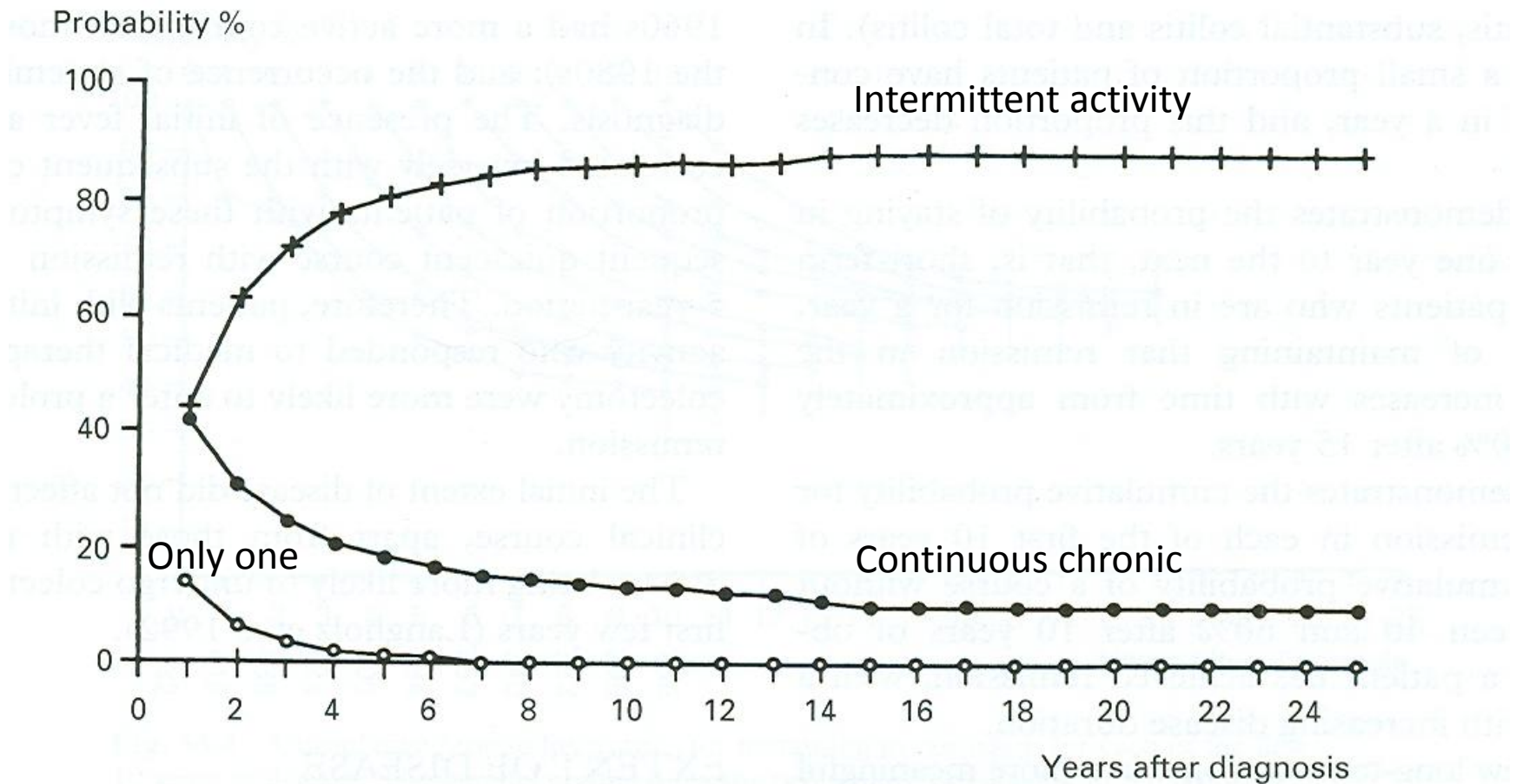
# Cumulative probability of CD patients experiecing: "only one attack"

