Colorectal cancer surveillance in IBD

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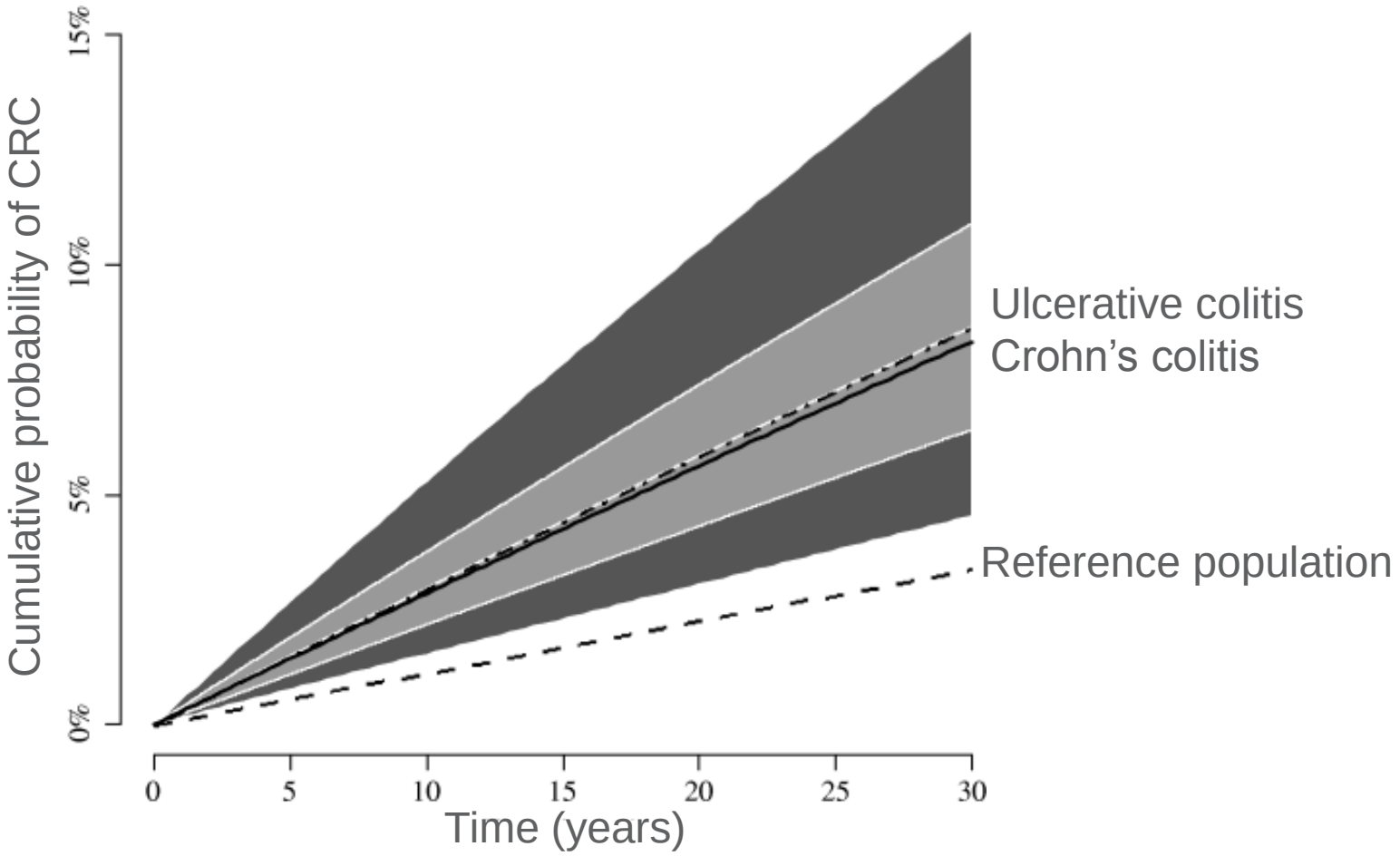
Increased risk of CRC in IBD



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Canavan, APT, 2006

Risk Factors for dysplasia or CRC in IBD

- Duration of disease
- Extensive disease (6-15x)
- Inflammatory polyps (2.5x)
- Increased histologic activity (3x)
- Stricture (5x)
- Family history of CRC <50 years (9x)
- Primary sclerosing cholangitis (4x)

Ekbom, NEJM, 1990
Soderlund, Gastro, 2009
Lutgens, IBD, 2013
Askling, Gastro, 2001
Lindberg, DCR, 2001
Rutter, Gastro, 2004
Velayos, Gastro, 2006
Soetikno, Gastroint Endosc, 2002
Rubin, CGH, 2013
Gupta, Gastro, 2007

