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MICROBIOTA-TARGETED THERAPIES FOR PREVENTION OF COLORECTAL ADENOMA RECURRENCE AFTER POLYPECTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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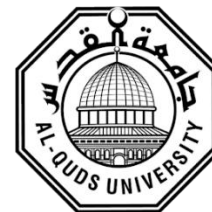
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Abstract

Background: Colorectal cancer is the third most common malignancy worldwide, with approximately 1.9 million new cases annually. Despite effective removal of premalignant lesions, colorectal adenoma recurrence remains a major clinical challenge, affecting up to 60% of patients within five years after polypectomy. Current chemopreventive strategies are limited by modest efficacy or safety concerns. Aspirin benefits only a narrow population, while NSAIDs and nutritional supplements have shown no consistent benefit. Emerging evidence implicates gut microbiota dysbiosis in colorectal carcinogenesis, providing a strong biological rationale for microbiota-targeted interventions.

Objectives: To conduct a systematic review and meta-analysis pooling probiotics, prebiotics, and microbiome-modulating agents under a unified framework to estimate their collective and class-specific efficacy in preventing colorectal adenoma recurrence following polypectomy, and to assess the certainty of evidence.

Methods: This systematic review and meta-analysis was conducted in accordance with PRISMA 2020 guidelines and registered with PROSPERO (CRD420251247058). PubMed, Embase, CENTRAL, and Web of Science were searched from inception through November 2025 for randomized controlled trials evaluating microbiota-targeted therapies versus placebo or no treatment in adults post-polypectomy. The primary outcome was adenoma recurrence at surveillance colonoscopy. Risk ratios (RR) were pooled using random-effects models. Risk of bias was assessed using Cochrane RoB 2, and certainty of evidence was evaluated using GRADE.



Results: Four randomized controlled trials ($n = 1,808$) were included, evaluating berberine, *Lactobacillus casei*, *Clostridium butyricum*, and lactulose. Probiotic-only analysis (2 trials, $n = 778$) showed no significant reduction in adenoma recurrence (RR 0.89, 95% CI 0.76–1.05; $p = 0.159$; $I^2 = 0\%$). In contrast, pooled analysis of all microbiota-targeted therapies demonstrated a significant 20% relative risk reduction (RR 0.80, 95% CI 0.67–0.96; $p = 0.015$; $I^2 = 49.4\%$), corresponding to a number needed to treat of 11. Subgroup analysis showed the strongest effect with lactulose (RR 0.41) and a significant effect with berberine (RR 0.77), while probiotics alone were not effective. The certainty of evidence was low.

Conclusions: Microbiota-targeted therapies may reduce colorectal adenoma recurrence with a number needed to treat of 11, comparable to aspirin but without its restricted eligibility criteria. This effect appears to be driven primarily by prebiotics and microbiome-modulating agents rather than probiotics alone. Given the low certainty of evidence, larger high-quality trials are required before clinical implementation.

Keywords: Colorectal adenoma; Adenoma recurrence; Chemoprevention; Gut microbiota; Probiotics; Prebiotics; Berberine; Polypectomy; Systematic review; Meta-analysis.