Munkholm P. SJG 1995;30:699 & DanMed Bull 1997;44(3):287-302



# The cumulative probability for -one episode of UC, -continuous activity & -intermittent activity

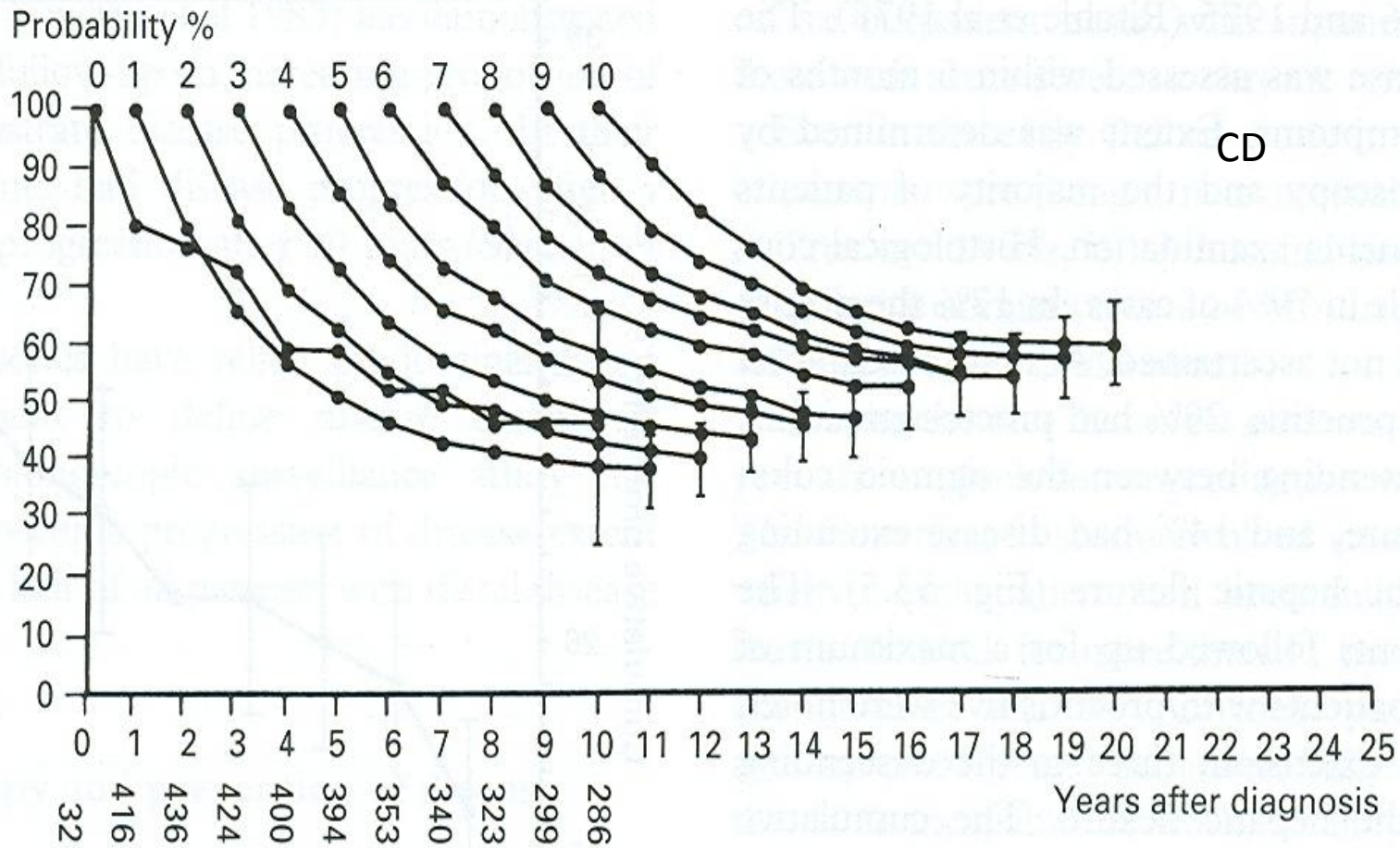
Langholz E. Gastroenterology 1994





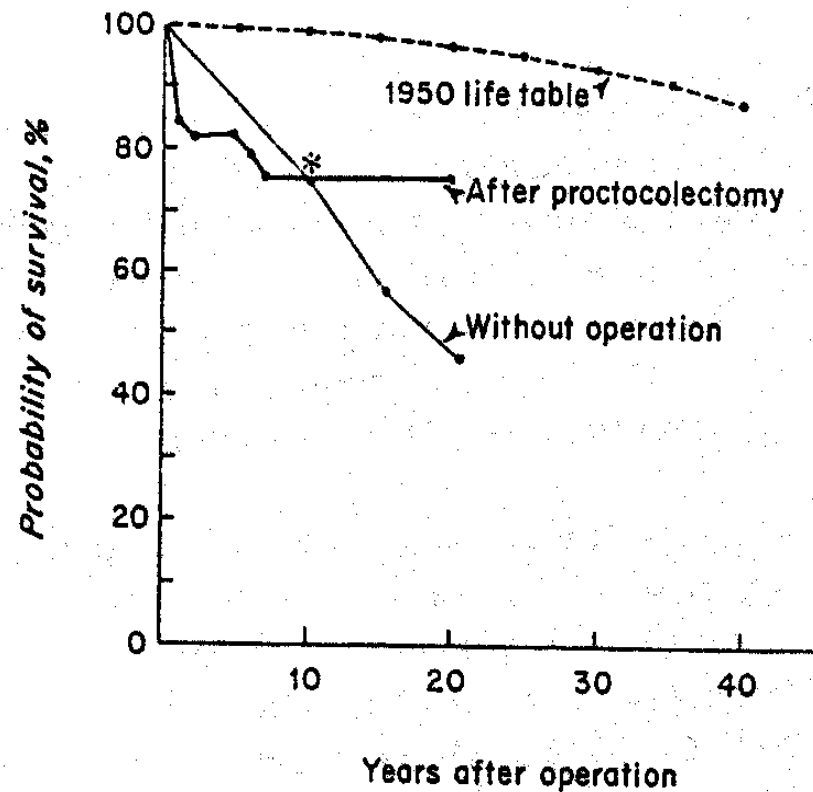
# Cumulative probability for remaining in remission for each of the first 10 years of disease. UC & CD burns out?

