McGill UNIVERSITY

Centre universitaire de santé McGill | McGill University Health Centre

Approaches to Dysplasia

Talat Bessissow, MDCM MSc FRCPC

Associate Professor, Department of Medicine

Division of Gastroenterology

McGill University Health Center

FRIDAY, November 5, 2021

MENTORING in IBD XXII

THE MASTER CLASS

Disclosure

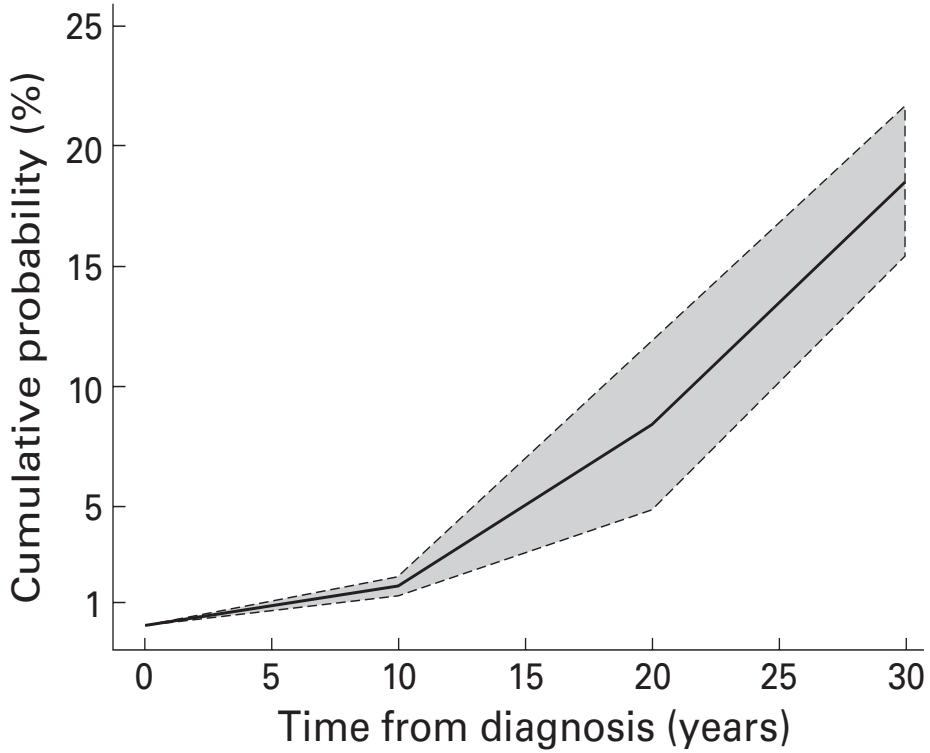
- Advisory board
  - Abbvie, Alimentiv, Amgen, Bristol Myers Squibb, Janssen, Pfizer, Roche, Sandoz, Takeda
- Speaker
  - Janssen, Abbvie, Takeda, Ferring, Bristol Myers Squibb, Merck, Gilead, Viatris
- Research grant
  - Abbvie, Janssen, Takeda

Objectives

- Brief Summary of the overall approach to surveillance
- Current and novel techniques for endoscopic surveillance of dysplasia including chromoendoscopy
- Endoscopic management of flat and polypoid dysplasia

COLON CANCER RISK

Cancer in IBD - meta-analysis 2001



Eaden J et al Gut 2001;48:526

Colon Cancer Risk

- 178 million person-years follow up

	No of CRC	Relative Risk of CRC
Ulcerative colitis	268	1.07 (0.95-1.21)
Crohn's disease	70	0.85 (0.67-1.07)
Total IBD	338	

UC and PSC RR 9.13 (4.52-18.5)

Patients diagnosed 1979-1988 RR 1.34 (1.13-1.58)

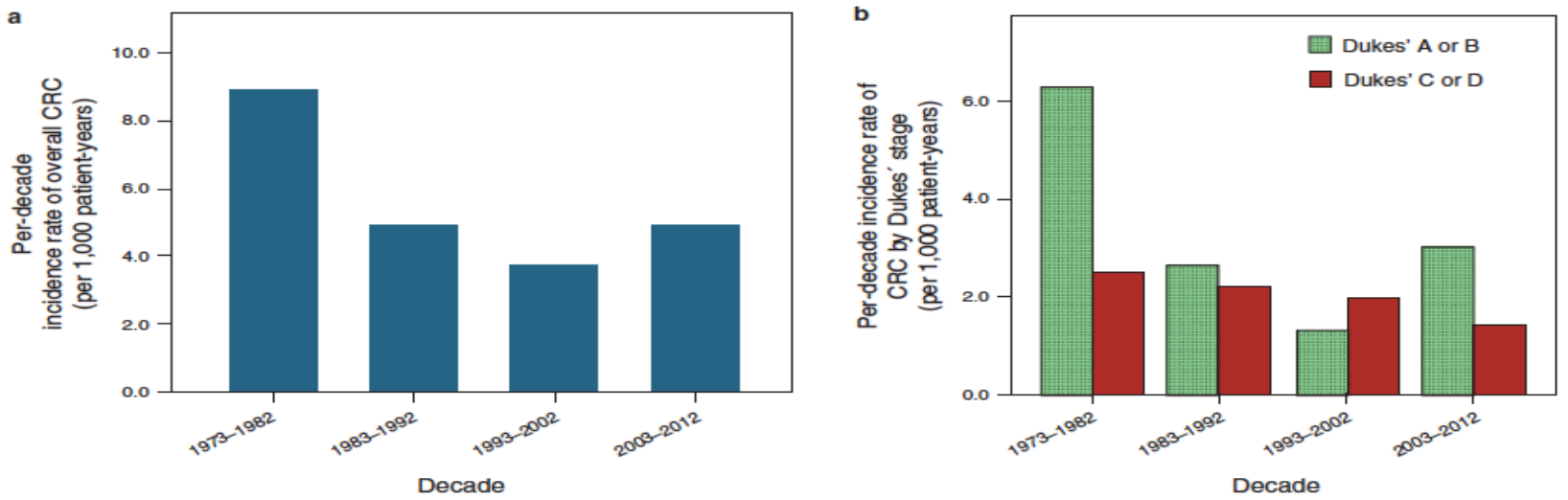
Jess et al. Gastroenterology 2012;143(2):375-381

Cancer risk-update

Duration of UC (up to *n* years)	10	20	30	40	50
Number at risk	1,345	1,086.5	635.5	290.5	99.5
Censored	60	455	385	255	107
CRC incidence	1	31	25	10	4
Cumulative incidence of CRC	0.07%	2.9%	6.7%	10.0%	13.6%
s.e.	0.001	0.005	0.009	0.013	0.022
Hazard rate	0.007%	0.29%	0.40%	0.35%	0.41%
s.e. of hazard rate	<0.001	<0.001	<0.001	0.001	0.002