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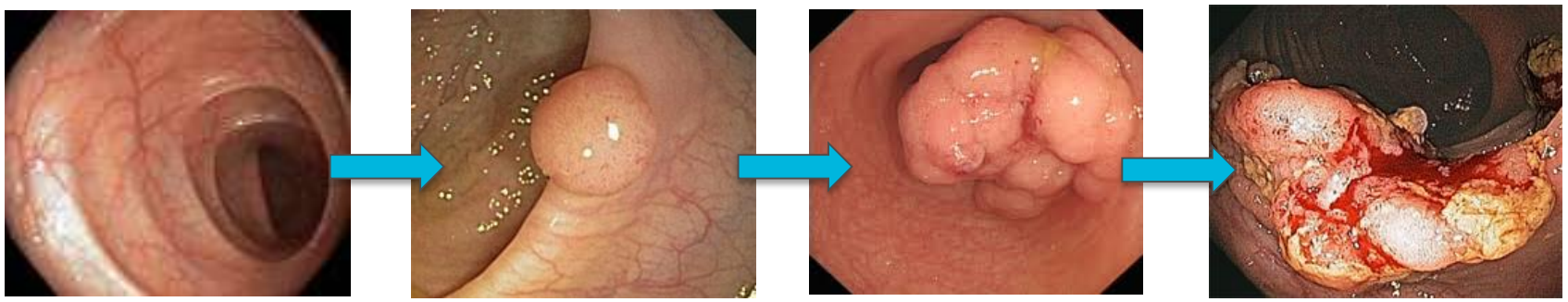
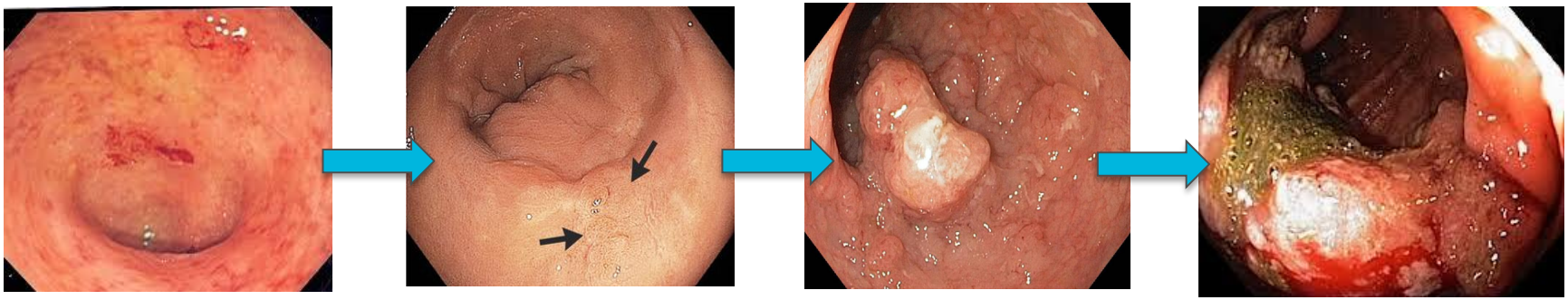
Pathogenesis of colitis-associated CRC

Non-IBD



normal | early adenoma | late adenoma | carcinoma

Colitis



inflammation | low grade dysplasia | high grade dysplasia | carcinoma

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Guidelines for surveillance colonoscopy

Society	Screening	*Surveillance colonoscopy
ACG (2010)	- All patients 8-10 yrs - Immediately in PSC	- Every 1-2 yrs - Yearly in PSC
AGA (2010)	- All patients 8 yrs - Immediately in PSC	- Every 1-2 yrs after screening - Every 1-3 yrs after 2 negative examinations - Yearly in PSC
**ASGE (2014)	- All patients 8 yrs - Immediately in PSC	- Every 1-3 years - Every year in: active inflammation, stricture, pseudopolyps, history of dysplasia, FH CRC, PSC - Histologically normal mucosa on >2 colonoscopies may lengthen interval

*Surveillance in CD>1/3 colon, excludes proctosigmoiditis
**Chromoscopy preferred over white light/random biopsies

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Kornbluth, Am j Gastro, 2010
Farraye Gastro, 2010
Committee AsoP, GIE, 2014

Missed lesions more common in IBD

- SEER database 1998-2005
- 55,008 CRC patients
- 304 Crohn's, 544 UC

	Miss rate
Control	5.8%
Crohn's	15.1%
UC	15.8%

Wang, Am J Gasro, 2013

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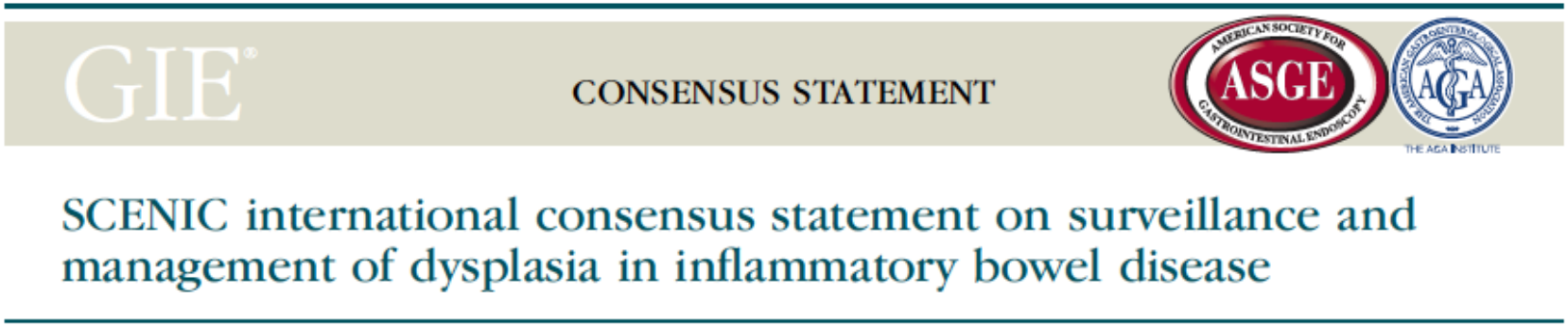

