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# Diagnostic techniques for surveillance of dysplasia

Gerhard Rogler, Department of Gastroenterology and Hepatology, University Hospital Zürich



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## Case: R.B., ♂, born 1977

- **2001** first diagnosed with left sided ulcerative colitis (age 24)
- Insufficient response to 5-ASA
- Steroid dependent disease course
- **03/2003** ACT 2 clinical trial: Remicade® for UC;
- **2006:** good clinical condition under Remicade®, 3-4 bowel movements/day; 2-3 times per month abdominal pain; increasing symptoms 6 weeks after infusion;

medication: Prednisolone 10 mg/day

Imurek 150 mg

Pentasa 3g

## Case: R.B., ♂, born 1977

- **01/2007** stable clinical situation
- **07/2008** colonoscopy: histologically moderate – severe chronic inflammation, pancolitis
- **2/2009** aggravation of clinical symptoms; 10 bloody bowel movements/day → steroids
- **11/2009** ongoing clinical symptoms; evaluation for Millenium study (vedolizumab in UC)

## Case: R.B., ♂, born 1977

- 11/2009

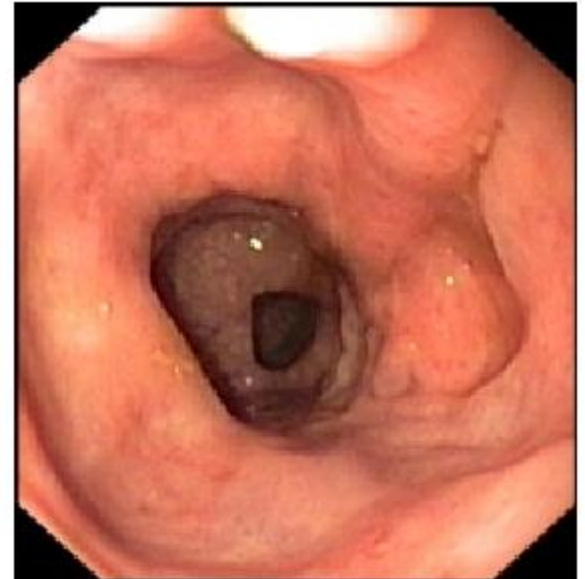
70 cm ab ano



60 cm ab ano



50 cm ab ano



## Case: R.B., ♂, born 1977

- 11/2009

30cm ab ano



## Case: R.B., ♂, born 1977

- **26/11/2009** start study medication; 5 bowel movements
- **12/2009** 6 – 7 bowel movements; sometimes blood; sometimes pain left upper quadrant
- **2/2010**

Befund ca. 15cm ab ano



Befund ca. 30cm ab ano



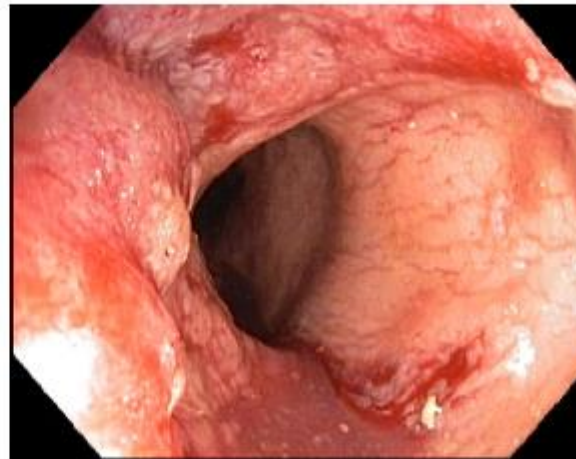
## Case: R.B., ♂, born 1977

- **03/2010** 2-3 bowel movements; no blood
- **07/2010** worsening of condition; 5-8 bowel movements
- **08/2010** again abdominal pain, bloody diarrhea
- **10/2010**

Bx 3



Bx 4 (45cm)





