TITLE: A SYSTEMATIC REVIEW OF SELF-MANAGEMENT INTERVENTIONS FOR CHILDREN AND ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE

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CONFLICT OF INTERESTS AND SOURCE OF FUNDING

Both authors declare that they have no conflict of interests.

This research was unfunded.

ABSTRACT

Background

Self-management of inflammatory bowel disease is complex. Children and adolescents (CA) with inflammatory bowel disease (IBD) often have difficulty with managing aspects of their condition, resulting in treatment non-adherence and impaired psychosocial function. Self-management interventions are developed to help support patients and their parents/carers to effectively self-manage. The aim of this systematic review was to evaluate the efficacy of self-management interventions in children and adolescents with IBD.

Methods

The review was conducted in accordance with PRISMA guidelines. A systematic literature search of the following databases; Medline, Embase, Cochrane, CINAHL and PsychINFO was conducted to identify controlled trials of interventions aiming to enhance IBD self-management in CA. Two reviewers screened articles for inclusion.

Results

Nine trials (eleven articles) met the inclusion criteria. Most were underpowered with seven recruiting fewer than 50 participants. The interventions aimed to enhance psychological wellbeing (n=5), medication adherence (n=3) or calcium intake (n=1). There was considerable heterogeneity in intervention content and outcomes assessment. Some benefits were reported in disease activity, adherence and psychological well-being but findings were inconsistent.

Conclusions

Self-management is difficult for CA with IBD, however this review identified only a small number of interventions to support self-management, most of which were under-powered and only one that was conducted outside the US. Clinical consensus is required on which self-management activities should be recommended to patients and targeted in interventions and which core outcomes should be assessed. Adequately powered trials of interventions are required to identify how best to support self-management in CA with IBD.

Keywords: Inflammatory Bowel Disease, Self-management, Children, Adolescents

INTRODUCTION

The role that the patient plays in the day-to-day management of their disease is commonly referred to as self-management[1, 2]. Chronic disease self-management involves several tasks, including medical management, coping with the emotional impact of having a chronic disease and adapting one's life roles to any limitations incurred by the disease[3]. For children and adolescents (CA) with inflammatory bowel disease (IBD), medical management may include attending regular hospital appointments, taking medication, nutritional therapy, eating a balanced diet, staying hydrated, managing symptoms such as diarrhoea, pain and fatigue and the early detection of symptoms that can lead to a flare-up[4, 5]. Role management may involve managing school and social relationships[6]. Emotional management, may include coping with stress and the potential embarrassment arising from having IBD[7].

Difficulties in IBD self-management experienced by CA include treatment non-adherence[8, 9] and impaired psychosocial function[10, 11]. Proactive participation in IBD self-management, particularly among adolescents often aids a successful transition into adult care[12]. In collaboration with healthcare professionals it is likely to improve treatment adherence[13] and disease outcomes[1,14].

There is evidence that self-management interventions for CA can help to improve disease outcomes[15, 16]. Self-management interventions have been found to be effective for adults with IBD[4] and also for CA with other chronic diseases[16] such as asthma[17, 18] and diabetes[19]. This review aims to examine the efficacy of self-management interventions for CA with IBD.

METHODS

Studies meeting the following criteria, defined by Population, Intervention, Comparator, Outcome and study design (PICOS)[20] were included.

Inclusion Criteria:

Population: CA up to 19 years old with IBD, in line with the World Health Organization definition of adolescence[21]. As many interventions for CA include parents/carers, trials that included parents/carers of CA with IBD were also eligible for inclusion.

Intervention: Self-management interventions i.e. interventions that aimed to enhance participants' ability to manage their condition and could include interventions to enhance medication adherence, lifestyle, diet, and coping with emotional and social aspects of living with IBD.

Comparator: Treatment as usual, an alternative intervention or a waiting list comparator.

O*utcomes:* Outcomes of interest included clinical, behavioural and psychosocial outcomes.

Study design: Controlled trials (randomised and non-randomised).

Exclusion Criteria:

Studies were excluded if they were:

- Articles that combined adults and CA with IBD or combined CA with IBD with other chronic diseases but did not report findings for CA with IBD separately.
- Observational studies.
- Written in languages other than English.
- Trials published as conference abstracts, editorials, or letters and articles that had not been subjected to a formal peer review.

Search strategy

An electronic search was conducted across the following databases from inception to June 2016: Cochrane Review, CINAHL, Embase, Medline and PsychInfo. Search terms used were: Inflammatory Bowel Disease; Ulcerative Colitis; Crohn's Disease; Self-manag*; Patient education; Health Promotion; Lifestyle; Psycho*; Patient Adherence; Coping; Program*; Intervention; Therapy. Relevant variations of search terms in the database thesauruses and MeSH terms were used. See Supplemental file 1 for the full search strategy.

