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Systematic Review: targets for interventions for faecal incontinence in Inflammatory
Bowel Disease

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Summary

Background: Prevalence of faecal incontinence is greater in patients with inflammatory bowel disease than in the general population. It is a major concern for patients with inflammatory bowel disease, even when disease is in remission. It is underreported and negatively affects quality of life.

Aims: To explore the evidence on the associations of faecal incontinence in inflammatory bowel disease and the effectiveness of interventions.

Methods: Databases searched in October 2017: Web of Science, MEDLINE, EMBASE, CINAHL, PsycINFO, British Nursing Index and Scopus. Manual search of reference lists was also conducted. Four researchers independently screened references and extracted data.

Results: Eighteen studies were included in the review (14 on associations, four on interventions). Presence of faecal incontinence was reported as 12.7-76% among 5924 participants, varying in definitions adopted and populations studied. Factors associated with faecal incontinence included disease activity, loose stool, female gender, childbirth, previous surgery, anal sphincter weakness or fatigability, anxiety and depression. The cross-sectional design of studies means causation cannot be inferred. Interventions included surgery (sphincter repair and sacral nerve stimulation) and tibial nerve stimulation which each improved faecal incontinence. However, the four intervention studies were small (34 participants in total) and uncontrolled.

Conclusions: There is a high prevalence of faecal incontinence in inflammatory bowel disease, associated with various sociodemographic, clinical and psychosocial factors which could be targeted in future interventions. Future intervention studies with control

groups, targeting likely underlying causes such as disease activity, loose stool, psychological factors and anal sphincter function, are needed.

Key words: inflammatory bowel disease, faecal incontinence, interventions, systematic review

INTRODUCTION

Inflammatory bowel disease (IBD) mainly comprises Crohn's disease (CD) and ulcerative colitis (UC). IBD causes relapsing-remitting gut inflammation and a number of debilitating symptoms including abdominal pain, fatigue, diarrhoea and urgency, with or without faecal incontinence (FI).

FI is a distressing personal and social hygiene problem ^{1, 2}. Individuals may be unaware of bowel leakage (passive soiling) or feel sudden urgency but be unable to reach a toilet in time (urge incontinence) ¹. In the general population, 1-15% of adults experience FI ^{3 4 5}. The prevalence is greater amongst those with IBD, however, definitional differences of 'incontinence' and selective study samples have resulted in varying prevalence reports. A systematic review has reported a pooled prevalence (from six studies) of 24% FI in people with IBD ⁶. This previous review focused on anorectal function rather than wider, potentially modifiable, associations.

FI has a negative emotional and psychosocial impact and often leads to social isolation and poorer quality of life². Fear of FI can be as restricting as the event itself in terms of daily and social functioning. Some IBD patients do not leave their homes for fear of experiencing FI ¹. Despite bowel control being reported as one of the main concerns of patients with IBD, it remains a taboo subject between patients and physicians^{1,7}. Of IBD patients reporting FI, only 38% had sought help for the symptom and less than half of these felt satisfied with the help they received ⁸. Patients find FI embarrassing to discuss whilst clinicians avoid raising the issue due to limited knowledge on how to manage it ². Understanding the factors associated with FI and reviewing the interventions available to manage this symptom should identify targets for future health interventions.

In the general population, management of FI focuses on a stepwise trial of conservative treatments, such as diet regulation, biofeedback or pelvic floor exercises, before proceeding to more invasive procedures, such as irrigation or surgery^{9, 10}. These methods are often effective in non-IBD populations¹¹⁻¹³ but have not been reported in IBD.

AIMS

Review questions:

- Which clinical and psychosocial factors are associated with the presence, frequency and severity of IBD-related FI?
- What interventions have been used for the management of IBD-related FI and how effective are they?

METHODS

Protocol and registration

The review was registered as a novel systematic review:

http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017076928

[published 21.09.17]. The review methods, objectives and eligibility criteria

are specified in detail in this protocol.

Eligibility criteria

Study inclusion and exclusion criteria were pre-specified (Online Supplementary Table 1). We included people with IBD of any sub-type and all quantitative observational and

interventional designs. We excluded people with IBD and FI secondary to specific surgical procedures such as ileo-anal pouch formation as this has been reviewed elsewhere¹⁴ .

Searches

Databases were searched in October 2017: Web of Science [from 1900], MEDLINE [via OVID, from 1946], EMBASE [via OVID, from 1974], CINAHL [from 1996], PsycINFO [via OVID, from 2002], the British Nursing Index [from 1994] and Scopus [from 2004]. The reference lists of papers included were hand searched.

The search strategy involved free-text and subject heading searching [MeSH terms] and was modified for each database. Search terms related to IBD [IBD, inflammatory bowel disease, Crohn's disease, ulcerative colitis,] were combined with terms associated with FI [faecal/fecal incontinence, bowel incontinence, anal incontinence, accidental bowel leakage, defaecation/defecation, incontinence and continence] and terms related to factors [predictors, risks, factors, associations, causes, and relationship] and interventions [treatment, intervention, management, trial, therapy, and care].

Study selection

Studies identified in the search were exported to Endnote bibliographic software (EndNote7).

The searches retrieved 2,820 records. After duplicates were removed, one author (HP) examined all article titles and abstracts, excluding irrelevant papers. The remaining 53 papers and abstracts were read and 34 excluded; if there was doubt about eligibility,

consensus was reached by three authors (HP, CN, BK). . We attempted to contact authors for further details where only an abstract was found. As few full papers were retrieved, abstracts were included. Figure 1 shows the PRISMA flow diagram.

Data extraction

Data were extracted onto an Excel spreadsheet. Missing data were, if possible, retrieved from the original researcher.

QUALITY APPRAISAL

Quality of papers was reviewed independently by at least two of the authors using the appropriate Critical Appraisal Skills Programme (CASP) tool for each study design ¹⁵. Studies were classified as low, medium or high quality (Online Supplementary Table 2). Any disagreement between reviewers about quality scores was resolved through discussion.

