

## 1. Rationale and Background

Patients with longstanding ulcerative colitis and Crohn's colitis have a well-established increased risk of colorectal cancer (CRC). Surveillance colonoscopy is widely recommended and has been associated with a reduction in CRC-related mortality.(Bye *et al.*, 2017) However, variability in how surveillance is defined and implemented, and whether it leads to earlier cancer detection, remains a key question. This systematic review will focus on the impact of colonoscopic surveillance on the stage of CRC at diagnosis in IBD patients, specifically assessing whether surveillance is associated with early-stage detection. The review aims to shift the discussion from whether surveillance is beneficial to how adherence and strategy can be optimised to prevent late-stage CRC.

## 2. Objectives

Primary Objective:

- To determine whether surveillance colonoscopy is associated with increased detection of early-stage CRC (Dukes A/B or TNM Stage 0–2) and decreased detection of late-stage CRC (Dukes C/D or TNM Stage 3–4) in patients with IBD.

Secondary Objectives:

- To explore factors associated with late-stage CRC detection despite surveillance.
- To inform future research and policy efforts toward improving adherence to and optimisation of surveillance strategies.

## 3. PICO

Population: Adults with ulcerative colitis or Crohn's colitis and colorectal cancer.

Intervention: Any colonoscopic surveillance conducted with the intent to detect dysplasia or early CRC.

Comparator: No surveillance or colonoscopy not performed with surveillance intent (e.g., >3 years interval, symptomatic investigation only).

Outcome: Stage of CRC at diagnosis (early-stage vs late-stage).

## 4. Surveillance Definition Tiers

Given the variability in surveillance definitions, a tiered categorisation will be applied:

- Tier 1 (Strict): Colonoscopy performed at regular intervals (e.g., every 1–3 years) in line with accepted surveillance guidelines.
- Tier 2 (Liberal): Any colonoscopy conducted with surveillance intent, including single or non-interval colonoscopies.

Subgroup analyses will explore outcomes by tier.

## **5. Eligibility Criteria**

Inclusion:

- Observational cohort or case-control studies (or RCTs, if any) comparing tumour stage at CRC diagnosis between surveillance and non-surveillance groups.
- Patients with IBD (UC, Crohn's colitis, or IBD-unclassified).
- Report on tumour stage at CRC detection.

Exclusion:

- Case series without comparison groups.
- Studies where colonoscopy was diagnostic only or CRC staging was not reported.

## **6. Outcomes of Interest**

Primary Outcomes:

- Early-stage CRC detection: Dukes A/B or TNM Stage 0–2.
- Late-stage CRC detection: Dukes C/D or TNM Stage 3–4.

## **7. Search Strategy**

Databases: MEDLINE, EMBASE, CENTRAL, Cochrane IBD Register.

Other sources: ClinicalTrials.gov, WHO ICTRP, and abstracts from ECCO, DDW, UEGW, BSG (past 5 years).

Study period: From 2016 onward, no language restrictions.

## **8. Study Selection and Data Extraction**

Two reviewers will independently screen studies and extract data on:

- Study design, setting, and population.
- Surveillance definitions and adherence.
- CRC detection and tumour stage.

## **9. Risk of Bias**

Assessed using the ROBINS-I. Sensitivity analyses will exclude studies with high risk of bias or unclear surveillance definitions.

## **10. Data Synthesis**

Primary meta-analysis: Pooled odds ratios for early vs late-stage CRC between surveillance and non-surveillance groups.

Heterogeneity assessed with  $I^2$  and  $\text{Chi}^2$ . Random-effects model used if  $I^2 > 50\%$ .

Subgroup analyses by surveillance tier, IBD subtype, geography, and study decade.

## **11. GRADE Assessment**

GRADE applied to the primary outcome (stage of CRC at diagnosis) to assess certainty of evidence.

## **12. Ethics and Dissemination**

No ethical approval required. Findings will be submitted for publication in a peer-reviewed journal and presented at relevant scientific meetings.

## **13. Funding and Conflicts of Interest**

No external funding

## **14. Registration**

This protocol will be registered with PROSPERO /online repository.