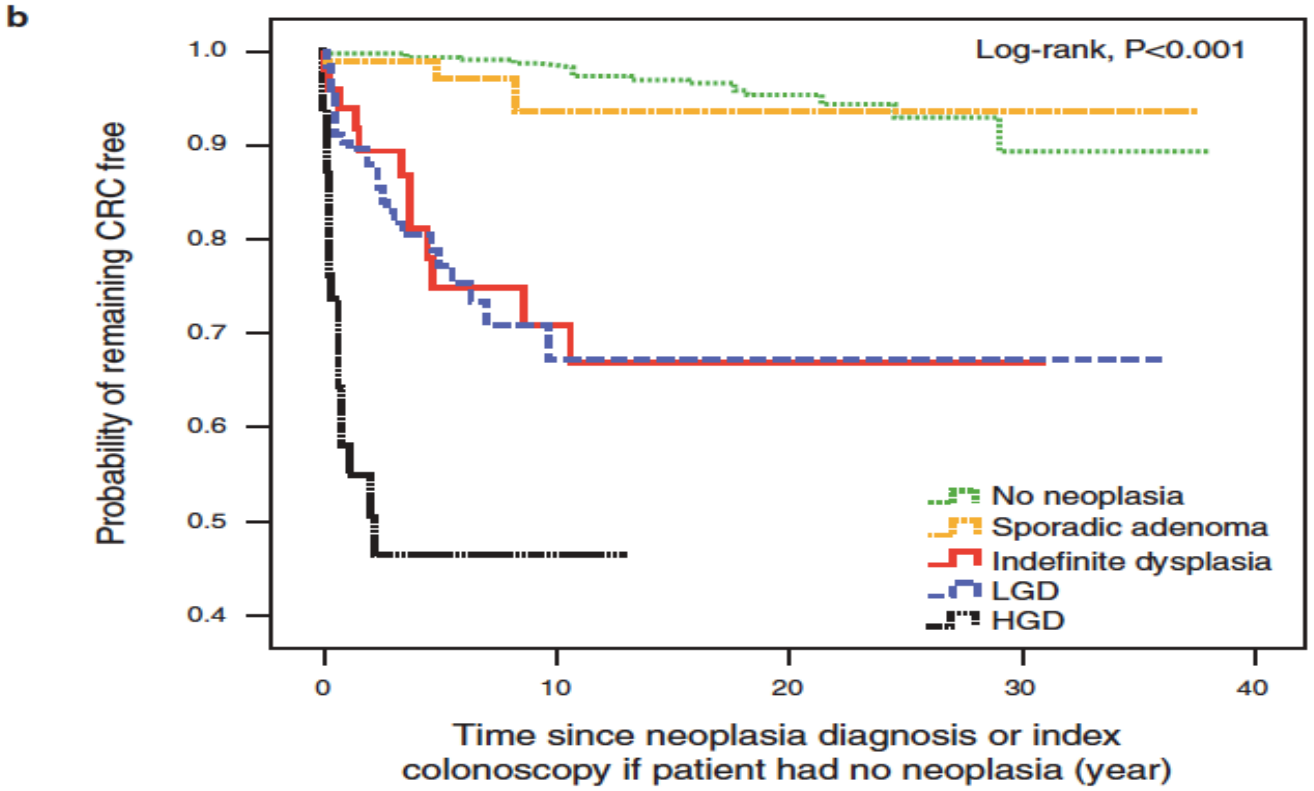
Choi et al. Am J Gastroenterol. 2015 Mar 31

Cancer risk-update



Choi et al. Am J Gastroenterol. 2015 Mar 31

Cancer Risk



Choi et al. Am J Gastroenterol. 2015 Mar 31

Risk Factors

- Extensive Colitis
- Long standing Inflammation
- Colonic Stricture
- Primary Sclerosing Cholangitis
- Personal History of Dysplasia
- Family history Colorectal Cancer
  - especially aged <50

Wijnands et al. Gastroenterology .2021 Apr;160(5):1584-1598.

Protective factors

- Surveillance colonoscopy
- 5-ASA
- Thiopurines
- Smoking

Wijnands et al. Gastroenterology .2021 Apr;160(5):1584-1598.

SURVEILLANCE TECHNIQUES

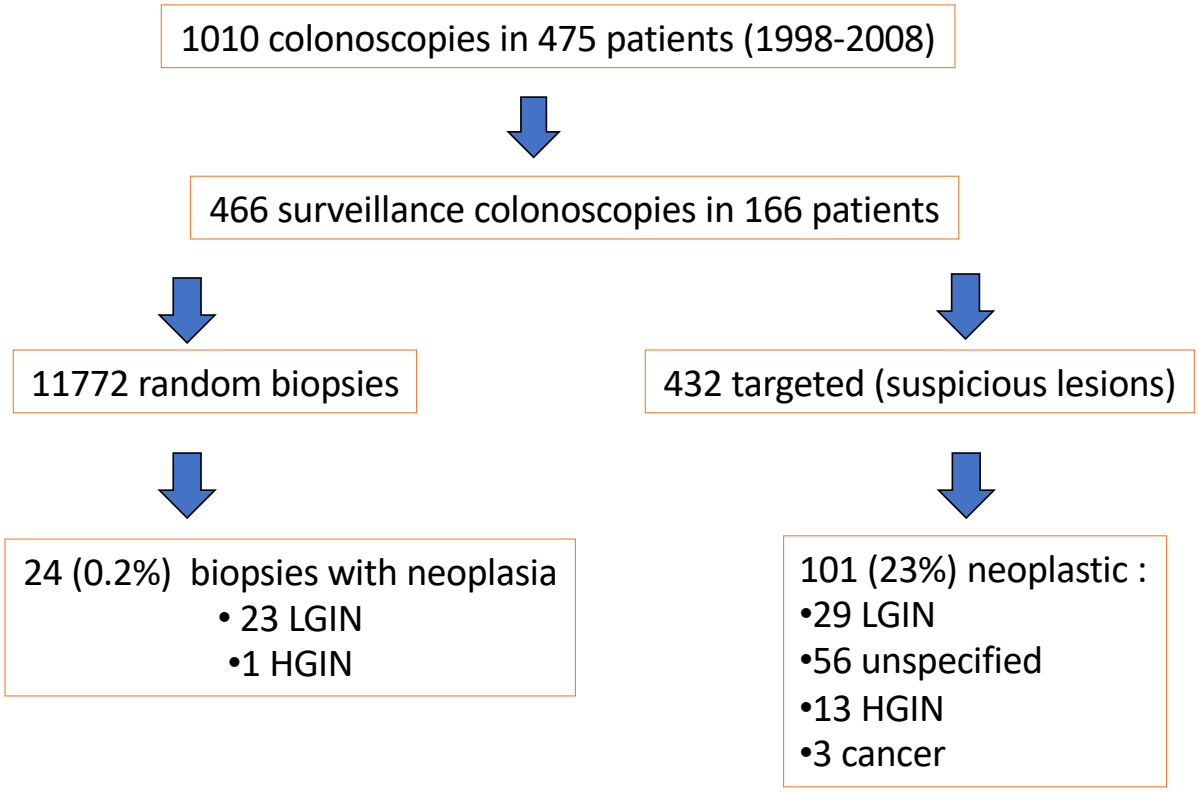
How can we see more at endoscopy ?

- Standard white light endoscopy
- **Zoom endoscopy**
- **Dye spraying endoscopy (chromoendoscopy)**
- **High definition endoscopy (like HD TV)**
- **Electronic virtual chromoendoscopy**
- **Confocal laser endomicroscopy**

Fundamentals for dysplasia detection

- Quiescent disease
- High-definition scopes
- Washing and careful inspection of the visible mucosa
- Target biopsies of suspicious mucosal abnormalities or site of prior dysplasia
  - Endoscopic resection preferred if well demarcated

Standard Biopsy Protocol



Van den Broek F et al. Am J Gastroenterol. 2011

Standard Biopsy Protocol

Adherence problem

Country	Adherence
Netherlands	25%
UK	57% take < 10 biopsies/pt
New Zealand	50% take < 17 biopsies/pt
Germany	9% adh; 50% < 10 biopsies

Obrador et al *Aliment Phar Ther* 2006;24:56
Eaden et al *GIE* 2000;51:123
Gearry et al *Dis Colon Rectum* 2004;47:314
Kaltz et al Z. *Gastroenterology* 2007;45:325