Detection of dysplasia

- High definition is recommended
  - *moderate quality evidence*
- Chromoendoscopy is recommended
  - *low quality evidence*
- Lack of consensus regarding random biopsies

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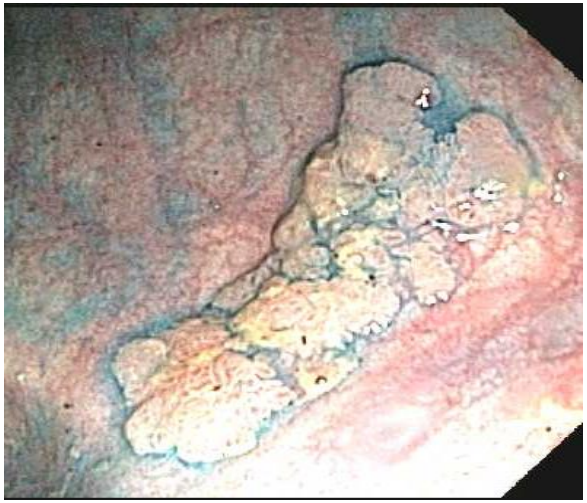
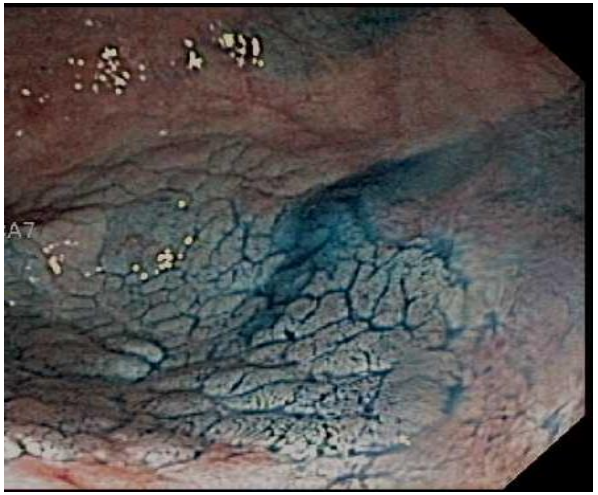
Chromoendoscopy

- Chromoendoscopy dye:
  - Indigo carmine 0.03%
  - Methylene blue 0.04%
  - Spray catheter or water jet
- Highlights mucosal irregularities
- Differentiation of neoplastic lesions (Kudo pit patterns)
- Improves delineation of borders





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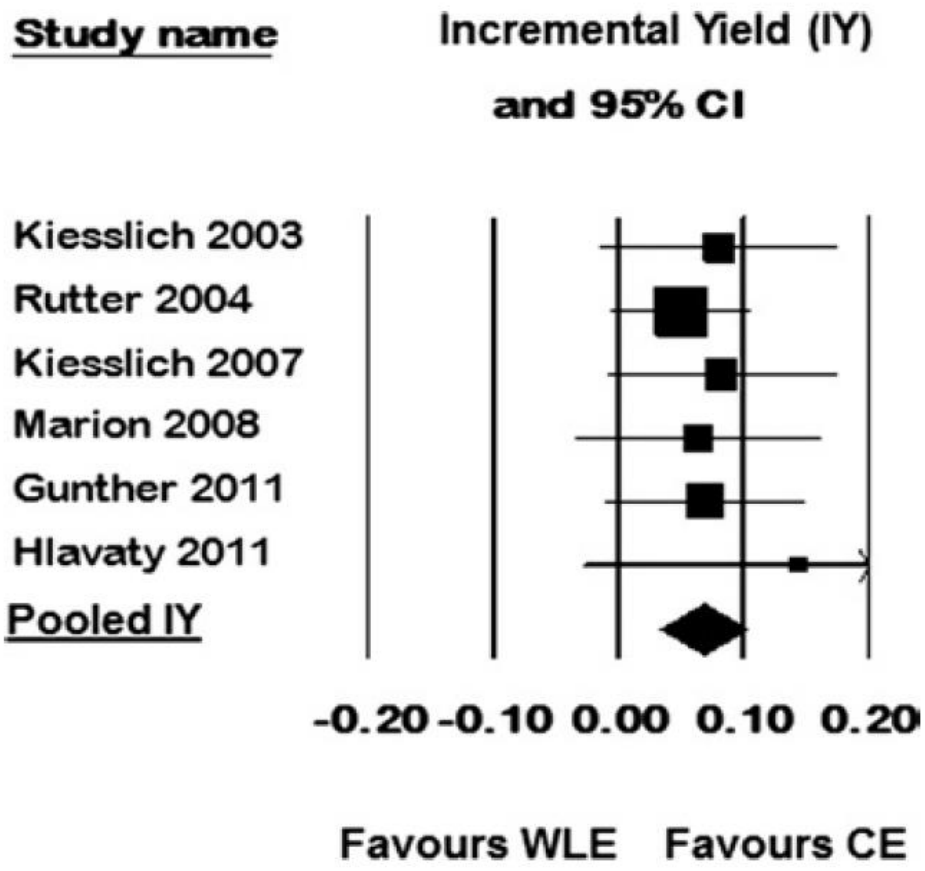
Chromoendoscopy detects more dysplasia



Incremental yield: 7% (3.3-10.3)

