Cancer Biology or Ineffective Surveillance? A Multicentre Retrospective Analysis of Colitis-Associated PCCRC

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THE NATIONAL BOWEL HOSPITAL

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Misha Kabir, Siwan Thomas-Gibson, Ahmir Ahmad, Rawen Kader, et al

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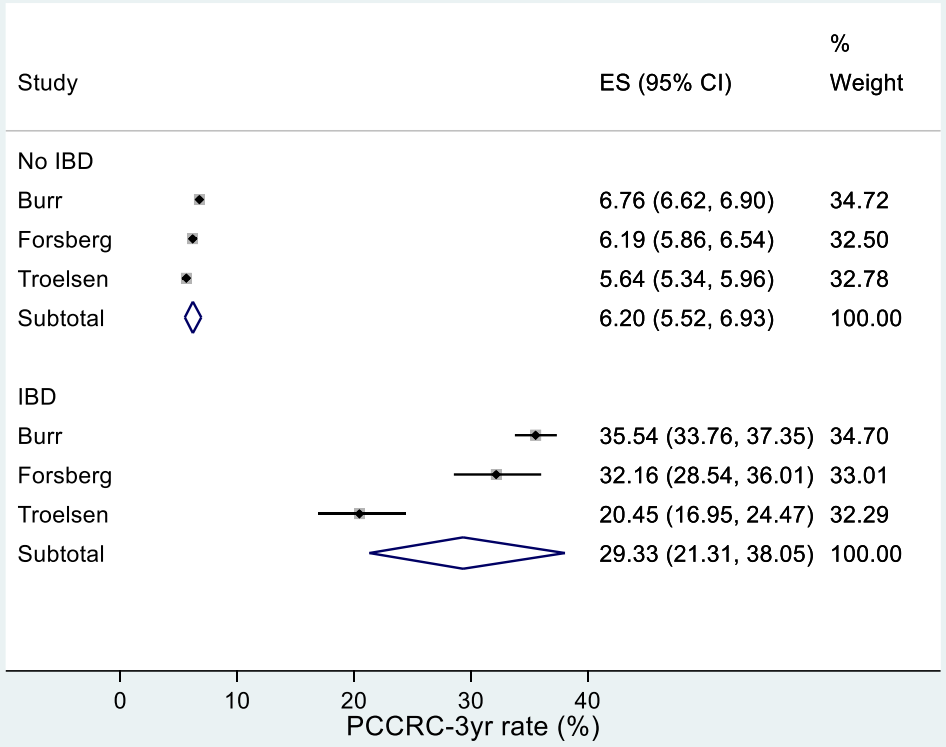
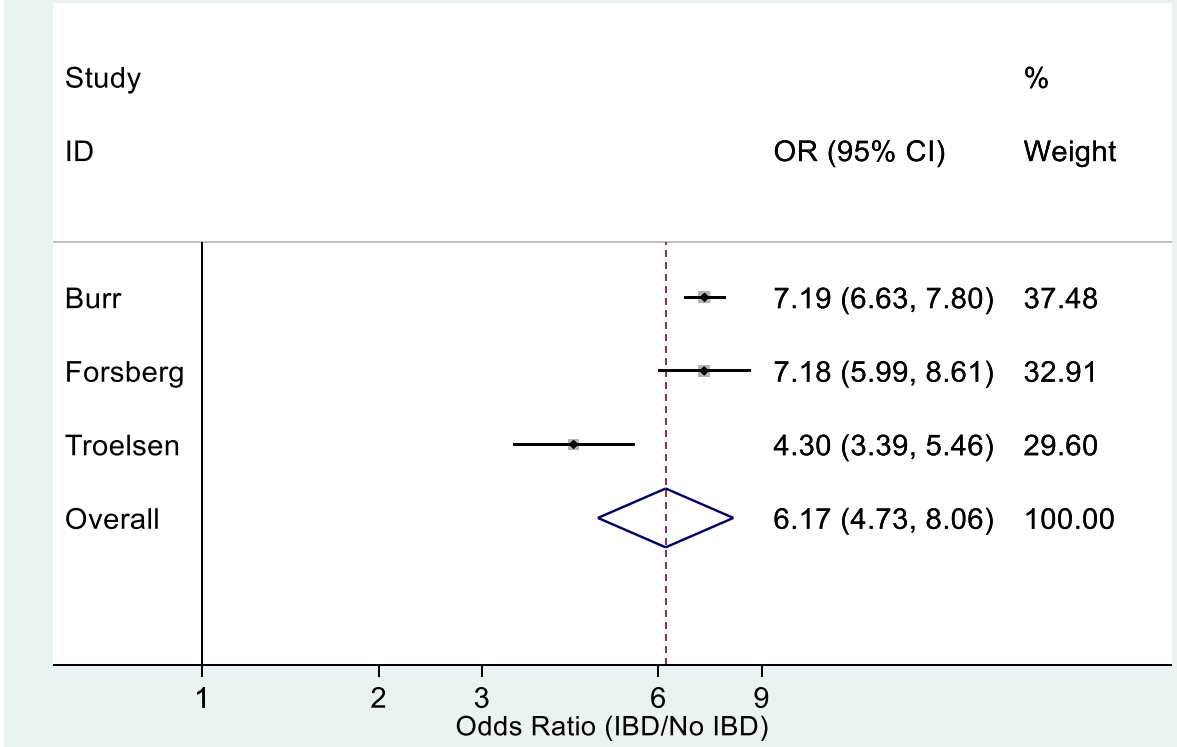
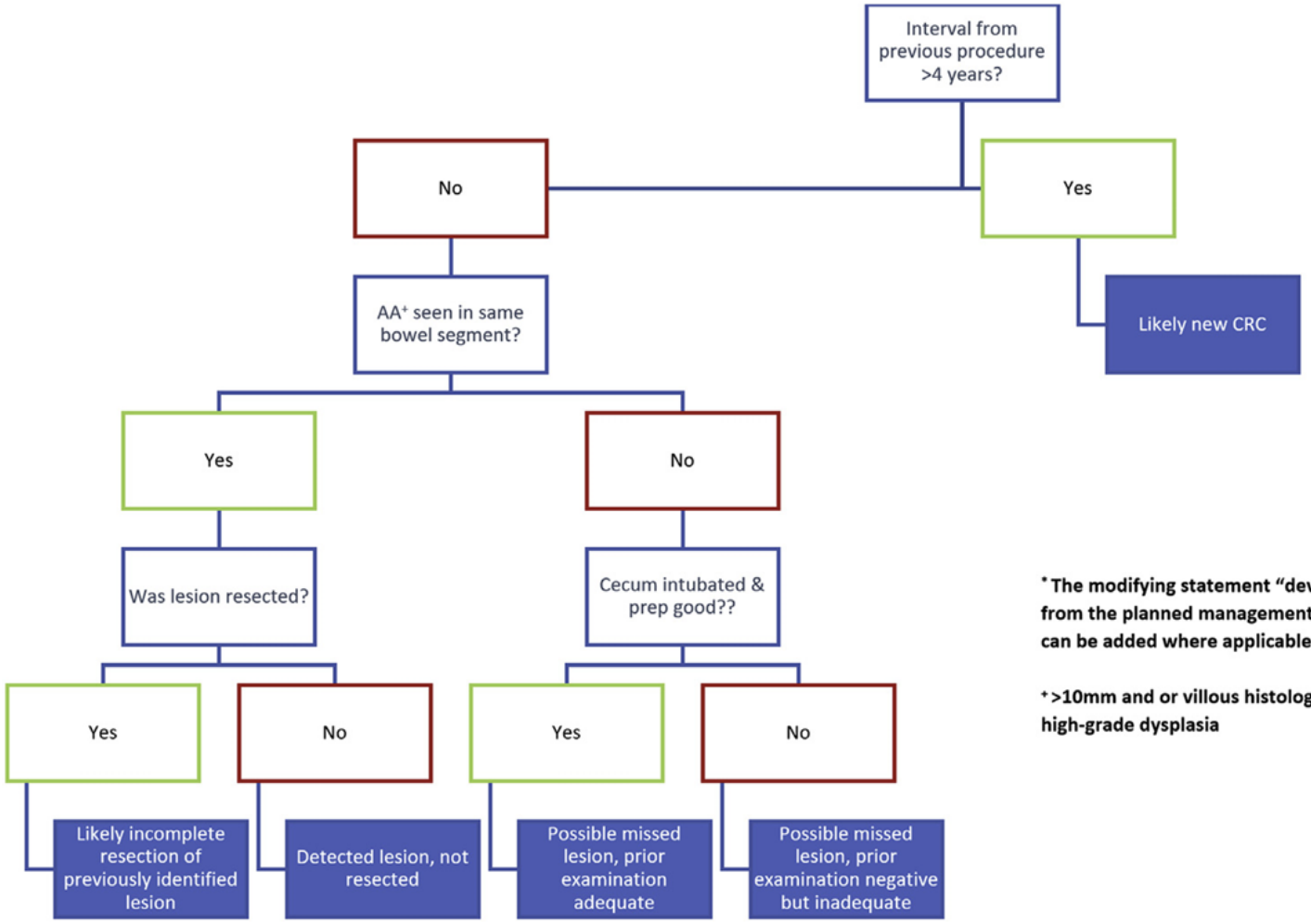
SYSTEMATIC REVIEW & META-ANALYSIS: IBD PCCRC - 3yr





