

48th Annual  
**NEW YORK COURSE**

December 12-13, 2024 • New York, NY



# IBD Dysplasia: Improving recognition and therapy

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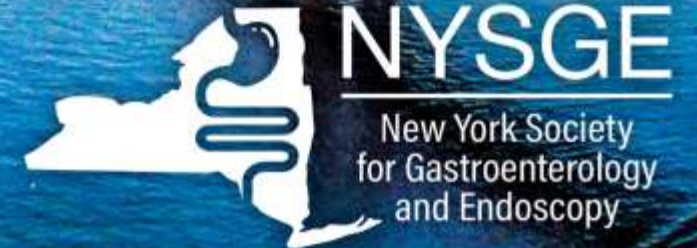
Consultant – Boston Scientific, Alexion Pharma, Iterative Health

Research support – Fujifilm, CDX Diagnostics

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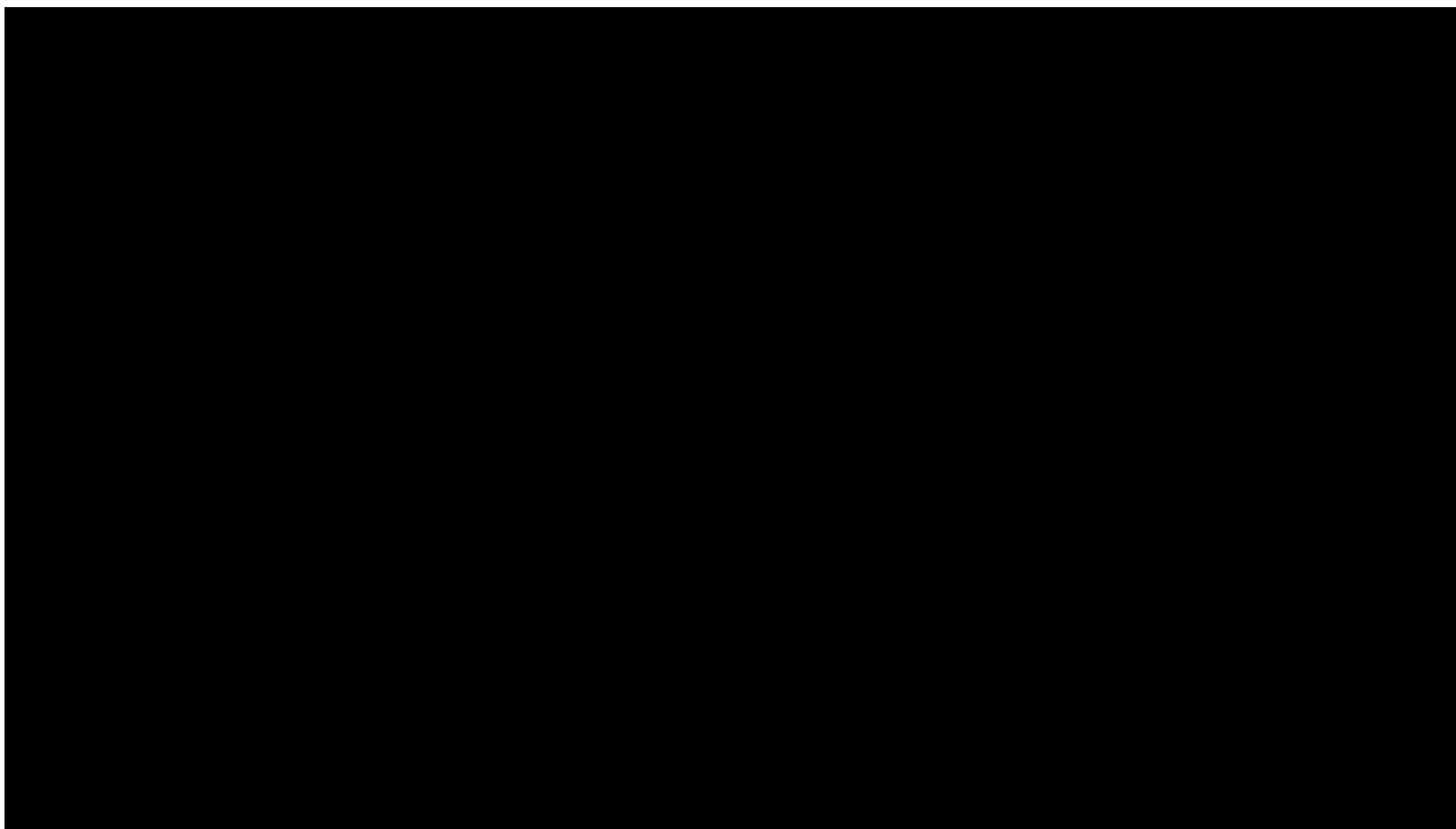
# LEARNING OBJECTIVE

- IBD surveillance guidelines
- IBD lesion morphology
- Management of IBD associated lesions

# Case

- 28 y/o male
- Crohn's colitis since age 15
- 2<sup>ary</sup> loss of response to adalimumab, now on Vedolizumab
- June 2023 – colonoscopy - right and left colon biopsies show low grade dysplasia
- Mayo – MRCP for ?Bile duct abnormalities on MRE – confirms PSC (normal labs)
- Sept 2023 - colonoscopy