Study selection

Retrieved articles were imported into Endnote version X7 and duplicates were removed. Two reviewers (LT, KM) independently reviewed potentially eligible studies' titles and abstracts and decided on the final inclusion of articles based on the full texts retrieved.

Data extraction and management

Relevant data were extracted from full text articles using an adapted Cochrane Data Extraction form[22]. Data were extracted on participant demographic and clinical characteristics, intervention characteristics and all reported outcomes.

Assessment of risk of bias

Study quality was assessed using the Cochrane "Risk of Bias" tool[24]. Trials were rated low, high or unclear across seven potential sources of bias: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias.

Analysis

Owing to the heterogeneity of interventions and outcome measures, a meta-analysis was not considered appropriate and a narrative synthesis was conducted.

ETHICAL CONSIDERATION

As this is a systematic review of published data, ethical approval was not required.

RESULTS

A total of 808 references were identified, of which eleven articles, reporting nine trials [23, 25-30,31, 32] were included (Figure 1).

Study and population Characteristics

Study and population characteristics are shown in Table 1.

All except one of the trials were conducted in the USA[23, 25-30, 32] Seven were randomized controlled trials (RCTs)[23, 25-30] and two were non-randomized controlled trials[31, 32]. Overall, 521 CA participated in the trials and in most trials parents/carers were involved except for one that included adolescents only[31]. A majority of trials were small with seven recruiting fewer than 50 participants[23, 26-28, 30-32]. Mean age ranged from 8.5-15 years and more than 68% were Caucasian. Most trials had an even gender distribution, except for two studies, one which consisted of 71.4% females[30] and the other recruited females only to ensure a homogenous group[32].

Eight trials reported separately for IBD subtypes, in which the proportions with ulcerative colitis (UC) ranged from 17.5% - 33.3%, Crohn's disease (CD) from 54% - 78.6% and Indeterminate Colitis (IDC) from 3%-12.5%, although one trial did not specify the IBD types[28]. Severity of IBD was reported in six studies, in which between 30-100% of participants had active disease[25-28, 30, 32].

One trial recruited only participants who had comorbid IBD and anxiety disorder[28] and two trials recruited participants with IBD who met the criteria for depression[29, 30].

Intervention characteristics (See Table 2)

Intervention Theoretical Framework and Content

Five interventions were based on cognitive behavioural theory (CBT) and aimed to improve psychological wellbeing[28,29, 30,31, 32].

Three interventions used skills training to improve medication adherence[25,26, 27].

The final intervention taught behavioural strategies to increase dietary calcium intake[23].

Intervention Delivery Mode

In only one trial, independent adolescent groups were conducted[31]. Three held CA sessions separately from the parent/carer sessions[26, 28, 30], in three other trials parents/carers were involved in some CA sessions (i.e. at the beginning or end of intervention sessions)[27, 29, 32] and in two the intervention was carried out as a family[25, 26].

Predominantly the interventions were delivered by clinical psychologists and psychology academics. Most were delivered face-to-face[23, 26-32], with one over the telephone[25] and one online[32]. The total number of sessions ranged from 4-13 and total duration ranged from 180 to 780 minutes.

Control/comparator groups

The trials comprised a mix of control and comparator groups. These were: wait-list (n=4)[25, 27, 31, 32]; treatment as usual (n=2)[26, 30]; nondirective supportive control (described as offering social and emotional support through non-directive techniques) (n= 2)[28, 29] and enhanced standard care (which included dietary counselling) (n=1)[23]. Among the five CBT trials, two compared the intervention to other CBT treatments[28, 29].

Risk of Bias

Risk of bias was high for performance bias across all the studies but low for reporting bias, and attrition bias (Figure 2). Attrition rates ranged from 2.4% to 55% (median 12.25%). Selection and detection bias were low to moderate.

Main Findings (See Table 3)

Clinical Outcomes

Disease Activity

Two CBT interventions measured disease activity as an outcome [28, 29] . A positive effect favouring CBT in reducing disease activity was found over time in,the larger trial (n=217) by Szigethy et al., 2014 [29] but not the smaller trial (n=22) by Reigada et al.[28].

Symptoms

One small trial of a coping skills intervention (n = 24) by McCormick et al.[32] reported on abdominal pain outcomes. There was no effect on abdominal pain, however somatization symptoms reduced over time in the intervention group but the between–group comparison was not significant.

Behavioural Outcomes

Medication Adherence

Three trials assessed medication adherence[25-27] but findings were inconsistent. Hommel et al. 2011 found a beneficial effect on adherence to one but not both of the assessed IBD medications[27]. Hommel et al. 2012found a beneficial effect on one of the assessed medications, but only for patient-reported adherence whereas other measures of adherence – pill count, electronic monitor and parent-report – were not significant[26]. Greenley et al. did not find an overall effect but reported an impact in a subgroup of participants aged over 16 years who were imperfect adherers at baseline[25].