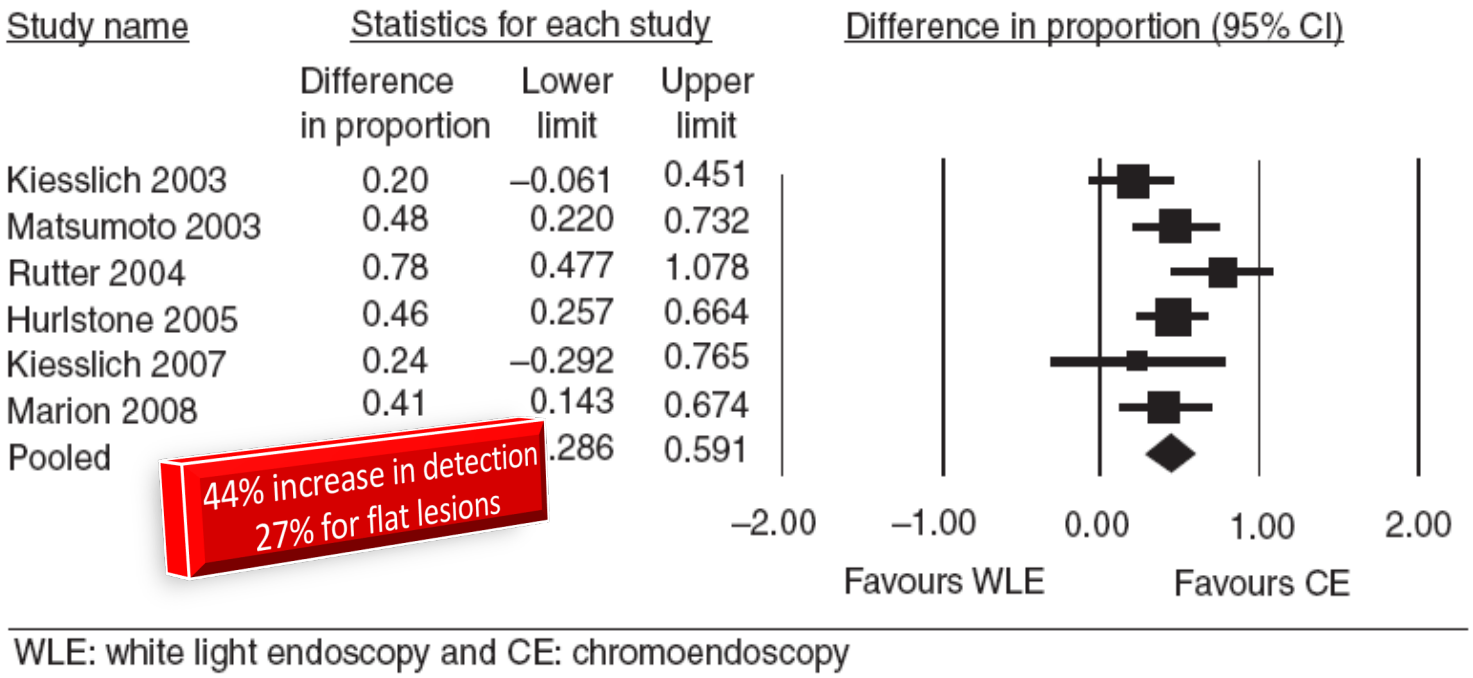
IBD-Dysplasia

A Randomized, Parallel-Group, Non-Inferiority Trial Comparing Random AND Targeted Biopsies to Targeted Biopsies Alone for Neoplasia Detection During Screening Colonoscopy in Adult Persons with Colonic Inflammatory Bowel Diseases: A Pilot Study (Short: “IBD-Dysplasia”)

CHROMOENDOSCOPY

CHROMO-ENDOSCOPY

Meta-analysis of chromo-endoscopy in UC screening



WLE: white light endoscopy and CE: chromoendoscopy

Subramanian *et al Aliment Pharmacol Ther* 2011; 33: 304–312

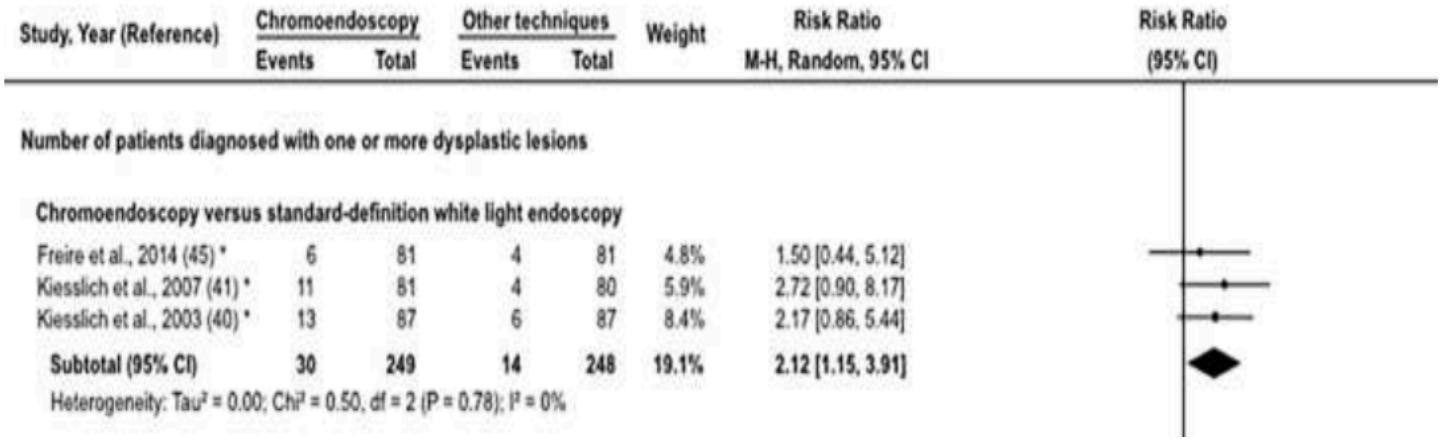
Meta-analysis-SCENIC group

TABLE 3. Proportion of patients with dysplasia and number of visible dysplastic lesions identified in studies comparing chromoendoscopy versus white-light colonoscopy

Study	Study type	Patients with dysplasia/all patients		RR (95% CI)	Absolute risk increase (95% CI)	No. of visible dysplastic lesions	
		Chromoendoscopy	White-light			Chromoendoscopy	White-light
Kiesslich[20]	Randomized parallel-group	13/84	6/81	2.1 (0.8-5.2)	8% (-2% to 18%)	32	10
Kiesslich[21]	Randomized parallel-group	11/80	4/73	2.5 (0.8-7.5)	8% (-1% to 17%)	19	2
Marion[24]	Prospective tandem	22/102	12/102	1.8 (0.96-3.5)	10% (0% to 20%)	35	13
Rutter[23]	Prospective tandem	7/100	2/100	3.5 (0.8-16.4)	5% (-1% to 11%)	9	2
Matsumoto[25]	Prospective tandem	12/57	12/57	1.0 (0.5-2.0)	0% (-2% to 2%)	18	8
Hlvaty[26]	Prospective tandem and additional cohort	4/30	2/45	3.0 (0.6-15.4)	9% (-5% to 23%)	6	2
Gunther[27]	Retrospective two-group	2/50	0/50	5.0 (0.3-101.6)	4% (-3% to 11%)	2	0
Chiorean[22]	Prospective tandem	No per-patient data given (N = 63)				41	18
SCENIC meta-analysis				1.8 (1.2-2.6)	6% (3%-9%)		

Laine et al. Gastrointest Endosc. 2015 Mar;81(3):489-501.e26

Chromoendoscopy



Iannone et al. CGH 2016

Contraindication

- Allergy or intolerance to methylene blue dye
- Renal insufficiency
- Pregnant or nursing women
- Need to warn patient that
  - Stool will be blue
  - Urine will be blue
- G6PD deficiency