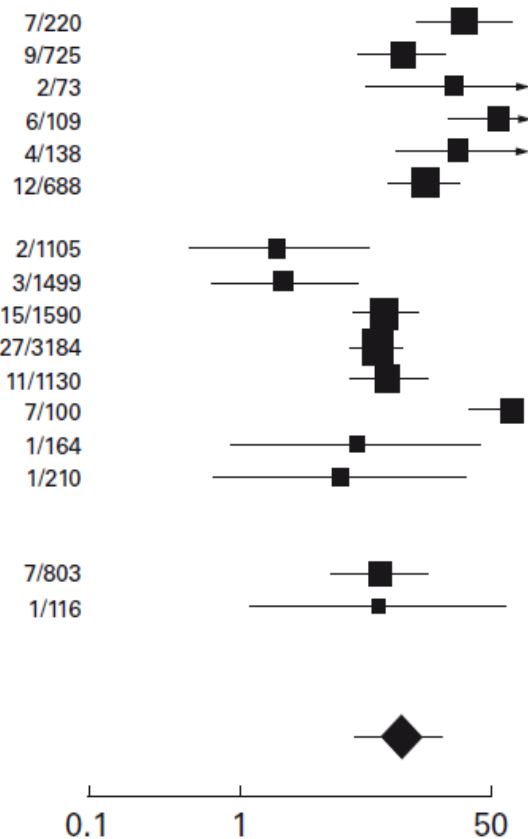
## Case: R.B., ♂, born 1977

- **03/2010** 2-3 bowel movements; no blood
- **07/2010** worsening of condition; 5-8 bowel movements
- **08/2010** again abdominal pain, bloody diarrhea
- **10/2010** endoscopy and biopsies: histology: moderately differentiated invasive CRC  
CT scan: liver metastases, lung metastases, bone metastases
- **11/2010:** colectomy: positive lymphnodes (21 of 29)