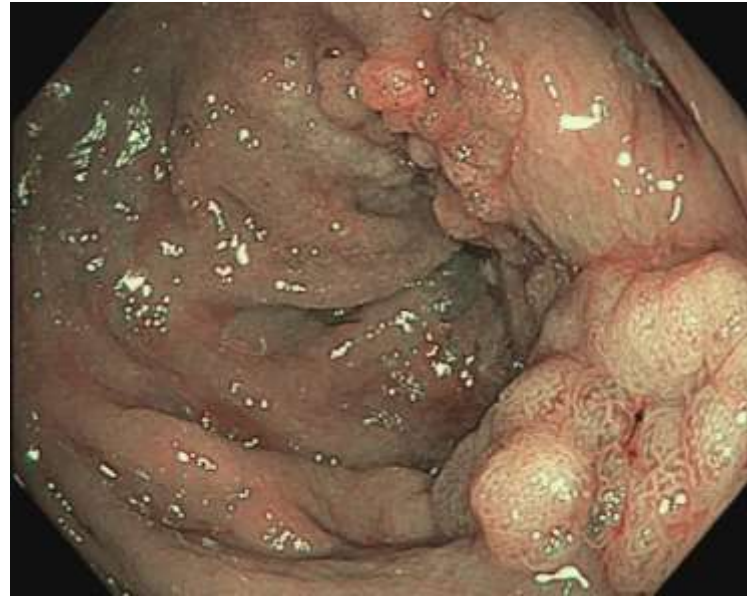
# Surveillance colonoscopy



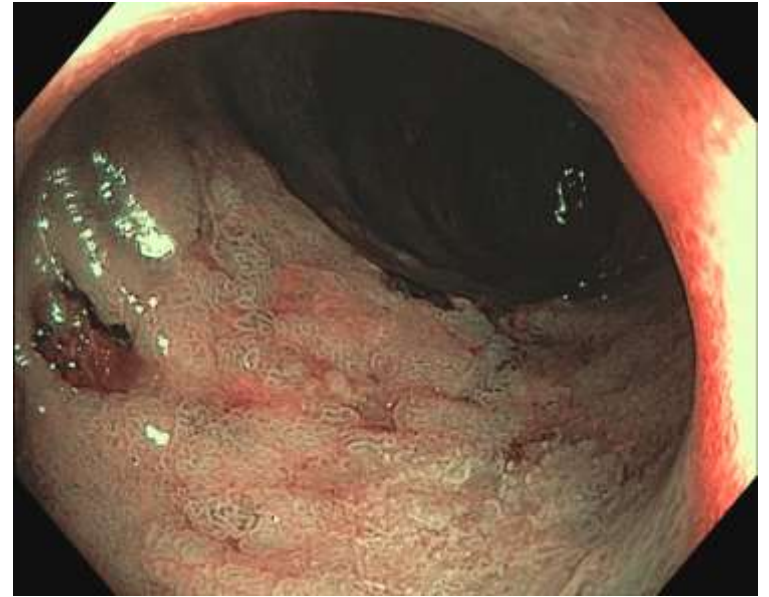
# pathology



Low grade dysplasia



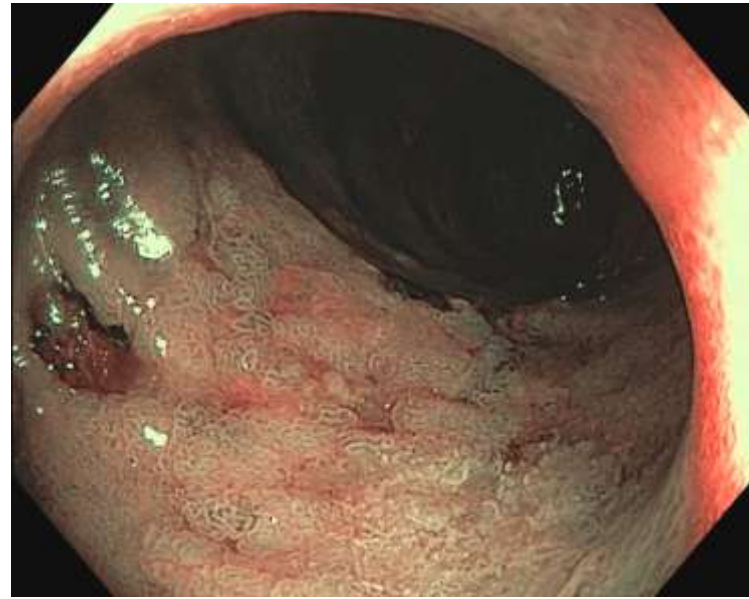
Indefinite dysplasia



Adenoca in a background of high grade dysplasia

# Colectomy – a week later

- 3.5 cm adenocarcinoma in cecum
- 2.4 cm adenocarcinoma in descending colon

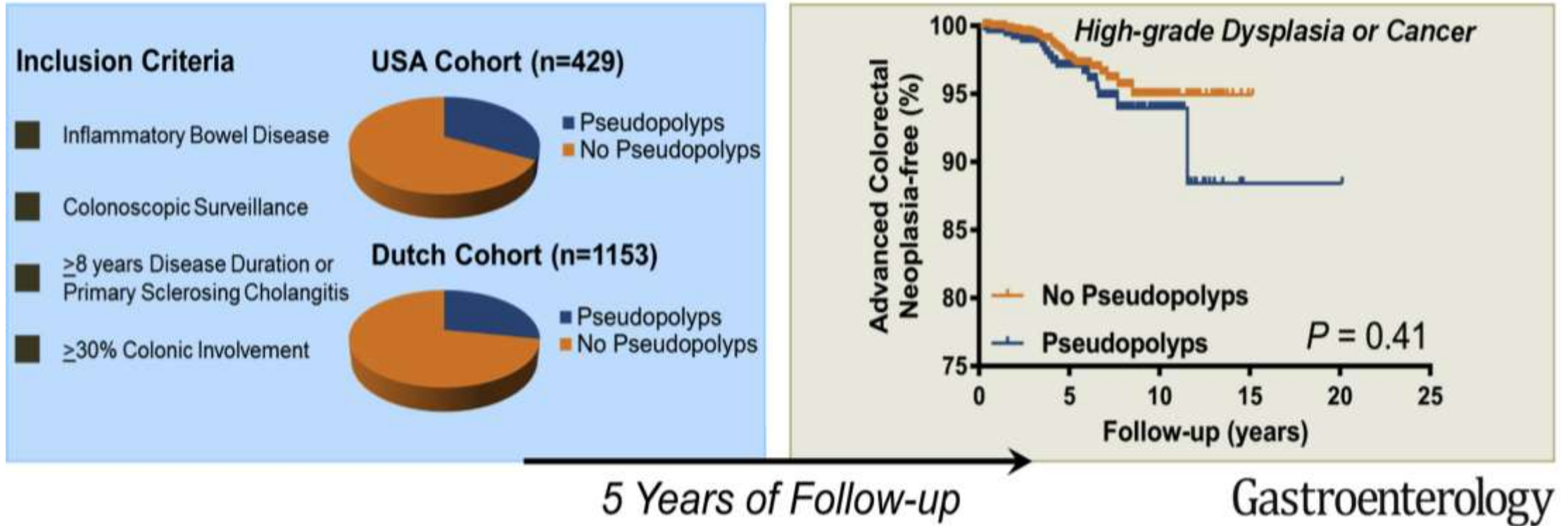


# Risk factors:

- Age at diagnosis:
  - pediatric-onset disease (UC: RR, 28.6; and CD: RR, 6.29)
- PSC
- Extensive disease
  - pancolitis (SIR, 2.4–14.8)
  - left-sided colitis (SIR, 1.4–2.8)
  - Proctitis (none)
- Active ongoing moderate-severe inflammation
- Scarred tubular colon
- Males

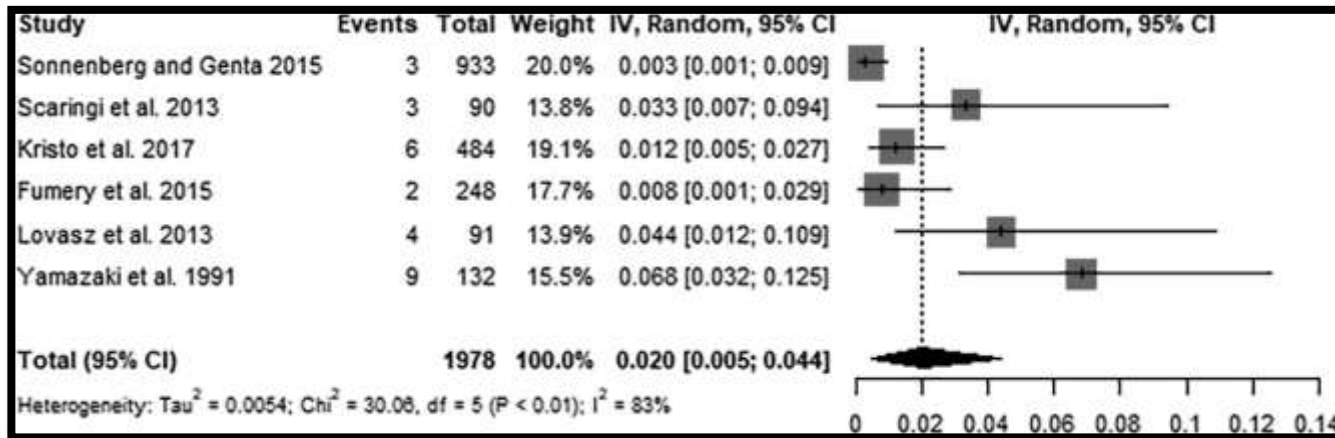
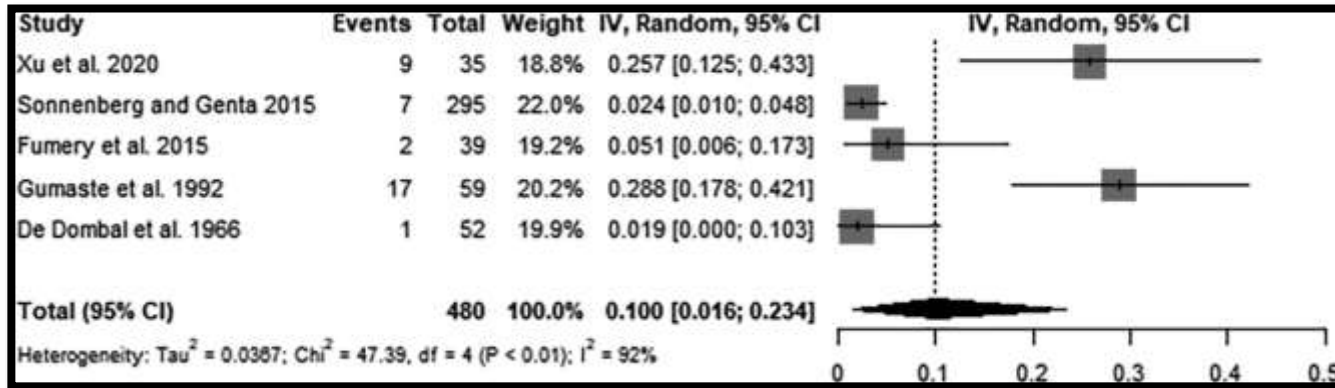


# Pseudopolyps do not increase risk of CRN



Mahmoud R et al; Dutch Initiative on Crohn and Colitis. No Association Between Pseudopolyps and Colorectal Neoplasia in Patients With Inflammatory Bowel Diseases. *Gastroenterology*. 2019

# Strictures confer increased risk in UC, not CD



## Meta-analysis:

- 2 case-control and 4 cohort studies
- UC (OR = 3.53, 95%CI 1.62–7.68, P = 0.001)
- CD (OR = 1.09, 95% CI 0.54–2.21, P = 0.811)
- Biopsy strictures in a separate jar

Zhan, Yanrong et al. "Risk and incidence of colorectal stricture progressing to colorectal neoplasia in patients with inflammatory bowel disease: a systematic review and meta-analysis." European journal of gastroenterology & hepatology vol. 35,10 (2023)

# When to start Surveillance

- 8-10 years after disease diagnosis of UC or CD colitis
- At time of diagnosis of concomitant PSC