VIRTUAL CHROMOENDOSCOPY

NBI Olympus, I-Scan Pentax, FICE Fuji

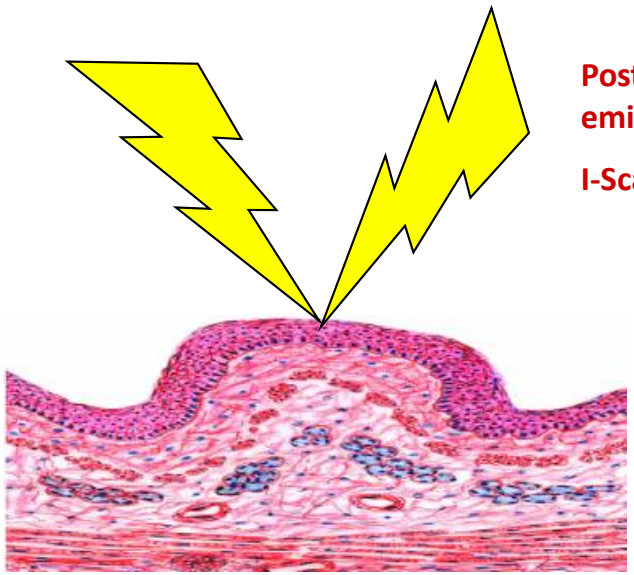
Electronic (Virtual) Chromoendoscopy

Narrowing of light spectrum

NBI

Post Processing of emitted light

I-Scan - FICE

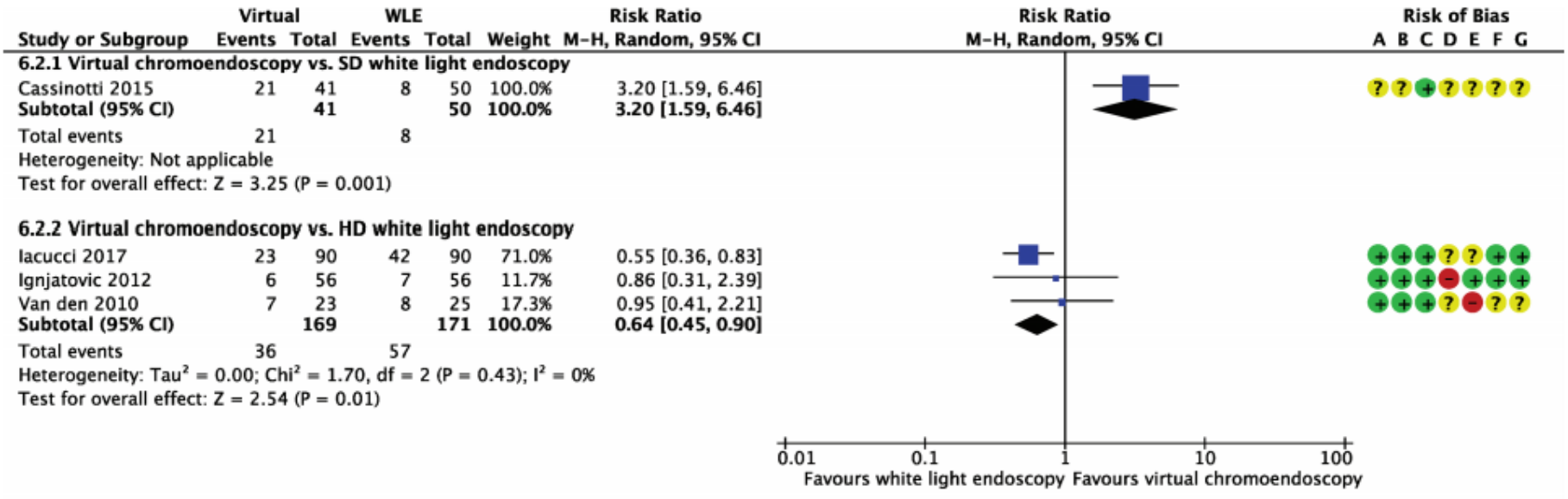


Effect:

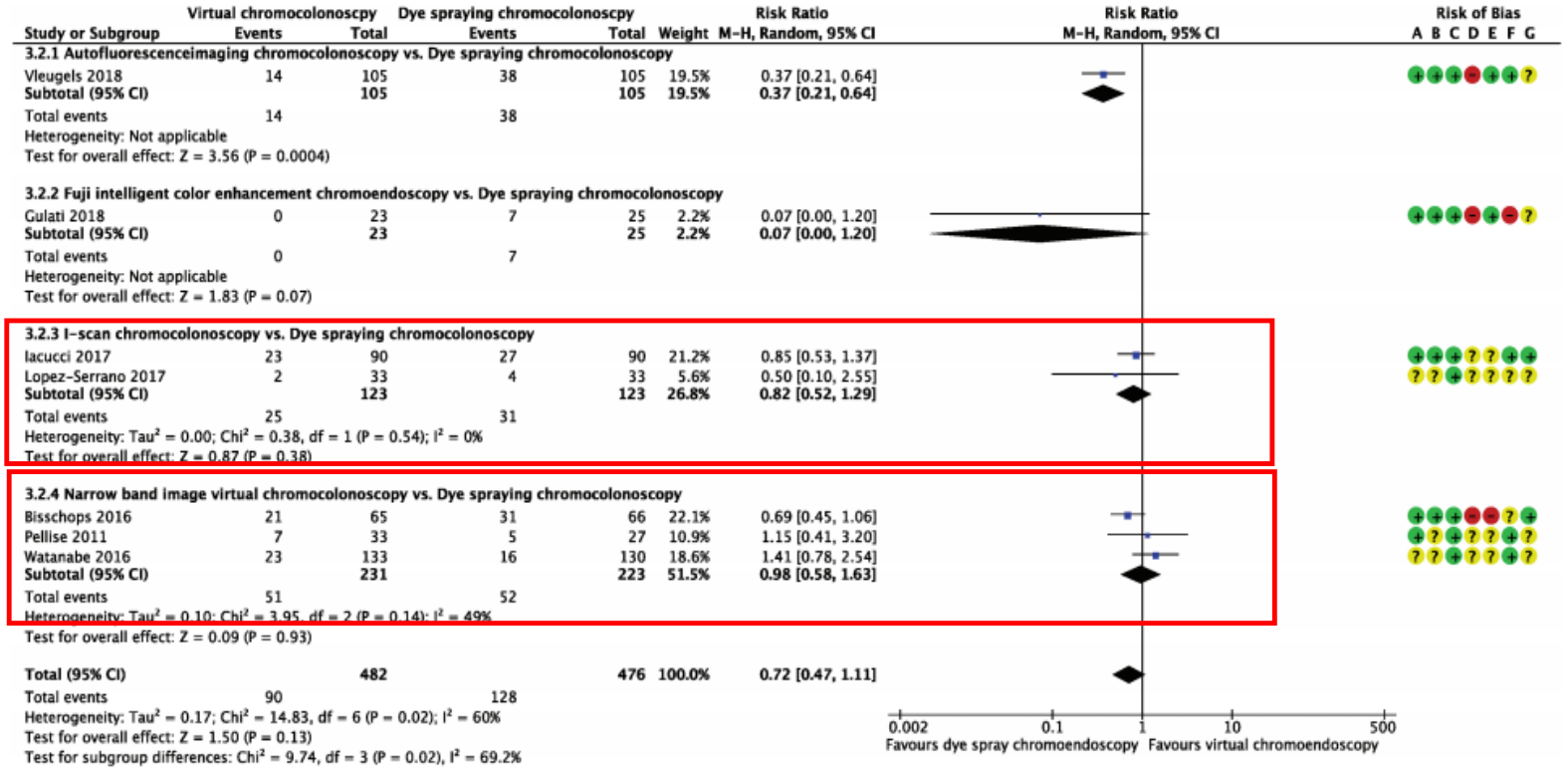
Vessel analyis

Effects:

Surface analysis Tissue analysis Vessel analyis



El-Dallal M et al. Inflamm Bowel Dis. 2020 Aug 20;26(9):1319-1329.



El-Dallal M et al. Inflamm Bowel Dis. 2020 Aug 20;26(9):1319-1329.