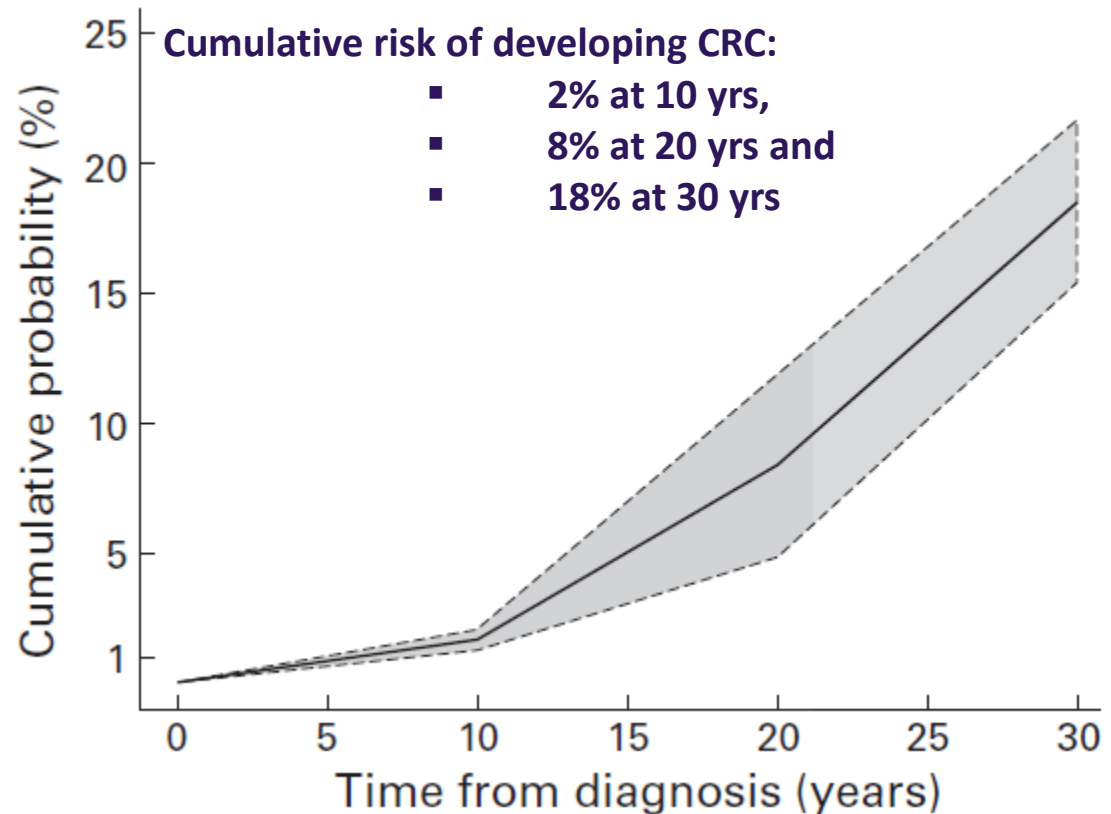


# Increased Risk of Colorectal Cancer in UC Patients

21–30 years



Meta-analysis of 116 