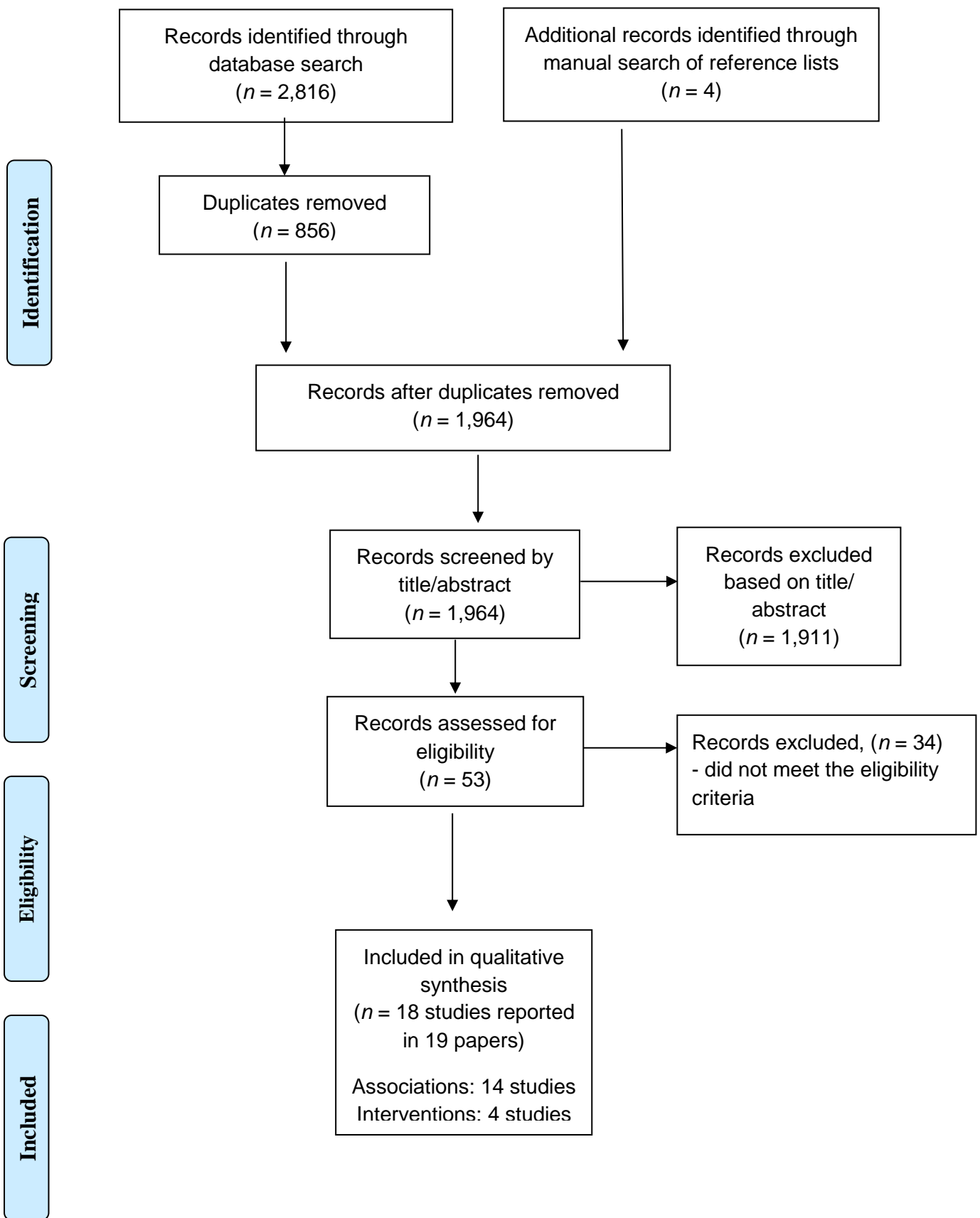


Figure 1. PRISMA flow diagram of citation retrieval and selection process.

Online Supplementary Table 2: Associations with faecal incontinence in IBD (by author)

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
Brochard [2017], France, cross-sectional.	<p>173 women on a database of perianal CD patients (107/173, 62%, had history of anal fistula), with confirmed CD of childbearing age (15-45 years old). Median age 38.2 years (IQR: 28.9-45.6).</p> <p>113/173 parous (65%). 134/173 (77%) reported treatment for CD.</p> <p>Questionnaires mailed to 327 consecutive females referred.</p>	<p>1. Cleveland Clinic Incontinence Score (CCIS) of ≥ 5.</p> <p>2. Obstetric outcomes: gestational age, date, number and term of birth, least and greatest birth weights, mode of delivery (Caesarean Section or vaginal), use of episiotomy, instrumental delivery (vacuum, forceps), vaginal tears (checked with hospital records); demographic and clinical characteristics of CD from hospital records: birth date, age at diagnosis, disease extent, perianal involvement and</p>	<p>65/173, 37.5% (CI 30.7-45.0) reported CCIS ≥ 5. 40/173, 23.1%, (CI 17.5-29.9) had severe FI (CCIS ≥ 9).</p> <p>Factors associated with FI in whole cohort (multivariate analysis): disease duration ($p=0.02$); history of anal fistula surgery ($p=0.008$); number of childbirths per woman ($p=0.02$); Harvey Bradshaw index >4 ($p=0.0001$); FI not associated with: age at IBD onset or age at most recent follow up ($p=0.72$); history of abdominal surgery ($p=0.08$); anal fistula at most recent follow-up ($p=0.57$); mode and characteristics of delivery (Caesarean Section vs. vaginal), instrumental delivery and experience of obstetric tears or episiotomy were not associated with FI (in univariate analyses, all $p>0.05$). Montreal classification not associated with FI in univariate analysis.</p>	<p>Quality: Medium</p> <p>Some data (pregnancy and deliveries) collected retrospectively.</p> <p>Response rate 56.3%. Patients recruited from a database of perianal CD patients at a tertiary referral centre - selection bias likely- may be increased prevalence of severe CD, and more likely to have perianal</p>

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
	56.3% (173) responded. Stoma and incomplete scores excluded (n = 11).	disease behaviour (Montreal classification), history of anal or major abdominal surgery.	In parous women FI associated with (multivariate analysis): abdominal surgery, anal fistula surgery and Harvey Bradshaw index >4 (p=0.0002). Not associated with number of childbirths or any other obstetric variable. Potential targets for intervention: disease activity	lesions than CD generally. Multivariable analysis conducted.
Duncan [2013], UK, cross-sectional.	380 people with IBD attending an outpatient clinic. 40% UC, 60% CD. 47% female. Median age 38 (IQR 31-50).	1. Any episode of FI in previous 3 months. ICIQ-B. St Marks FI score. 2. Disease activity	67% reported FI in past 3 months. 90% reported anal incontinence (FI + flatus incontinence). No difference in FI rates between CD and UC (p = 0.74). FI reported as strongly associated with current disease activity in CD (p<0.0001) but not in UC. 37% reported FI during both flares and remission. Potential targets for intervention: disease activity in CD	Quality: Abstract only. Author confirmed no further data available. Not clear if participants were consecutive or convenience sample.
Flor [2014], Spain, cross-sectional.	"Random sample" of 340/1004 IBD patients over 18 years attending an IBD clinic. No	1. Cleveland Clinic Incontinence Score: cut-off not stated.	Overall FI 53.6% FI in 58.3% with UC. FI in 49.4% with CD.	Quality: Abstract only. Unclear if truly a random sample,