Advantages

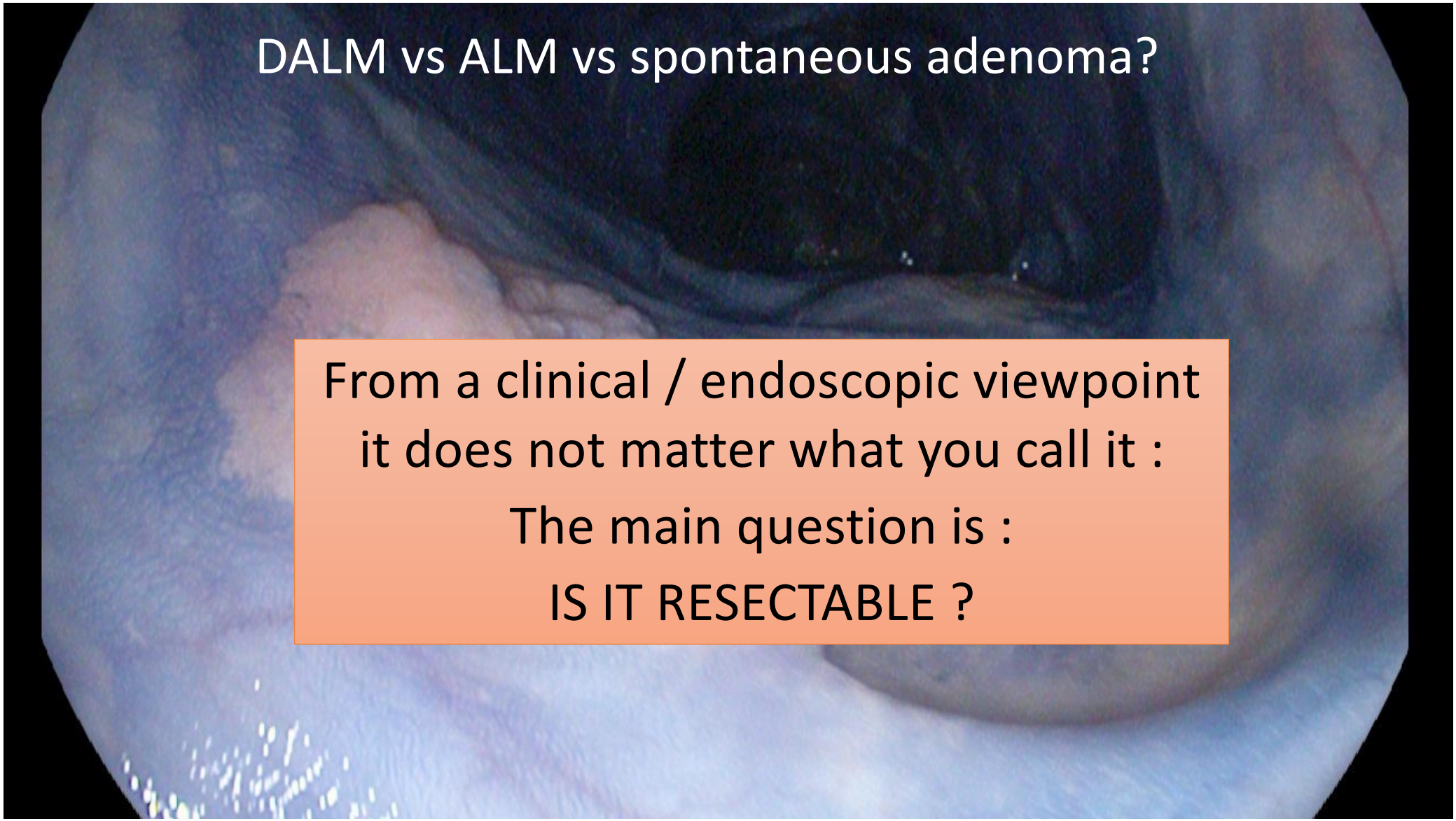
- ‘push the button’ application
- Easier to use in difficult colonoscopies
- Shorter withdrawal time
  - 26.87 ± 9.89 minutes for CE vs. 15.74 ± 5.62 minutes for NBI, $P < 0.01$
- No dye spraying
- No extra equipment
- Equal contrast of the mucosa

Bisschops et al. Gut 2015

Dysplasia Management

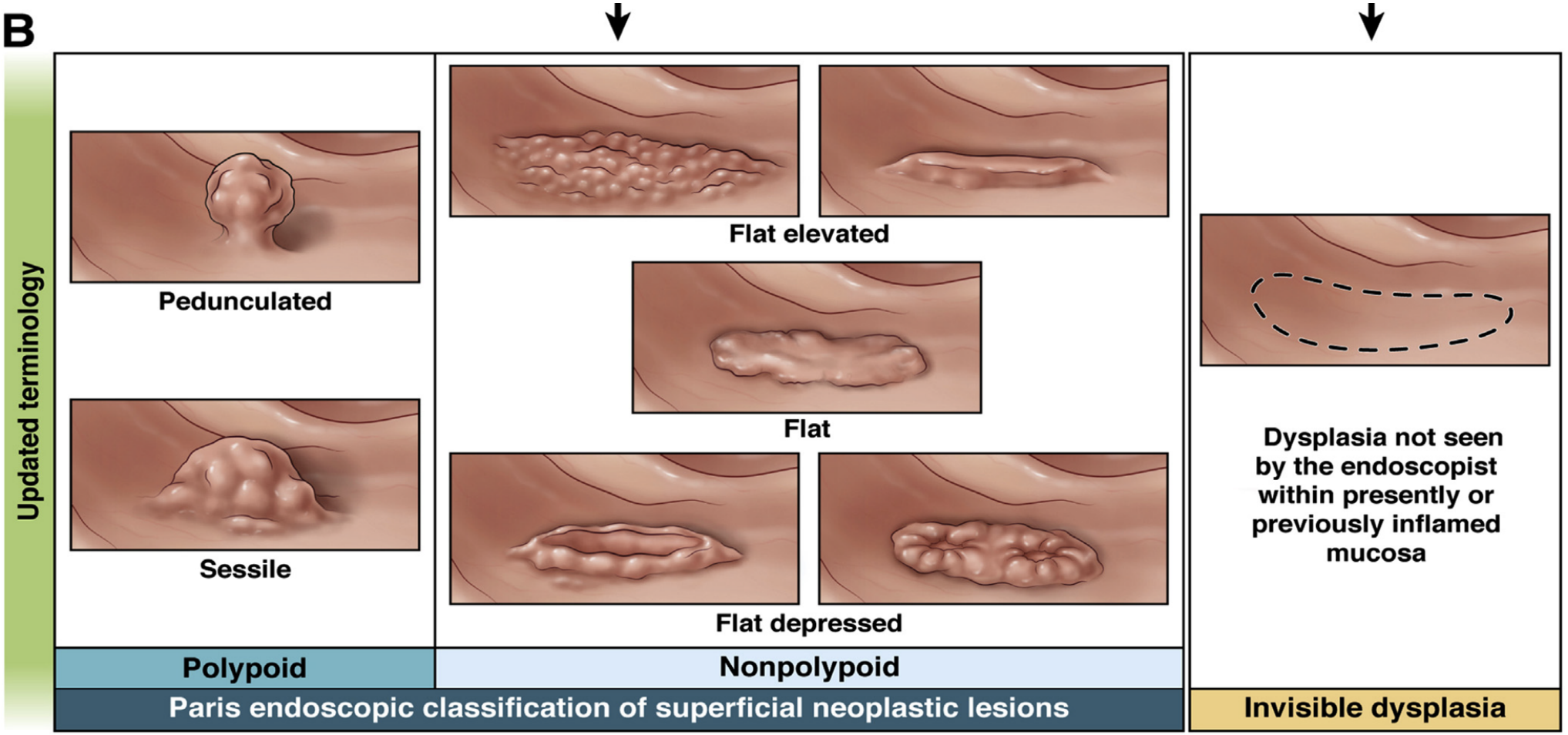
C	Timing of next colonoscopy when no dysplasia detected at present colonoscopy	
Physicians should err towards the more frequent surveillance category if at least one higher risk factor exists. Timing based on past and ongoing CRC risk factors and mucosal features that may obscure dysplasia.		
1 year	**2 or 3 years**	**5 years**
• Moderate or severe inflammation (any extent) • PSC • Family history of CRC in first degree relative (FDR) age < 50 • Dense pseudopolyposis • History of invisible dysplasia or higher-risk visible dysplasia < 5 years ago	• Mild inflammation (any extent) • Strong family history of CRC (but no FDR < age 50) • Features of prior severe colitis (moderate pseudopolyps, extensive mucosal scarring) • History of invisible dysplasia or higher-risk visible dysplasia > 5 years ago • History of lower risk visible dysplasia < 5 years ago	Continuous disease remission since last colonoscopy with mucosal healing on current exam, plus either of: • ≥ 2 consecutive exams without dysplasia • Minimal historical colitis extent (ulcerative proctitis or < 1/3 of colon in CD)