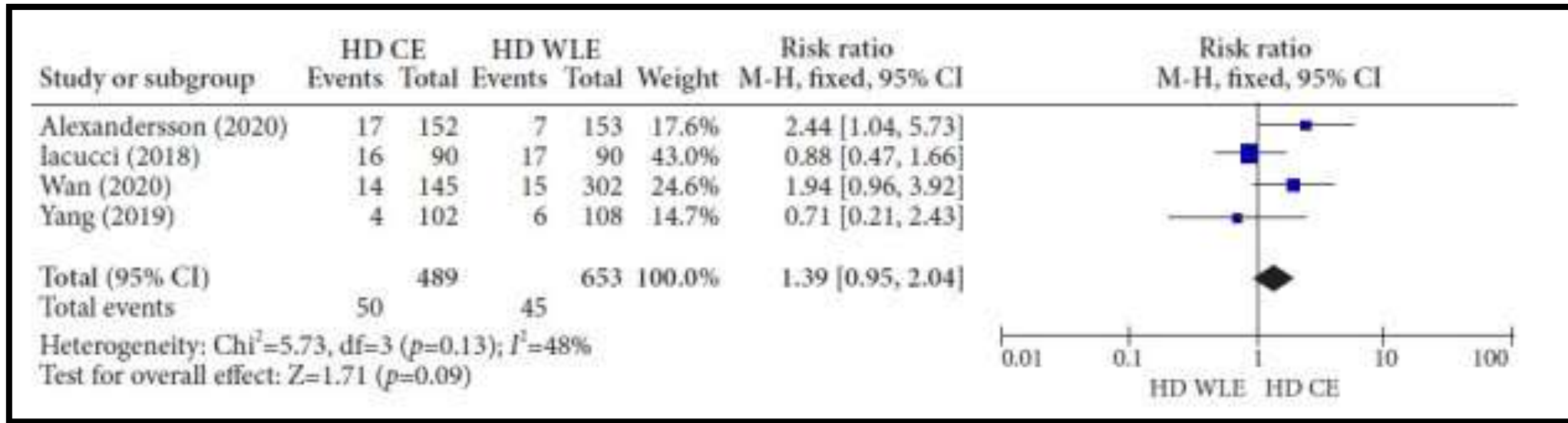
# High quality surveillance colonoscopy

- Bowel preparation
- Mucosal disease activity
- Endoscopist's experience/quality
  - Cecal intubation rate
  - ADR
- Type of endoscope
  - HD vs SD
- Use of enhanced imaging

# SCENIC guidelines (2015)

- High Definition (HD) scopes recommended
- Dye chromoendoscopy (DCE) recommended over White light endoscopy (WLE) for SD
- DCE suggested over WLE for HD
- NBI not suggested over DCE for HD

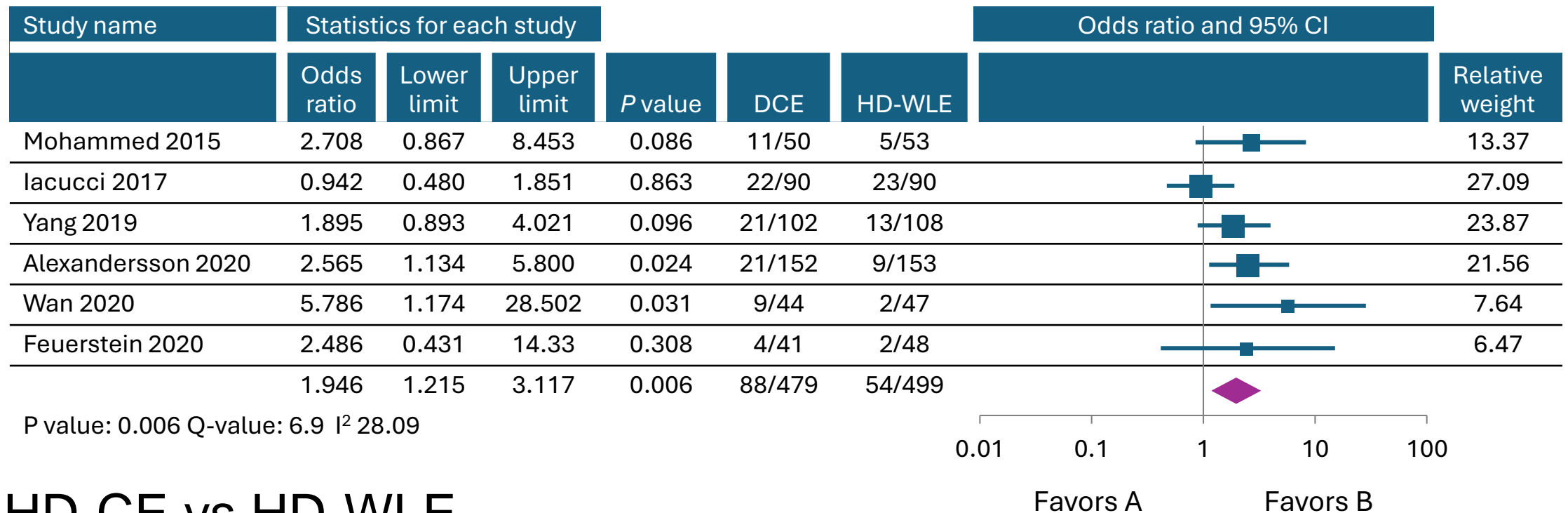
# NO difference in RR between dye-CE and HDWLE



HD-CE vs HD-WLE

RR, 1.39; 95% CI, 0.95–2.04

# Higher ODDS of dysplasia detection using DCE vs HD-WLE



HD-CE vs HD-WLE

**OR, 1.94; 95% CI 1.21-3.11**

Redrawn from: Mohamed et al: Am J Gastroenterol 2024;119:719-726

# No difference in detection of high grade dysplasia

Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI) <sup>a</sup>	Anticipated absolute effects	
				Risk with HD-WLE	Risk difference with DCE
Overall dysplasia detection	978 (6 RCTs)	High <sup>b</sup>	OR 1.94 (1.21–3.11)	108 per 1,000	83 more per 1,000 (20 more to 166 more)
High-grade dysplasia detection	889 (5 RCTs)	Low <sup>b,c</sup>	OR 2.21 (0.64–7.62)	7 per 1,000	8 more per 1,000 (2 fewer to 42 more)
Withdrawal time assessed with: minutes	798 (4 RCTs)	Low <sup>b,d,e</sup>	–	The mean withdrawal time was 15.8 min	MD 3.509 min higher (0.37 lower to 7.388 higher)

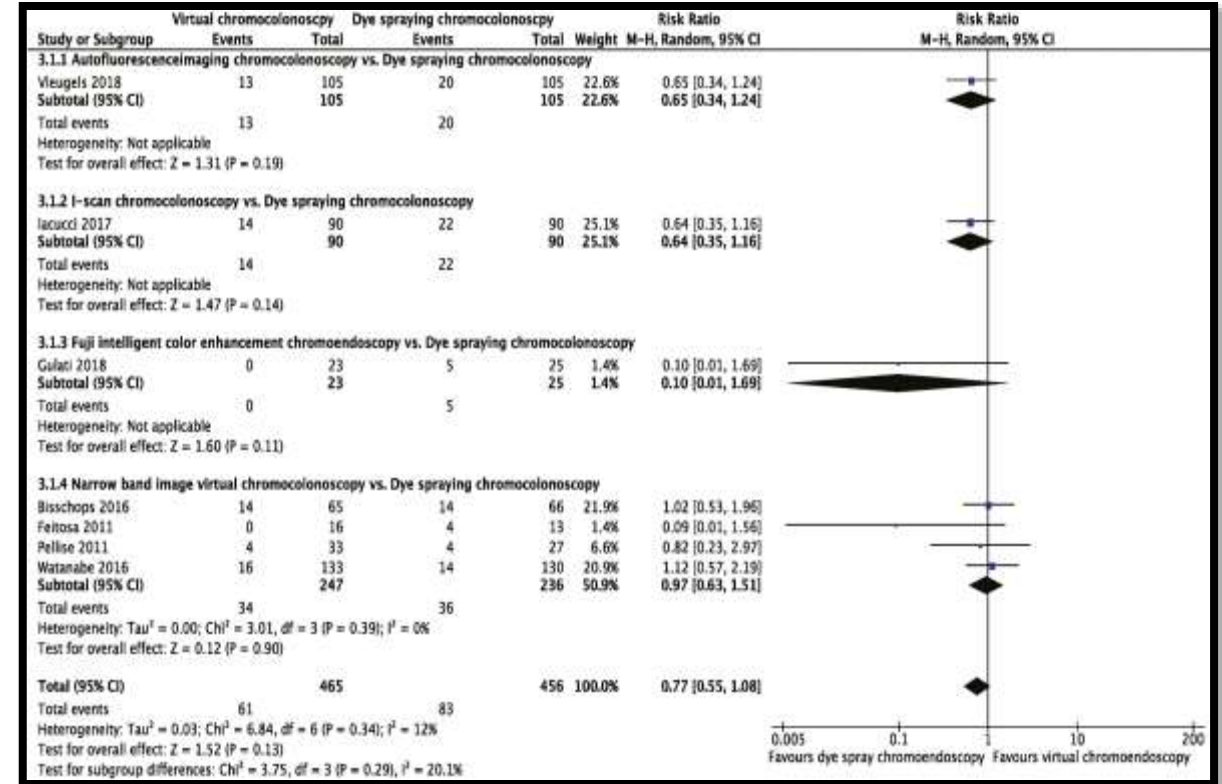
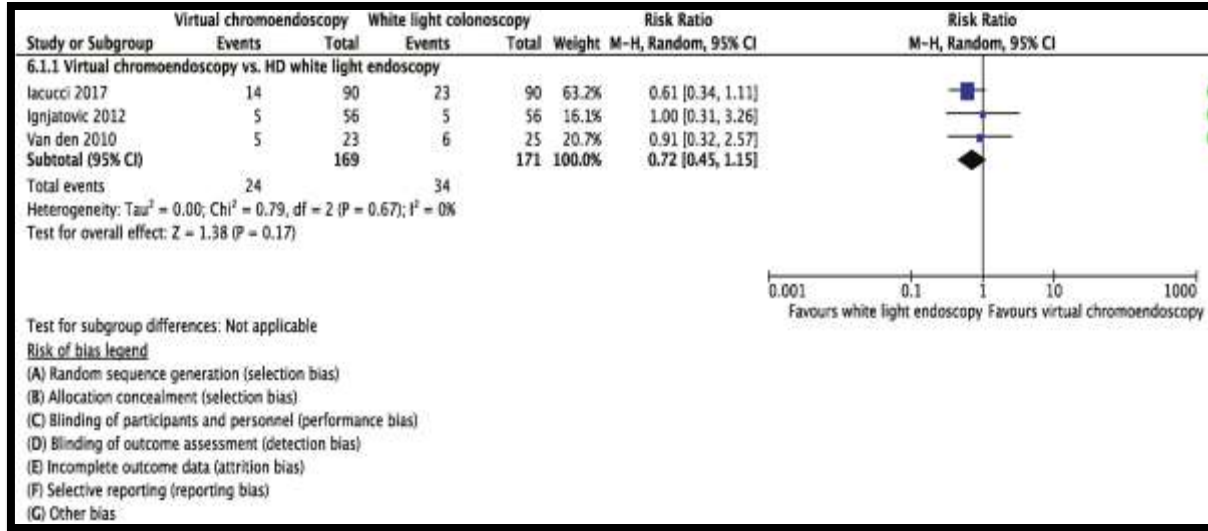