Nutritional Adherence

One trial, by Stark et al., that aimed to increase calcium intake found that a behavioural intervention was more effective than enhanced standard care[23].

Psychosocial Outcomes

Five trials reported on psychosocial outcomes, all of which were evaluations of CBT interventions[28-32].

Health-related Quality of Life (HRQoL)

Three trials assessed HRQoL. Szigethy at al. 2014 compared CBT to supportive non-directive therapy reported improvements over time but found no significant difference between the two conditions[29]. Greenley et al's. problem-solving skills training study did not report between-group findings but found an effect in the intervention group after two weeks of intervention although none found at four weeks[25]. In the third study by Grootenhuis et al.[31], a subscale of HRQoL, (patient's body image) detected a positive increase in the intervention group but no effect was found in other subscales.

Global Mental Health

A significant difference was found between the intervention and treatment as usual comparison groups in Szigethy et al's 2007 trial that recruited CA with subsyndromal depression[30]. However, Szigethy et al's 2014 trial comparing CBT with supportive non-directive therapy (SNDT) in participants with depression found no difference between treatments[29].

Anxiety and Depression

In a trial for participants with depression, Szigethy et al. 2014 found an improvement in both the CBT and SNDT groups but there were no differences between the groups in change over time and the trial did not include a usual care control group[29,33]. In a trial of CBT in participants with subsyndromal depression, Szigethy et al. 2007 found an impact of CBT on a measure of depressive severity but not on the number of depressive symptoms immediately post-intervention. The impact on depressive severity was not maintained at 6 or 12 month follow-ups[30,34].

Two trials measured anxiety; Reigada et al's trial of CBT for anxiety disorders saw a greater reduction in IBD-specific anxiety in the intervention group post-treatment and at 3 months follow-up [28] but there was no effect on trait anxiety (a predisposition to react to stressful situations with anxiety) in the other CBT trial by Grootehuis et al. [31].

Self-worth

Self-worth was assessed in one trial of CBT by Grootenhuis et al., in which the intervention group improved relative to the control group in global self-worth and physical self-perception but there was no effect found in five other sub-scales of the self-worth measure[31].

Behavioural-emotional problems

One trial of CBT by Grootehuis et al. assessed parent reports of their child's behavioural-emotional problems[31]. The intervention group reported a reduction in problems 6-8 months post baseline but between-group findings were not reported.

Coping

In a trial of coping skills training by McCormick et al., parents reported more adaptive pain coping by their child in the intervention group compared to the control and over time. Parents over protectiveness and irrational cognitions about pain experienced by the adolescents were also significantly reduced[32]. Parent outcomes were only reported in this one trial with a focus on changing their response or irrational thoughts about adolescents' pain[32].

Grootehuis et al. found that greater predictive control (optimism) about the further course of the disease was reported 6-8 months following CBT [31]. In another trial of CBT for subsyndromal depression, by Szigethy et al. 2007, an increase in perceived control was seen at 12-14wks[30].

Intervention acceptability

Treatment satisfaction and acceptability was measured in four trials (.,Hommel et al. 2012., Hommel et al. 2011, Reigada et al.)[25-28] and ratings were mostly positive. However, adolescents in the Problem-Solving Skills Training intervention reported by Greenley et al were less satisfied with discussing issues over the phone compared to their parents[25] and parents gave higher ratings than adolescents for two interventions by Hommel et al. to promote medication adherence[26, 27].

DISCUSSION

To our knowledge, this is the first systematic review of self-management interventions for CA with IBD. The review identified nine trials, which mainly focused on improving either medication adherence or psychological wellbeing. There was considerable heterogeneity in both the intervention content and the outcomes measured. Most trials recruited very small samples and although some benefits were reported, findings were inconsistent. There remains a need to identify how best to support self-management in CA with IBD and to ensure that interventions are evaluated in adequately powered trials.

Medication non-adherence is a common issue for adolescents with IBD[8, 9]. None of the three trials in this review that measured medication adherence were adequately powered. Although some positive outcomes were reported, these were not consistent across trials or assessment methods but were mainly found in sub-groups such as older non-adherent adolescents or the type of oral medication. How best to improve medication adherence in CA with IBD therefore remains unclear. The three interventions all used problem-solving approaches to address barriers to adherence. A meta-analysis of interventions to promote adherence in paediatric chronic illnesses[34] found that behavioural (e.g. problem-solving) and multi-component interventions (usually behavioural plus another modality such as social support or family therapy) had the greatest effect. Therefore, given the under-powered nature of the existing trials in IBD, problem-solving interventions should not be dismissed as a potential approach for improving adherence. A

study by Gray et al[35] found that barriers to adherence in adolescents with IBD were moderated by anxiety/depressive symptoms therefore interventions that aim to improve medication adherence need to consider a broader approach that also incorporates strategies to identify and reduce symptoms of anxiety and/or depression.