worldwide studies assessing the risk of CRC in CU patients



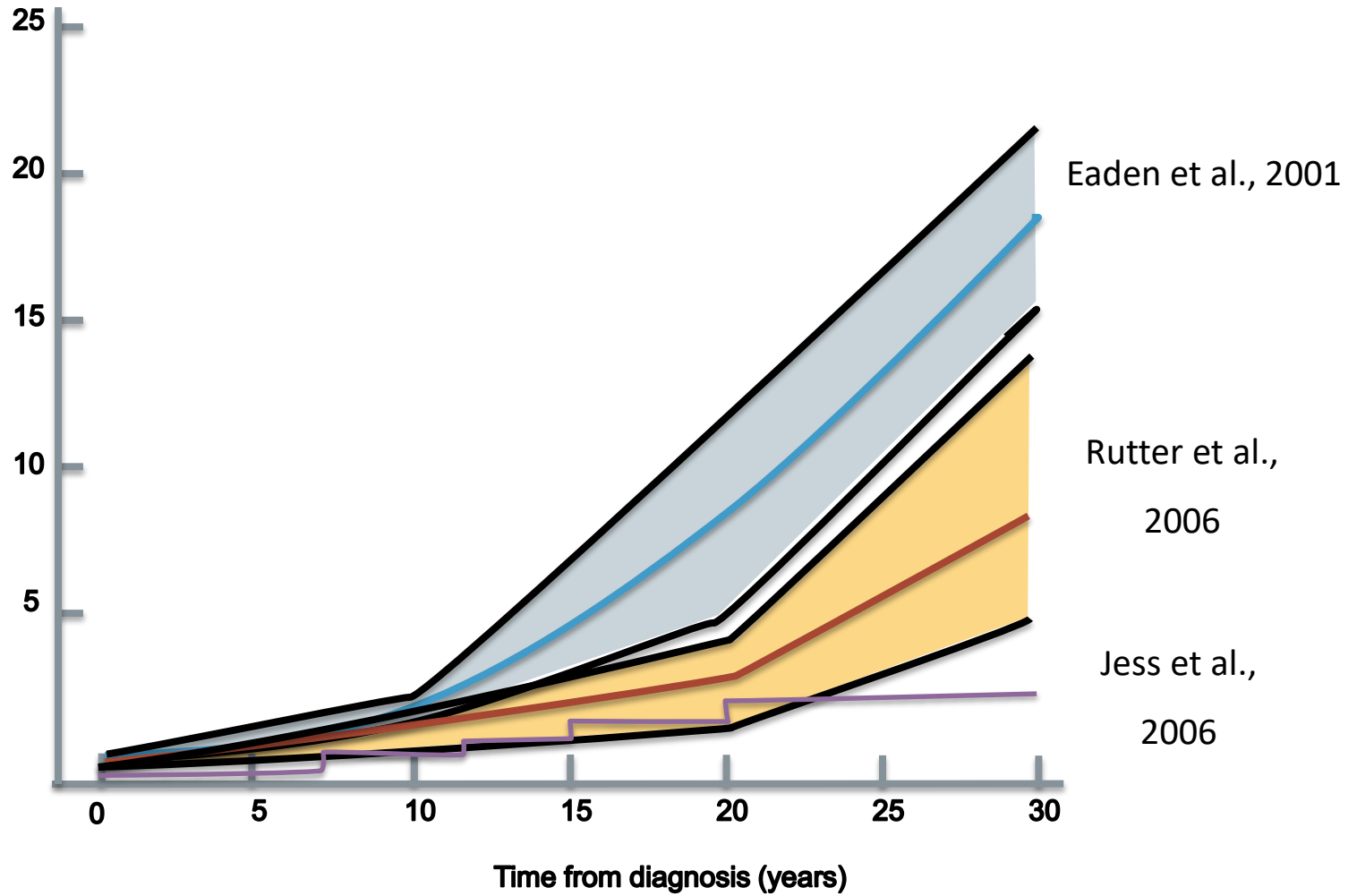
# Is the Risk Still The Same?