# HELIOS – HD-WLE with segmental reinspection non-inferior to HD-CE

- 563 patients randomized 2:2:1 to HD-WLE

	<b>HD-WLE with segmental reinspection</b>	<b>HD-CE</b>	<b>HD-WLE with single pass</b>
	234	214	115
Dysplasia detection rates	9.8%	13.1%	6.1%
Withdrawal time (median)	19.0	26.0	15.0

# VCE no different than dye-CE and HD-WLE



Per patient - similar rates of dysplasia detection comparing VCE with dye-based CE and HD-WLE

# Dye-CE shown to increase dysplasia detection in patients with prior dysplasia

Deepak P, Bruining D et al, 2016

- 95 patients
- Prior SD and HD WLE with invisible and visible dysplasia
- First CE - dysplastic lesions in 50 patients, including 34 new lesions

Dziegielewski C, Murthy SK et al, 2022

- 24 patients
- Prior HD-WLE with invisible or 'poorly defined' dysplasia
- 32 visible neoplastic lesions unmasked during DCE
- 29.4% with invisible dysplasia on HD-WLE – no visible lesion found

# Updated SCENIC 2022

- HD colonoscopy recommended
- DCE with targeted biopsy sampling recommended (over WLE) when using SD colonoscope
- DCE, WLE, NBI, and VCE with targeted biopsy sampling all acceptable modalities for surveillance when using HD colonoscope; endoscopist should have training or expertise in dysplasia detection using method of choice
- Random biopsy sampling (in addition to targeted biopsy sampling) should be used in highest risk patients, including those with PSC, previous neoplasia, active inflammation, or a tubular, scarred colon

# Chromoendoscopy – Tips/Pearls

- Not effective in
  - > mild inflammation
  - Inadequate bowel prep (lower than BBPS 2 in each segment)
    - Can mitigate by cleaning as you insert
- Mayo practice
  - terminal ileal examination
  - four segment random biopsies in addition to targeted
  - Visible lesions in segmental bottles

# IBD visible lesion - Five 'S's

- Shape
- Size
- Site
- Surface [Kudo pit pattern]
- Surrounding [mucosal activity and other lesions]

# Endoscopic reporting terminology

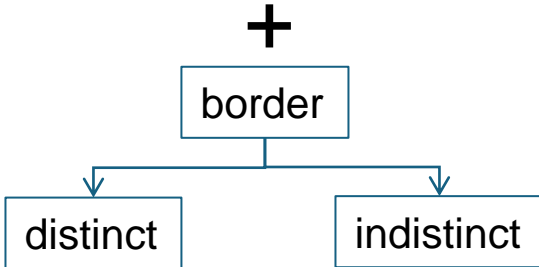
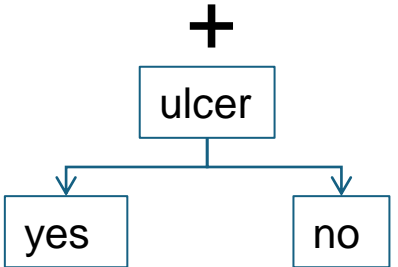
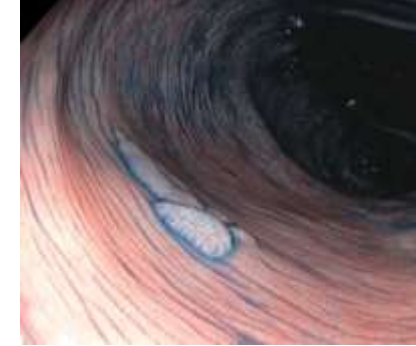
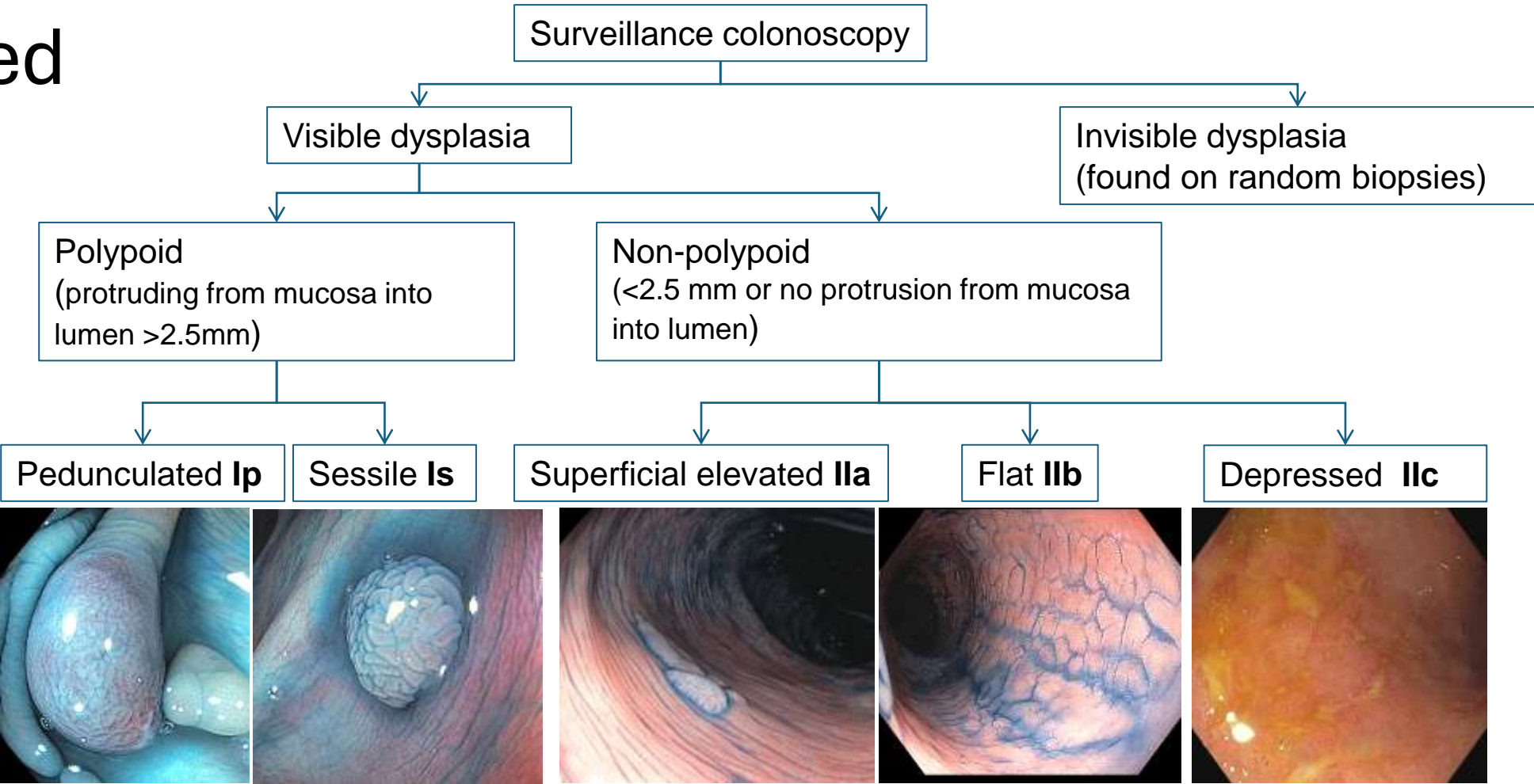


- **polypoid** ( $\pm$ 2.5 mm tall)
- **nonpolypoid** (<2.5 mm)
- **invisible** (detected on nontargeted biopsy)



- adenomatous polyp
- adenoma-like mass (ALM)
- dysplasia-associated lesion or mass (DALM)
- flat dysplasia