In terms of adherence to nutritional therapy, a beneficial increase in calcium food intake was achieved by training parents in behavior management strategies to encourage consumption of high calcium foods. No change was found in the comparison group that received education only, supporting the view that education as a standalone intervention is not sufficient to improve self-management in IBD[4]. Although diet is an important aspect of IBD management, this was the only intervention that addressed any aspect of dietary self-management. Hommel et al[36] have previously highlighted the need for further examination of dietary adherence in IBD.

Psychological well-being is an important aspect of managing IBD[13, 37]. Five trials focused on improving psychological wellbeing, however, several different outcomes were assessed and no single outcome measure was used in more than two trials. Some improvements were seen in depression in the short term however the lack of a usual care control group in one of the trials limits the validity of this finding. A benefit was also seen for IBD-specific anxiety but not trait anxiety. As the latter is considered a fairly stable personality characteristic, this is not unexpected and measuring disease-related anxiety may have been more appropriate. The interventions also showed some beneficial effect on adolescent self-esteem and coping whereas previously no efficacy was reported in a review of psychological interventions for adults with IBD[38]. This suggests that being in a position of thinking positively and increasing perceived control that starts in adolescence may better enable patients to emotionally manage their chronic illness into adulthood.

The effects on clinical outcomes such as disease activity were not well covered or reported in these studies. One of the trials, the largest in the review, did find an impact of CBT on disease activity. It is important that self-management interventions should assess the relationship between any change in self-management behaviours, psychosocial functioning and disease activity outcomes and also whether intervention efficacy is moderated by disease activity.

The interventions in this review did not address IBD self-management in the broad sense, as encompassed by the three tasks outlined by Corbin and Strauss[3]. The interventions focused on only a small part of medical management or emotional management but did not address how these factors may influence each other nor did they address any aspect of role management, such as managing IBD at school. This may be because there are no available guidelines regarding IBD self-management such as those that exist for CA with diabetes[39] or asthma[40]. Given the complex nature of IBD self-management, it is important that clear guidelines should be drawn up on what patients and families need to do to effectively self-manage IBD. This will inform the content of future interventions to support patients and families in self-managing IBD, which could then be more consistent in what they address. Consensus also needs to be achieved on which outcomes are important so that there is greater consistency in the outcome measures that are used in evaluations of intervention efficacy.

The important role that families play in helping CA to manage their IBD was recognised by the inclusion of families in most interventions. However, information on the parents/carers was sparse and only one trial reported parental outcomes. Parent stress has been found to be associated with poorer psychological adjustment in children with chronic illness[41], therefore trials of interventions that involve parents should also assess the impact of the intervention on parents and to what extent this mediates the impact of the intervention on the CA. Only one of the trials in this review recruited young children, for whom parents/carers would take most of the responsibility for IBD management. The intervention was effective in increasing calcium intake but research has not examined whether self-management interventions could improve other outcomes in young children with IBD or whether providing self-management support from a younger age could facilitate better self-management in adolescence.

Most trials in this review were conducted in the USA. Epidemiological data indicate that the burden of IBD is increasing in many other parts of the world[42], suggesting that IBD self-management interventions should be developed for and evaluated in these different healthcare systems.

STRENGTHS AND LIMITATIONS OF THE REVIEW

We conducted a systematic and comprehensive literature search and the review was conducted using PRISMA guidelines.

The review is limited by the underpowered studies and poor methodology of some trials that lacked a usual care control group. Generally, the trials were underpowered to provide reliable intervention estimation of effectiveness. The heterogeneity of outcomes made it difficult to directly compare across trials. Inadequate analysis was apparent in some trials, for example reporting only results over time but not between groups.

There was considerable heterogeneity in intervention structure, content, mode of delivery, and outcome measures, including diverse ways of reporting. In order to establish how effective self-management interventions are in CA with IBD, and to better enable comparable analysis across trials, there needs to be a consensus on the content and assessment of self-management interventions for CA with IBD.

CONCLUSION

Identification of patient education interventions to improve self-management was rated as the top priority for IBD nursing and allied health professional research[43] in a recent Delphi survey. This review identified some benefits of self-management interventions but there was a lack of well-designed, adequately powered trials. Most of the trials were conducted in recent years suggesting that self-management in CA with IBD is a relatively new and developing area. Further work is necessary to build clinical consensus on the self-management activities that CA with IBD need to perform and the core outcomes to be assessed. Interventions should then be developed to target those key self-management activities and evaluated using the agreed core outcomes.