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
	<p>details on gender or age. Survey administered by a gastroenterologist in person or by phone.</p> <p>334 of 340 responded.</p>	<p>2. Quality of life; stool consistency (unclear how measured; disease flare (unclear how measured)).</p>	<p>Associated with disease flares (64%) and liquid stools (90.5%), gastroenterological surgery and older age in UC.</p> <p>Not related to disease type (UC vs CD), sex. Quality of life worse with FI.</p> <p>Potential targets for intervention: disease activity, liquid stools.</p>	<p>or a convenience sample as abstract also states “selected”.</p>
<p>Gonzalez-Ortiz [2015], Mexico, cross-sectional.</p>	<p>96 with IBD. 78 with UC: 54% female, mean age 43 years; 56% pan-colitis; 82% less than 2 relapses per year, 5% with a pouch. 18 with CD: 67% female, mean age 55 years.</p>	<p>1. Cleveland Clinic Incontinence Score: cut-off not stated.</p> <p>2. Harvey Bradshaw index for CD; Mayo score for UC.</p>	<p>FI in 31% with UC: associated with disease activity (OR 7.5; p = 0.002). FI in 44% with CD: associated with inflammatory behaviour.</p> <p>Potential targets for intervention: disease activity</p>	<p>Quality: Abstract only.</p> <p>Selection of participants and cut off for FI not stated.</p>

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
Kangas, [1992], Finland, case-control.	63 people with CD and 10 controls. CD: 11/63 partially incontinent, 3/63 totally incontinent.	1. Measure of FI not stated. 2. Anorectal manometry. Diarrhoea (measure not stated).	14/63 (22%) with CD had some FI. Incontinent patients had lower resting ($p<0.01$) and squeeze pressures ($p<0.05$) and different (? lower – not stated) rectal capacity than continent people with CD and controls. Potential targets for intervention: diarrhoea, anal resting and squeeze pressure, rectal capacity.	Quality: Abstract only.
Kanis [2015] Netherlands, cross-sectional.	343 women recruited through a patient organisation or social media. 61.5% CD. Mean age 41.8 years (SD 13).	1. St. Mark's Incontinence score (range 0-24). 2. Online survey.	24.0% never had FI. 29.2% seldom had FI. 29.8% sometimes had FI. 8.9% weekly FI. 8.1% daily FI. Median FI score 7 (IQ range 5-10). No difference between CD and UC.	Quality: Abstract only

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
	Median of 16 years since last delivery. 61 had perianal disease. 51.2% nulliparous. 40% had one or more vaginal deliveries.		Univariable analysis: FI score higher if had a previous vaginal delivery (median 8 vs 7, $p=0.02$), but this relationship was lost in multivariable analysis controlling for perianal disease and menopause. FI score higher if postmenopausal (median 8 vs 6, $p=0.001$). Postmenopausal: 66.1% FI; premenopausal 45.9% FI ($p = 0.03$): childless women also increased FI prevalence post-menopausal. Potential target for intervention: menopause therapy?	
Keogh [2017], Ireland, cross-sectional.	250 IBD patients, tertiary care centre. 117 completed the questionnaire	1. International Consultation on Incontinence Questionnaire-IBD.	77/117 (66%) reported any FI. 46.1% of patients were in remission. 30% FI episode in past 3 months. 70% urgency in past 3 months.	Quality: Medium Cut off used for anxiety and

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
	(47% response rate) 46 UC (39%); 71 CD (61%). Female: 66 (56%). Mean age 49 (range not given).	2. Hospital Anxiety and Depression Score (HADS); disease activity index (Harvey Bradshaw Index for CD; Walmsley Index for UC); demographic data; date of diagnosis.	<p>Overall: 52% reported anxiety, 31% depression. Anxiety significantly higher than depression ($p < 0.001$). Anxiety ($p < 0.001$) and depression ($p < 0.005$) were significantly higher in patients with FI compared to those without FI.</p> <p>With FI, 65% reported anxiety; 41% depression. Without FI: 28% reported anxiety; 16% depression.</p> <p>No association between FI and age ($p = 0.69$), gender ($p = 0.99$), disease duration ($p = 0.72$), disease type (CD or UC, $p = 0.71$). No association found between levels of anxiety ($p = 0.43$) or depression ($p = 0.07$) experienced and disease duration. 58% reported that no health professional had addressed the topic of FI during consultations.</p> <p>Potential targets for intervention: anxiety, depression.</p>	<p>depression unclear. No statistical test reported for relationship between disease activity and FI.</p> <p>No multivariable analysis.</p>

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
Neill [2016], USA, cross-sectional.	37 CD patients, outpatient clinic. 36 completed questionnaires (97.2% response rate). Male: 17 (47.2%) Female: 19 (52.8%). Mean age 39.9 (range not given). Mean duration of disease 13.6 years (range 1-34 years)	1. Crohn's Disease Activity (CDAI). Faecal Incontinence Severity Index (FISI). 2. Quality of Life; Short Quality of Life in Inflammatory Bowel Questionnaire (SIBDQ) and Medical Outcomes Short Form 12 (SF-12)	CDAI and FIS were strongly associated with SF12 p <0.001 Correlation Coefficients: SIBDQ and CDAI, -0.79, SIBDQ and FISI, -0.53. Potential targets for intervention: None	Quality: Medium

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
Norton [2013], UK, cross-sectional.	10,000 members of a national Crohn's & Colitis Organisation, selected randomly by computer, sent a postal questionnaire; 4,827 (48%) responses received; 3,264 complete and without a stoma (32.6%) [1,599 UC (49%); 1,543 CD (47%)]; 126 other IBD (4%); 6 missing diagnosis (0.2%). 67% female. Mean age 50.3 years (range 19-92).	1. International Consultation on Incontinence Questionnaire-Bowels) 2. Questionnaire developed by authors, including: demographics, IBD, medical, obstetric history, symptoms & perceptions of stress, anxiety, diet, other factors on FI; Bristol Stool Chart; urinary continence (ICIQ-UI); quality of life (IBDQ). Disease activity: Harvey Bradshaw Index (HBI) for CD; SCCI for UC.	74% (CI 72-75%) of respondents reported some FI. For 9% this was regular. If all non-responders are considered to have no FI, then 24% (CI 23-25%) of people with IBD have some FI; 3% regularly. Multivariable significant variables for presence of FI: age, peaking at 51-60 years (p = 0.05); female gender (OR 0.76 for males, p = 0.003); ileo-anal pouch (OR 2.53, p = 0.04); anal fistula surgery (OR 1.75, p = 0.007); anal fissure (OR 2.32, p = 0.03); abdominal surgery for IBD (OR 1.59, p <0.001) and urinary incontinence (OR 3.34, p <0.001). Vaginal delivery not significant after adjusting for effects of other variables. Multivariable significant variables for frequency of FI: all the above except pouch surgery. For CD, 1 unit HBI increase, increased risk of FI by 25% (p<0.001). For UC, 1 unit SCCI increase, increased FI risk by 28% (p<0.001).	Quality: Medium Self-reported IBD with no verification of diagnosis. Poor response rate. Multivariable analysis conducted.