Murthy et al. AGA clinical practice update Gastroenterology 2021;161:1043–1051


DALM vs ALM vs spontaneous adenoma?
From a clinical / endoscopic viewpoint
it does not matter what you call it :
The main question is :
IS IT RESECTABLE ?

When can you resect?

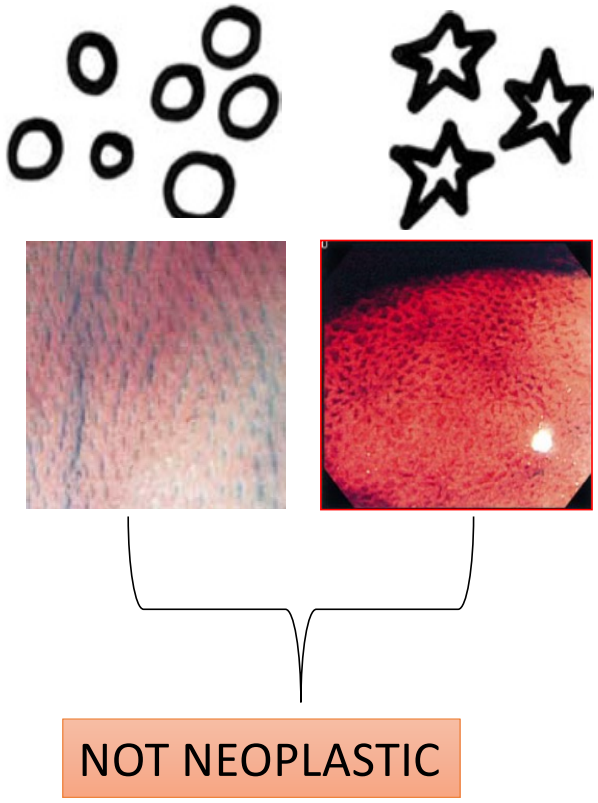
- Good delineation of borders
- No deep invasion
- Adequate submucosal lift



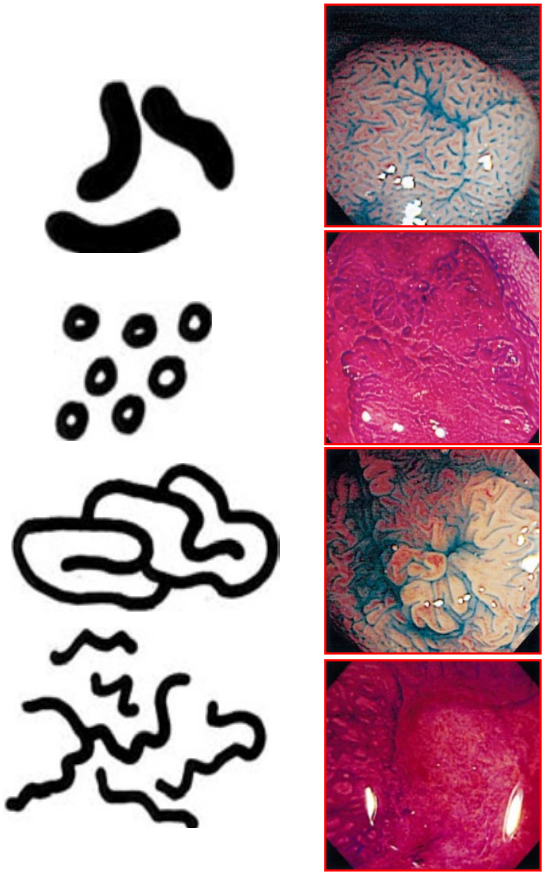
In addition to Paris classification, report lesion size, morphology, border clarity, ulceration, location, if within area of colitis, completeness of resection, and any special techniques used to visualize.