# Modified PARIS

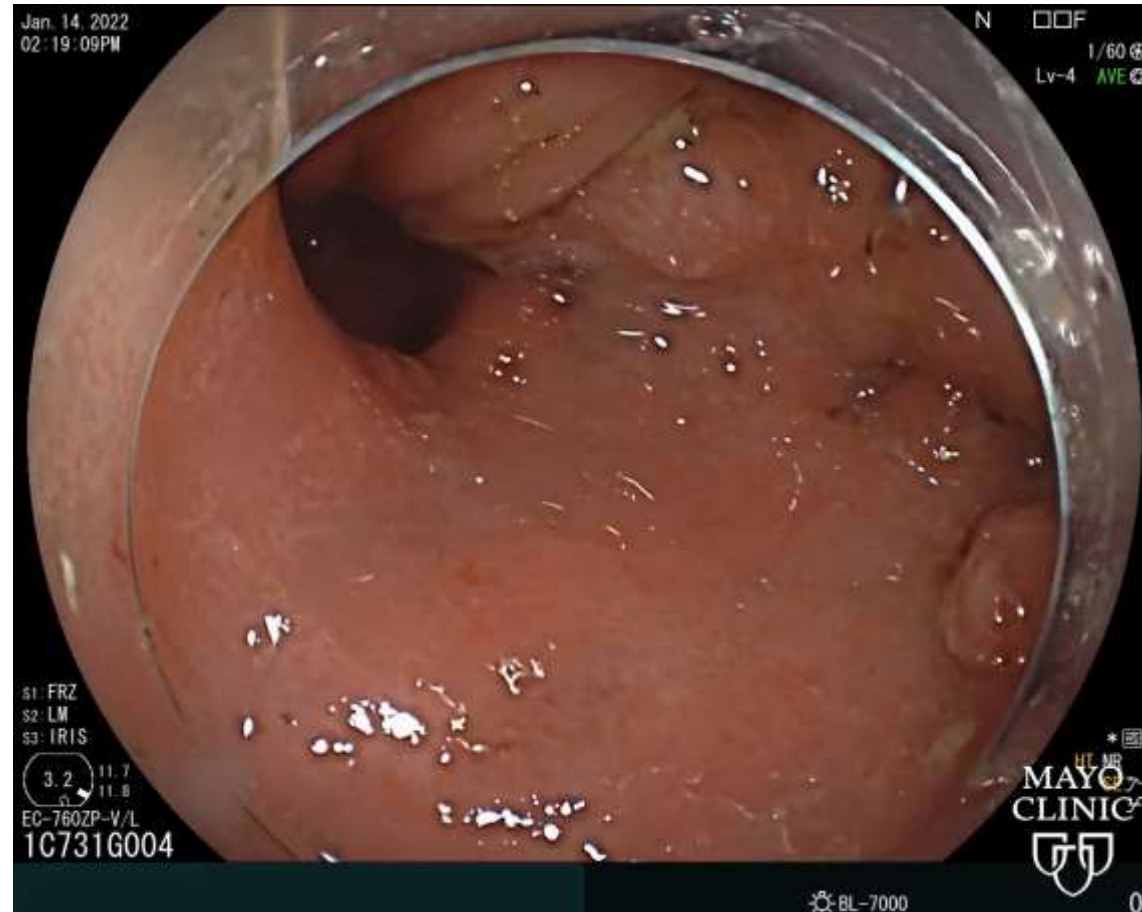




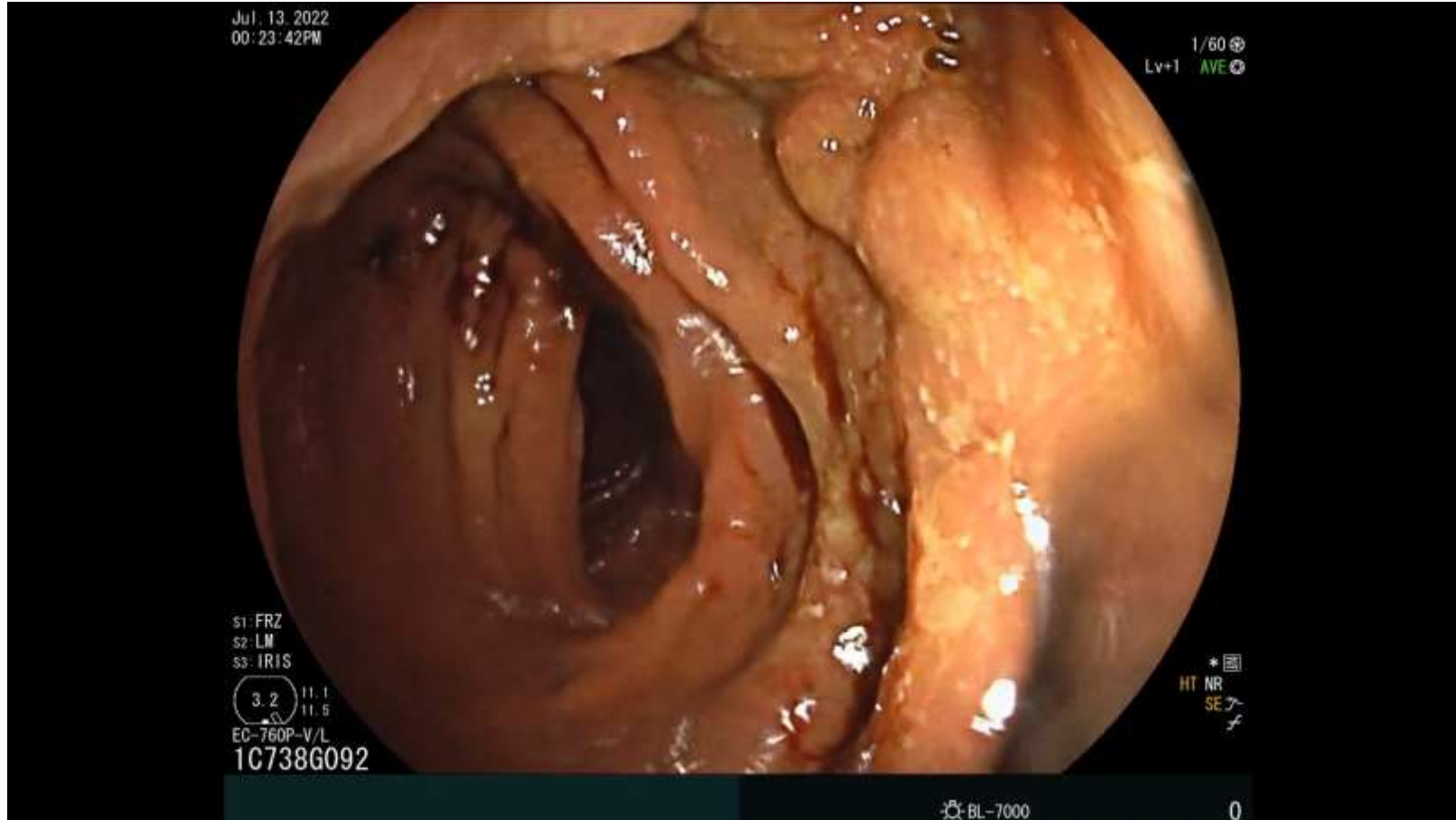
# Paris IIb - LGD – poorly defined margins - unresectable



# Paris IIc – high grade dysplasia

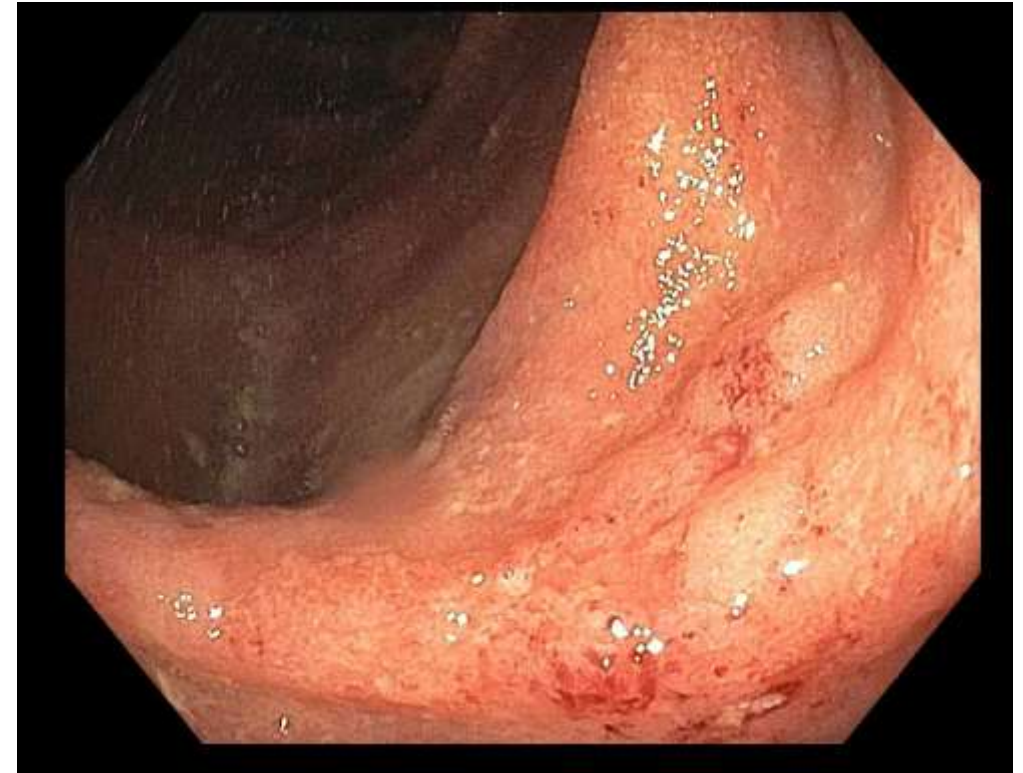
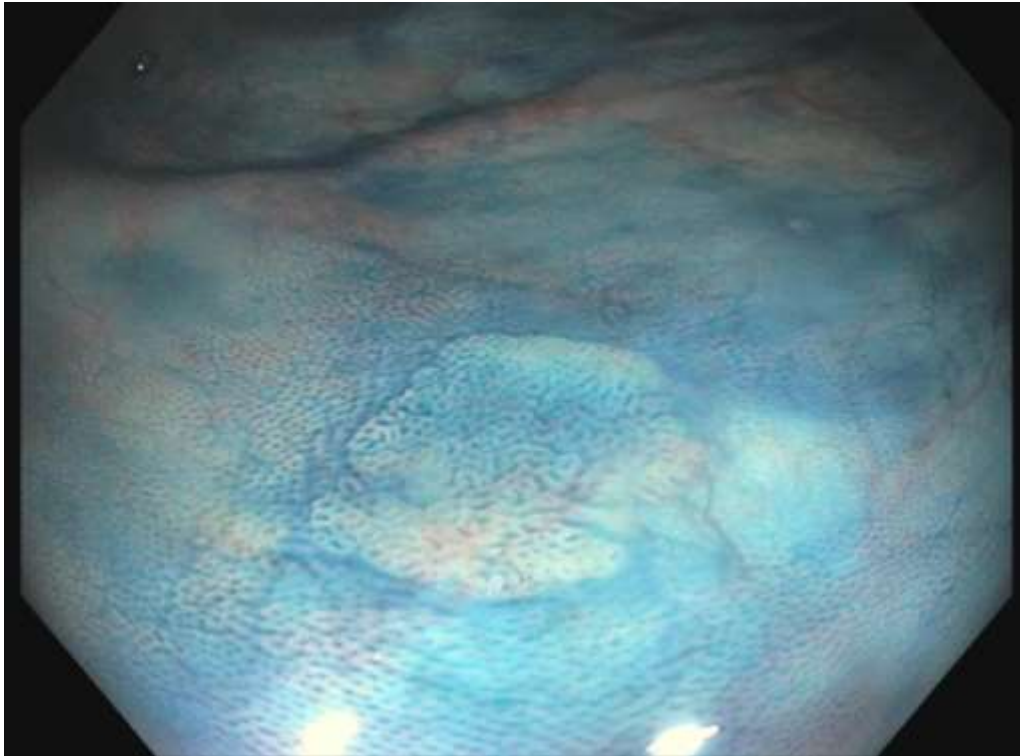