FUNDING

n/a

ACKNOWLEDGEMENTS

n/a

AUTHORS' CONTRIBUTIONS

Both authors were involved in the conception and design of the study. LT conducted the searches and collected the journal articles, LT and KM screened studies for inclusion, LT extracted and analysed the data under the guidance of KM. Both authors were involved in data interpretation. LT drafted the manuscript and KM was involved in revising the manuscript. Both authors approved the final version for publication.

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Table 1. Study population characteristics

Author (Year); Country	Study Design	Sample Size Total (n)	Total Attrition (%)	Age Range; Mean Age (SD); Gender (%); Ethnicity (%)	IBD type (%)	Disease Severity (%)	Reported Parents/Carers demographics can include; age, gender, marital status, education level, income
Greenley et al (2015); USA[25]	RCT	I = 50 C = 26 n = 76	14.5	11-18; 14.54 (1.84); F (45); White/Caucasian (88)	CD (72) UC (25) IDC (3)	None/Remission (70); Mild (25); Moderate (5); Severe (0)	Female Carers (93%)
Grootenhuis et al (2009); Netherlands[31]	NRCT	I = 22 C = 18 n = 40	20	12-18; I: 15.7 (1.5), C: 15.4 (1.4); F (54); Ethnicity NR	CD (69) UC (22.5) IDC (8.5)	NR	NR
Hommel et al (2012); USA[26]	RCT	I = 20 C = 21 n = 41	2.4	11-17; 15.4 ± 1.5; M (50); White/Caucasian (90)	CD (75) UC (17.5) IDC (7.5)	CD: Inactive (28); Mild (55); Moderate/Severe (17). UC/IDC: Inactive (40); Mild (40);	Mean age 46.2 ± 4.9; Married (87.5%);College degree (45%); Annual income: $100,001-

Author (Year); Country	Study Design	Sample Size Total (n)	Total Attrition (%)	Age Range; Mean Age (SD); Gender (%); Ethnicity (%)	IBD type (%)	Disease Severity (%)	Reported Parents/Carers demographics can include; age, gender, marital status, education level, income
						Moderate/Severe (20)	$125,000
Hommel et al (2011); USA[27]	RCT	I = 7 C = 8 n = 15	6.6	11-18; 14.89 ± 2.01; F (71); White/Caucasian (100)	CD (78.6) UC (21.4)	CD: Inactive (36.4); Mild (63.6) UC: Inactive (66.7); Moderate (33.3)	Mean age 45.87 ± 3.79; Married (100%); College degree (43%) Annual income: $75,000-$100,000
McCormick et al (2010); USA[32]	NRCT	I = 29 C = 11 n = 31	55	11-17; SD NR; F (100); White/Caucasian (92)	CD (54.2) UC (33.3) IDC (12.5)	IBD: Inactive (50); Mild (29); Moderate (21); Severe (0)	NR
Reigada et al (2015); USA[28]	RCT	I = 11 C = 11	0	9-17; 13.65 ± 2.08; F (59);	NR	Active (100)	Annual income: <$120,000 (59%)

Author (Year); Country	Study Design	Sample Size Total (n)	Total Attrition (%)	Age Range; Mean Age (SD); Gender (%); Ethnicity (%)	IBD type (%)	Disease Severity (%)	Reported Parents/Carers demographics can include; age, gender, marital status, education level, income
		n = 22		White/Caucasian (68)			> $120,000 (41%)
Stark et al (2005); USA[23]	RCT	I = 19 C = 19 n = 38	16	5-12; I: 10.30 ± 2.38, C: 10.64 ± 2.10; M (53); White/Caucasian (84.5)	CD (75) UC (22) IDC (3)	NR	I: Mothers age 38.1 ± 3.9; Fathers age 40.3 ± 6.5. C: Mothers age 42.2 ± 6.0; Fathers age 43.8 ± 7.0. Annual income >$50,000 (66%)
Szigethy et al (2014) &	RCT	I = 110 C = 107 n = 217	18	9-17; I: 14.3 (2.5), C: 14.3 (2.3); M (47);	CD (74) UC (26)	NR	NR

Author (Year); Country	Study Design	Sample Size Total (n)	Total Attrition (%)	Age Range; Mean Age (SD); Gender (%); Ethnicity (%)	IBD type (%)	Disease Severity (%)	Reported Parents/Carers demographics can include; age, gender, marital status, education level, income
				White/Caucasian (89)			
(2015);		I = 82	10	14.3 (2.4);	CD (100)		
USA[29,33]		C = 79		M (46);			
		N =161		White/Caucasian (88)			
Szigethy et al (2007); USA & Thompson et al (2012); USA[30,34]	RCT	I = 22 C = 19 n = 41	7.3	11-17; 14.99 (2.01); F (51); White/Caucasian (78)	CD (71%) UC (29%)	IBD: Moderate/Severe (93%)	College education (15%) and more than 4 years of college (60%). Annual income: $75,000 - $90,000