R.Kader et al (unpublished data)

WEO - PCCRC ROOT CAUSE ANALYSIS (RCA)



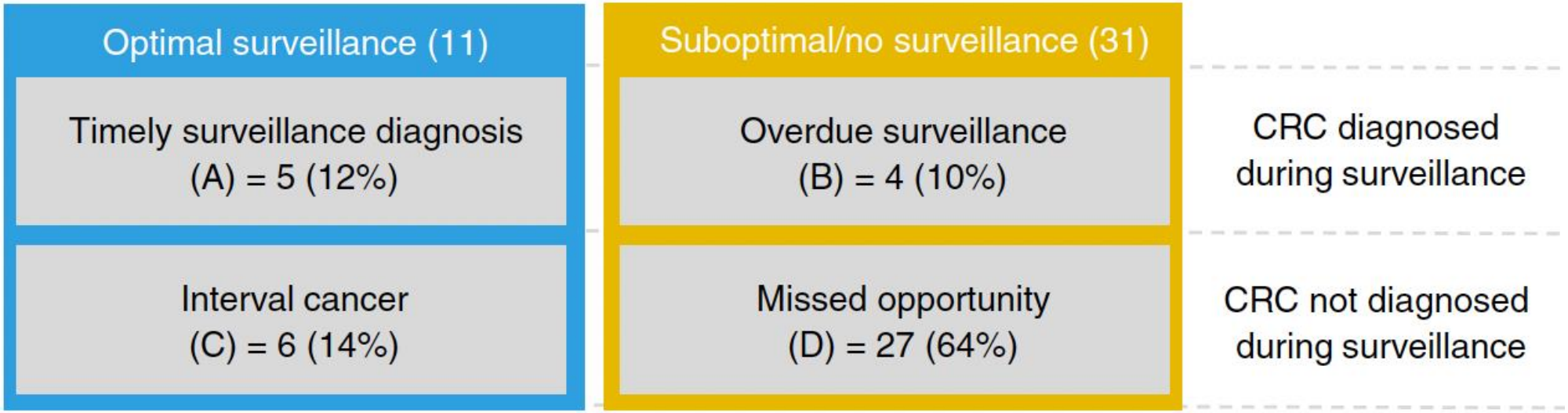
***The modifying statement "deviation from the planned management pathway" can be added where applicable**

+>10mm and or villous histology and/or high-grade dysplasia

Rutter MD, Beintaris I, Valori R et al, WEO Consensus Statement, Gastroenterology (2018)

IBD PCCRC RCA

- 1st RCA of IBD PCCRCs published in 2020
- Retrospective single-center study
- Study cohort = 1998 to 2019



Gordon C et al. Root-cause analyses of missed opportunities…Aliment Pharmacol Ther (2021)

STUDY OVERVIEW

AIM

To identify preventable factors that contribute to IBD PCCRCs

STUDY DESIGN

Retrospective study to evaluate the quality of surveillance undertaken in IBD pts who have developed CRCs at UK tertiary referral IBD centres

METHODOLOGY - SITES

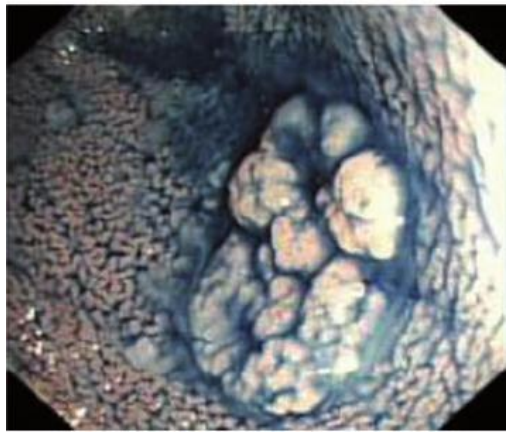
Tertiary Centers (UK)

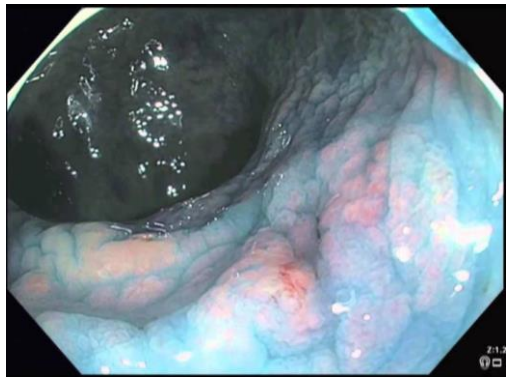
- St Mark's The National Bowel Hospital
- NHS Oxford University Hospitals NHS Foundation Trust
-  NHS University College London Hospitals NHS Foundation Trust
- Barts Health NHS NHS Trust