Murthy et al. AGA clinical practice update Gastroenterology 2021;161:1043–1051

How to characterize lesions : Kudo's pit pattern classification

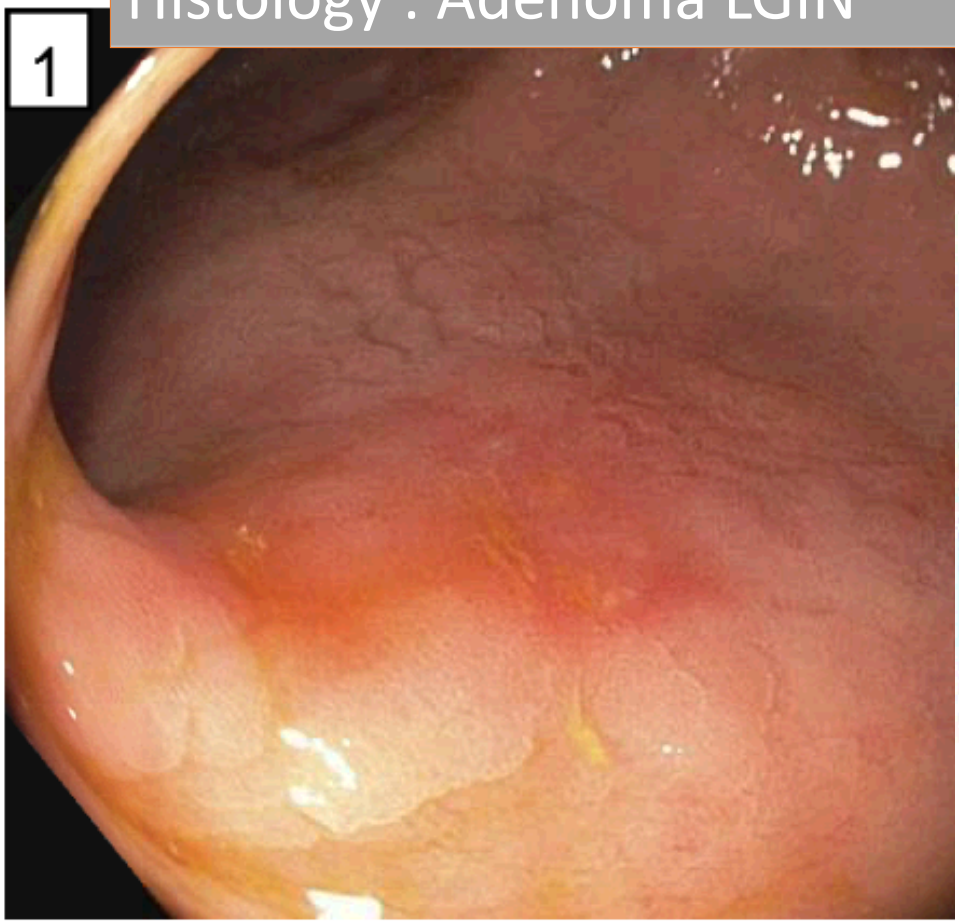


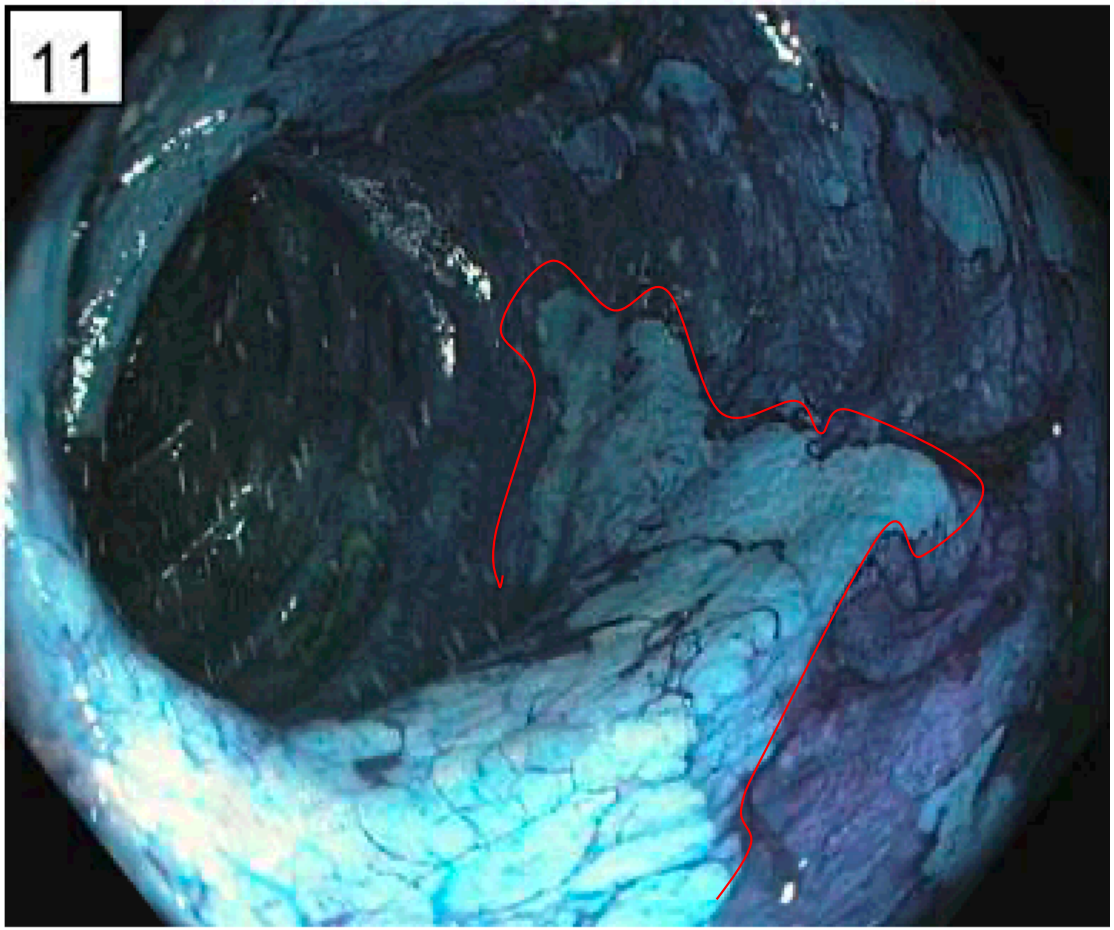
NOT NEOPLASTIC



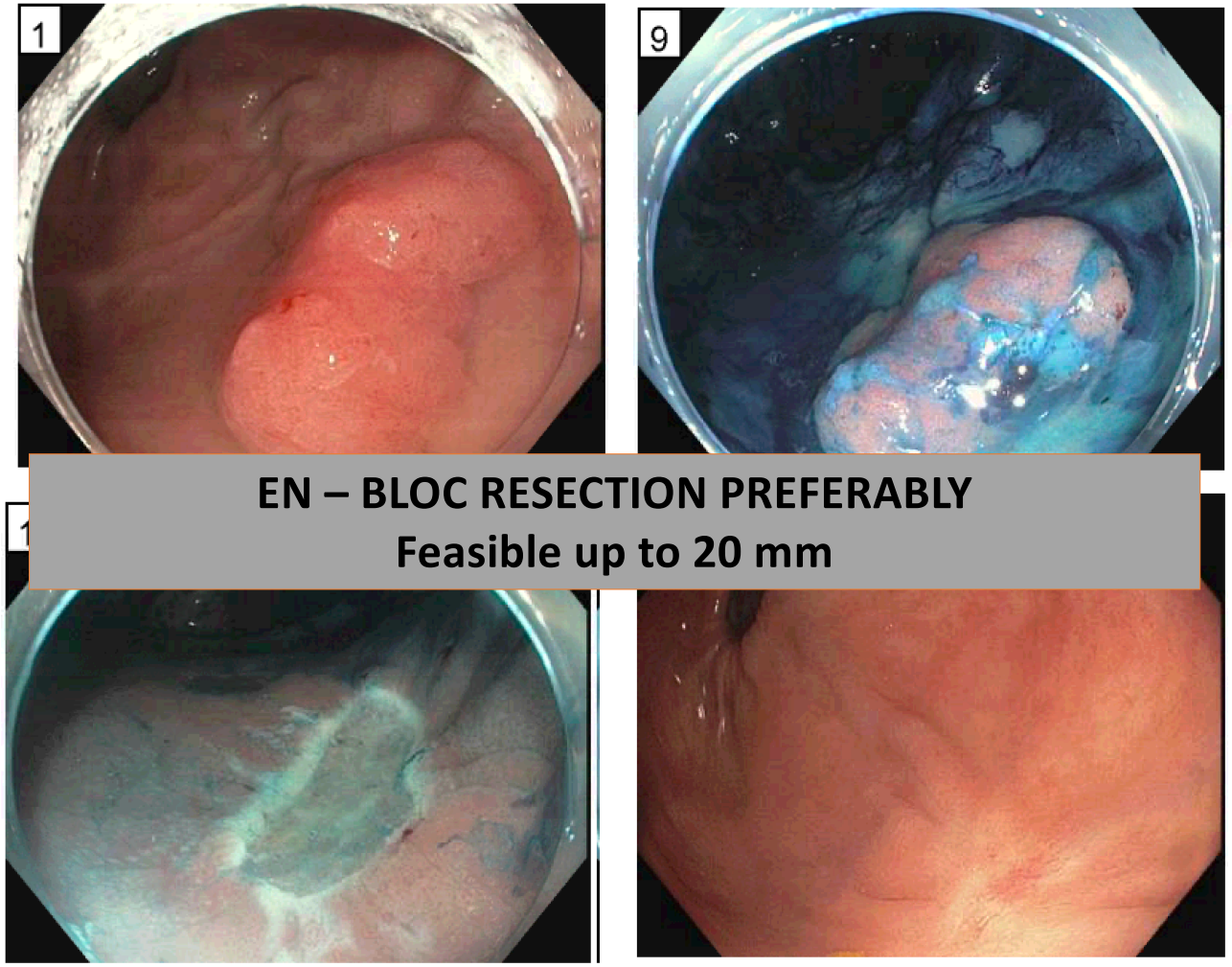
Kudo et al : J Clin Pathol 1994; 47: 880
Hurlstone et al British Journal of Surgery 2002, 89, 272