C – Control group; CD – Crohn's disease; I – Intervention group; IDC - Indeterminate Colitis; UC – Ulcerative colitis

Table 2. Intervention Characteristics

First author Year Country	Theoretical Framework	Structured or Tailored Intervention Group	Intervention group (I) / Control or Comparison Group (C)	Independent sessions or with family involvement	No. of weekly Intervention Sessions. Duration (range). Mode of delivery	Providers
Greenley, 2015, USA[25]	Problem-solving	Tailored	I: Up to 4 sessions of phone based problem-solving skills training (PSST) tailored to address each family's adherence barriers. C: Wait-list Comparison Group	Family sessions	2 or 4 sessions; 45–90 mins; Telephone	Psychology graduates
Grootenhuis, 2009, Netherlands[31]	CBT	Structured	I: Psychoeducational group intervention to strengthen coping by teaching adolescents to actively use coping strategies. C: Wait-list Control Group	Independent Adolescent groups sessions.	6 sessions; Duration NR; Face to Face	NR

Hommel, 2012, USA[26]	NR	Structured	I: Family-Based Group Behavioural intervention involved IBD education and organisation, goal setting, problem solving skills, positive reinforcement, adherence monitoring and on improving communication in the family. C: Treatment as Usual Control Group	Patients and parents meet independently in 3 sessions. Family involvement in the last session only.	4 sessions; 60-90 mins; Face to Face	Doctoral clinical psychologists, postdoctoral psychology fellows
Hommel, 2011, USA [27]	NR	Tailored	I: Manualised individually tailored behavioural treatment included IBD education and organisational intervention, goal setting, problem solving skills, positive reinforcement, adherence monitoring and on improving communication C: Wait-list Control Group	Family sessions	4 sessions; 60-75 mins; Face to Face	Doctoral clinical psychologists, postdoctoral psychology fellows
McCormick, 2010, USA[32]	CBT	Structured	I: Cognitive Behavioural Therapy aimed to effectively help patients cope with IBD symptoms, restructure maladaptive	Independent parents and adolescent's sessions with some	1-day (6hrs), 6 web-based and	Clinical psychology graduates, clinical psychologist

			thoughts, use distraction techniques and communication skills. Parents training in providing helpful responses. C: Wait–list Control Group	family involvement.	30 mins online weekly chat sessions; Face to Face & Web Based	
Reigada, 2015, USA[28]	CBT	Tailored	I: CBT Treatment of Anxiety and Physical Symptoms related to IBD (TAPS + IBD), patient self-care training was provided in IBD symptoms and anxiety management, in addition to relapse prevention strategies. The parent sessions involved a stepwise training in cognitive and behavioural strategies. C: Nondirective Supportive Therapy Control Group offered social and emotional support only, no cognitive reappraisal, exposure or explicit	Independent adolescent and parent sessions with some family involvement.	I: 13 sessions, 2 posttreatment (monthly) 1-hr booster sessions. Three 1-hr parent sessions; C: 13 face-to face sessions	Psychology doctoral students (n=6); postdoctoral clinical fellow (n=1)

			instructions for practicing skills.			
Stark, 2005, USA[23]	NR	Tailored	I: Behavioural Intervention, a stepwise approach was used in each parent session that focused on increasing calcium intake and training was provided in child behaviour management. Age-appropriate entertaining educational activities were delivered to IBD- CA. C: Enhanced Standard Care Comparison Group was an approximate of the dietary counselling that would be routinely available in a medical centre.	Independent children and parent group sessions.	I: 6 sessions over an 8-week period; C: 3 sessions over an 8-week period; Approx. 60 mins/session; Face-to-face sessions	Ph.D. psychologist, postdoctoral fellow, research assistants (n=2)
Szigethy, 2014, 2015, USA [29,33]	CBT	Structured & Tailored	I: CBT Primary and Secondary Control Enhancement Therapy-Physical Illness taught IBD-CA to recognize and challenge negative thoughts, weekly assignments were on behavioural activation and cognitive reframing.	CA independent group sessions with family involvement at the end.	I&C: Up to 12 sessions; 45 mins; Face-to-face and telephone.	MSc social workers, psychology interns, psychologists, child psychiatry fellows, psychiatrist