NNT 14.3 (9.7-30.3)

OR all dysplasia 8.9 (3.4-23)

OR flat dysplasia 5.2 (1.7-15.9)

Mean difference procedure time 10.9 mins (9.1-12.6)

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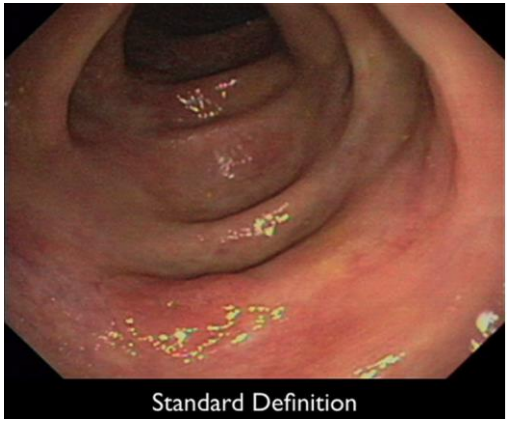
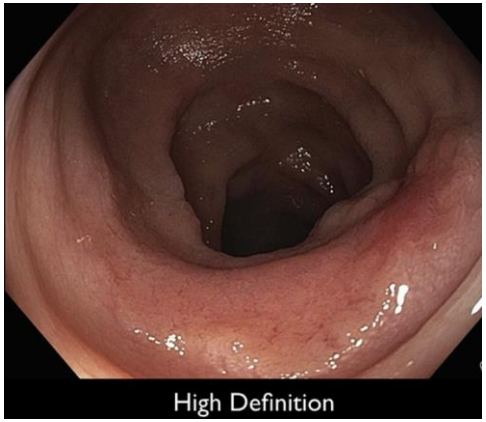
Soetikno, Gastro, 2013

Majority of dysplasia is visible

	High definition WLE	Chromo	Std definition WLE
Random	9.4%	9.8%	19.6%
Targeted	90.6%	90.2%	80.4%





Soetikno, Gastro Endo Clin N Am, 2014
SCENIC Guidelines, GIE, 2015

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"And this is where they switched to High Definition."

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HD WLE versus HD chromoendoscopy

- Longstanding (>10 years) extensive colitis
- Randomized to HD WLE versus HDCE
- 103 patient randomized

	HD WLE (n=53)	HD CE (n=50)
Dysplastic lesions	6/5 patients (9%)	14/11 patients (22%)
HGD	0	1

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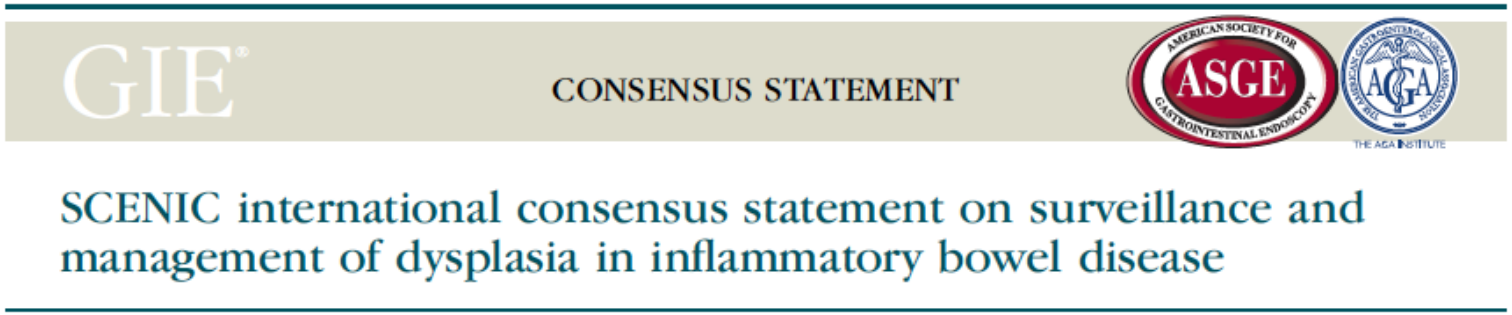
Mohammed et al, DDW, 2015



Management of dysplasia

- Polypoid and nonpolypoid resectable lesions can be followed by surveillance endoscopy
  - *very low quality evidence*
- Invisible dysplasia should be evaluated by expert in chromoendoscopy
  - *very low quality evidence*