METHODOLOGY – STANDARDIZED IBD SURVEILLANCE

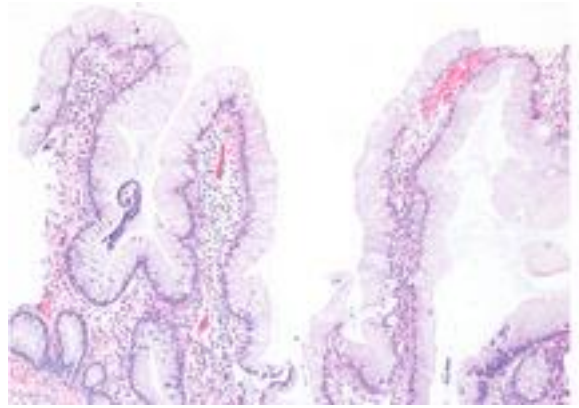
High-Definition

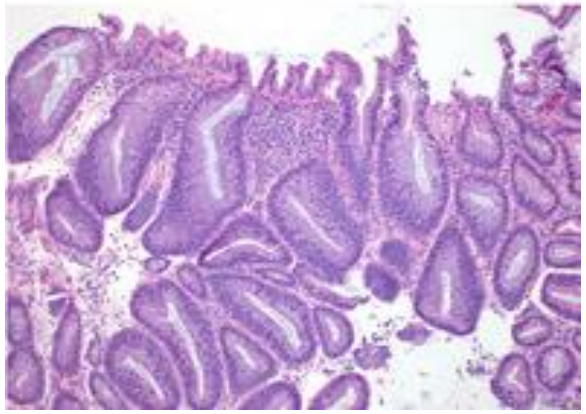
Chromoendoscopy



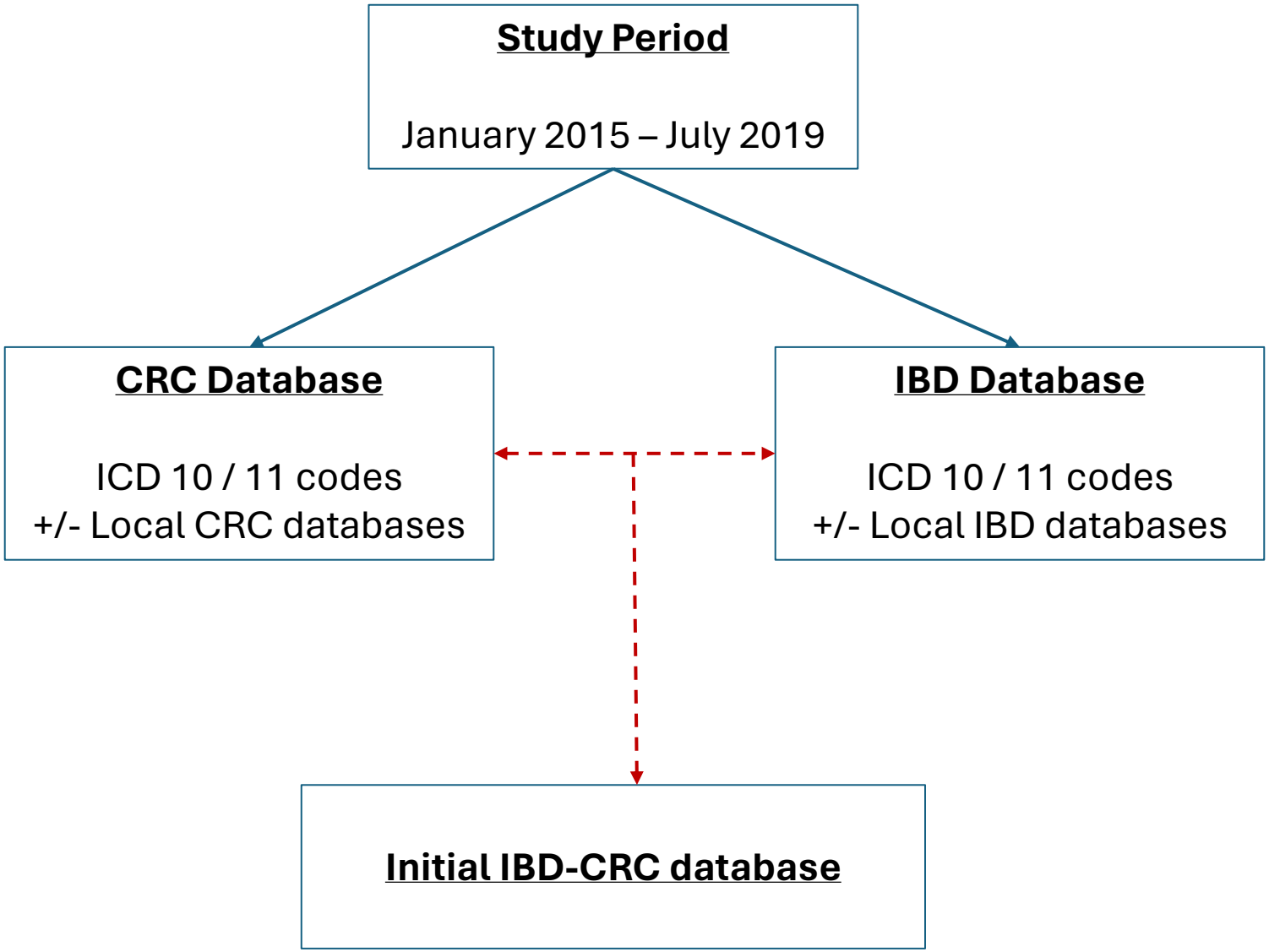


Expert GI Histopathologists

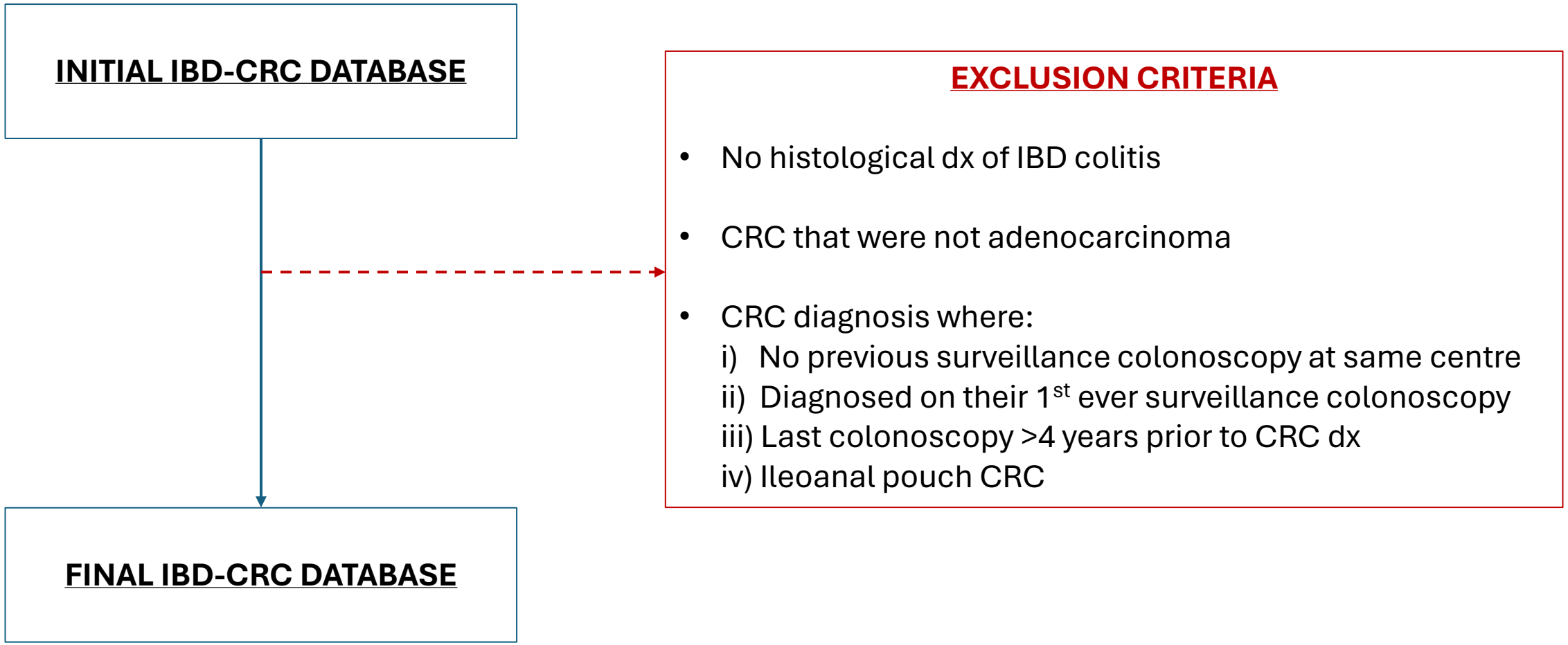




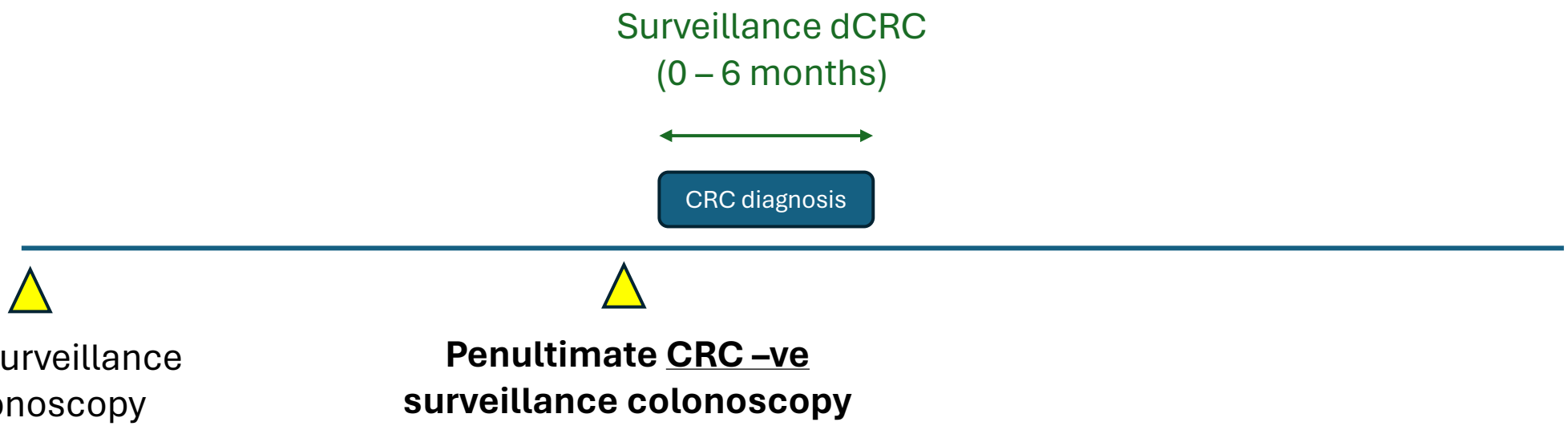