# Paris IIc - Adenocarcinoma



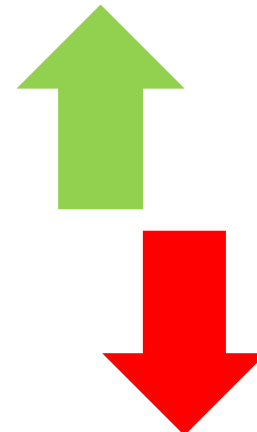
# Adenoma detection using ai (cade)

Current AI algorithms exclude IBD population



# Results

Performance of original CADe IN IBD  
WHITE LIGHT DATASET



Best for dysplastic polyps

Worst for pseudopolyps and serrated changes

Pathology of IBD lesion	Original CADe algorithm							
	IBD image total	TP	FN	FP	Sens	PPV	FPR	F1
<b>Dysplastic</b>	254	208	46	8	0.82	0.96	3.1%	0.89
<b>Non-dysplastic</b>	197	150	47	8	0.76	0.95	4.1%	0.85
<b>Pseudopolyps</b>	1380	468	912	10	0.34	0.98	0.7%	0.5
<b>Serrated changes</b>	57	35	22	4	0.61	0.90	7.0%	0.73
<b>Serrated adenomas</b>	128	101	27	5	0.79	0.95	3.9%	0.86
<b>Total</b>	2016	962	1054	35	0.50	0.97	1.7%	0.64

# Results

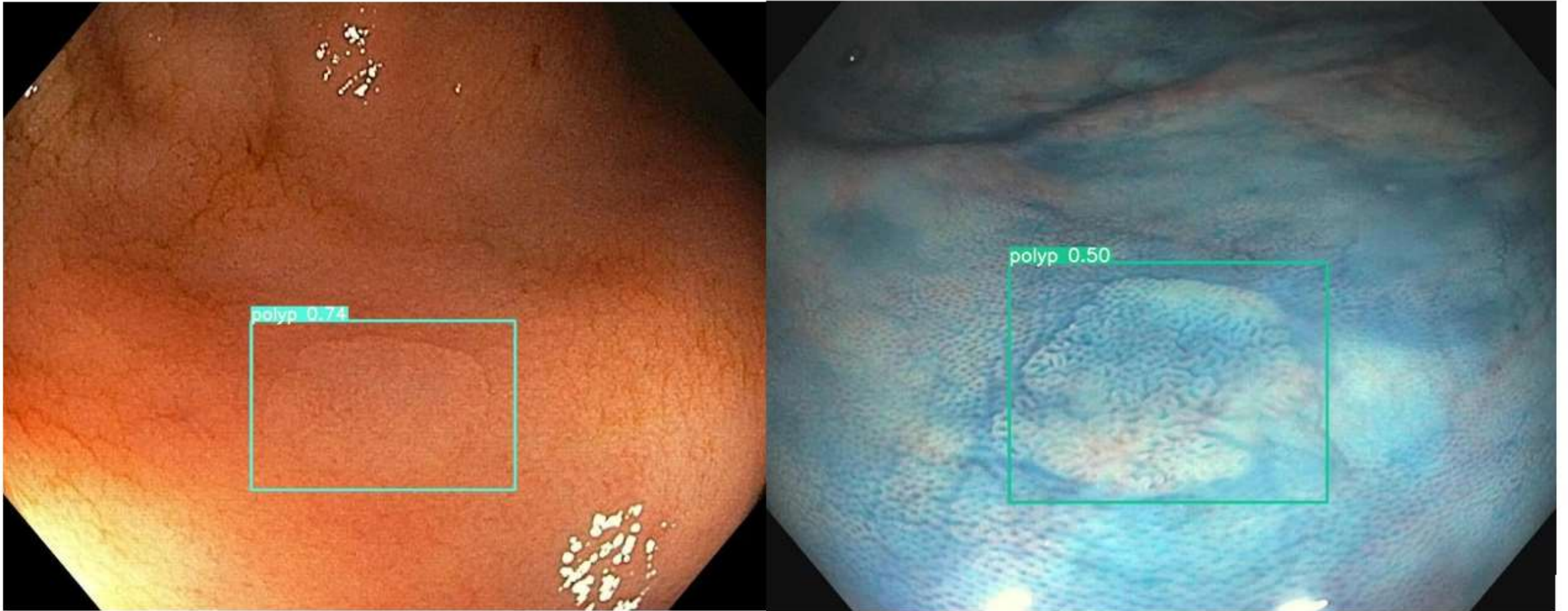
## Performance of IBD-CADe AFTER RETRAINING WITH IBD LESIONS

All performance metrics significantly improved after retraining the AI system with IBD lesions

Pathology of IBD lesion	IBD-CADe model							
	Images in test set	TP	FN	FP	Sens	PPV	FPR	F1
<b>Dysplastic</b>	30	27	3	0	0.90	1	0%	0.95
<b>Non-dysplastic</b>	21	19	2	1	0.90	0.95	4.7%	0.93
<b>Pseudopolyps</b>	108	107	1	8	0.99	0.93	7.4%	0.96
<b>Serrated changes</b>	7	6	1	0	0.85	1	0%	0.92
<b>Serrated adenomas</b>	13	11	2	0	0.84	1	0%	0.92
<b>Total</b>	179	170	9	9	0.95	0.95	5.0%	0.95

# Morphology:

- Lesions with flat morphology (Paris IIa and IIb) and mixed morphology were most frequently missed by IBD-CADe.
  - IBD-CADe performed best with Paris Ip, Is and IIa lesions.