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
			<p>Looser stool associated with more regular FI (p<0.001), regular FI associated with flatus, poorer QoL and restricted social function vs rare/no FI (all p<0.001).</p> <p>Potential target for intervention: disease activity, loose stool, pelvic floor function (urinary incontinence)</p>	
Ong [2007], UK, case-control.	<p>777 regional members of a National Colitis and Crohn's Organisation; male members asked to complete the questionnaires on behalf of their unaffected female partner as a control group.</p> <p>491 (63%) responses. 477 completed forms; 346 women with IBD [153 UC</p>	<p>1. Questionnaire developed by authors: symptoms of FI. Emphasis on time of onset of FI in relation to IBD diagnosis and childbirth mode of delivery.</p>	<p>229/346 (66.2%) women with IBD parous; CD 67%, UC 65%; 116/131 (88.5%) women without IBD parous.</p> <p>37/229 (16%) women with IBD had caesarean section (CS). 15/116 (13%) women without IBD had had CS (difference for CS rates: $\chi^2=0.62$, p = 0.62).</p> <p>Parous women with IBD: 58/229 (25%) reported FI; 62% attributed this to IBD, 28% dated this to time of vaginal delivery. Parous women without IBD: 6/116 (5.2%). 2/116 (2%) reported FI dating to vaginal delivery.</p> <p>Potential target for intervention: mode of delivery?</p>	<p>Quality: Low</p> <p>Subjective reporting of symptoms, timing and attributions.</p> <p>No multivariable analysis.</p>

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
	(32%); 193 CD (40%)] and 131 female partners without IBD (27%). Age NR			
Papathanasopoulos [2010, 2013], Greece, case-control.	72 total; 58 consecutive patients with IBD at a tertiary centre: 20 UC; 38 CD. 14 healthy controls recruited via advert. Excluded: over 70 years, significant co-morbidities, 3 or more vaginal	1. Faecal Incontinence Severity Scale (FISS) (self-reported). 2. Perianal disease activity index (PDAI); Crohn's disease activity index (CDAI); Simple Clinical Colitis Activity Index (SCCI) for UC. Bristol Stool Chart; daily bowel diary. Oral glucocorticoid use; presence of proctitis; perianal disease.	27/58 (47%) with IBD reported urgency. 13/58 (22%) reported FI. Multivariable analysis: FISS associated with active disease (p = 0.033); anal sphincter fatigue rate index (p = 0.037); defects on ultrasound in the internal (but not external) anal sphincter (p =0.0008); rectal urge volume (p =0.009). Model explained 62% of variance (p < 0.0001). People with IBD and urgency had a more fatigable anal sphincter than people with IBD and no urgency than in healthy controls (p < 0.001).	Quality: Low Very similar or identical data presented in the two papers. Multivariable analysis conducted.

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
	deliveries, current perianal sepsis. 25/72 (34.7%) female. Mean age 42 (IBD) /45 (controls) years.	Anorectal manometry to measure: external anal sphincter fatigability (fatigue rate; anal contractility (maximum squeeze time), and fatigue rate index; rectal compliance. Endoanal ultrasound to detect anal sphincter defects.	FISS scores correlated with looser stool consistency and higher stool frequency. Fatigue rate index and rectal compliance were significantly different in IBD than in healthy controls. Potential target for intervention: disease activity; decrease fatigability of anal sphincter; improve rectal compliance; improve stool consistency and frequency.	
Rao [1988], UK, cross-sectional.	110 assessments carried out in 96 patients with histological proven UC. 60/96 active (endoscopically/histologically); 50/96 quiescent; twice during	1. Symptom questionnaire: presence of FI (defined as the "inability to control defecation voluntarily resulting in leakage of motions and/or soiling of garments").	FI: 14/110 (13%) (12 women, 2 men) with active colitis reported FI (all except 2 were over 60 years of age). There was greater prevalence of FI in those with active UC than quiescent disease in both total and distal colitis (p<0.01). Patients with active disease exhibited higher prevalence of: urgency, incomplete	Quality: Low No multivariable analysis.

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
	active and quiescent periods, hence, 110 assessments. Female: 59/110 (54%). Mean age 48 (range 19-80).	2. Presence/absence of: urgency (an urgent and irresistible desire to defecate); incomplete evacuation (strong, persistent desire to evacuate after defecation); tenesmus (continual inclination to evacuate bowels accompanied by painful straining); pain (lower abdominal or rectal pain, with or without any relation to defecation); perianal soreness (intense discomfort or itching of perianal skin; stool consistency (loose, formed or hard); night time defecation; average daily bowel frequency.	evacuation, tenesmus, pain, anal soreness and FI compared with those with quiescent colitis. Prevalence of symptoms did not vary between total and distal disease. Potential target for intervention: disease activity	
Subasinghe [2016], Sri Lanka, cross-sectional.	184 [153 UC (83%); 31 CD (17%)]	1. St. Mark's Incontinence score (range 0-24).	48/184 (26%) reported FI. 10% of those with FI reported regular FI. 33% reported flatus incontinence. No association between FI and type of IBD. Significant association of FI with	Quality: Medium

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
	IBD patients at a tertiary care hospital. 101/184 (54.9%) female. Mean age 45 (range 20-78).	2. Sociodemographic data, disease characteristics, management details and history; QoL (IBDQ-32)	<p>age, gender and quality of life. Females had significantly higher FI scores than males (79.9 vs 79.34, $p<0.05$).</p> <p>Of those with FI, 70.8% were women.</p> <p>No significant difference between CD and UC in mean FI score (CD=14.45, UC=13.79, $p=0.63$) or bowel symptoms (CD=22.39, UC=21.11, $p=0.22$), social (CD=11.10, UC=11.91, $p=0.3$), systemic (CD=12, UC=12.46, $p=0.56$) and emotional symptoms (CD=34.77, UC=34.04, $p=0.61$).</p> <p>No difference in FI between those who had surgical or medical management of IBD.</p> <p>The extent of colitis was significantly associated with FI scores ($p=0.002$) - patients with distal colitis had higher scores.</p> <p>Association of total IBDQ and FI score was statistically significant ($p<0.001$). Weak association between FI and emotional and systemic QoL components ($r_s<0.3$), moderate association between FI and social QoL ($r_s=0.3-0.7$), strong association between FI and bowel-related QoL ($r_s>0.7$).</p> <p>Potential target for intervention: disease activity (distal colitis)</p>	<p>Main focus on determinants of quality of life. Some values quoted for score are outside the range possible (e.g. score of 79 quoted for incontinence score when the maximum score possible is 24).</p> <p>No multivariable analysis.</p>