Langholz E. Gastroenterology 1994; Munkholm P. SJG 1995



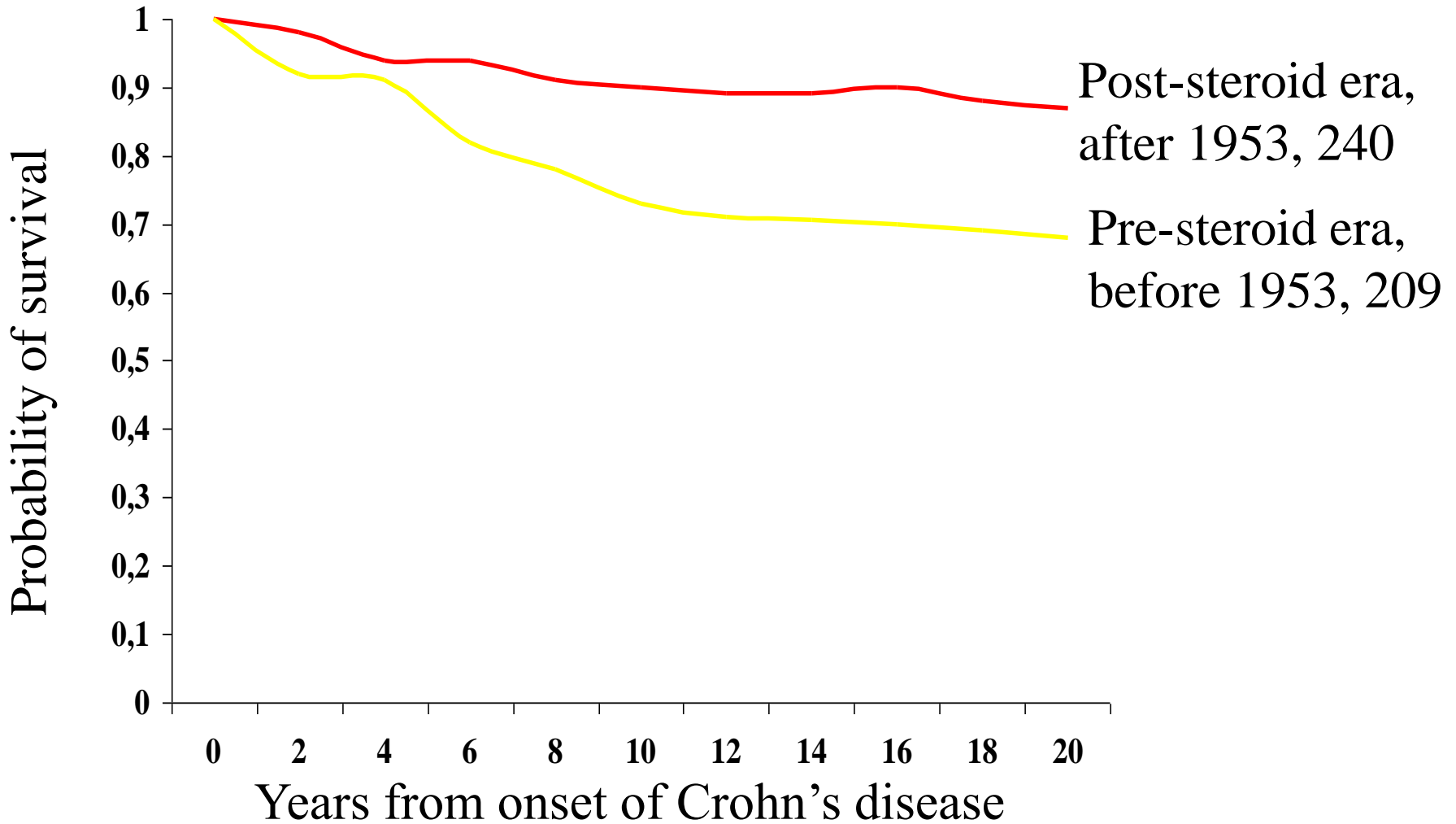
# Mortality

# History-Devroede et al. NEJM 1971



Of 396 children 40 had colectomy-survival improved(MAYO)

# Children diagnosed Crohn's disease 1921-1965



Weedon D, NEJM 1973

# Meta-analysis

## Mortality cause UC-population based cohorts

1.1 (95% CI, 0.9 – 1.2; p = 0.42).

Causes of deaths	No. of studies	Lowest SMR	95% CI	Highest SMR	95% CI	Pooled SMR	95% CI
Cancer	5	0.7	0.5 - 0.9*	1.5	1.2 - 1.8*	1.0	0.7 - 1.3
Colorectal cancer	4	0.9	0.4 - 1.8	4.4	3.2 - 5.9*	1.9	1.0 - 3.8
Pulmonary cancer	2	0.3	0.1 - 1.0	0.4	0.1 - 1.3	0.3	0.1 - 0.9*
Leukemia	1	-	-	2.9	0.4 - 10.3	2.9	0.4 - 10.3
Cardiovascular diseases	5	0.6	0.4 - 0.9*	1.1	0.9 - 1.4	0.9	0.7 - 1.1
Ischemic heart disease	2	0.9	0.8 - 1.1	1.0	0.8 - 1.3	0.9	0.8 - 1.1
Pulmonary embolism	1	-	-	4.0	1.5 - 8.7*	4.0	1.5 - 8.7*
Respiratory diseases	5	0.9	0.3 - 2.0	2.0	1.1 - 3.5*	1.6	1.3 - 2.0*
COPD	4	0.6	0.1 - 2.3	3.4	1.7 - 5.9*	1.6	0.7 - 3.7
Pneumonia	2	1.3	0.3 - 3.7	3.4	2.1 - 5.0*	3.1	2.0 - 4.6*
Gastrointestinal and liver diseases	4	1.6	0.8 - 2.8	4.0	1.9 - 7.3*	2.5	1.9 - 3.2*
All exclusive ulcerative colitis	3	0.5	0.2 - 1.1	2.8	1.7 - 4.4*	1.7	0.8 - 3.6
Non-alcoholic liver diseases	3	0.9	0.1 - 4.9	4.8	2.1 - 9.5*	4.0	2.5 - 6.5*
Genitourinary tract diseases	4	1.0	0.4-2.3	1.6	0.4 - 4.1	1.2	0.7 - 2.2
Suicide	4	0.8	0.3-1.8	2.1	1.0 - 3.9	1.3	0.8 - 2.0
Accidents/Injuries	5	0.5	0.2-1.2	0.8	0.3 - 1.9	0.7	0.5 - 1.0

\*95% confidence interval excluding 1.0 (p<0.05). COPD, chronic obstructive pulmonary disease (bronchitis, emphysema, and asthma)

# Meta-analysis

## Mortality cause UC

- 10 population based studies:
  - Overall mortality all causes 1.1 (95% CI, 0.9 – 1.2; p = 0.42)
- 5 population based reported UC-related mortality:
  - first years of follow-up, in patients with extensive colitis, and in patients from Scandinavia.
  - Ulcerative colitis-related mortality 17%(11%-30%)  
mean percentage death
  - Colorectal cancer 37%(24%-44%)
  - Surgical & post-operative complic. 44%(17%-100%)  
perforations, peritonitis, cardiovascular
  - Remaining: **severe disease, i.e. toxic megacolon, intestinal perforation, intestinal- & myocardial -infarction, infarction second to anaemia, & end-stage liver disease second to PSC**