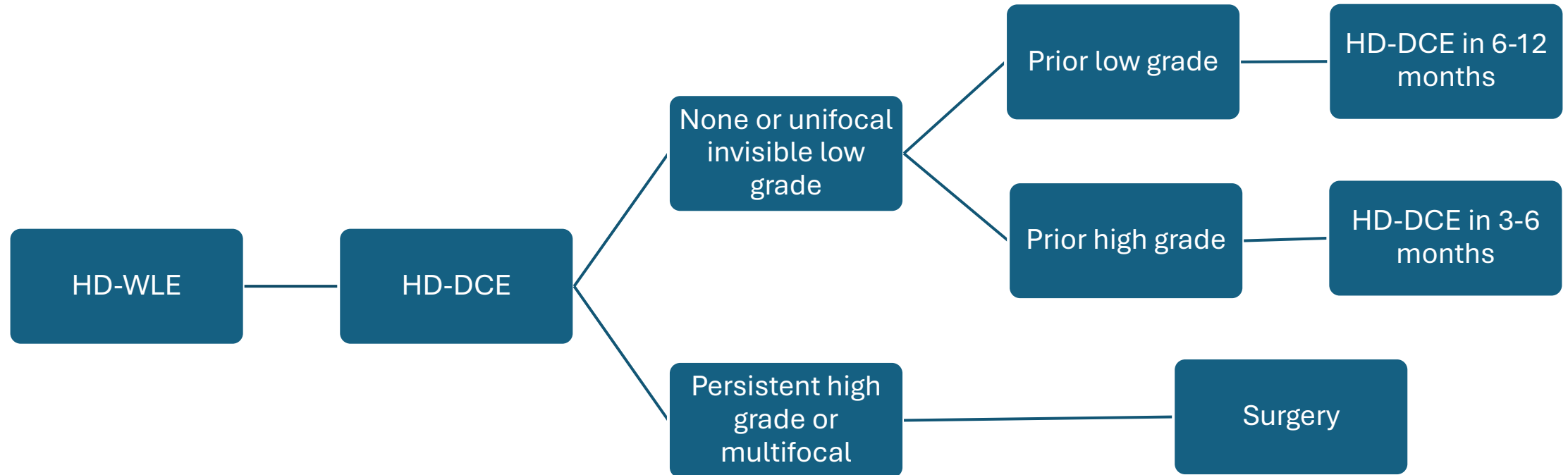


# Random biopsies – highest yield in PSC and prior dysplasia

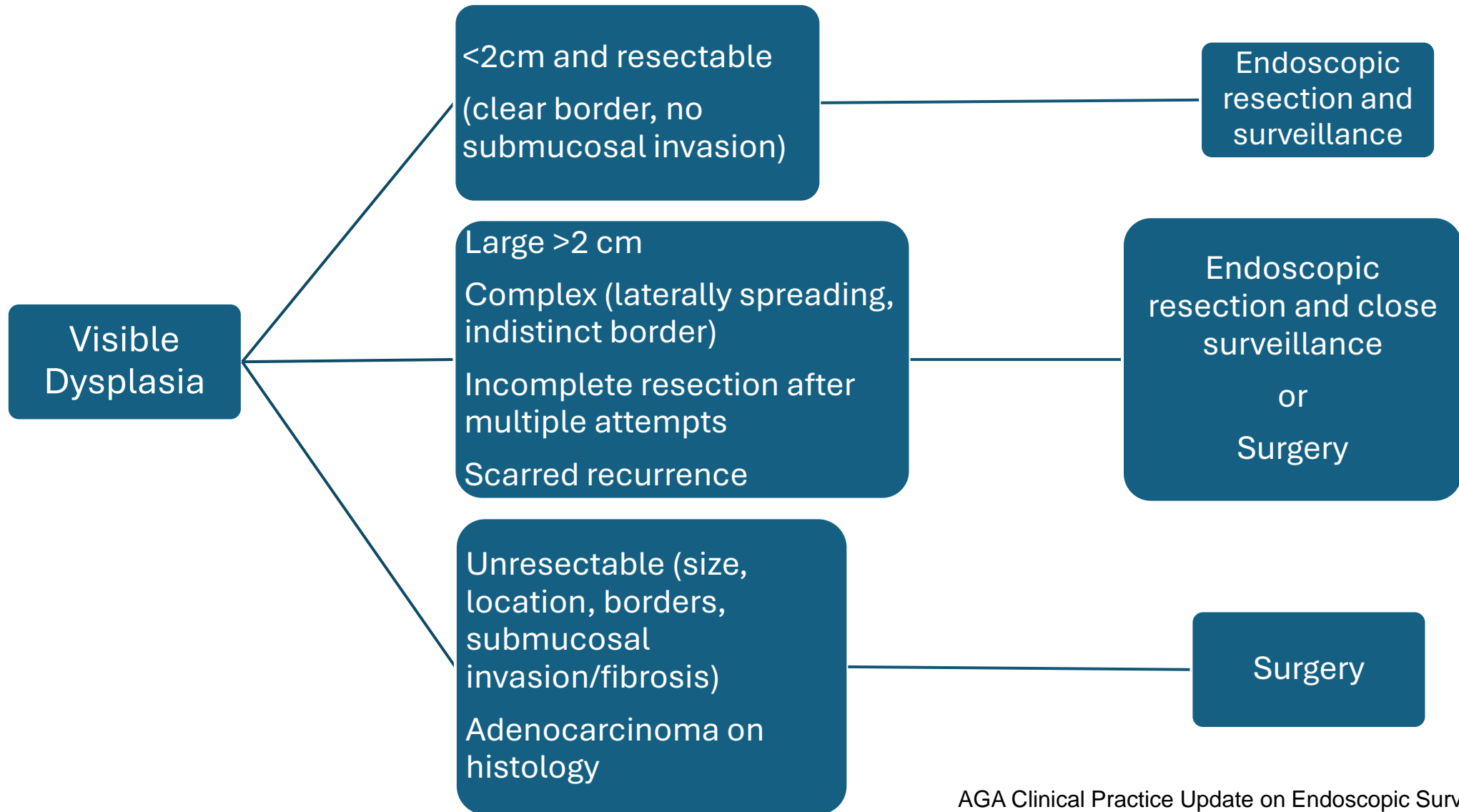
Author (year)	% Colonoscopies with dysplasia on random biopsies	% Colonoscopies with dysplasia only on random biopsies	Type of colonoscopic exam
Van den Broek (2014)	1.2%	0.5%	SD and HD scopes
Mooiweer (2015)	Not reported	1.7%	All SDWLE
Gasia (2016)	0.8% w/HDWLC	0.8% (0.9% w/non-HDWLC)	SDWLE, HDWLE, VCE, Dye-CE
Moussata (2018)	1.9%	1.2%	All with SD Dye-CE
Coelho-Prabhu (2021)	4.8%	Not reported	HDWLE and dye-CE
Hu (2021)	18%	12%	SDWLE, HDWLE and dye-CE