- ▶ 600 patients with extensive UC at St. Mark's in London followed for 5932 person-years
- ▶ 30 CRCs detected (annual risk: 0.5% or 1/200)
- ▶ Cumulative probability of CRC was
  - 2.5% at 20 years,
  - 7.6% at 30 years and
  - 10.8% at 40 years
- ▶ Linear regression suggested that CRC risk declined over the course of the study.

Rutter MD, et al. Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. *Gastroenterology* 2006;130:1030-1038



# Is the Risk Still The Same?



Rogler G.  
Cancer Lett. 2014 10;345(2):235-41.  
Chronic ulcerative colitis and colorectal cancer.

# The declining risk of CRC in ulcerative colitis

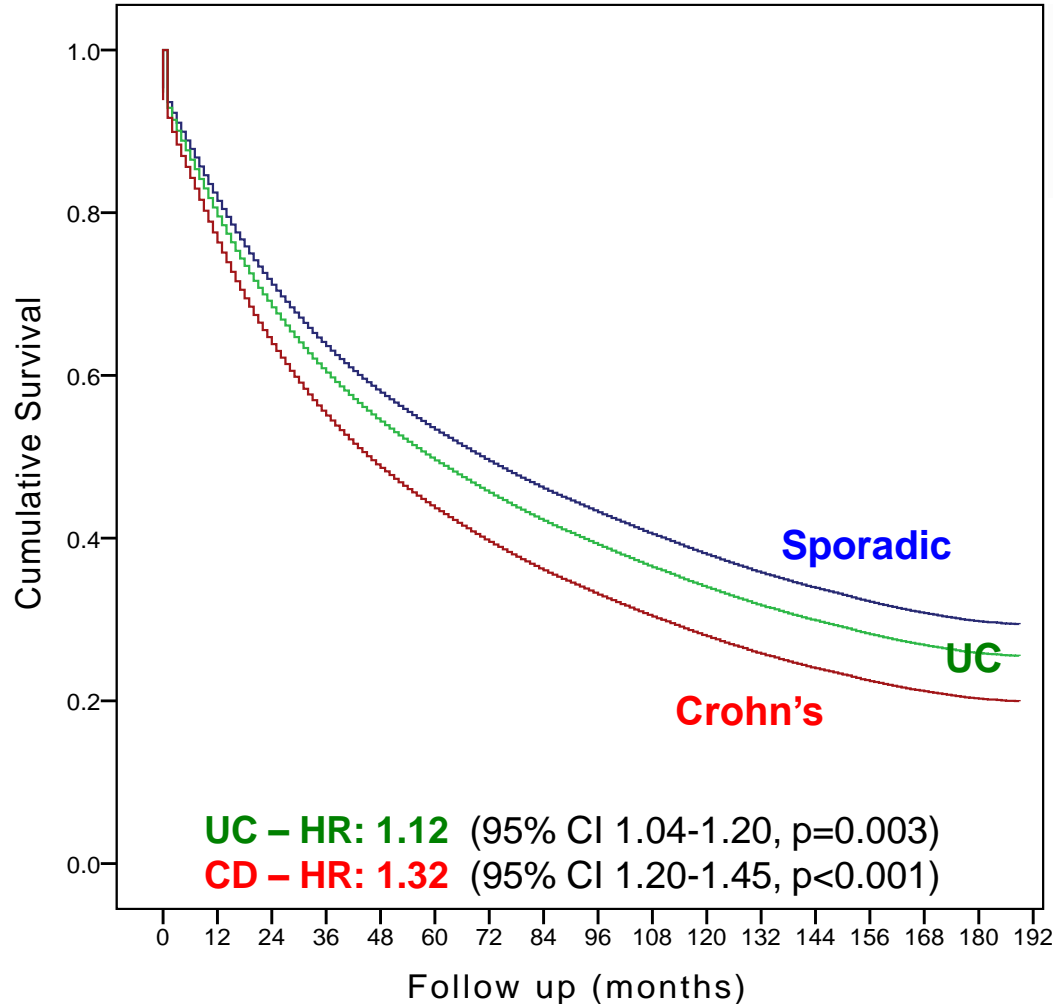
Risk of developing CRC in UC stratified by decade of publication of studies