# Crohn's disease related mortality from unselected, population-based cohorts published since 1992

Author (ref)	Location	Cohort type	Study period	No	Median or mean follow up (y)	Overall SMR (95% CI)
Ekbom <sup>1</sup>	Uppsala, Sweden	Incidence (89%) and prevalence (11%)	1965–83	1655	NA	→ 1.6 (1.4–1.9)
Probert <sup>5</sup>	Leicestershire, UK	Incidence	1972–89	610	NA	0.7 (0.5–1.0)
Persson <sup>2</sup>	Stockholm County, Sweden	Incidence	1955–84	1251	NA	→ 1.5 (1.3–1.7)
Jess <sup>3</sup>	Copenhagen County, Denmark	Incidence	1962–87	374	17	→ 1.3 (1.0–1.6)
Card <sup>8</sup>	GPRD, UK	Incidence (31%) and prevalence (69%)	1987–??	5960	3.6	→ 1.7 (1.5–2.0)
Masala <sup>4</sup>	Florence, Italy	Incidence	1978–92	231	15.4	→ 1.5 (1.1–2.1)
Jess <sup>6</sup>	Olmsted County, USA	Incidence	1940–2001	314	13	1.2 (0.9–1.6)
Wolters <sup>12</sup>	EC-IBD, Europe and Israel	Incidence	1991–93	371	10	→ 1.9 (1.3–2.5)