			Parent sessions were focussed on parent coaching and encouraging their children to use CBT skills. C: CBT Standard Nondirective Treatment Control Group focussed on establishing rapport through listening and providing empathy, while encouraging youth to seek out resources for help.			
Szigethy, 2007 & Thompson, 2012, USA[30,34]	CBT	Structured	I: CBT Primary and Secondary Control Enhancement Therapy-Physical Illness (PASCET-PI) teaching skills via a manual to improve cognitions and behaviour in IBD-CA. Positive thinking, problem solving. C: Treatment as Usual Comparison Group in addition received an information sheet on the signs of depression and treatment options available.	Independent adolescent and parent sessions.	I: 9 to 11 sessions; 60 mins; Face-to-face and telephone.	Psychiatrists (n = 2), psychologists (n = 2), clinical social workers (n = 2)

Table 3. Main Findings

Author (Year); Country	Time points assessed	Outcome		Main Findings
		Outcome assessed	Measuring Instrument	
Greenley et al (2015); USA[25]	Baseline Post 2wks Post 4wks	Behavioural - oral medication adherence	MEMS Track Caps	Between-group findings were not reported. No significant change in treatment adherence was found after two weeks of the intervention in the full sample or after four weeks in the group who received the extended intervention. A statistically significant increase in adherence after two weeks was found among a small subgroup (n=14), aged >16-18 years, ($p < 0.05$; d=0.95).
		HRQoL	PedsQL	Between-group findings were not reported. A significant improvement in HRQoL was found for the full sample after two weeks of intervention (t (66) = -2.83, p=0.006; d = 0.49) but no further change was found after four weeks in the group who received the extended intervention.
		Intervention Ratings - Intervention	5-point Likert scale	Participants were overall highly satisfied with the intervention, Youth mean rating (4.38) and Parent mean rating (4.20). Parents were more satisfied (4.48) with discussing issues over the phone

		acceptability		compared to the Youth (3.90). Youth felt that their medication taking behaviour improved (4.10) while the parents did not rate this as high (3.78). The lowest rating was in the information learned about child's IBD and medication regime amongst parents (3.53).
Grootenhuis et al (2009); Netherlands[31]	Baseline Post 6wks Follow-up at 6-8mth	Psychosocial – Coping	Cognitive Control Strategies Scale	The Intervention group reported greater optimism about the course of the disease (Predictive Control subscale), (p<0.01; β = 0.43). No effect on the Vicarious control or Interpretative control subscales.
		Self-esteem	Self-perception Profile for Adolescents	Intervention group reported more favourable self-perception for physical appearance (p<0.01; (β = 0.41) and global self-worth (p<0.01; β = 0.27) but no effect was found on the School competence, Social acceptance, Athletic competence, Behavioural conduct or Close friends subscales.
		Anxiety	State Anxiety	No intervention effect on anxiety.
		Behavioural-emotional problems	Parent reported - Dutch Child Behaviour Checklist	Pre-post, Parents reported fewer behavioural-emotional problems about their children. (p<0.05) but no difference found between intervention and control.

		HRQoL	Daily Functioning Dutch Children's AZL/TNO Quality of Life Questionnaire	Effect on Body image favouring the Intervention group, (p<0.05; β = 0.39) but no effect on the Home functioning or Emotional functioning subscales or on Total functioning.
Hommel et al (2012); USA[26]	Baseline Post 4wks	Behavior - Medication adherence	Pill Count, Electronic Monitor Assessment, Parent-reported and Patient-reported adherence assessment	No significant differences between Intervention and Control from baseline to post-treatment assessments were found across pill count, electronic monitor and parent-reported adherence assessment. No significant difference was found between Intervention and Control on patient-reported adherence to 6-MP/azathioprine but there was a statistically significant effect of the intervention in patient-reported mesalamine adherence (Condition × Time interaction, F = 13.32, p< .05; δ = .69).
		Intervention Rating - Intervention acceptability	7-point Likert scale.	Overall intervention was favourably accepted. Parents highly liked the group format compared to adolescents (6.65 vs 5.70), they also thought that the group format was helpful (6.41 vs 5.75). Parents used the behavioural skills more than adolescents (5.15 vs 4.79).

				Both parents (5.41) and adolescents (5.25) highly rated the intervention for helping to improve adherence. Adolescents rated the convenience of attending the sessions lower (4.95) compared to their parents acceptability mean range of (5.88). The structure of the intervention (information, no. sessions, length and commitment time) had similar ideal ranges of high acceptability mean ratings between parents and adolescents.
Hommel et al (2011); USA [27]	Baseline Post 4wks	Behavior - Medication adherence	Pill Count	A statistically significant difference favouring the Intervention group was found in post intervention adherence to 6-MP/azathioprine ($t=2.72$, $p<0.05$), but not mesalamine ($t=1.09$, $p=0.31$)
		Intervention Rating - Intervention acceptability	7-point Likert scale. Higher scores reflect higher satisfaction.	Overall adolescents and parents rated the intervention as highly acceptable 70-100%. Parents rated the individualized format higher than adolescents (6.62 vs 5.86) and thought the format was helpful (6.50 vs 5.43). Total time commitment for treatment was rated lower by adolescents (3.86) compare to parents (4.36). Parents used the behavioural skills more (5.15 vs 4.79) and felt that the treatment improved their child's adherence (5.92 vs 5.43). The structure of the intervention (information, no. sessions, length and commitment time) had similar ideal ranges of high acceptability mean