METHODOLOGY – STUDY COHORT



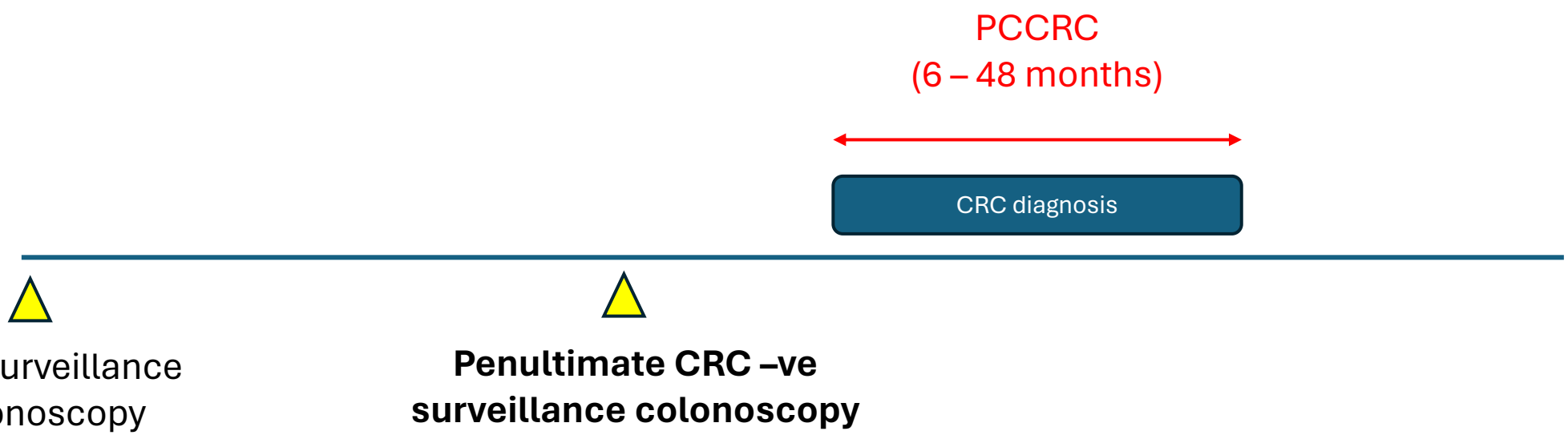
METHODOLOGY – EXCLUSION CRITERIA



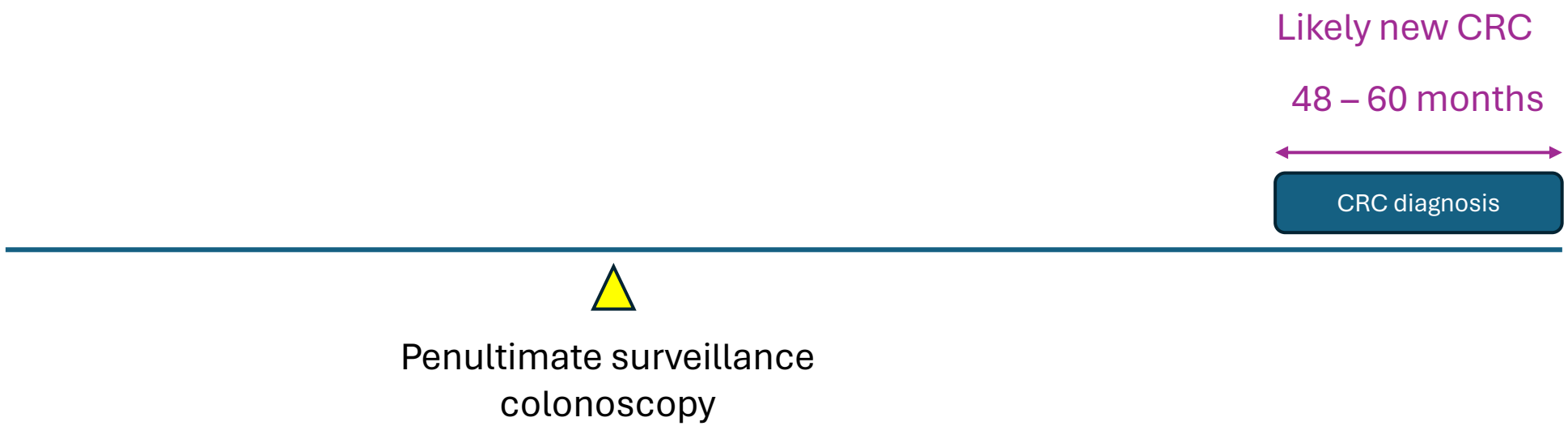
METHODOLOGY – Surveillance dCRC



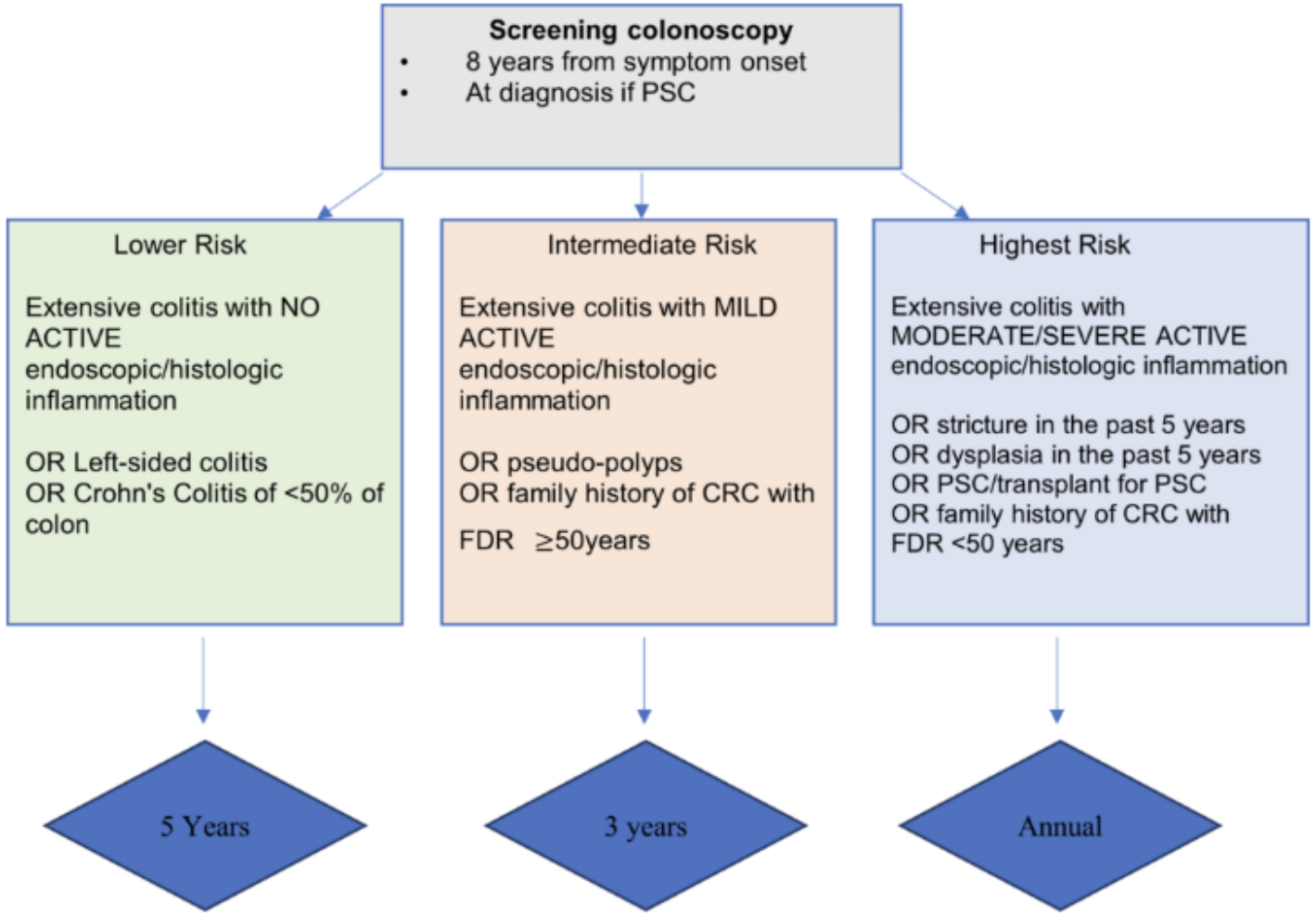
METHODOLOGY – Surveillance PCCRC



METHODOLOGY – NEW CRC (EXCLUDED)