Author, year, country, design	Population	1.Faecal incontinence measure/definition 2.Other measures/outcomes	Main findings Potential targets for intervention	Quality of study and comments
Vollebregt [2017], Netherlands, cross-sectional.	Questionnaires sent to 528 CD patients between 2003-2013. 325 completed (62%). 215/325 (66%) female. Median age 42 years (range 19-88).	1. St Mark's incontinence score and Cleveland Clinic incontinence score. 2. Obstetric history, current and past perianal disease, current perianal symptoms, presence of liquid stools, current symptoms of FI, impact of FI on QoL (Faecal Incontinence QoL questionnaire).	65/325 (20%) reported FI for liquid/solid stools at least once in the last 4 weeks. 29/325 (9%) reported gas incontinence only. Multivariate analysis: liquid stools ($p<0.0001$), stricturing disease behaviour ($p=0.02$) and perianal disease ($p=0.03$) were all significantly associated with IBD-FI. Age and diagnosis age lost association with IBD-FI. Those who reported FI more than weekly scored lower on all QoL scales (lifestyle, coping, depression, embarrassment) than those who reported FI less than weekly (all $p<0.05$). Potential target for intervention: liquid stools	Quality: High Multivariable analysis performed.

CCIS, Cleveland Clinic Incontinence Score; CD, Cohn's disease; FI, faecal incontinence; IBD, inflammatory bowel disease; ICIQ-B, Incontinence Symptoms and Impact on Quality of Life; IBD-U, IBD unclassified; UC, ulcerative colitis; QoL, Quality of Life; IBDQ, inflammatory bowel disease questionnaire; NR, Not reported.

RESULTS

A total of 18 studies reported in 19 papers were included. Two very similar papers apparently reporting the same participants were amalgamated^{16, 17}. Fourteen studies reported prevalence and associations of FI (summarised in Table 1, with more detailed data in Online Supplementary Table 2). There were a total of 5,924 participants. Four studies tested interventions for FI with 34 participants (Table 2). Some focused only on female participants to determine the role of childbirth in IBD-related FI^{18, 19}. Some reported both patients with UC and CD whilst others included either CD or UC patients alone. Some studies included IBD patients and a healthy control group whilst others consisted of IBD patients only. Quantitative synthesis such as meta-analysis was not appropriate due to the heterogeneity of the data, thus, a narrative review is presented.

Presence and associations of FI in IBD

Rates of FI varied from 12.7 to 76% across the 14 studies (Table 1). Various definitions of FI were used and response rates varied (Online Supplementary Table 2).

Table 1: Summary of prevalence and associations of faecal incontinence in IBD (by author, year)

Author, year	Number (%) respondents	Percentage of participants reporting FI	Definition of FI to be counted as experiencing FI	Associations
Brochard [2017]	173 (56.3%)	37.5%	Cleveland Clinic Score \geq 5	Disease activity; parity; mode of delivery; surgery
Duncan [2013]	380 (% NR)	67%	Any episode in previous 3 months	Disease Activity in CD only
Flor [2014]	334 (98.2%)	53.6%	Not stated	Disease activity in CD only; loose/ liquid stools
Gonzalez-Ortiz [2015]	96 (% NR)	31-44%	Cleveland Clinic Score: cut off not stated	Disease activity; surgery
Kangas [1992]	63 (% NR)	22.2%	Not stated	Loose/ liquid stools; anal sphincter structure or function
Kanis [2015]	343 (% NR)	76%	Any FI	Post-menopausal
Keogh [2017]	117 (47%)	66%	Any FI	Anxiety; depression
Neill [2016]	36 (97.2%)	20.4%	Faecal Incontinence Severity Index (FISI).	Disease activity; PCS & MCS domains of SF-36
Norton [2013]	3264 (32.6%)	74%	Any FI	Disease activity; age; gender; surgery; loose/ liquid stools; anal sphincter structure or function
Ong [2007]	491 (63%)	25% parous women	Any soiling or wearing a pad	None reported
Papathanasopoulos [2010, 2013]	58 (100%)	22.4%	FI in last 3 months	Disease activity; loose/ liquid stools; anal sphincter structure or function
Rao [1988]	96 (% NR)	12.7%	Any FI	Disease activity
Subasinghe [2016]	184 (% NR)	26%	Any FI	Disease activity; age; gender; surgery

Vollebregt [2017]	325 (62%)	20%	FI at least once in past 4 weeks	Loose/ liquid stools
Total	5960			

Key: FI, faecal incontinence; NR, not reported; CD, Crohn's disease; PCS, Physical Component Summary; MCS, Mental Component Summary; SF-36, Short Form 36.

Note: further details of the studies, their method, results and quality appraisal are given in Online Supplementary Table 2.

Table 2: Interventions for faecal incontinence in IBD (by author)

Author, year, country, design	Population	Intervention	Faecal incontinence measure and outcomes of intervention	Quality of study and comments
Alvarez [2011], Spain, cohort study	10 patients with CD. 3/10 female; mean age 37 years (range 21-53) and complex perianal fistula and an anal sphincter defect; FI to solid stool. Mean of 3 previous fistula procedures (range 1-10).	Induction therapy with Infliximab 5mg/kg at weeks 0, 2 and 6. Then surgical repair of sphincter; fistula also cored out and seton inserted for 3 patients. Infliximab continued each 8 weeks and azathioprine 2.5mg for at least 6 months. 2 patients delayed surgery until proctitis settled on drug regimen. Antibiotics for 7 days post-operatively. No covering stoma. Seton removed	Measures: Cleveland Clinic Incontinence Score (CCIS); other continence symptoms. Outcomes: CCIS score improved from 18.0 (baseline) to 10.0 post-operatively (p= 0.003) and 9.3 at 48 months (p= 0.001). Results appeared worse if urgency was present pre-operatively (p=0.003). 6/10 fully continent; 3/10 FI for liquid stool; 1/10 incontinent of flatus. 7/10 reported improved quality of life. No difference between patients who continued or discontinued Infliximab. All patients reported that they would repeat the procedure again.	Quality: High Variable disease course post-operatively: 7/10 had change in drug regimen over time. No control group.