NON Polypoid slightly elevated
Kudo III L
Histology : Adenoma LGIN





Elective resection of larger lesions

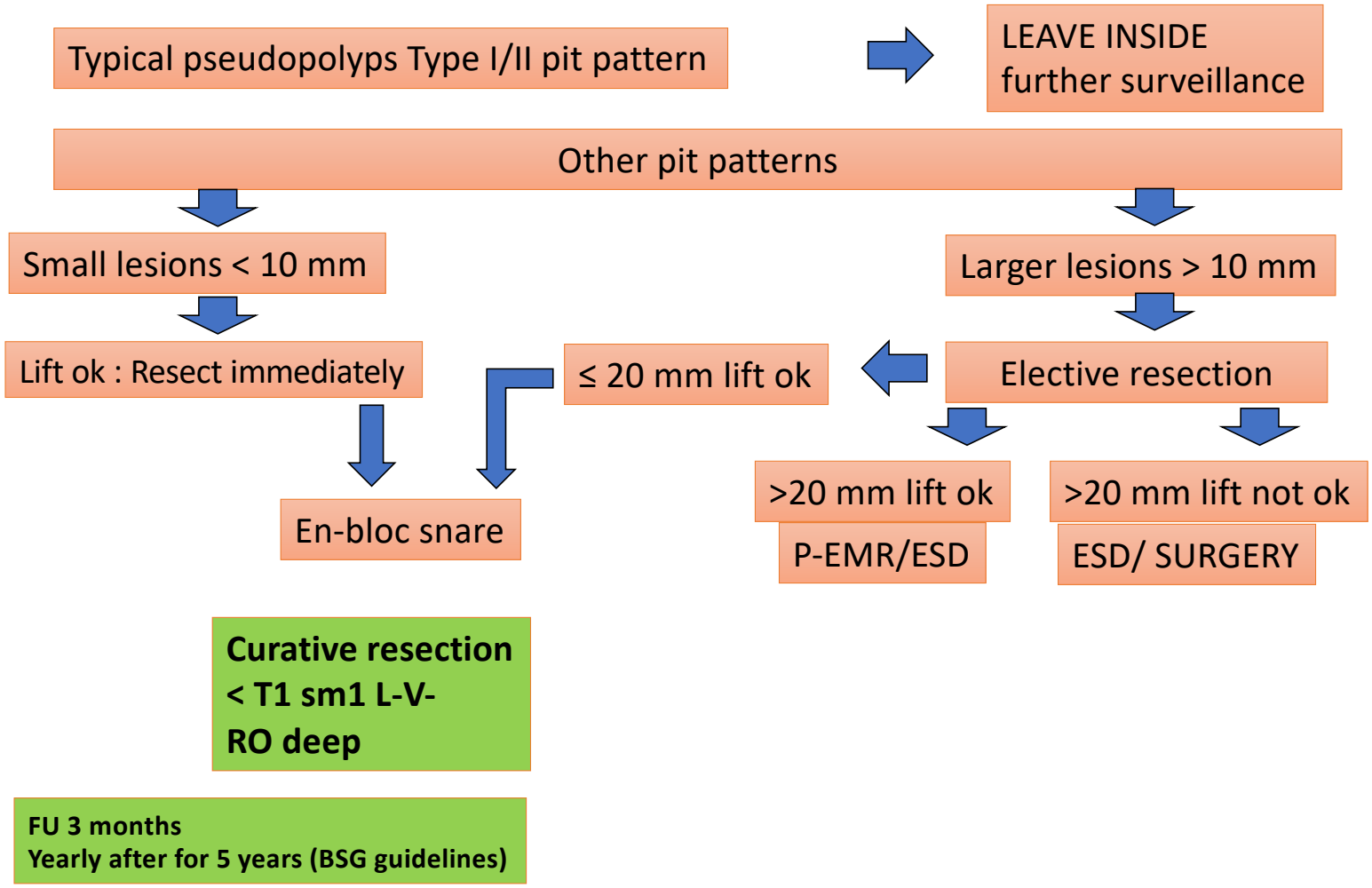


Post resection Risk

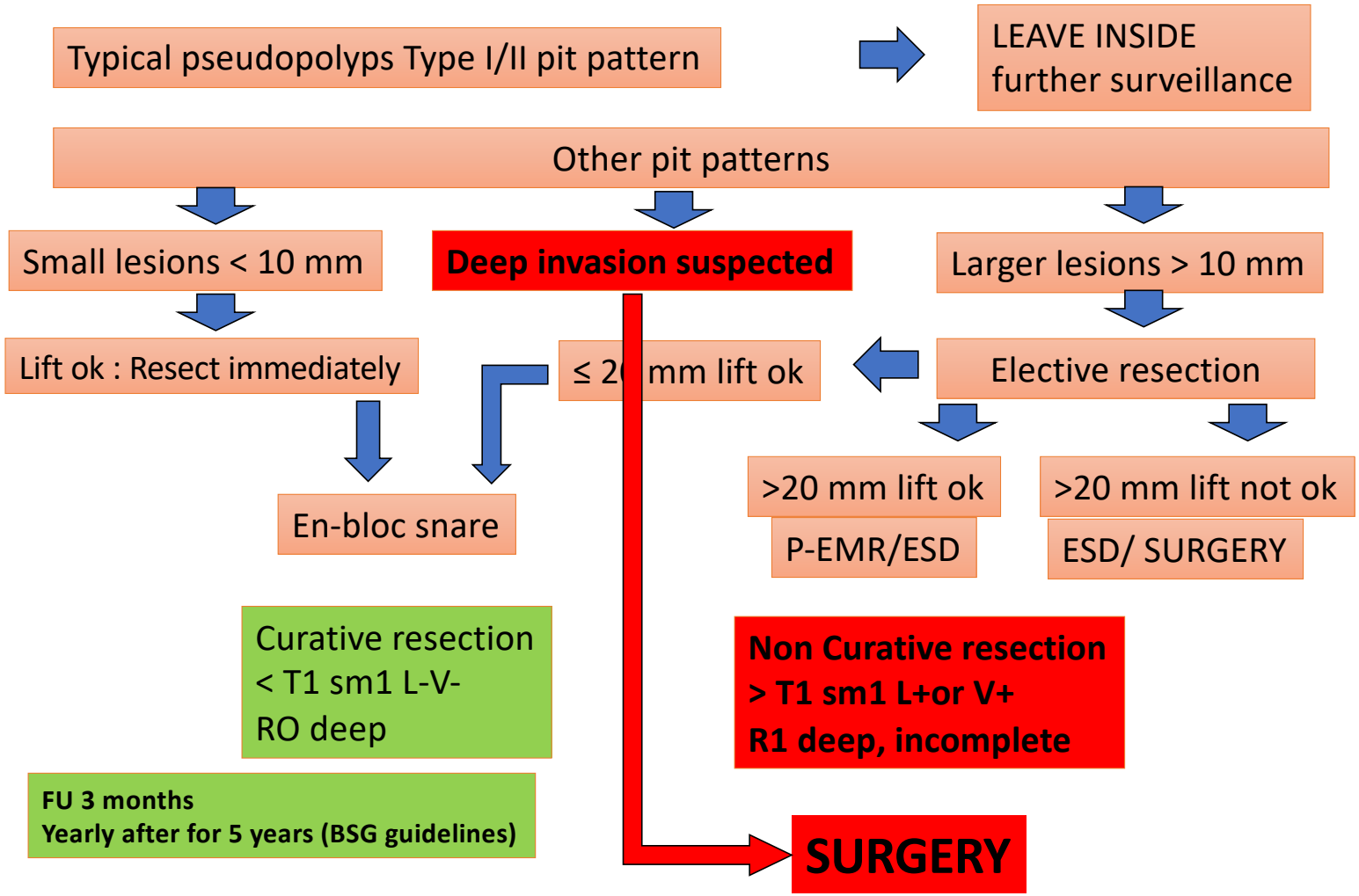
- Meta-analysis on recurrent CRC after endoscopic resection of polypoid lesions in IBD
  - 376 patients with 1704 pt years FU
  - Risk of CRC : 0.5% per year.

Wanders et al CGH 2014; 12: 756-764

Treatment of colitis lesions in relation to characterisation



Treatment of colitis lesions in relation to characterisation



Summary/Take home

- Increased risk of neoplasia in longstanding colonic disease (highest in PSC)
- Chromoendoscopy is method of choice for surveillance (VCE is a good alternative)

- Terminology DALM/ALM should be abandoned (resectable or not)

- Endoscopic resection of neoplasia is possible if
  - Can delineate lesion
  - Submucosal lifting and en bloc resection