METHODOLOGY – IBD Surveillance Intervals (BSG Guidelines)



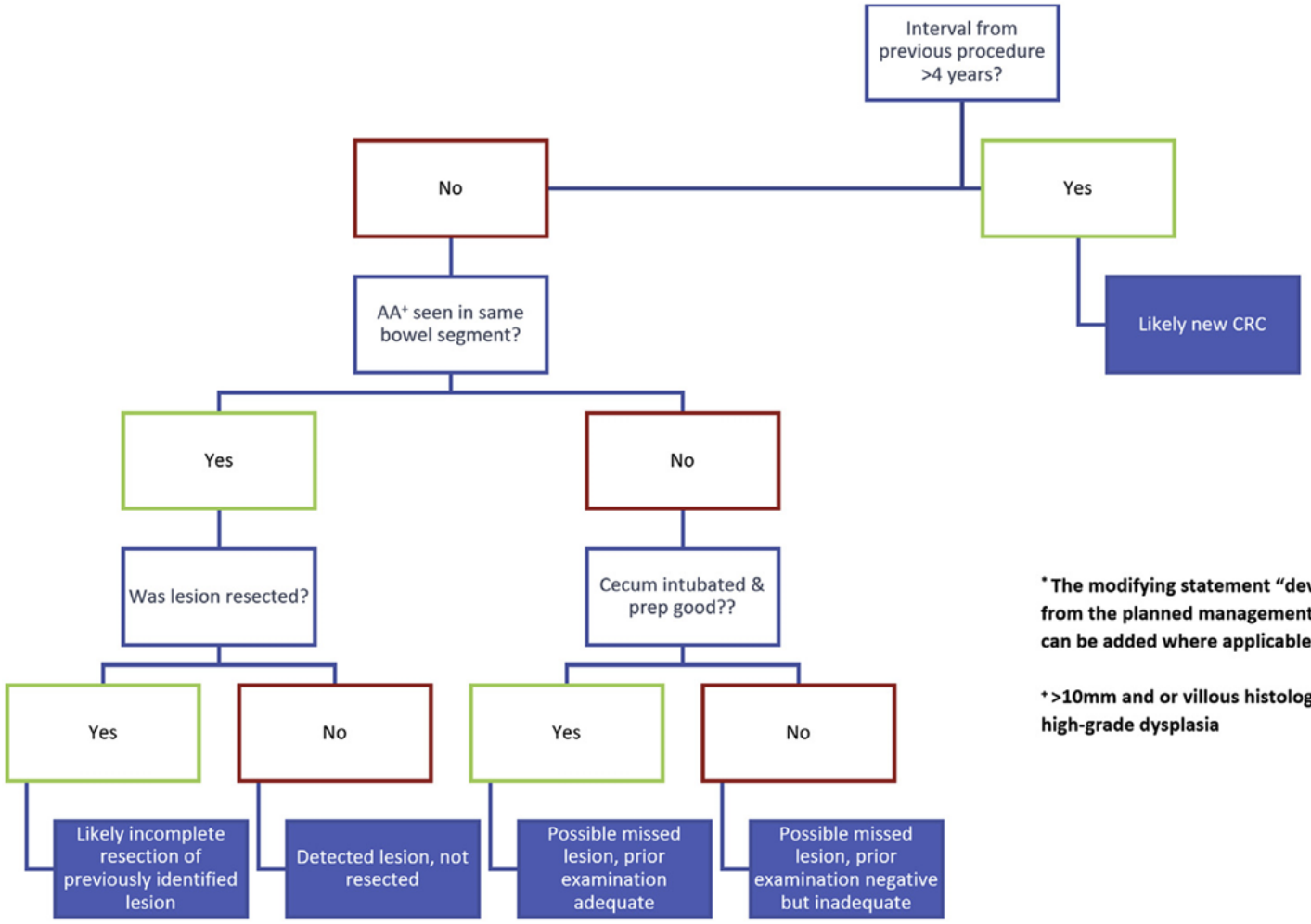
METHODOLOGY – SURVEILLANCE PCCRC

Table 2. Post-Colonoscopy Colorectal Cancer Subcategories

	PCCRC subcategories			
		Non-interval type		
	Interval type	Type A	Type B	Type C
	Detected before recommended screening/surveillance interval	Detected at recommended screening/surveillance interval	Detected after recommended screening/surveillance interval	Where no screening/ surveillance interval had been recommended

Rutter MD, Beintaris I, Valori R et al, WEO Consensus Statement, Gastroenterology (2018)

WEO - PCCRC ROOT CAUSE ANALYSIS (RCA)



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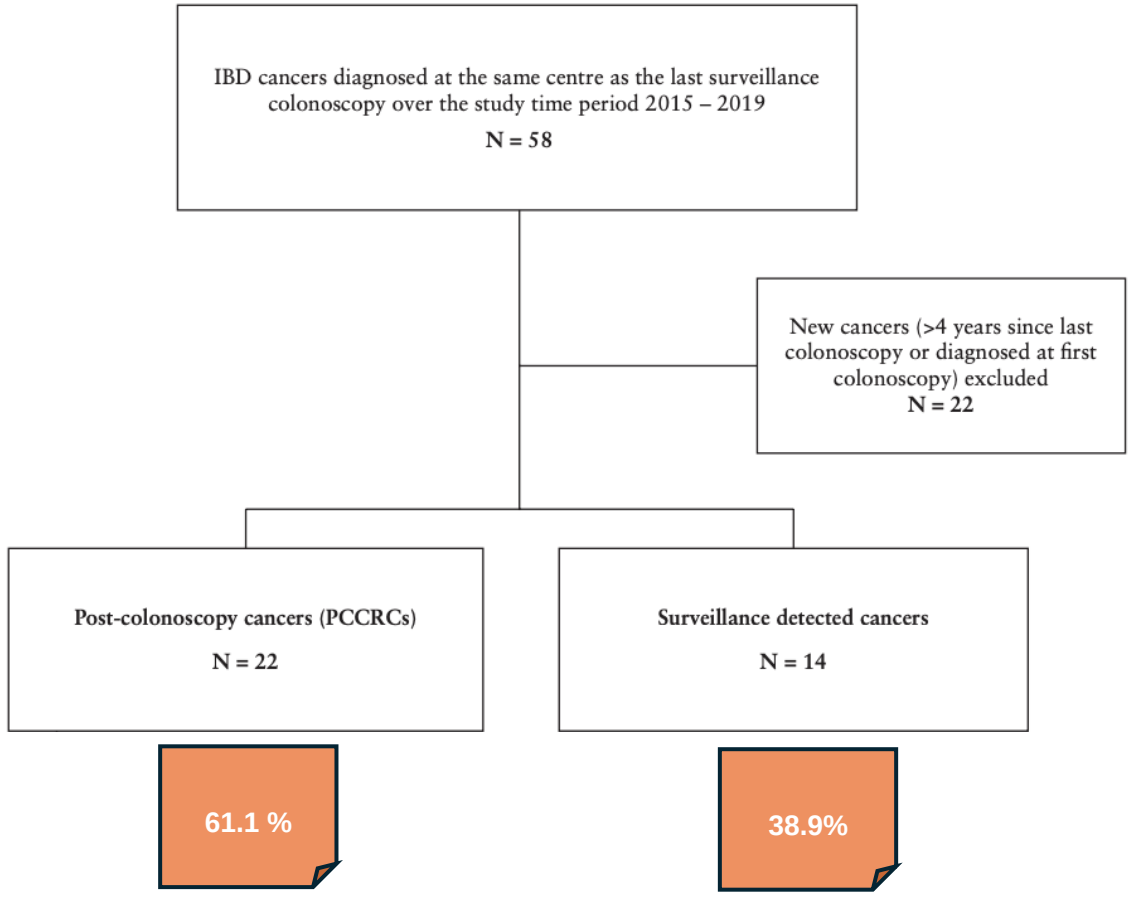
Rutter MD, Beintaris I, Valori R et al, WEO Consensus Statement, Gastroenterology (2018)