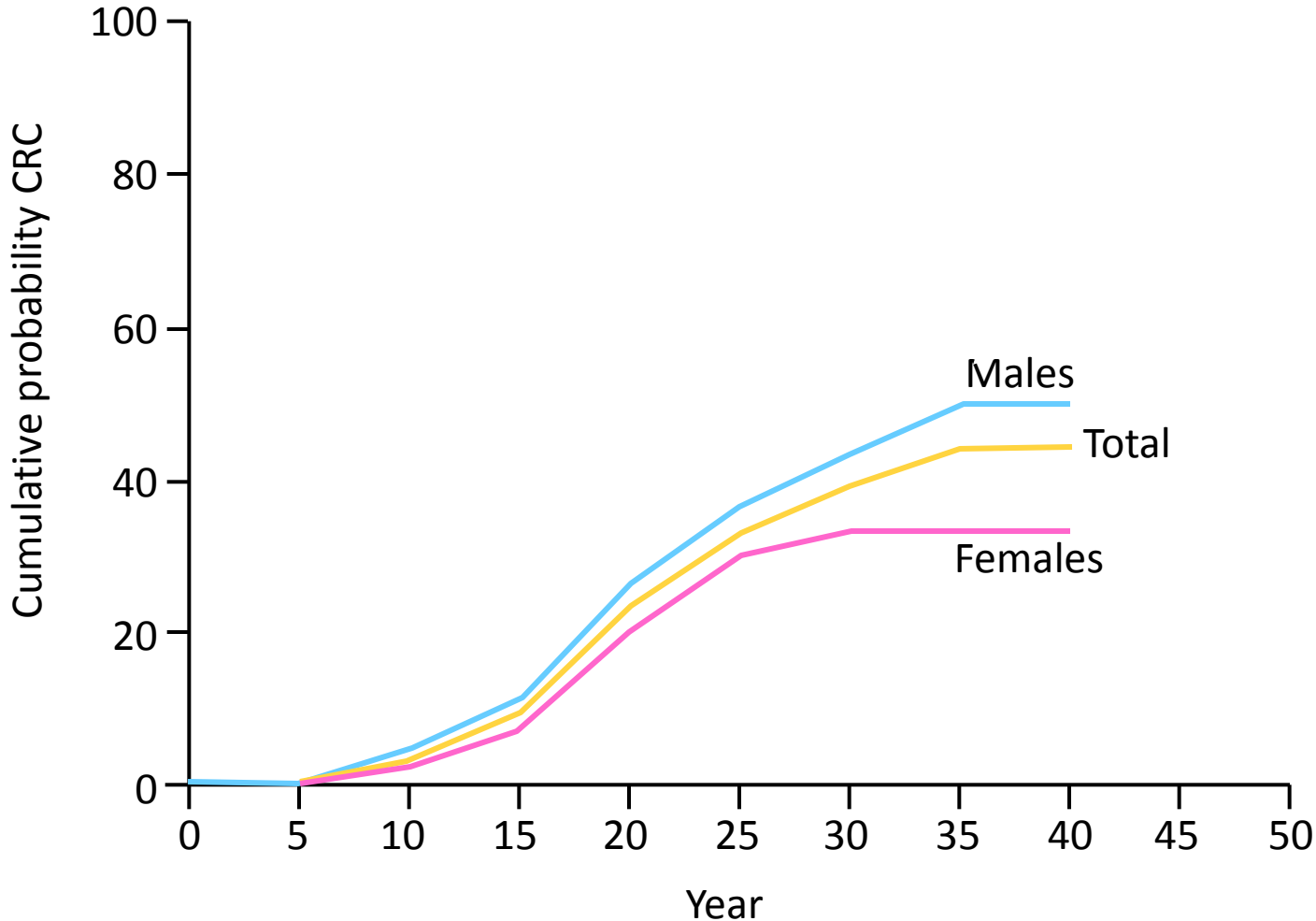
# Meta-analysis Mortality cause CD

## DEATH

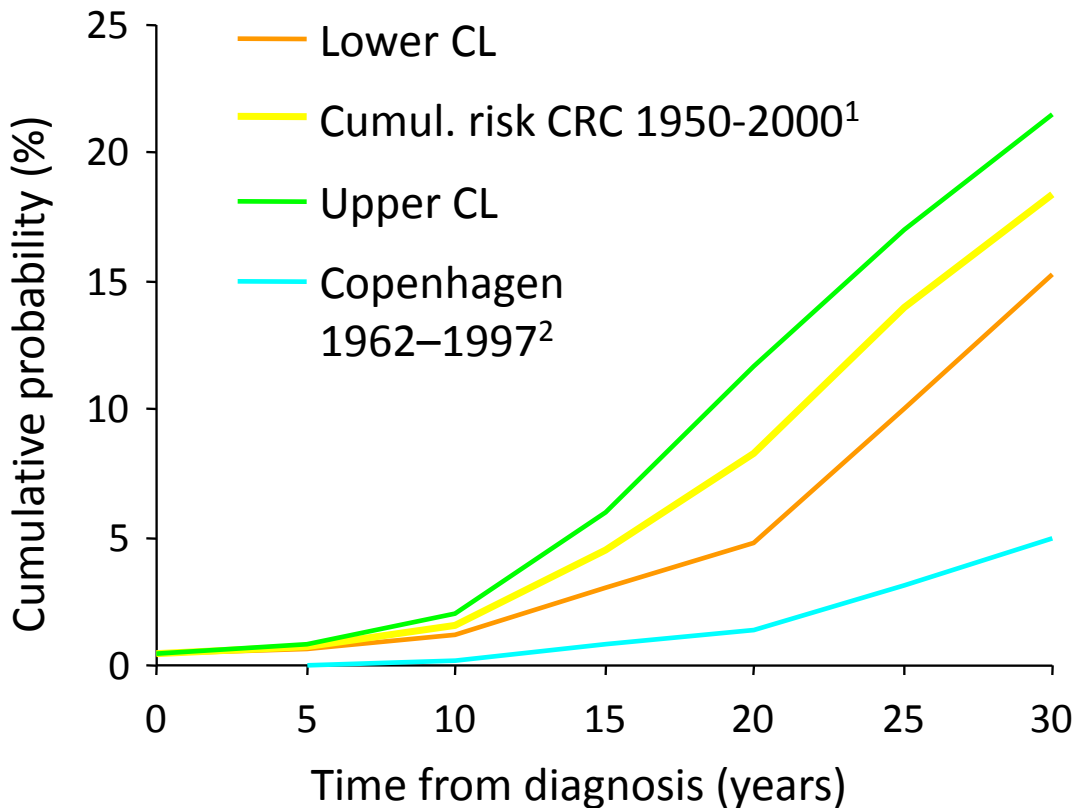
- Assumed 51% greater chance of death from CD than in general population.



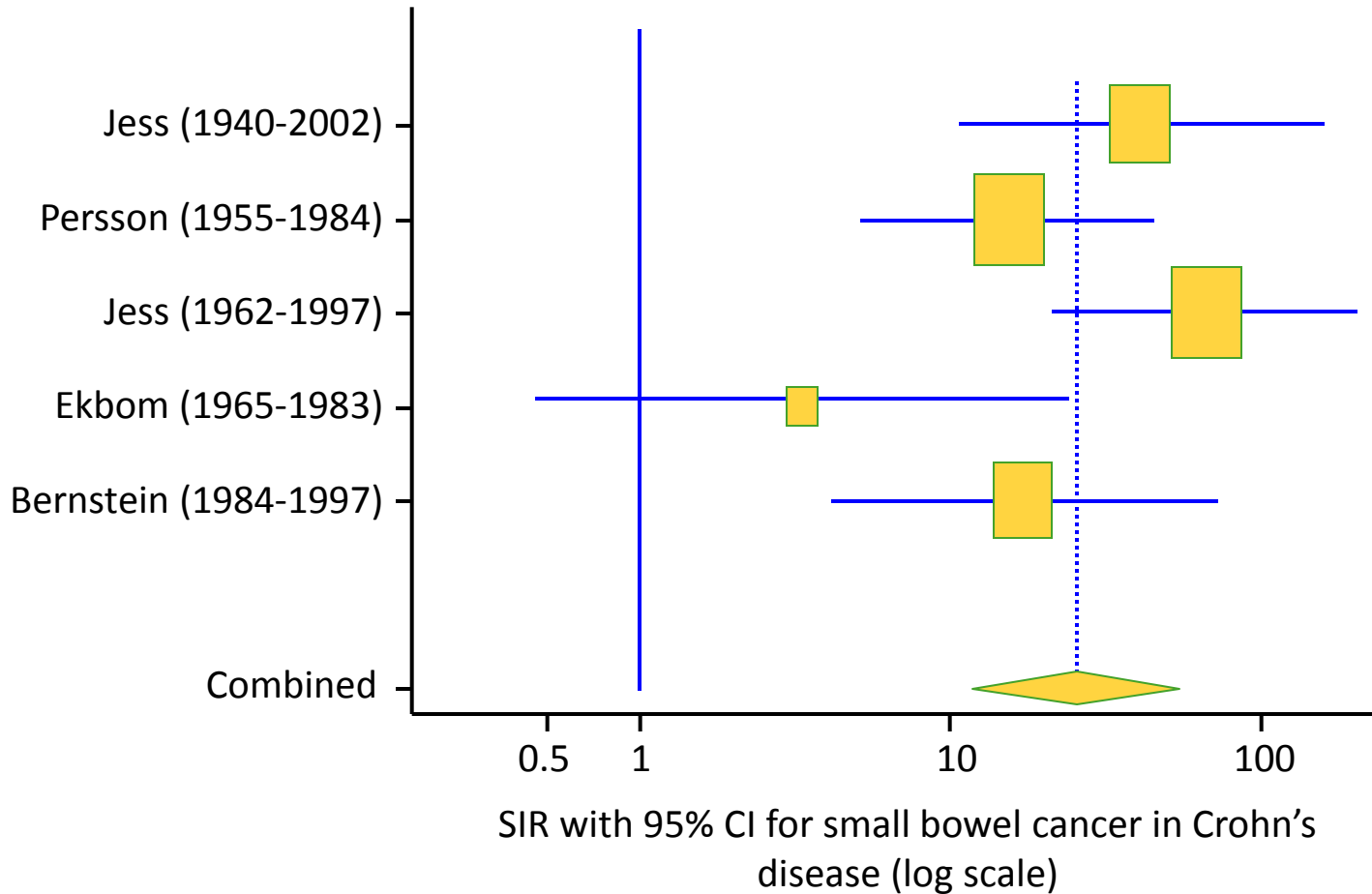
## History: estimated cumulative probability of development of colorectal cancer in UC