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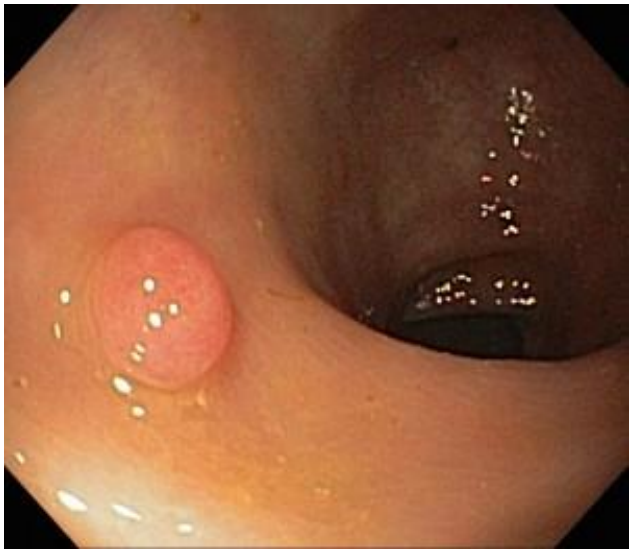
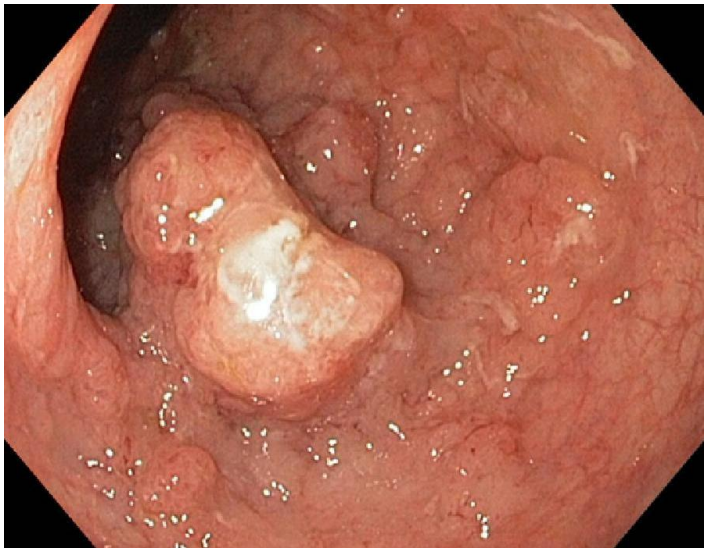
Raised dysplasia

Resectable



Adenoma-like mass (ALM)
Colitis-associated adenoma
Sporadic adenoma

Unresectable



Dysplasia-associated lesion or mass (DALM)

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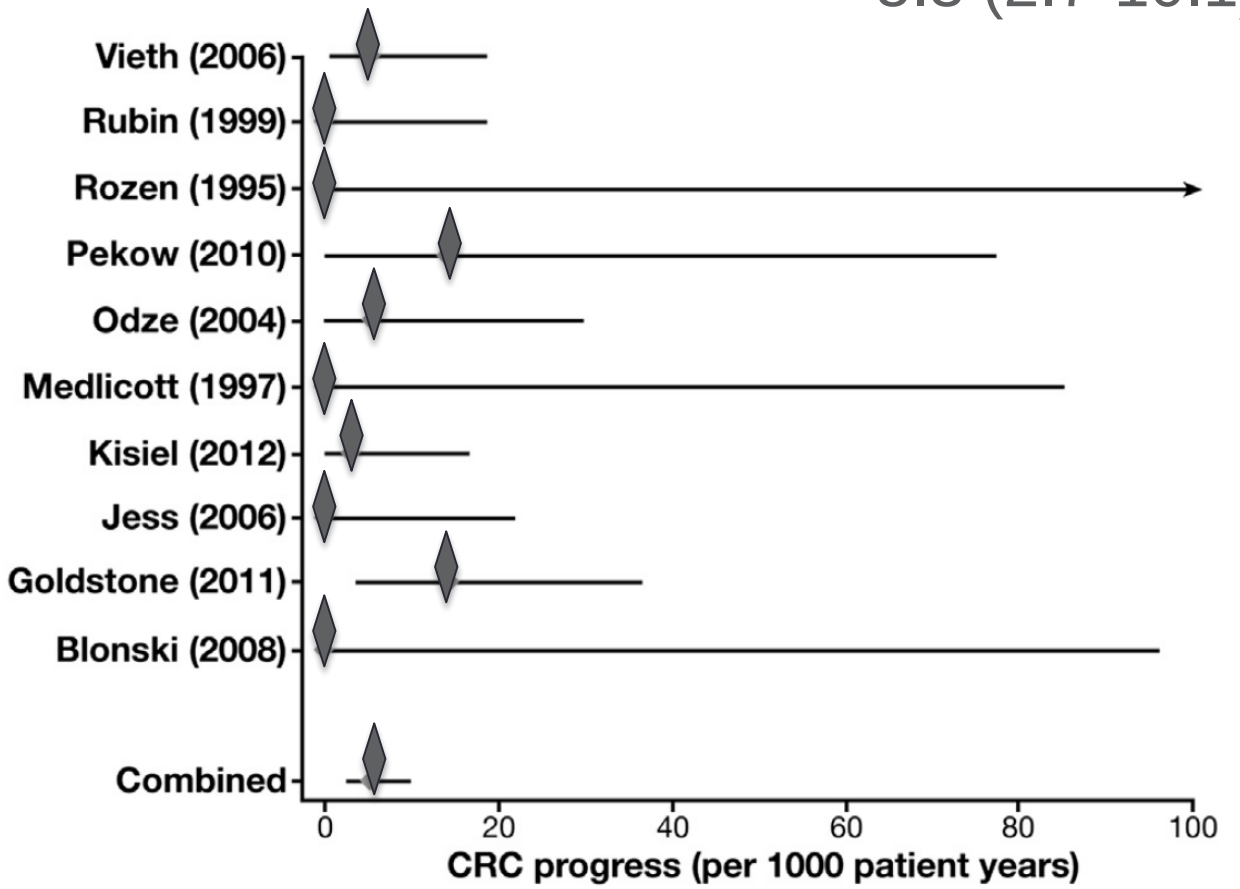
Low risk of CRC after polypoid dysplasia resection