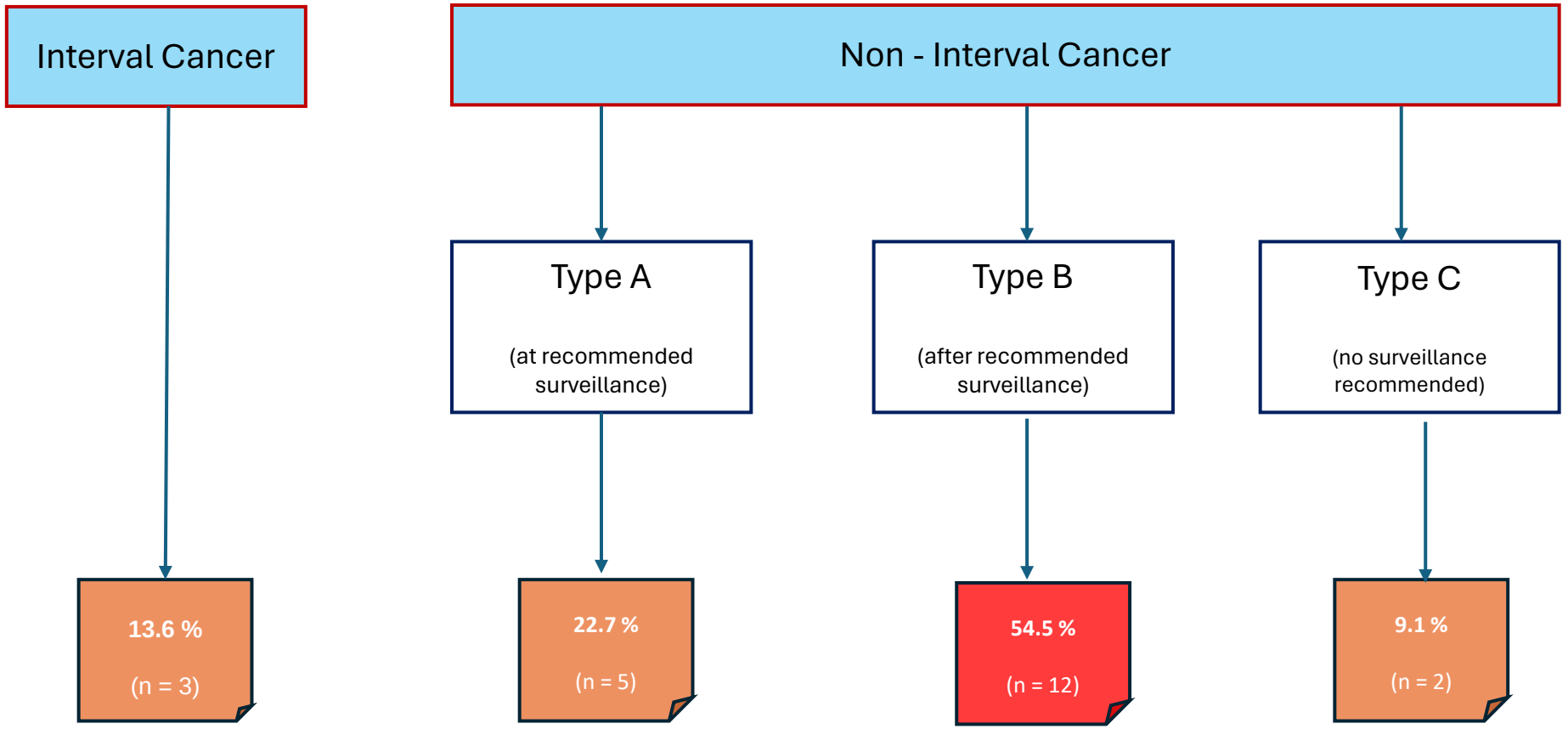
RESULTS

RESULTS - SURVEILLANCE PCCRC



Patient demographics and disease characteristics	PCCRCs [*n* = 22]	Surveillance-detected cancers [*n* = 14]	*p*-value
Median age at time of cancer diagnosis [years]	61.5 [IQR 38.8–74.3]	58.0 [IQR 49.0–68.0]	0.470
Median duration of IBD at cancer diagnosis [years]	20.0 [IQR 15.0–25.3]	29.0 [IQR 15.0–32.0]	0.301
Male gender	63.6% [*n* = 14/22]	64.3% [*n* = 9/14]	0.968
Non-Caucasian ethnicity	27.3% [*n* = 6/22]	50.0% [*n* = 7/14]	0.166
IBD type			
Ulcerative colitis	72.7% [*n* = 16/22]	85.7% [*n* = 12/14]	0.441
Crohn's disease	27.3% [*n* = 6/22]	14.3% [*n* = 2/14]	
History of extensive colitis [extending proximal to splenic flexure in ulcerative colitis and > 50% of the colon in Crohn's disease]	77.3% [*n* = 17/22]	84.6% [*n* = 11/13]	0.689
Medication use at time of CRC diagnosis			
5-Aminosalicylate	75.0% [*n* = 15/20]	81.8% [*n* = 9/11]	
Immunomodulator	50.0% [*n* = 10/20]	40.0% [*n* = 4/10]	
Biologic	25.0% [*n* = 5/20]	0.0% [*n* = 0/11]	0.133
Primary sclerosing cholangitis	13.6% [*n* = 3/22]	0.0% [*n* = 0/14]	0.537
Presence of multiple post-inflammatory polyps	38.1% [*n* = 8/21]	58.3% [*n* = 7/12]	0.261
Previous or existing stricture within last 5 years	14.3% [*n* = 3/21]	8.3% [*n* = 1/12]	—
Previously diagnosed dysplasia within last 5 years	47.6% [*n* = 10/21]	66.7% [*n* = 8/12]	0.290
Had extensive moderate–severe active inflammation on their last cancer-negative surveillance colonoscopy	50.0% [*n* = 11/22]	28.6% [*n* = 4/14]	0.204
High-risk surveillance interval categorization based on risk factors [i.e. meets criteria for annual surveillance]	81.8% [*n* = 18/22]	71.4% [*n* = 10/14]	0.683
Investigation mode of cancer diagnosis			
Endoscopy	63.6% [*n* = 14/22]	28.6% [*n* = 4/14]	0.172
Surgery	27.3% [*n* = 6/22]	64.3% [*n* = 9/14]	
Radiology	9.1% [*n* = 2/22]	7.1% [*n* = 1/14]	
Location of CRC			
Distal colon/rectum	63.6% [*n* = 14/22]	64.3% [*n* = 9/14]	0.968
Proximal colon	36.4% [*n* = 8/22]	35.7% [*n* = 5/14]	
TNM stage			
Early stage [I–II]	54.5% [*n* = 12/22]	71.4% [*n* = 10/14]	0.311
Advanced stage [III–IV]	45.5% [*n* = 10/22]	28.6% [*n* = 4/14]	
Cancer-related deaths	40.9% [*n* = 9/22]	14.3% [*n* = 2/14]	0.142