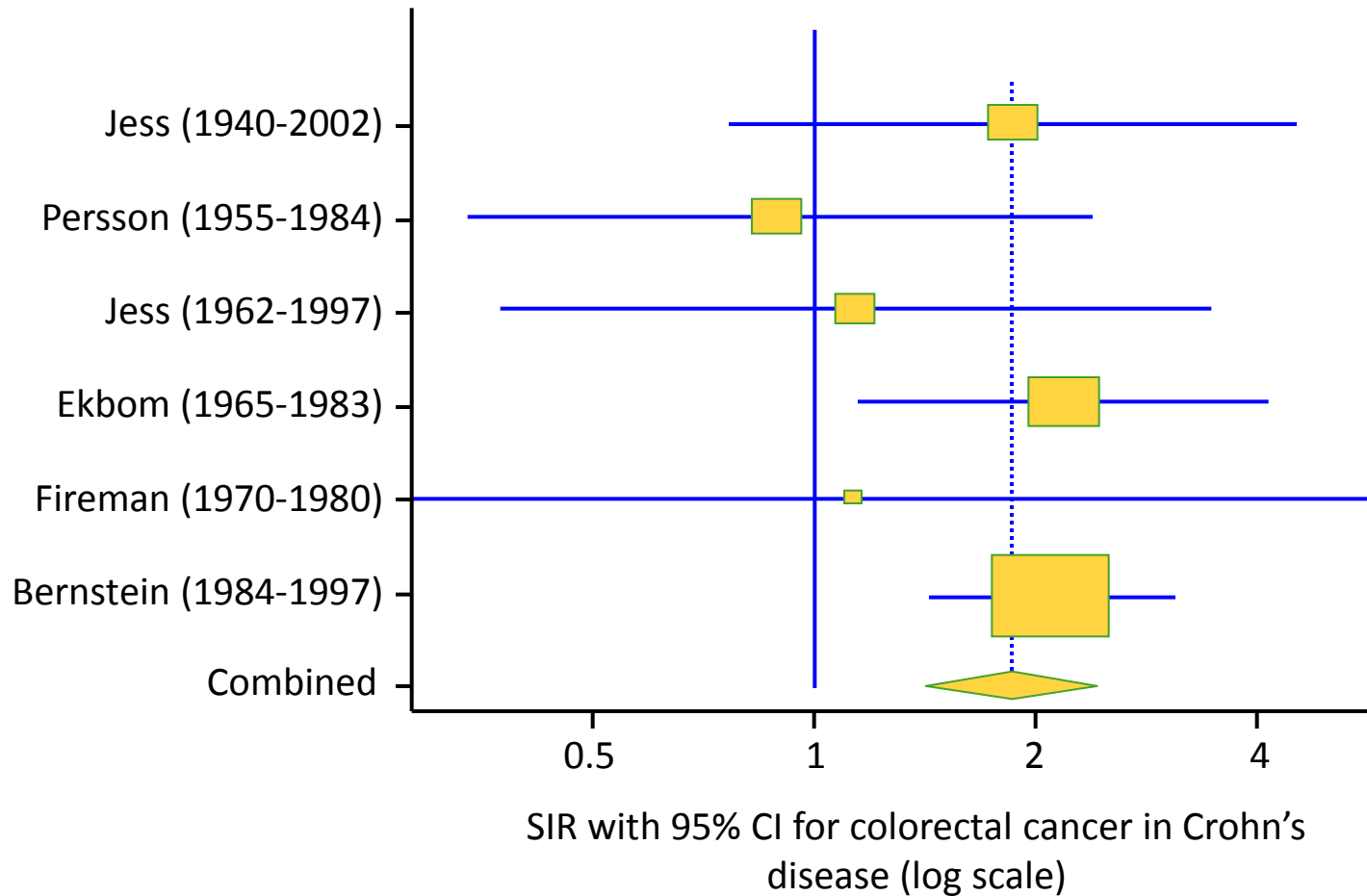
# Meta-analysis: Cumulative risk of developing CRC in UC