5.3 (2.7-10.1)/1000 pt-yrs



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Wanders, CGH, 2014

Significant variability in progression of "invisible" LGD

Study	Setting	LGD (n)	Rate
Connell 1994	St Mark's	9	54% @5y
Ullman 2002	Mayo Clinic	18	33% @5y
Ullman 2003	Mount Sinai	46	53% @5y
Rutter 2006	St Mark's	36	25% @5y
Van Schaik 2010	6 Dutch centers	21	37% @5y
Lindberg 1996	Huddinge	37	35% @20y
Befrits 2002	Karolinska	60	2% @10y
Lim 2003	Leeds, UK	29	10% @10y
Pekow 2010	U of Chicago	13	8% @ 5 y

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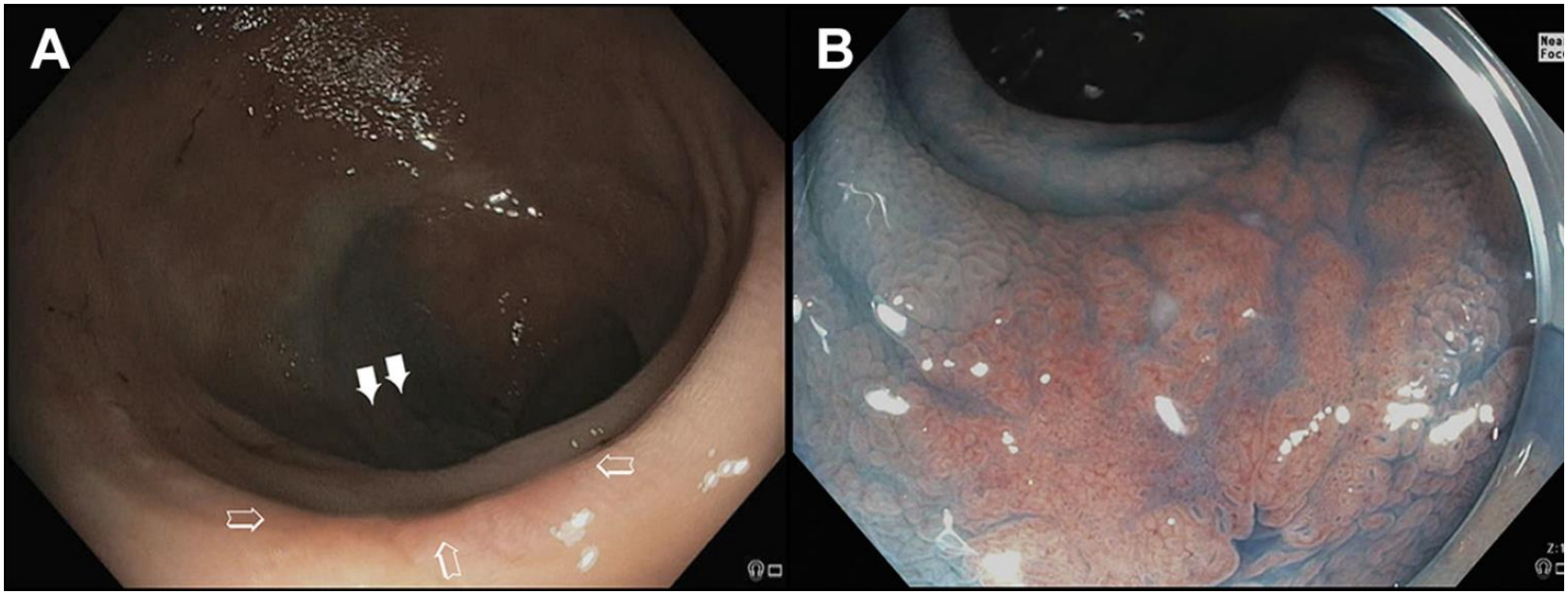
Does invisible dysplasia = flat dysplasia?