RESULTS - SURVEILLANCE PCCRC



Characteristics of the last cancer-negative surveillance colonoscopy	PCCRCs, *N* [%] or median [IQR]	Surveillance-detected CRCs, *N* [%] or median [IQR]	*p*-value
Median duration from last surveillance colonoscopy to cancer diagnosis [months]	15.0 [IQR 10.0–27.3]	2.0 [IQR 1.0–5.0]	**0.001**
Median interval between penultimate and last surveillance colonoscopy [months]	14.5 [IQR 8.5–27.3]	17.0 [IQR 6.0–21.0]	0.530
Inappropriately delayed surveillance interval before or after last surveillance colonoscopy [delayed by at least 2 months from recommended surveillance interval due to patient non-attendance, endoscopist non-compliance with recommendations, administrative booking delays]	59.1% [*n* = 13/22]	53.8% [*n* = 7/13]	0.762
Inadequate bowel preparation	9.1% [*n* = 2/22]	7.1% [*n* = 1/14]	1.000
Dye spray chromoendoscopy use			
Yes	45.5% [*n* = 10/22]	78.6% [*n* = 11/14]	**0.049**
No [due to inadequate bowel preparation or active inflammation]	45.5% [*n* = 10/22]	14.3% [*n* = 2/14]	
No [reason not clear]	9.1% [*n* = 2/22]	7.1% [*n* = 1/14]	
Endoscopist expertise			
Consultant endoscopist with specialist expertise in complex polypectomy	50.0% [*n* = 11/22]	42.9% [*n* = 6/14]	—
Other consultant endoscopist	31.8% [*n* = 7/22]	50.0% [*n* = 7/14]	
Non-consultant endoscopist	18.2% [*n* = 4/22]	7.1% [*n* = 1/14]	
Incomplete colonoscopic examination to caecum or anastomosis [due to poor bowel preparation, impassable stricture, technical difficulty, or unclear reason]	13.6% [*n* = 3/22]	7.1% [*n* = 1/14]	1.000
Rectal retroflexion photo-documented	68.2% [*n* = 15/22]	75.0% [*n* = 9/12]	1.000
Histologically active inflammation at the location of subsequent cancer			
Quiescent/normal	47.6% [*n* = 10/21]	35.7% [*n* = 5/14]	—
Mild	23.8% [*n* = 5/21]	42.9% [*n* = 6/14]	
Moderate	28.6% [*n* = 6/21]	14.3% [*n* = 2/14]	
Severe	0.0% [*n* = 0/21]	7.1% [*n* = 1/14]	
Lesion detected within colonic segment of subsequent cancer	54.5% [*n* = 12/22]	85.7% [*n* = 12/14]	0.076
Morphology of lesion detected within colonic segment of subsequent cancer			
Polypoid	33.3% [*n* = 4/12]	25.0% [*n* = 3/12]	—
Non-polypoid	50.0% [*n* = 6/12]	66.7% [*n* = 8/12]	
Stricture	8.3% [*n* = 1/12]	0.0% [*n* = 0/12]	
Invisible [detected on random biopsy]	8.3% [*n* = 1/12]	8.3% [*n* = 1/12]	
Histology of visible lesions biopsied within colonic segment of subsequent cancer:			
Low-grade dysplasia [LGD]	41.7% [*n* = 5/12]	50.0% [*n* = 6/12]	—
High-grade dysplasia [HGD]	33.3% [*n* = 4/12]	41.7% [*n* = 5/12]	
Regenerative/inflammatory/no dysplasia	25.0% [*n* = 3/12]	8.3% [*n* = 1/12]	
Visible lesion at colonoscopy located at site of subsequent cancer, detected and/or resected by:	*N* = 11 Detected: Resected:	*N* = 11 Detected: Resected:	—
Endoscopist with specialist expertise in complex polypectomy	72.7% [*n* = 8] 0.0%	54.5% [*n* = 6] 0.0%	
Other consultant endoscopist	27.3% [*n* = 3] 0.0%	45.5% [*n* = 5] 0.0%	

WEO - PCCRC ROOT CAUSE ANALYSIS

WEO – PCCRC CATERGORY A

Likely incomplete section of previously identified lesion

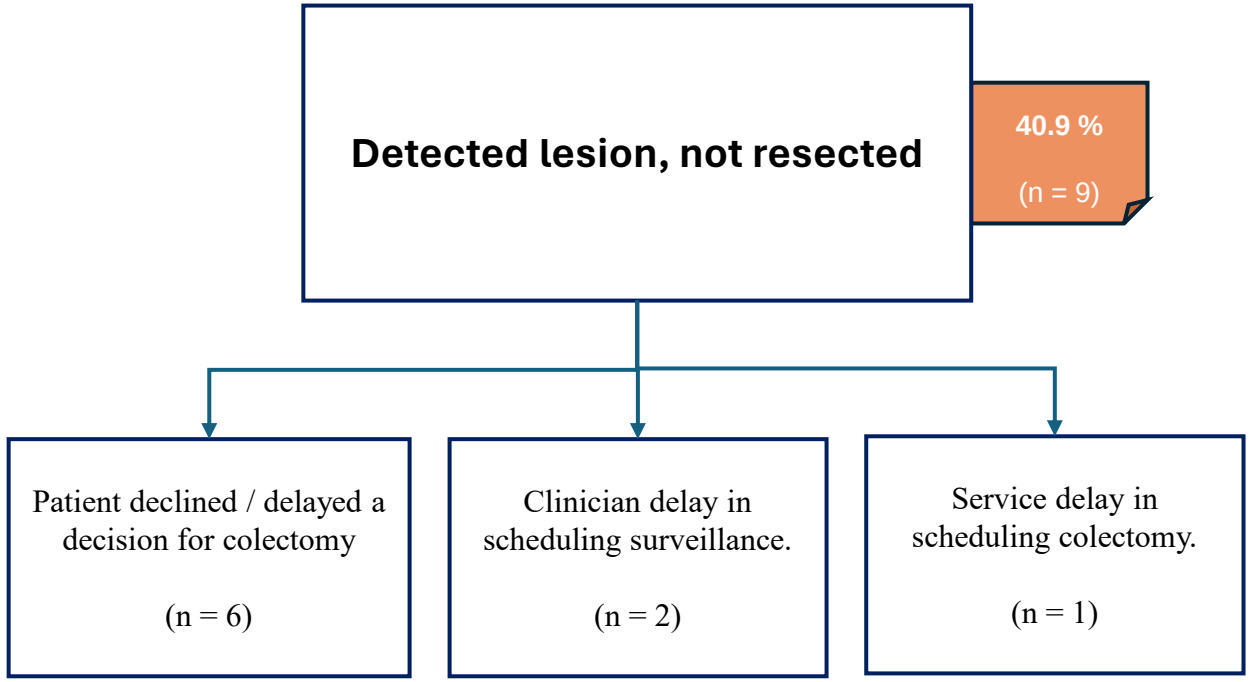
0 %

(n = 0)

KEY MESSAGE

- Reflection of centralizing resections to specialist expert endoscopists

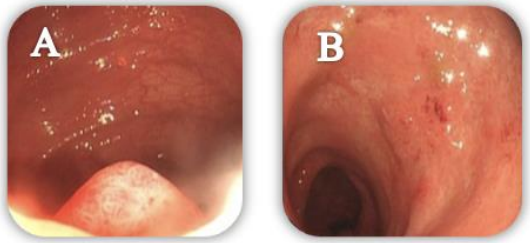
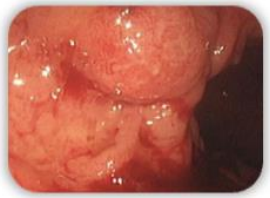
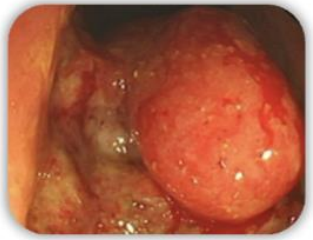
WEO – PCCRC CATEGORY B



- All high-risk annual surveillance category (*known dysplasia, colonic stricture or active pancolitis).*
- Most performed by expert endoscopists (77.8%; n = 7/9)
- No lesions endoscopically resectable
  - LGD (55.5%; n = 5/9)
  - HGD (44.4%; n = 4/9)
  - Majority (88.9%) within segments of active inflammation
- Most [77.8%; n = 7/9] dx at an early stage [TNM I–II]

KEY MESSAGES

- Specialist expert endoscopist for high-risk surveillance = appropriate diagnosis and management of detected lesions
- Patient education requires improvement
- Service optimisation required

Case details (including risk factors before LSC)	Second from last (penultimate) surveillance colonoscopy findings before CRC diagnosis	Last surveillance colonoscopy findings before CRC diagnosis	Time from LSC to CRC diagnosis	Cancer detection method
Ulcerative colitis, Montreal E3 **Intermediate-high risk CRC factors:** ▪ Moderate active pancolitis ▪ Post-inflammatory polyps ▪ Previous invisible LGD	▪ Performed by consultant endoscopist without subspecialist expertise in complex polypectomy ▪ Mild active pancolitis ▪ 10mm LGD lesion in transverse colon resected (A) ▪ Indefinite for dysplasia from rectal biopsies (B) 	▪ Re-examination 4 months later by consultant endoscopist without subspecialist expertise in complex polypectomy supervising trainee ▪ Moderate active pancolitis. 30mm unresectable lesion in rectum. LGD detected on biopsy but not escalated to IBD MDT ▪ Seen in clinic 10 months later. Repeat colonoscopy requested 	11 months	▪ Delayed surveillance colonoscopy detected 50mm exophytic rectal and sigmoid cancers (TNM stage IV) 

WEO – PCCRC CATEGORY C

Possible missed lesion, prior exam adequate

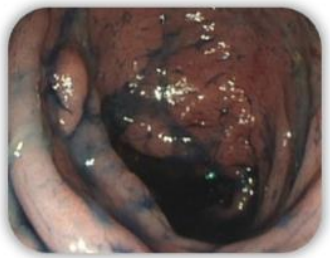
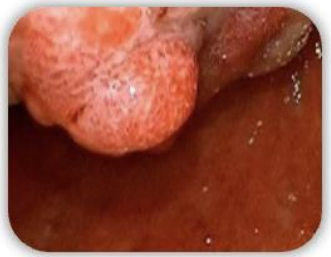
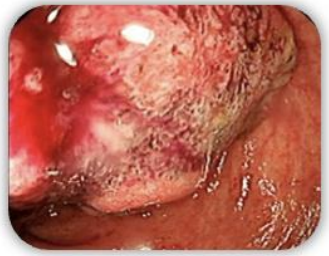
36.4 %