Decade	N. of studies	Patient-yrs	Number of cases of CRC	Cumulative incidence per 1000 py (95% CI)	Incidence rate per 1000 py (95% CI)
1950s	3	4.759	22	33.15 (0.58-65.73)	4.29 (0.95-7.64)
1960s	7	19.304	80	31.43 (20.21-42.65)	4.18 (2.67-5.68)
1970s	4	12.909	40	29.47 (2.47-56.37)	3.22 (0.67-5.77)
1980s	14	123.866	310	31.37 (20.36-42.38)	2.58 (1.81-3.34)
1990s	12	87.499	132	15.59 (9.6-21.57)	1.53 (1.06-2)
2000s	23	369.829	525	14.26 (10.47-18.05)	1.29 (1-1.58)
2010-2013	18	861.478	1180	9.05 (6.8-11.3)	1.21 (0.95-1.48)

Py, patient-years; CI, confidence interval

# Survival in UC associated CRC versus sporadic

Overall Survival (OS) in Sporadic, UC and CD colorectal cancer



Hospital Episode Statistics (HES)

All admission in England 1997-2012

Total of 286,591 patients underwent surgical resection for CRC

UC: 1,546 (0.5%)

CD: 776 (0.3%)

Age at CRC diagnosis:

■ IBD-CRC: median 64 years

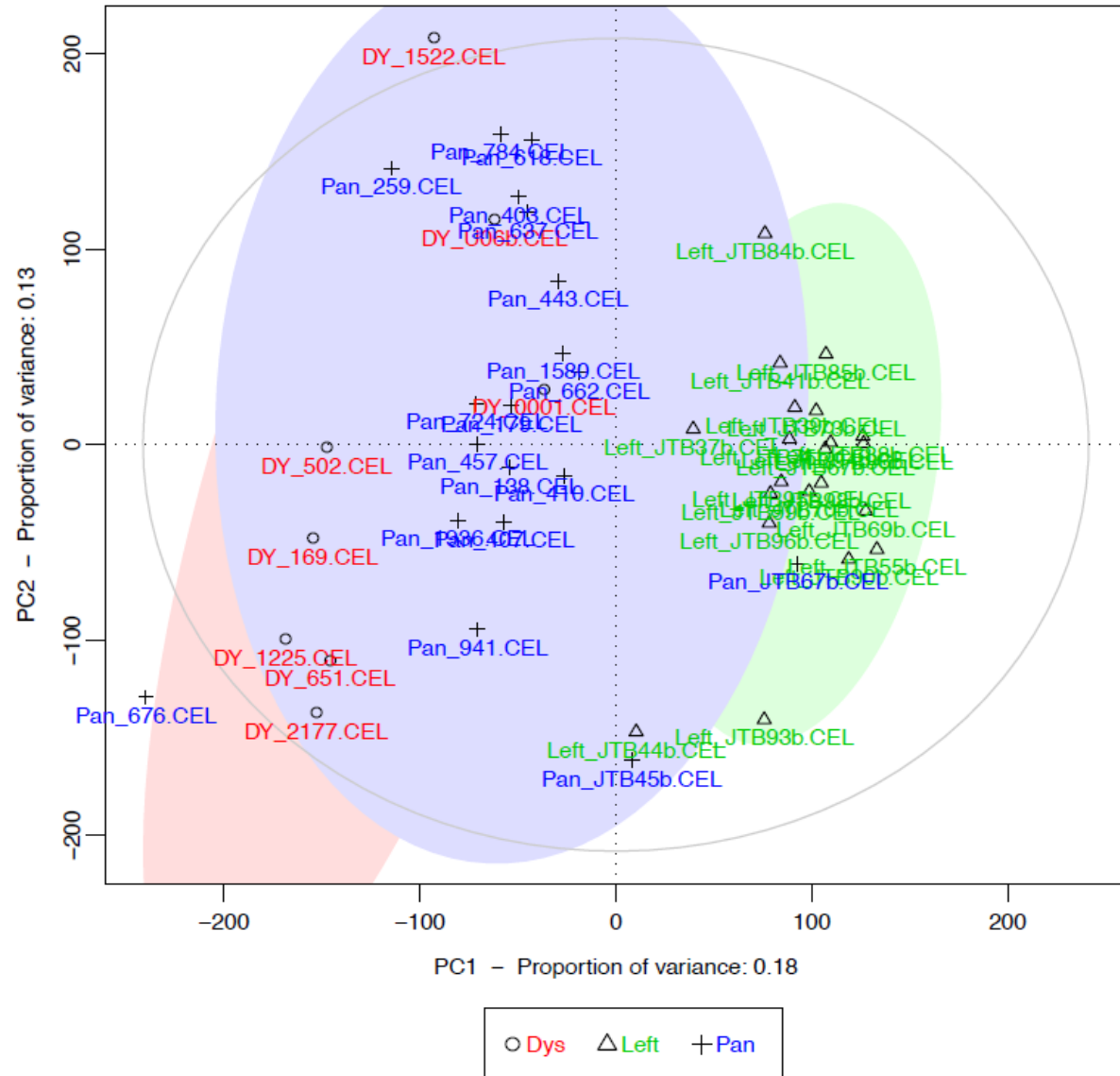
■ Sporadic CRC: median 71 years

# Dysplasia has specific genetic signatures

Bjerrum JT, Nielsen OH, Riis LB, Pittet V, Mueller C, Rogler G, Olsen J

Inflamm Bowel Dis. 2014 Dec;20(12):2340-52.

Transcriptional analysis of left-sided colitis, pancolitis, and ulcerative colitis-associated dysplasia.



# Who is at increased risk for colorectal cancer?

## ECCO Statement 9 B + C

- ▶ Risk is highest in patients with extensive colitis, intermediate in patients with left-sided colitis, and not increased in proctitis [EL2].
- ▶ Patients with early onset of disease (age < 20 years at onset of disease) and patients with UC-associated primary sclerosing cholangitis (PSC) may have a particularly increased risk [EL2].
- ▶ Persistent inflammation and family history of CRC may contribute to the risk of CRC in patients with UC [EL3]

Biancone et al. for the European Crohn's and Colitis Organisation (ECCO) European evidence-based Consensus on the management of ulcerative colitis: Special situations *Journal of Crohn's and Colitis* (2008) 2, 63–92





# Factors influencing CRC risk

- ▶ Disease duration,
- ▶ more extensive disease,
- ▶ primary sclerosing cholangitis,
- ▶ and a positive family history of sporadic CRC
  
- ▶ Colonic strictures in patients with UC and/or
- ▶ a shortened colon, and/or
- ▶ multiple post-inflammatory pseudopolyps
  
- ▶ Inflammation is a risk factor for progression to colorectal neoplasia.

Farraye FA, Odze R, Eaden J, Itzkowitz S. Diagnosis and management of colorectal neoplasia in inflammatory bowel disease. *Gastroenterology* 2010; 138:746-774.