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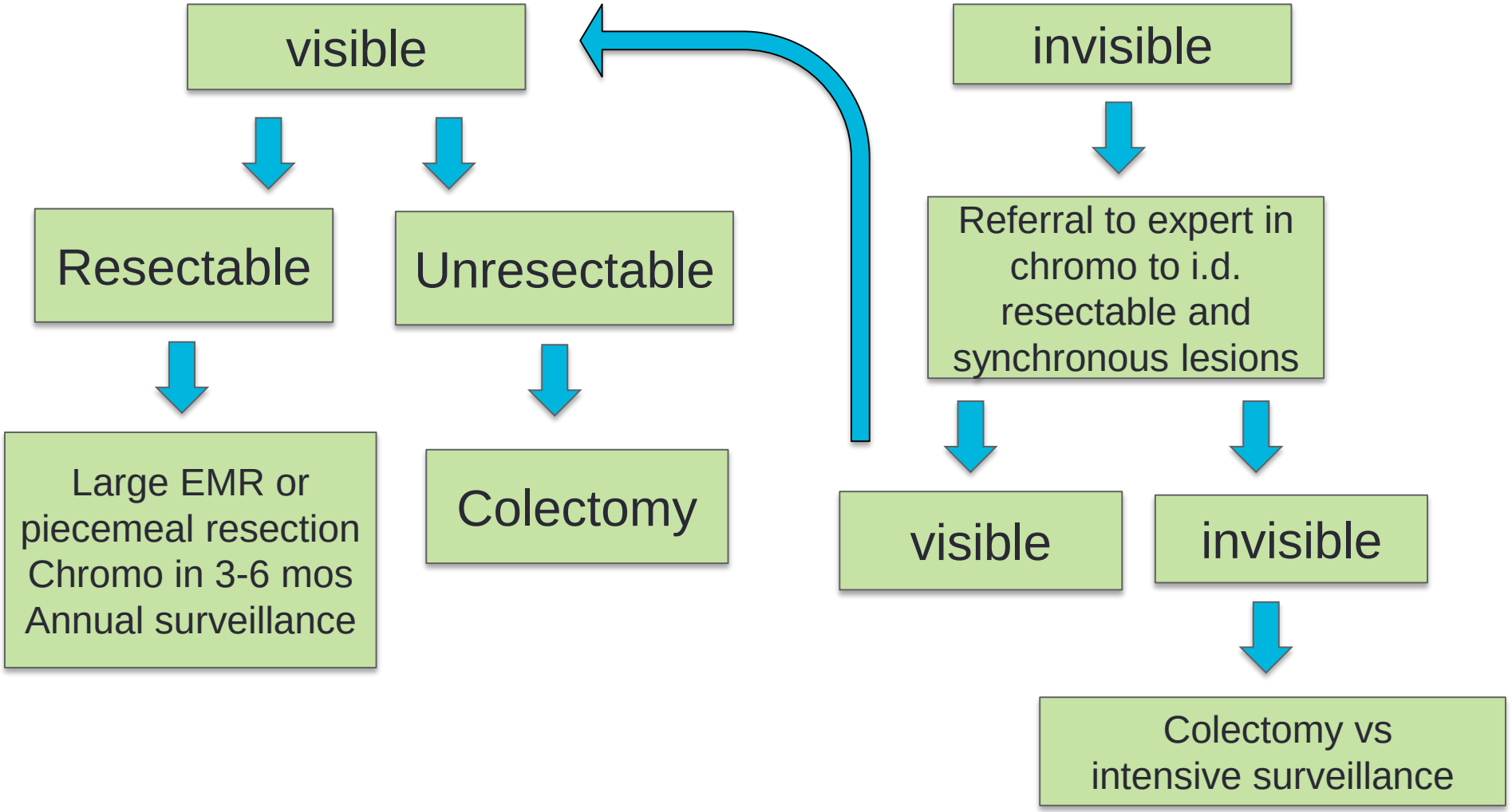
Soetikno, Gastro Endo Clin N Am, 2014

SCENIC guidelines for dysplasia management



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Chromoscopy: new standard of care?

- Detection of more dysplasia is not the goal of surveillance
- Long-term studies of relevant outcomes are needed
- Risk of over-diagnosis particularly in low-risk patients
  - Finding less aggressive lesions with unknown natural history
  - More procedures, potential for complications, stress, financial
- Lack of standardization is problematic
  - Operator dependence/ training (IBD dysplasia detection rate)
  - Random biopsies or targeted biopsies only in chromo?
  - WLE followed by chromo or chromo alone?
- What is the appropriate interval based on the natural history of dysplasia in IBD? What is the negative predictive value of a normal index chrmoendoscopy?

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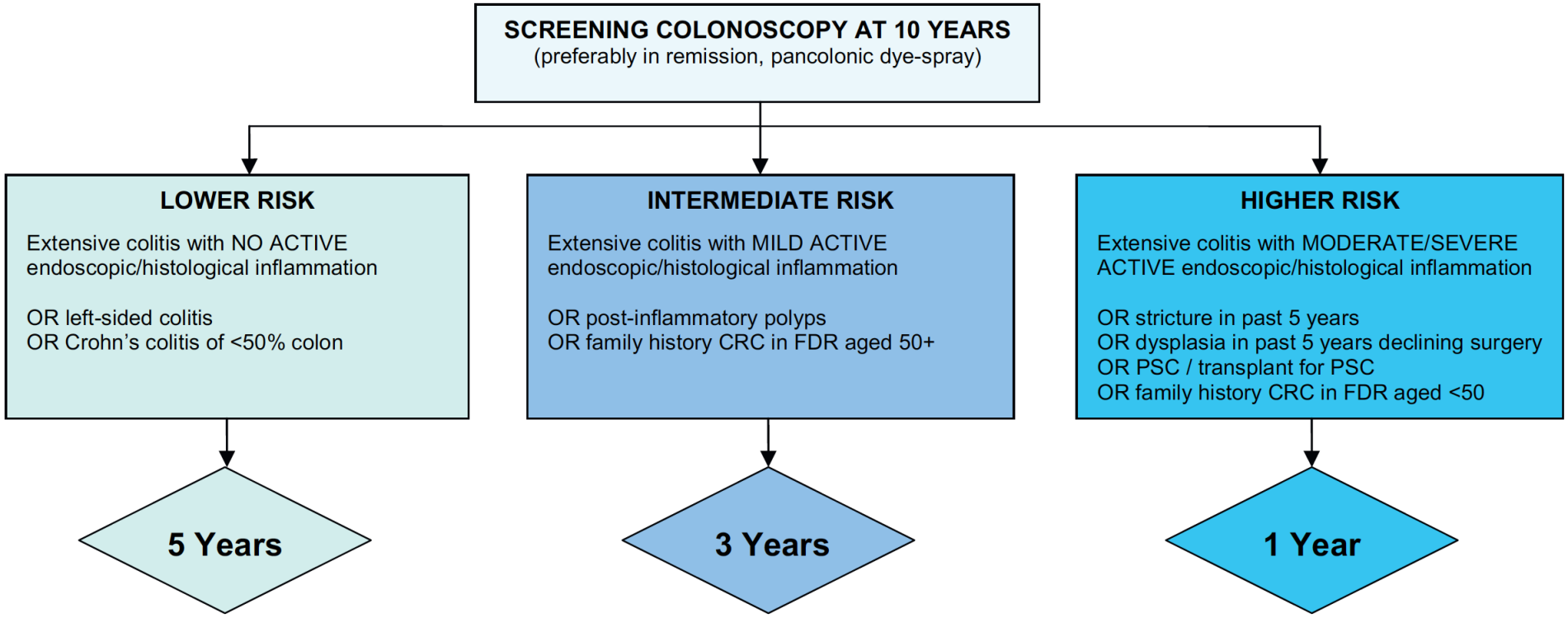
Risk Stratification