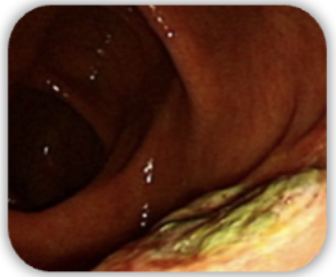
(n = 8)

- 75% (n=6) had high CRC risk factors + colonoscopy by non-expert endoscopist
- 87.5% (n=7) CRCs located in colonic segments with active inflammation / post-inflammatory change on last cancer-negative surveillance colonoscopies.
  - Only 3 endoscopists prompted escalated treatment
  - New rectal stricture dx but not biopsied (subsequent cancer)
- Chromoendoscopy not used in 62.5% (n=5) due to active inflammation
- 87.5% (n=7) had inappropriately prolonged surveillance intervals either before or after their last surveillance colonoscopy.

KEY MESSAGES

- Non-specialist expert endoscopist = higher lesion miss-rate in high-risk surveillance
- Patient education requires improvement
- Service optimisation required

Case details (including risk factors before LSC)	Second from last (penultimate) surveillance colonoscopy findings before CRC diagnosis	Last surveillance colonoscopy findings before CRC diagnosis	Time from LSC to cancer detection	Cancer detection method
Ulcerative colitis, Montreal E3 **Intermediate-high risk CRC factors:** ▪ Moderate active pancolitis ▪ Post-inflammatory polyps	▪ Performed by non-consultant independent endoscopist ▪ Mild active pancolitis ▪ Post-inflammatory polyps noted in the descending colon – no dysplasia on biopsy 	▪ Surveillance 18 months later (patient did not attend scheduled annual surveillance) by non-consultant independent endoscopist ▪ Moderate active pancolitis ▪ Lesion in descending colon thought to be post-inflammatory. Reactive atypia on biopsy 	10 months	▪ Interval inpatient sigmoidoscopy performed for flare assessment ▪ 60mm descending colon CRC detected ▪ TNM stage II 

Case details (including risk factors before LSC)	Second from last (penultimate) surveillance colonoscopy findings before CRC diagnosis	Last surveillance colonoscopy findings before CRC diagnosis	Time from LSC to cancer detection	Cancer detection method
Ulcerative colitis, Montreal E3 **Intermediate-high risk CRC factors:** ▪ Previously resected LGD ▪ Mild active inflammation ▪ PSC	▪ Performed by non-consultant independent endoscopist ▪ Quiescent colitis ▪ No dysplasia detected with chromoendoscopy	▪ Surveillance 14 months later by non-consultant independent endoscopist (service delay in scheduling) ▪ Mild active inflammation in proximal colon ▪ No dysplasia detected with chromoendoscopy	14 months	▪ Next surveillance colonoscopy detected ulcerated cancer in ascending colon (TNM stage III) 

WEO – PCCRC CATEGORY D

Possible missed lesion, prior exam negative but inadequate

13.6 %

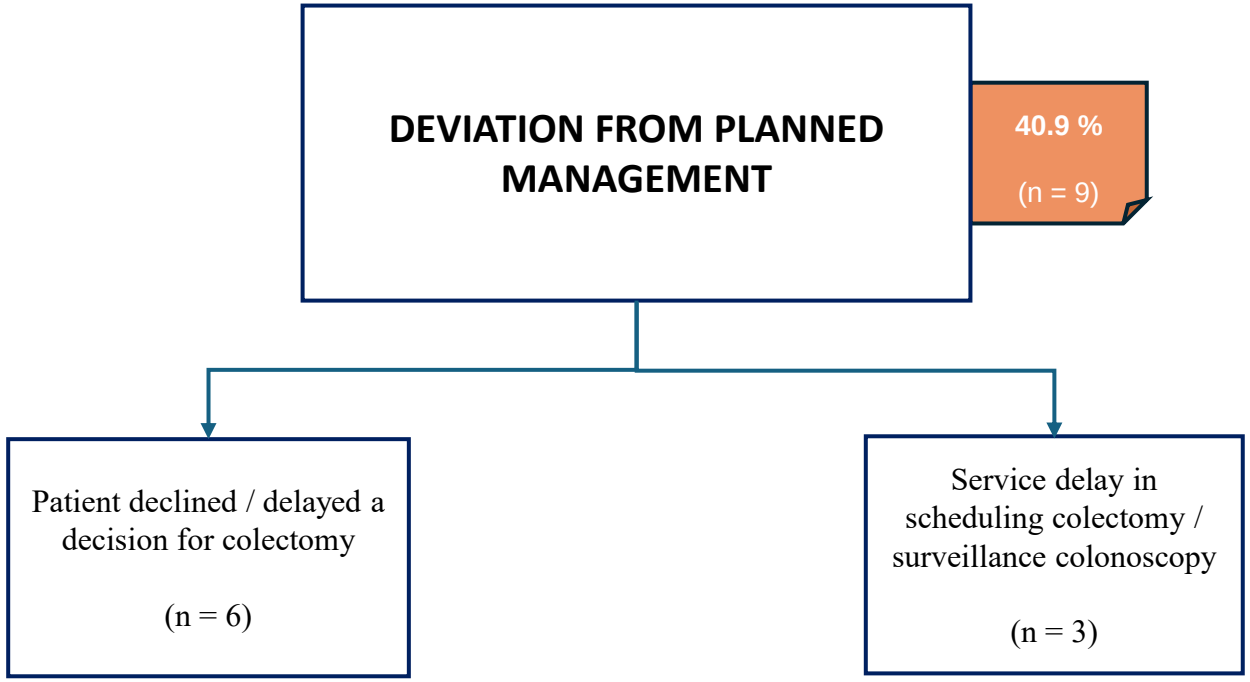
(n = 3)

- All located caecum and ascending colon (n = 3)
  - Inadequate caecal pole visualised (n = 2)
- No dye chromoendoscopy (n = 3) due to poor prep / active inflammation
- Surveillance in all inappropriately scheduled for > 12 months (patient and service delays)

KEY MESSAGES

- Patient education requires improvement
- Service optimisation requires improvement

WEO – PCCRC CATEGORY E ‘ OTHER’



KEY MESSAGES

- Patient education requires improvement
- Service optimisation requires improvement

Pre-procedural

IDENTIFY THE RIGHT PATIENTS:

-Maintain prospective surveillance database

-Risk stratify and prioritise intermediate/high-risk patients

SCHEDULING SURVEILLANCE:

-Dedicated time slots (at least 45 mins)

-Intermediate/high-risk patients on most experienced endoscopist lists

PREPARATION:

-Endoscopist training in chromoendoscopy, dysplasia detection and resection

-Patient education to optimise bowel preparation, medical therapy and interval adherence

-Proactive assessment and therapy escalation for active inflammation

Intra-procedural

OPTIMISE LESION DETECTION:

-Right equipment: high definition, dye spray and virtual chromoendoscopy

-Targeted biopsies but random where mucosal assessment diffcult e.g. active inflammation, post-inflammatory change, or consider in high-risk cases e.g. previous dysplasia

LESION ASSESSMENT:

- Aim to resect lesions en-bloc (may require referral to specialist endoscopist)
- Take peri-lesional biopsies
- Targeted biopsies including strictures, isolated ulcers and large (15 mm) post-inflammatory polyps
- Biopsy extensively if a lesion is unresectable

Post-procedural

CONSIDER MISSED LESIONS:

- Early repeat if inadequate mucosal visualisation
- If suspicious lesion but negative biopsies, review histology or early repeat
- Further imaging for strictures and unexplained rectal pain
- Escalate medical therapy if active inflammation and repeat

MANAGEMENT OF DYSPLASIA:

- Discuss all cases at a multi-disciplinary team meeting
- Fast-track unresectable high-grade dysplasia for colectomy
- Early discussion regarding colectomy with high-risk patients, particularly if difficult surveillance e.g. extensive post-inflammatory change

EDUCATION:

- Root cause-analysis of cancers with closed feedback loop

QUESTIONS?

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