Author, year, country, design	Population	Intervention	Faecal incontinence measure and outcomes of intervention	Quality of study and comments
		after 2 post-operative infliximab doses.	3/10 had postoperative complications with one delayed healing (5 months) and 2 abscess and recurrent fistulae.	
Vitton [2009], France, cohort study	12 patients with IBD (7 CD, 3 UC, 2 IBD-U; 9/12 female. Median age 51 years (range 29-64). 9/12 previous abdominal surgery; 6/12 with anal fistula. FI reported for 6-240 months, median 59 months. Median continence score 13.5 at baseline.	Transcutaneous posterior tibial nerve stimulation 20 minutes daily for 3 months: self-administered via TENS machine at home. Stimulation at 10Hz, 200 μ s, 10-30 mA, set at just below sensory threshold	Measures: Cleveland Clinic Incontinence Score (CCIS); 0-5 VAS: 0-100 QoL scale. Outcomes at 3 months: CCIS: Improved in 4; unchanged in 6; worse in one. VAS improved in 5/12 (42%); QoL also improved in these 5, who all continued treatment after the study. 3 patients reported greater time to defer defecation.	Quality: Low Text reports only 1/12 improved on CCIS; Table reports 4 improved this score. Methods describe statistical tests but no results are presented. No control group.
Vitton [2008], France, cohort study	5 patients with CD. 3/5 female. Median age 48 years (range 27-67). Perineal lesions with internal and external anal sphincter defects and CCIS >5/20.	Sacral nerve stimulation: temporary for 3 weeks then permanent implant.	Measures: Cleveland Clinic Incontinence Score (CCIS). Number of daily stools. VAS QoL. Outcomes (at median 14 months, range 3-36 months): no figures given but CCIS reported to have decreased by at least 50%, number of stools and episodes of FI (all p<0.05). QoL also reported to have improved by over 50%.	Quality: Low No figures reported for any of the outcome measures. No control group. Unclear if some patients had

Author, year, country, design	Population	Intervention	Faecal incontinence measure and outcomes of intervention	Quality of study and comments
				temporary stimulator only and were excluded.
Scott [1989], UK, cohort study	7 patients with anorectal CD. 6 reported as one lost to follow up. 5/6 female. Age 12-48 years. All with previous perianal surgery (3 abscess, 3 fistula) + 1 obstetric trauma as well. All with colonic resection.	Overlapping anal sphincter repair (1 + rectopexy & hemicolectomy; 1 + closure of rectovaginal fistula); 5 with covering stoma (closed 2-20 months post operatively).	Measures: FI measure not specified. Unclear how FI was assessed (clinician recorded in medical notes?) One wound breakdown at 16 days, re-repair, persisting FI and permanent colostomy. 5/6 reported as fully continent at mean of 7.8 years (range 1.5-16 years).	Quality: Low No control group. Unclear how patients were selected and if this is a complete series. No information on how outcomes were assessed.

Abbreviations: CCIS = Cleveland Clinic Incontinence Score, CD = Cohn's disease, FI = faecal incontinence, IBD = inflammatory bowel disease, IBD-U= IBD unclassified, UC = ulcerative colitis, QoL = Quality of Life. VAS = visual analogue scale.

Associations of FI in IBD: targets for health interventions

Disease Activity

A significant positive association between FI and IBD disease activity measured by a disease activity index (DAI) was found in all but one study which measured this ²⁰. Active disease was significantly associated with the presence ^{2, 16, 18, 21} and the severity of FI ¹⁶. However, when using the inflammatory biomarker C-reactive protein (CRP), the relationship between disease activity and FI was not significant ¹⁶. Other studies found that FI persisted in remission and was also present in those with low DAI scores, suggesting that FI is not always associated with active disease ^{2, 20}.

Stool consistency

Self-rated loose stools ^{2, 17, 22} were associated with more frequent ^{2, 22} and severe FI¹⁷.

Anorectal physiology and pelvic floor function

FI severity scores were positively associated with lower rectal urge volume ¹⁷, lower mean anal resting pressure ¹⁷ and a more fatigable anal sphincter compared to controls ¹⁶. A significant association was found between FI severity and internal and external anal sphincter defects, as detected by endoanal ultrasound ¹⁶.

Anxiety, depression and fear

Significantly higher levels of anxiety and depression were found in those with FI compared with continent people ²⁰. Fifty-eight percent of participants reported anxiety and stress worsened FI symptoms ². Patients who experienced FI more

frequently were more likely to ruminate about possible future FI occurrences and were negatively affected by such thoughts ². Sixty-seven percent who had not experienced FI reported thinking about possible future FI, suggesting that FI-related anxiety is not necessarily associated with previous FI experiences ². Parous women with IBD feared the possibility of postpartum FI ¹⁹.

Associations with FI not amenable to interventions

The review also identified associations between FI and IBD which are unlikely to be modifiable.

Duration and type of IBD

No significant association was found between disease type (CD or UC) and the presence of FI ^{2, 17, 20, 23}. Patients with UC had increased risk of more frequent FI than CD patients ². In CD FI was found more likely to occur in patients with stricturing or perianal disease than in those without ²². Patients with distal colitis had higher FI scores than those with total colitis ²³. Others found that this difference was non-significant ²¹. Patients with a longer disease duration were at greater risk of FI ¹⁸. This relationship was non-significant in another study ²⁰.

Age

There were mixed findings on age and FI. Some studies found that older patients reported more FI ^{18, 22}, or more frequently². However, this was not found in other studies.²⁰ In univariate analysis, a significant association was found between age and prevalence ^{18, 22} and frequency ² of FI: younger individuals had lower prevalence and less frequent FI. This finding was not significant in other univariate ²⁰ and multivariate analyses ^{18, 22}. FI frequency was positively associated with age in

multivariate analysis ². Age was only significantly associated with FI prevalence in patients with CD where FI was most prevalent in 51-60 year olds and the 81+ age group and not associated in those with UC ². Age at diagnosis was not associated with FI in multivariate analyses ²².

Gender

Female gender was significantly associated with the prevalence and frequency of FI ^{2, 23}. This association was found in multivariate analysis for FI frequency and a significant association between female gender and FI prevalence remained in CD but not in UC ². This was not found in other studies ²⁰. Gender may be confounded by childbirth and being post-menopausal ²⁴.

Childbirth

Findings on obstetric factors associated with FI were mixed, including number of childbirths; mode of delivery (vaginal, assisted or caesarean section); episiotomy and other complications (such as breech birth and forceps delivery) ^{2, 18, 19}. The number of childbirths was associated with the presence of FI ¹⁸. Vaginal delivery increased the risk of FI ^{2, 19} by more than 50% compared with caesarean section ². This was not found in all studies ¹⁸ and was not significant in multivariate analysis ². Obstetric complications including perineal tears, episiotomy and instrumental delivery did not significantly increase the risk of FI ^{2, 18}. Eighty-eight percent of those who attributed their FI to vaginal delivery had experienced episiotomy ¹⁹. However, this was a patient-reported, retrospective attribution, without objective clinical assessment.