BIOPSY PROTOCOL
Pancolonic dye spraying with targeted biopsy of abnormal areas is recommended, otherwise 2-4 random biopsies from every 10 cm of the colorectum should be taken

OTHER CONSIDERATIONS
Patient preference, multiple post-inflammatory polyps, age & comorbidity, accuracy & completeness of examination

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Cairns, *Gut*, 2010

Maximizing yield of surveillance

- Disease should be in remission
- Excellent bowel prep (remove mucus and debris)
- Recognize limitations: pseudopolyps
- Careful withdrawal with attention to visible lesions
  - Biopsy or resect (EMR) all mucosal alterations
  - Special attention to Kudo III, IV
  - Peri-polyp biopsies to identify spreading dysplasia
  - Random biopsies may not be necessary
- Chromoendoscopy for high risk groups (PSC), patients with known dysplasia, better visualization of known lesions

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Summary

- CRC risk is increased in IBD and colon cancer surveillance is recommended
- Chromoendoscopy and high definition WLE detect more dysplasia than standard WLE, but it is not clear whether these methods improve relevant outcomes
- Visible, resectable dysplasia can be managed with polypectomy and close surveillance with chromoendoscopy preferred
- Management of non-targeted LGD dysplasia is controversial
  - Multidisciplinary approach
  - Patient involvement in decision making

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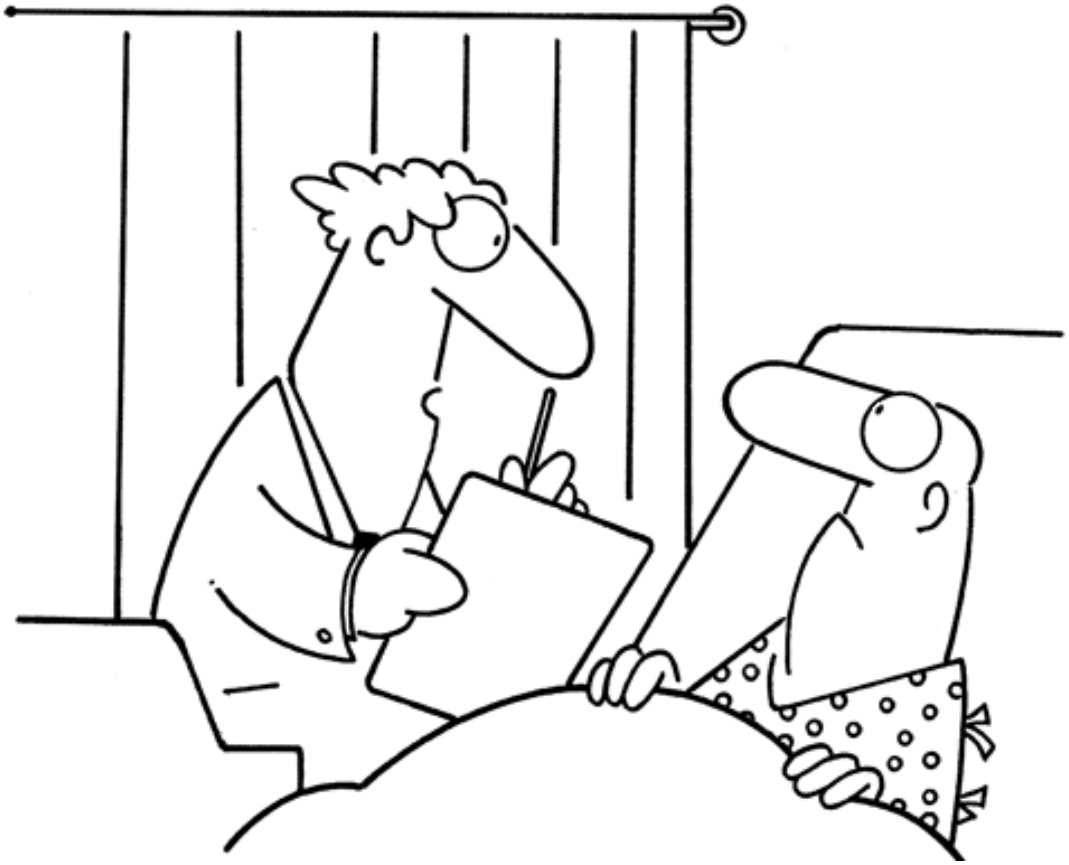

"You don't need a colonoscopy, but I'm sending you for one, because, quite frankly, I don't like you."

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