# AGA - Management of invisible dysplasia



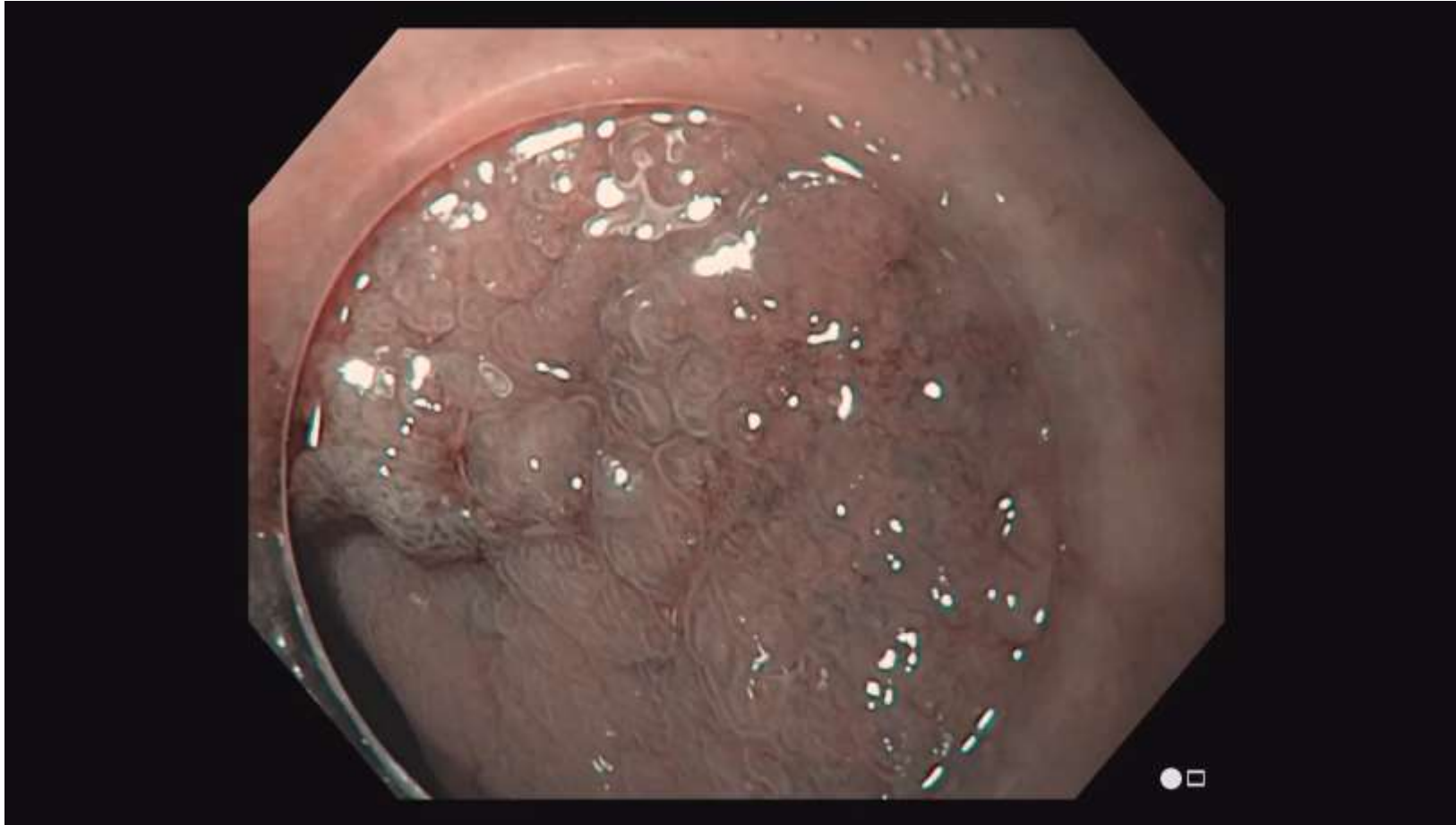
# AGA – Management of Visible dysplasia



# EMR and ESD are safe and effective

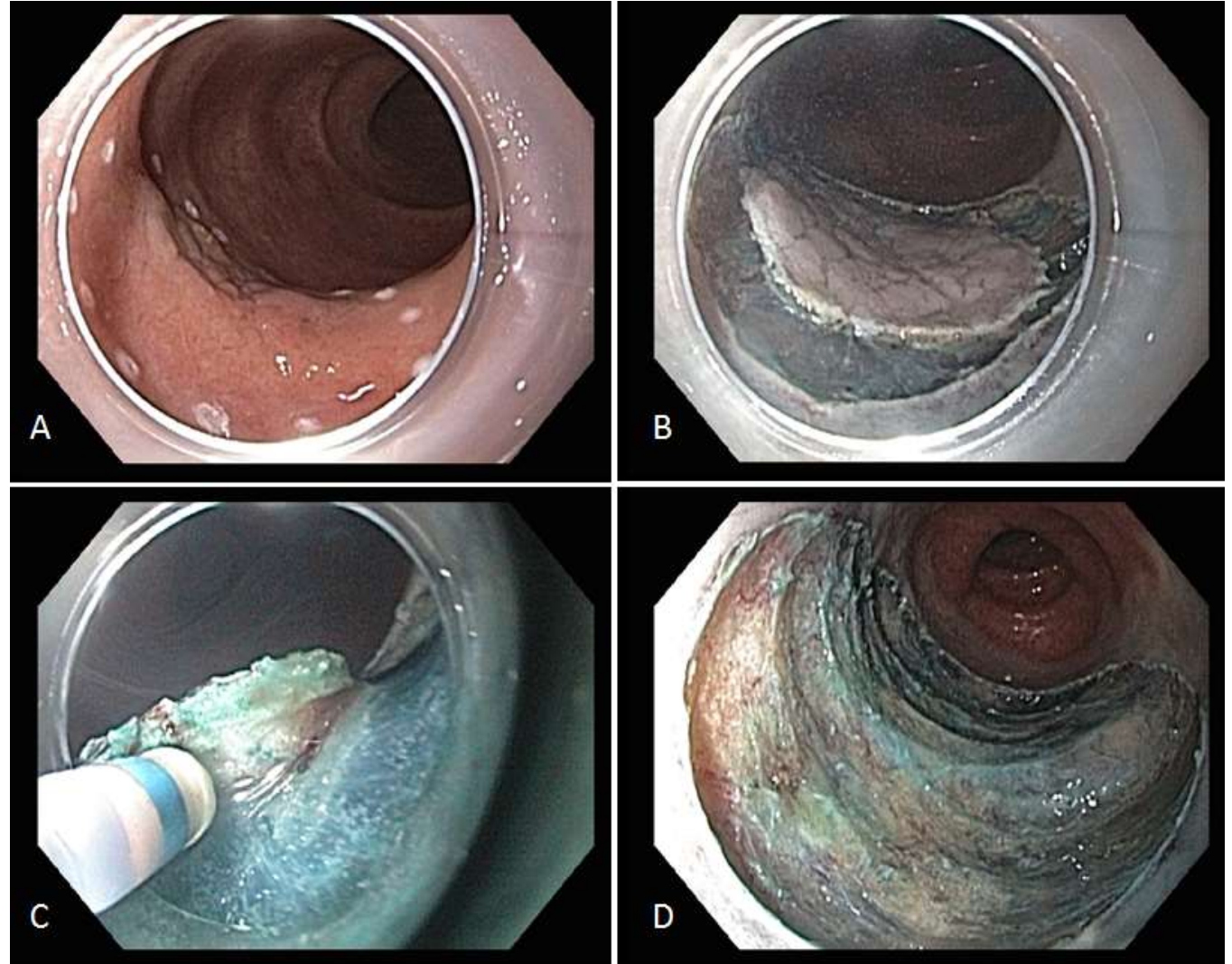
	Endoscopic mucosal resection (n= 347)	Endoscopic submucosal dissection (n= 190)	Hybrid endoscopic s-ubmucosal dissection (n= 73)
Lesion characteristics			
• Mean size (mm)	14.6	25.1	26
• Proportions of lesions < 20 mm (%)	71.3	36.8	NA
• Submucosal fibrosis (%)	2.3	88.1	75.3
Polyp morphology (%)			
• Polypoid	43.8	11.1	32.8
• Non-polypoid	56.2	88.9	67.1
Rate of incomplete resection (%)	0.6 (95% CI: 0%–2.7%, I <sup>2</sup> 6.3%)	3.8 (95% CI: 0.2%–10%, I <sup>2</sup> 25.6%)	0
Rate of en bloc resection (%)	79.7 (95% CI: 63%–90.3%, I <sup>2</sup> 92.6%)	85.7 (95% CI: 72.2%–95.8%, I <sup>2</sup> 73.6%)	74.6 (95% CI: 63.1%–84.8%, I <sup>2</sup> 0%)
Rate of adverse events (%)	0.7 (95% CI 0%–2.7%, I <sup>2</sup> 0%)	4.4 (95% CI 0.07%–10%, I <sup>2</sup> 11.8%)	11 (95% CI 4.3%–19.6%, I <sup>2</sup> 0%)
Rate of recurrence during follow-up (%)	3.5 (95% CI 0%–11.5%, I <sup>2</sup> 83.4%)	1.7 (95% CI 0%–6.5%, I <sup>2</sup> 33.5%)	4.4 (95% CI 0.1%–11.8%, I <sup>2</sup> 0%)

# Challenging esd - fibrosis

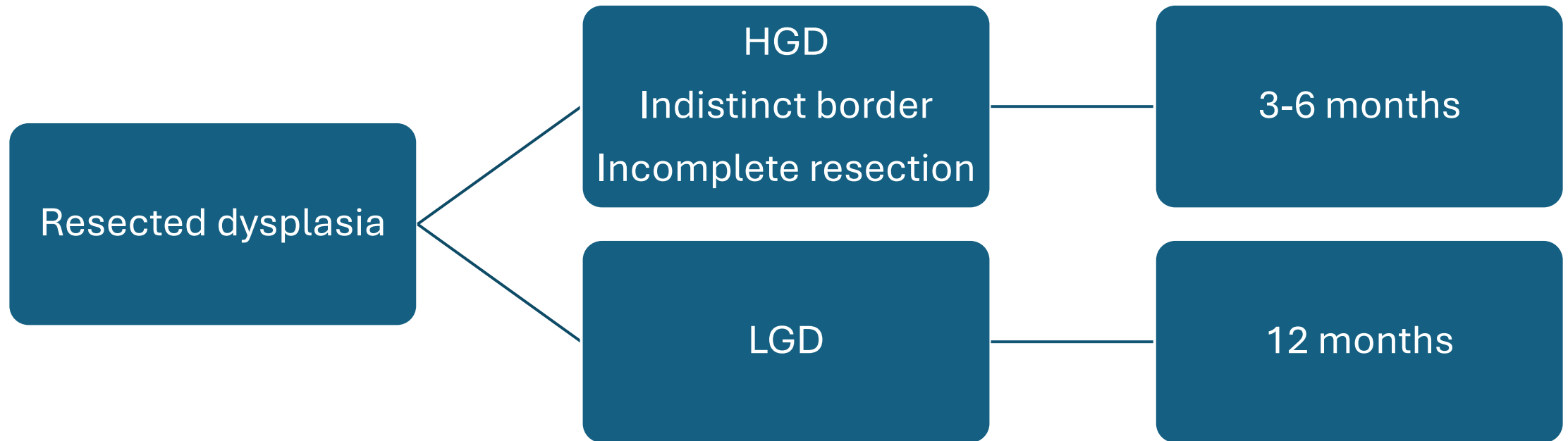


# ESD for IBD dysplasia

- Meta-analysis
- 25 studies – 585 patients
- Median 24 mth f/u
  
- En bloc resection 0.88 (95% CI 0.82-0.92)
- R0 resection 0.78 (95% CI 0.72-0.83)
  
- Very low recurrence upto two years



# AGA – Surveillance of visible dysplasia



# AGA - Surveillance – no dysplasia

## 1 year

- Moderate-severe inflammation
- PSC
- Family h/o CRC in 1<sup>st</sup> degree relative <50
- Dense pseudopolyps
- h/o invisible or high-risk dysplasia <5 years

## 3 years

- Mild inflammation
- Strong family history of CRC
- Features of prior severe colitis – mucosal atrophy
- h/o invisible or high-risk dysplasia >5 years
- h/o low-risk visible dysplasia <5 years

## 5 years

- Sustained disease remission since last colonoscopy with mucosal healing +
  - $\geq 2$  consecutive exams without dysplasia
- Minimal historical disease extent



## CONTINUE SURVEILLANCE AFTER IPAA

Mayo - 1327 patients with IBD and IPAA from  
January 1981 to February 2020

10 (0.8%) patients developed dysplasia or  
adenocarcinoma

4 in pouch

5 in rectal cuff

1 in prepouch, pouch and cuff

Risk factors at time of IPAA surgery:

Rectal dysplasia

PSC

Pancolitis

Backwash ileitis



# Summary

- High quality surveillance colonoscopy imperative to ↓ CRC risk
- Make the invisible visible
  - Use enhanced imaging techniques, especially for lesions delineation
- Endoscopic management when possible
- Outcome data similar for EMR and ESD
- Tailor surveillance intervals

# QUESTIONS & ANSWERS

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