# Meta-analysis-population-based cohorts: Small bowel cancer in Crohn's disease



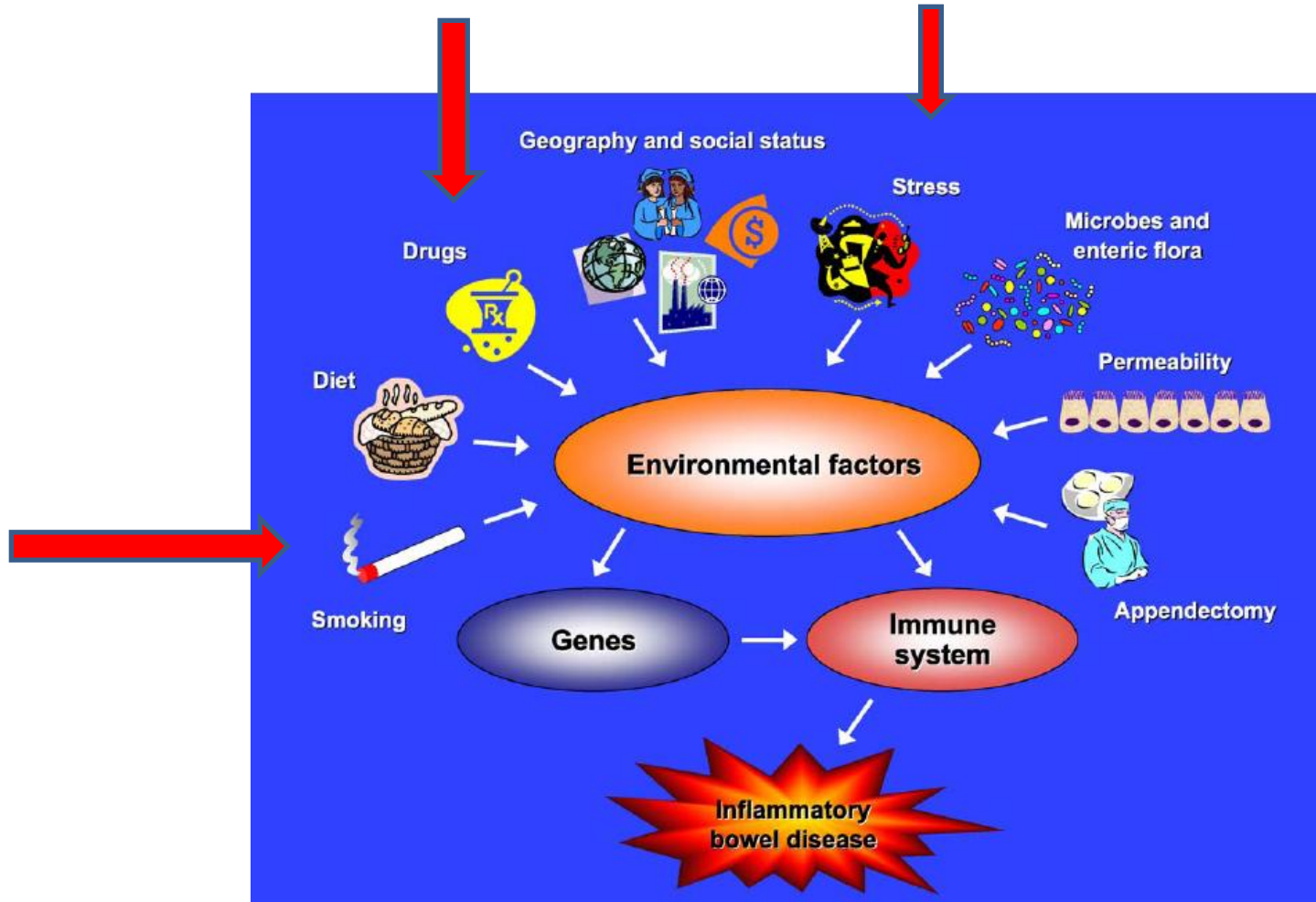
# Meta-analysis: colorectal cancer in Crohn's disease



# Small Bowel Adenocarcinoma risk in CD

29 cases SBA vs 87 controls (- SBA)	OR(IC 95%)	p
Multivariate less risk: 		
intestinal resections	0.04(0.01-0.28)	0.001
5-asa long-term > median 2 yrs	0.16(0.03-0.79)	0.02
Time to resection longer(ns) 15,9 yrs vs 8,2 yrs		0.02
Age, sex, Montreal phenotype		ns

# Impact of environmental factors on inflammatory bowel disease



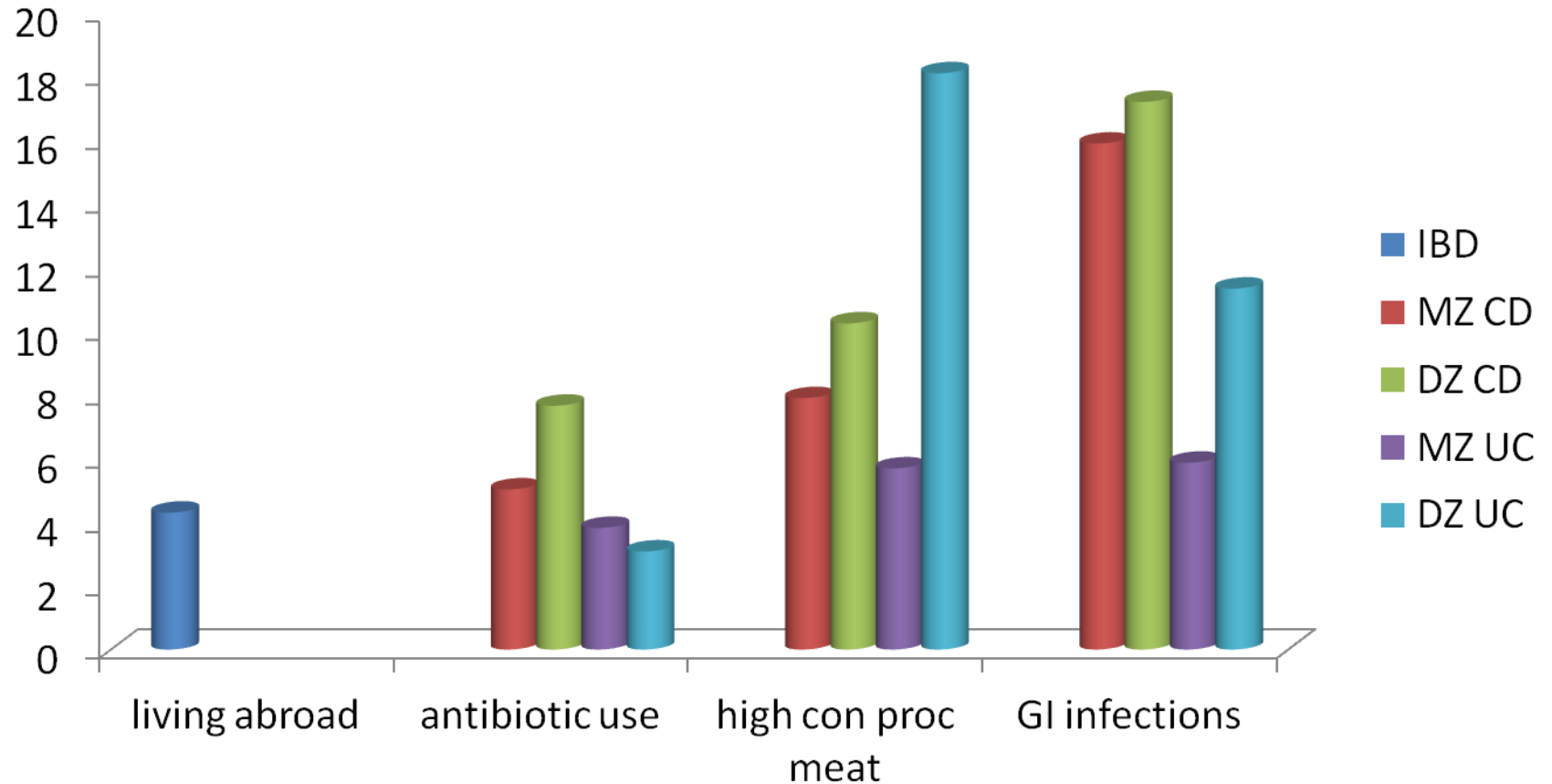
Danese S. Autoimmunity Reviews 2004;3(5):394-400.