# How to perform surveillance colonoscopy in UC?

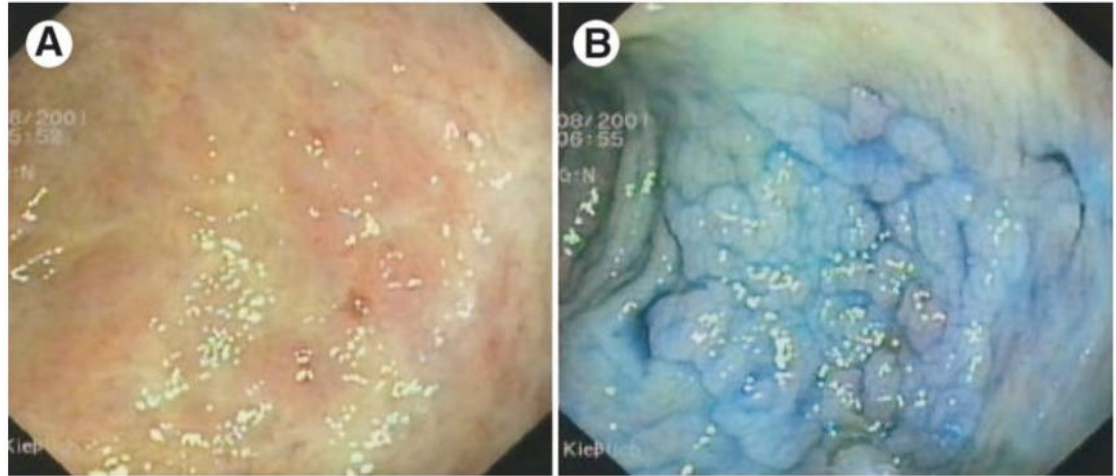
## ECCO Statement 9H

- ▶ Random biopsies (4 every 10 cm) and targeted biopsies of any visible lesion should be performed during surveillance colonoscopy [EL2b, RGB].
- ▶ Methylene blue or indigo carmine chromoendoscopy is an alternative to random biopsies for appropriately trained endoscopists and is superior to random biopsies in the detection rate of neoplastic lesions [EL1b, RG B]

*Livia Biancone, et al.: European evidence-based Consensus on the management of ulcerative colitis: Special situations Journal of Crohn's and Colitis (2008) 2, 63–92*



# Chromoendoscopy



318 patients

	Pat. with at least one dysplasia
conventional colonoscopy	10/154 (6,5%)
+ 0,1% methylen blue	24/164 (14,6%)      p=0,028

→ 2,2x detection rate with chromoendoscopy with methylene blue

Kiesslich R, Fritsch J, Holtmann M, Koehler HH, Stolte M, Kanzler S, Nafe B, Jung M, Galle PR, Neurath MF. Methylene blue-aided chromoendoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. *Gastroenterology*. 2003 Apr;124(4):880-8.

Kiesslich R, Goetz M, Lammersdorf K, Schneider C, Burg J, Stolte M, Vieth M, Nafe B, Galle PR, Neurath MF. Chromoscopy-guided endomicroscopy increases the diagnostic yield of intraepithelial neoplasia in ulcerative colitis. *Gastroenterology*. 2007 Mar;132(3):874-82.

# Impact of NBI – so far not better than WL

## 42 Patients

Low grade n=9	NBI missed 5 WL missed 3
High grade n=5	NBI missed 2
Karzinom n=3	NBI missed 1 WL missed 2

*Dekker E, van den Broek FJ, Reitsma JB, Hardwick JC, Offerhaus GJ, van Deventer SJ, Hommes DW, Fockens P.*

*Narrow-band imaging compared with conventional colonoscopy for the detection of dysplasia in patients with longstanding ulcerative colitis.*