Surgery

A history of abdominal and anal surgery was associated with FI ^{2, 18, 22}. This included anal fistula ^{2, 18}, colorectal surgery, total/partial colectomy, previous colostomy, anal fissure, anal stretch, ileo-anal pouch, small bowel surgery and bowel resections ^{2, 22}. Others found non-significant associations between FI and previous surgeries including anal surgery ¹⁷, anal fistula and ileo-anal pouch surgery.

Interventions for FI in IBD

Four small cohort intervention studies which addressed FI in IBD were found ²⁵⁻²⁸, with a total of 34 participants (Table 2). These studies involved anal sphincter repair surgery ^{27, 28}, sacral nerve stimulation ²⁶ and transcutaneous posterior tibial nerve stimulation (TPTNS) ²⁵. In all but one study ²⁵, patients had FI secondary to perianal disease. All studies reported improvements in FI post-treatment. However, only 42% of patients reported reduced FI after 3 months of TPTNS treatment ²⁵. In two studies, FI improvements were accompanied by improved faecal urgency ²⁶, decreased need to defecate ²⁶, increased retention time ^{25, 26} and more solid stool consistency.²⁶ Two studies reported improved quality of life after treatment ^{25, 26}.

DISCUSSION

Fourteen studies that explored correlates of FI in IBD and four that tested interventions for FI were analysed. Overall, there is a lack of robust evidence on both the mechanism and associations of FI in IBD and, in particular, the effectiveness of interventions. This contrasts with FI in the general population, where there more literature ¹⁰.

The recent review which reported a pooled prevalence from six studies of 24% FI in IBD ⁶, as in the present review, found that most studies were of clinic attenders or members of a patient organisation and so may be a biased sample. Studies of anorectal function in IBD and FI have not reported a consistent pattern of association, except FI being associated with anal sphincter defects ⁶.

We have identified that few potential targets for interventions have been tried. Disease activity and loose or liquid stool would appear to be the most obvious

factors which could potentially be changed. Other targets have not been robustly investigated. In some studies, active disease was predictive of the presence^{2, 16, 18, 21, 29} and severity of FI¹⁶. Others found that patients with less active disease still experienced FI, suggesting that FI is not always the result of active disease^{2, 20}.

Disease activity indices correlate poorly with objective markers of disease activity³⁰. When using C-reactive protein to determine disease activity, no significant association was found with FI¹⁶. C-reactive protein has been reported as an insensitive biomarker of endoscopic inflammation as it is altered by infections non-specific to IBD¹⁶. Future studies should employ more robust biomarkers of active disease¹⁸.

It is unclear why IBD patients continue to experience FI when in remission. It may be the result of rectal scarring (fibrosis). Alternatively, psychosocial factors may have a perpetuating role in FI in periods of remission.^{2, 20} Anxiety and depression levels were significantly higher in patients who had previously experienced FI compared with those who had not.²⁰ However, it is difficult to establish causality within this finding. Over half of patients reported that anxiety and stress exacerbated FI.² All patients who experienced FI reported worrying about possible future accidents.² Yet, over 60% of those who had never experienced FI reported similar concerns.² This suggests that the possibility of future FI may be anxiety-provoking for patients with IBD regardless of previous FI experiences.

Some associations are not amenable to modification. The relationship between age and FI may be confounded by other factors, such as increased likelihood of anal surgery and longer disease history in older patients.² Some found FI more commonly in females than males^{2, 23} possibly confounded by childbirth.²

The relationship between FI and obstetric factors was inconsistent. Brochard and colleagues ¹⁸ challenged others' findings that vaginal delivery increased the risk of FI compared with caesarean section. This lack of relationship between FI and childbirth is also found in the general population ⁵.

Different factors may be associated with the occurrence of FI in UC and CD patients. Whilst there was no significant difference in the prevalence of FI between IBD diagnoses ^{2, 16, 20, 23}, UC patients experienced more frequent FI than CD patients ². The differences between UC and CD in FI should be explored further to ensure appropriate management of FI in the two conditions.

Some studies found that previous abdominal and anal surgery for IBD increased patients' likelihood of experiencing FI ^{2, 18, 22, 31}. Others found that this relationship was non-significant^{2, 17, 32, 33}. Knowing which surgical procedures in which patients carry greater risks of subsequent FI and may enable formulation of more effective informed consent and treatment plans for patients who are more susceptible to FI.

We propose some possible targets for FI management intervention based on this review in Figure 2.