# Environmental factors in unselected IBD cohort 2003-04

- Being breastfed >6 months (OR, 0.50; 95% CI, 0.23-1.11)
- tonsillectomy (OR, 0.49; 95% CI, 0.31-0.78) decreased the odds for IBD
- appendectomy dec UC only (OR, 0.29; 95% CI, 0.12-0.71)
- Vaccination against:
  - pertussis (OR, 2.08; 95% CI, 1.07-4.03) &
  - polio (OR, 2.38; 95% CI, 1.04-5.43) increased the odds for IBD
  - measles infection increased the odds for UC (OR, 3.50; 95% CI, 1.15-10.6)
- Low consumption of fibres & high consumption of sugar significantly associated with development of CD and UC
- Smoking increased the risk for CD and protected against UC

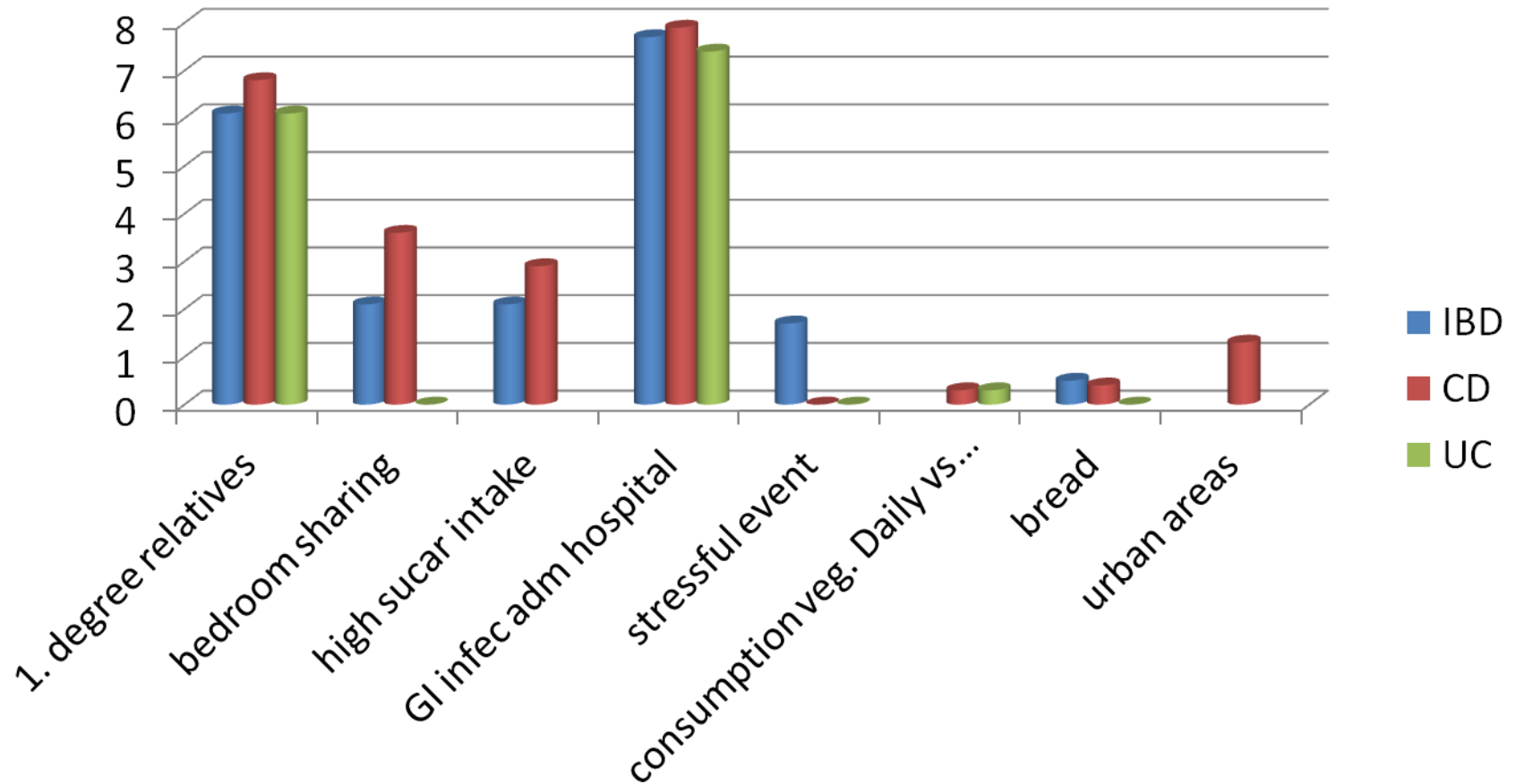
# Life style & alteration of gut flora

## IBD Twins





# Environmental factors in a Danish pediatric inception cohort 2007-9



Have a nice ECCO Congress 2012