*Endoscopy. 2007 Mar;39(3):216-21.*



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## 48 Patients

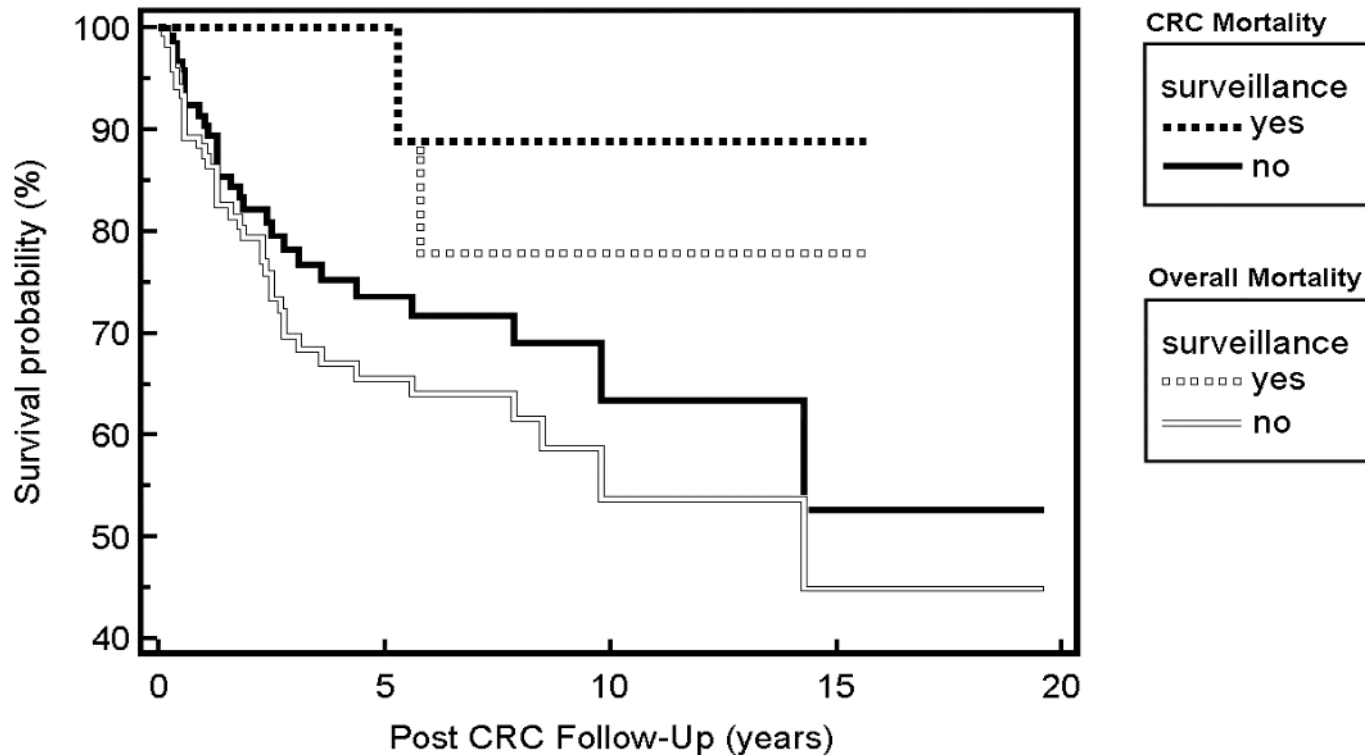
Low grade n=16	NBI targeted 11 (69%) WL targeted 13 (82%) random 3
High grade n=0	
Karzinom n=0	

*van den Broek FJ, Fockens P, van Eeden S, Stokkers PC, Ponsioen CY, Reitsma JB, Dekker E. Narrow-band imaging versus high-definition endoscopy for the diagnosis of neoplasia in ulcerative colitis. Endoscopy. 2011 Feb;43(2):108-15.*



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# Is surveillance in colitis effective?



Number at risk

Group: non-surveillance

124      44      11      5      1

Group: surveillance

21      9      3      1      0

# Summary

- The pathomechanism of CRC in IBD is different from sporadic CRC; already dysplasia have a unique expression pattern
- Severity of inflammation, extend of disease, disease duration, presence of pseudopolyps, family history and PSC are risk factors
- CRC in UC patients usually is more aggressive and has a worse prognosis
- The magnitude of CRC risk in IBD is uncertain: not all studies report an increased risk: Decreasing incidence of CRC in IBD over the last 50 years
- Surveillance is effective and strongly recommended but should be stratified to the risk profile. *But what to do with the increasing prevalence of dysplasia????*



# Thank you for your attention



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