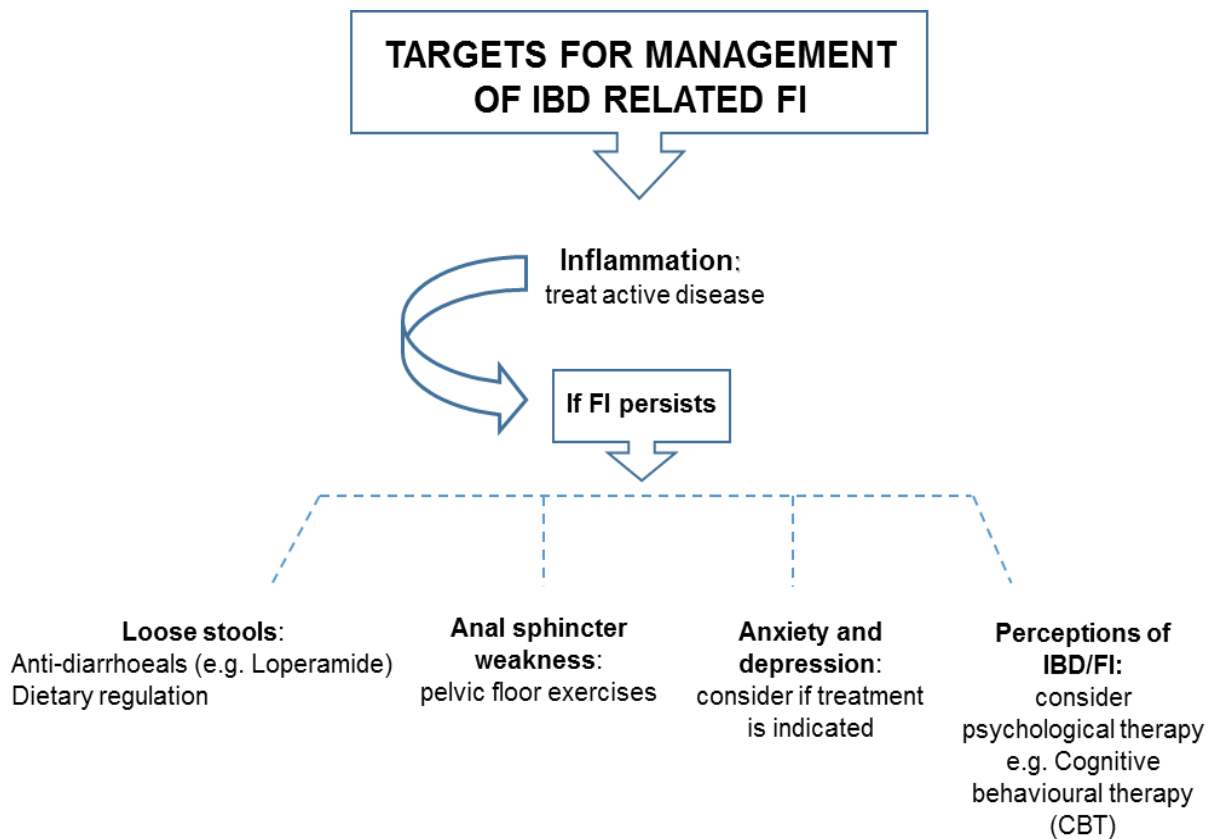


Figure 2. Possible targets for health interventions for IBD-related FI

Many intervention studies have been conducted for FI generally ¹⁰. However, most have specifically excluded participants with IBD. Only four studies tested interventions for FI in IBD. This is remarkably few studies given the high prevalence and heavy burden of FI in IBD. There is an ongoing study³⁴ in which a nurse-led behavioural intervention for IBD-related FI is being tested; the results are not reported. All intervention studies had small samples, short follow-up, selective patient groups and possible placebo effects.

Anxiety, depression and fear are associated with FI and may exacerbate this symptom, even during remission.^{2, 20}. There is no research directly targeting the

psychological correlates of FI. More holistic approaches to targeting FI-specific anxiety in IBD patients could be considered. There is evidence of benefit of cognitive-behavioural therapy (CBT) for other gastrointestinal disorders which exhibit FI and urgency, such as irritable bowel syndrome (IBS) ³⁵; it is plausible that CBT could help in IBD. Techniques such as biofeedback and pelvic floor exercises used for FI in the general population¹¹ might also help.

LIMITATIONS

The findings of the review should be considered in light of limitations. Six different measures of FI were utilised, with varying cut-offs ³⁶⁻⁴¹ and lack of validation in an IBD population.

Whilst some studies conducted rigorous measures to determine patients' IBD diagnosis ^{16-18, 21-23, 33}, others did not^{2, 19, 29}. Others did not report how diagnosis was ascertained ^{20, 31, 32, 42-44}. This is important to assess because IBD shares similar symptom complaints with IBS.⁴⁵

Most studies on associations of FI only conducted a univariable analysis. Future studies should recruit a sufficient sample to allow multivariable analysis, allowing more robust conclusions on associations.

Participants were recruited from either an IBD organisation^{2, 19} or a tertiary referral centre.^{16-18, 20, 23, 29}, with likely sampling bias in both of these subpopulations, individuals who experienced FI may have been more likely to participate, thus overestimating the prevalence of FI in IBD.² Patients from a referral centre may have more severe IBD. Some studies did not report recruitment sources ^{21, 33}; others

recruited extremely selective samples^{22, 31, 32, 42-44}. Many studies used cross-sectional designs limiting causal inferences^{2, 18, 20-23, 29}.

RECOMMENDATIONS FOR CLINICAL PRACTICE

Clinicians need to ask actively about FI⁹ as patients may be reluctant to discuss this symptom⁸. There should be no assumption that FI will always resolve when IBD is in remission. First line intervention for FI in IBD will be to manage active disease, likely using disease-modifying medication. If FI is not resolved when IBD is in remission or if stool remains loose, anti-diarrhoeal medication or dietary modifications to firm up the stool should be considered. Pelvic floor exercises, urge resistance techniques, possibly biofeedback and practical advice on managing FI may be helpful.⁹

Clinicians should also consider whether referral for psychological support or intervention is warranted.

CONCLUSIONS

This systematic review has highlighted various sociodemographic, clinical, and psychosocial factors associated with IBD-related FI. and highlights the need for further longitudinal studies with larger, representative samples and more extensive psychosocial measures. Only when the factors associated with FI in IBD are established can we develop effective interventions for this debilitating symptom.

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AUTHORSHIP

Guarantor of the article: Hannah Proudfoot.

Author Contributions: CN and HP designed the study and drafted the protocol; HP and BK conducted the searches; HP, MA, ED, SK, CN and BK extracted data; CN, MA, SK, ED and HP conducted quality appraisal of included studies. All authors contributed to manuscript preparation.

All authors approved the final version of the manuscript.

Online Supplementary Table 1

Table 1. Inclusion and exclusion criteria for studies in the review

	Inclusion criteria	Exclusion criteria
Population	<ul style="list-style-type: none"> - Individuals of any age with any type of IBD (CD, UC or IBD-U). - Individuals with IBD who may also have a perianal fistula or an ileo-anal pouch. 	<ul style="list-style-type: none"> - Individuals without IBD (unless as a control group). - Individuals who experience FI not related to IBD (unless as a control group). - Individuals who do not experience FI (unless as a control group). - Individuals with IBD who have a stoma. - Individuals with FI secondary to specific surgical procedures (e.g. ileo-anal pouch or anal fistula surgery).
For intervention review: Intervention/Exposure	<ul style="list-style-type: none"> - Any intervention approach or management strategy for FI (conservative and/or surgical). 	
Comparator for associations	<ul style="list-style-type: none"> - No comparison/control group. - Healthy individuals (without IBD and without FI). - Individuals with FI but not IBD. - Individuals with other gastrointestinal disorders (e.g. Irritable Bowel Syndrome) where results are analysed in comparison with IBD patients' results. 	
Comparator for interventions	<ul style="list-style-type: none"> - No comparator or any other intervention. 	
Outcome for associations	<ul style="list-style-type: none"> - Factors associated with FI in IBD examined as a primary or secondary outcome (including sociodemographic, clinical, and/or psychosocial factors). 	<ul style="list-style-type: none"> - Presence of FI measured but no associations explored.
Outcome for interventions	<ul style="list-style-type: none"> - FI frequency or severity measured by any means. - Quality of life. 	<ul style="list-style-type: none"> - Interventions in people with IBD but no measure of FI.
Study design	<ul style="list-style-type: none"> - Experimental studies (RCTs, quasi-experimental RCTs, non-RCTs, pilot & feasibility studies). - Quantitative studies (case control, cohort, cross-sectional, longitudinal) 	<ul style="list-style-type: none"> - Qualitative studies - Case studies - Reviews - Editorials and letters. - Non-English language studies.

CD, Crohn's disease; FI, faecal incontinence; IBD, inflammatory bowel disease; IBD-U, inflammatory bowel disease-unclassified; RCTs, randomised controlled trials; UC, Ulcerative colitis.

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