



REVIEW ARTICLE

# Fecal microbiota transplantation as therapy for inflammatory bowel disease: A systematic review and meta-analysis



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## KEYWORDS

Fecal microbiota transplantation;  
Inflammatory bowel disease;  
Microbiome;  
Systematic review;  
Meta-analysis;  
Mucosal healing

## Abstract

**Background and aims:** Fecal microbiota transplantation (FMT) has gained interest as a novel treatment option for inflammatory bowel diseases (IBD). While publications describing FMT as therapy for IBD have more than doubled since 2012, research that investigates FMT treatment efficacy has been scarce. We conducted a systematic review and meta-analysis to evaluate the efficacy of FMT as treatment for patients with IBD.

**Methods:** A systematic literature search was performed through May 2014. Inclusion criteria required FMT as the primary therapeutic agent. Clinical remission (CR) and/or mucosal healing were defined as primary outcomes. Studies were excluded if they did not report clinical outcomes or included patients with infections.

**Results:** Eighteen studies (9 cohort studies, 8 case studies and 1 randomized controlled trial) were included. 122 patients were described (79 ulcerative colitis (UC); 39 Crohn's disease (CD); 4 IBD unclassified). Overall, 45% (54/119) of patients achieved CR during follow-up. Among the cohort studies, the pooled proportion of patients that achieved CR was 36.2% (95% CI 17.4%–60.4%), with a moderate risk of heterogeneity (Cochran's  $Q$ ,  $P = 0.011$ ;  $I^2 = 37\%$ ). Subgroup analyses demonstrated a pooled estimate of clinical remission of 22% (95% CI 10.4%–40.8%) for UC ( $P = 0.37$ ;  $I^2 = 0\%$ ) and 60.5% (95% CI 28.4%–85.6%) for CD ( $P = 0.05$ ;  $I^2 = 37\%$ ). Six studies performed microbiota analysis.

**Abbreviations:** FMT, fecal microbiota transplantation; CR, clinical remission; IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; CDI, *Clostridium difficile* infection; PICOS, Population, Intervention, Control, Outcomes, Study design; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; ACG, American College of Gastroenterology; DDW, digestive disease week; AIBD, advances in IBD; ECCO, European Crohn's and Colitis Organization; NASPGHAN, North American Society for Pediatric Gastroenterology, Hepatology and Nutrition; ESPGHAN, European Society for Pediatric Gastroenterology, Hepatology and Nutrition.

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**Conclusions:** This analysis suggests that FMT is a safe, but variably efficacious treatment for IBD. More randomized controlled trials are needed and should investigate frequency of FMT administration, donor selection and standardization of microbiome analysis.

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## 1. Introduction

Fecal microbiota transplantation (FMT) has become an increasingly popular avenue of inquiry for patients with inflammatory bowel disease (IBD). Prior to 2013, research that explored the treatment efficacy of FMT was generally limited to patients with *Clostridium difficile* infections (CDI). Data from this body of research demonstrated excellent results within this patient population.<sup>1</sup> FMT research has been sparse outside of the context of CDI and is limited to case reports alone for the IBD patient population.<sup>2–9</sup> As a result, the two systematic reviews of this topic were completed in 2012 and 2013 and were predominantly comprised of case reports.<sup>10,11</sup> These studies included IBD patients both with and without co-morbid CDI and were limited in quantitative analysis due to the statistical limitations of existing publications.

In this updated systematic review and meta-analysis, we investigate the efficacy of FMT as therapy for IBD. We performed a pooled analysis and meta-analysis with data from the first published cohort studies on this topic. Secondly, we examined the safety of FMT among the IBD population and treatment efficacy associated with microbiota analysis.

## 2. Methods

### 2.1. Search strategy and study selection

A systematic literature search was performed and used MOOSE, PRISMA and Cochrane guidelines.<sup>12–14</sup> The MOOSE checklist was followed accordingly.<sup>12,14</sup> The systematic literature search was conducted using EMBASE (1947–May 2014), MEDLINE (1950–May 2014), the Cochrane library and Biomed Central Cases Database. Proceedings from annual meetings of national and international gastroenterology conferences (American College of Gastroenterology (ACG), Digestive Disease Week (DDW), Advances in IBD (AIBD), European Crohn's and Colitis Organization (ECCO), North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN), European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the British Society of Gastroenterology annual meeting) were searched manually from 2010 up to and including May 2014.

A Population, Intervention, Comparison, Outcomes, Study (PICOS) design question was designed to determine inclusion and exclusion criteria. Databases were searched with the following alternatives for fecal microbiota transplant: "fecal",

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