				ratings between parents and adolescents.
McCormick et al (2010); USA[32]	Baseline Post 6wks Follow-up at 6mths	Symptoms - Abdominal pain	Abdominal Pain Index (API; Parent and Child Report)	No effect of intervention on abdominal pain.
		Psychosocial – Somatic Symptoms	Child Somatization Inventory (CSI; Parent and Child Report)	Within group comparison: Statistically significant reduction in somatic symptoms from pre-post treatment. Parent-reported [F (1,12) = 7.48, p=0.009, n2p = 0.384] and Patient-reported [F (1,12) = 8.32, p=0.007, n2p = 0.410] but no significant group differences.
		Parents cognitions	Adult Responses to Children's Symptoms: Protect Scale (ARCS; Parent Report)	A significant reduction in overly protective parents of adolescents' pain/symptoms pre/post at 6wks [F (1,12) = 4.35, p=0.030, n^2_p = 0.266] and at 6mth follow-up [F (1,8) = 7.69, p=0.010, n^2_p = 0.435].
		Coping	Pain Coping Questionnaire	Parent-reported PCQ approach scale had significantly higher scores compared to Control group at the end of the treatment [F (1,12) = 7.87, p =

			(PCQ; Parent and Child Report)	0.005, n^2_p = 0.282] and in PCQ distraction [F (1,20) = 7.87, *p* = 0.005, n^2_p = 0.282]. Parent-reported significant improvement from pre/post 6wks in the Intervention group for their adolescents' use of approach coping strategies: [F (1,12) = 9.11, *p*=0.006, n^2_p = 0.432] and distraction techniques: [F (1,12) = 6.44, *p*=0.013, n^2_p = 0.349] but there was no significance PCQ approach and distraction in the adolescent group. PCQ emotional avoidance coping strategies was nonsignificant in the intervention however in the control an improvement was reported in adolescents [F (1,12) = 4.95, *p*=0.027, n^2_p = 0.355].
		Parents and adolescents' cognitions about pain	Pain Catastrophizing Scale for Children (PCS-C) and Pain Catastrophizing Scale for Parents (PCS-P)	Significant reduction in parents own irrational cognitions about adolescent's pain [F (1,12) = 3.25, *p*=0.048, n^2_p = 0.213] but no significance in adolescent's own view.

Reigada et al (2015); USA[28]	Baseline Post 13wks Follow-up 3mths	Clinical – Disease activity	Paediatric Ulcerative Colitis Activity Index and Paediatric Crohn's Disease Activity Index	No statistically significant effect of treatment condition or time was found.
		Psychosocial - Anxiety	IBD-Specific Anxiety Scale	A significant reduction in Intervention compared to Control group at post intervention, (F (8.25), p=0.01, d = 1.21) and at 3-month follow-up (F (4.62), p=0.05, d = 0.75).
		Treatment expectancy and satisfaction	Narratively reported	Parents and patients reported moderate beliefs that the intervention can improve IBD and address nervousness. Parents were very satisfied following treatment and would recommend the program, patients felt that the intervention helped them a lot and the therapist cared very much.
Stark et al (2005); USA[23]	Baseline Post 8wks	Behavioural - Calcium intake	Dietary food diaries	Intervention group achieved significantly higher calcium intake than the control group (Condition by time interaction [F(1,30) =23.09, p< 0.001] δ = 0.44). There was an average increase of 984mg/Ca/day in the intervention group compared to 274 mg/Ca/day in the control group. At posttreatment

				81% of Intervention participants achieved the 1500mg calcium per day compared to 19% of control participants, (χ^2 = 12.50, p<0.001).
Szigethy et al (2014) & (2015); USA[29,33]	Baseline Post 3mths	Clinical – Disease activity	Paediatric Ulcerative Colitis Activity Index (PUCAI) and Paediatric Crohn's Disease Activity Index (PCDAI)	There was a statistically significant difference in reducing disease activity favouring CBT over time. (z = 2.01, p = 0.04)
		Psychosocial - Depression	The Children's Depression Rating Scale (CDRS-R) Kiddie-Schedule for Affective Disorders and Schizophrenia – Present Version (K-SADS-PL)	No significant difference between interventions but an improvement was seen over time in both groups. In the CD sample, depressive severity improved over time for CBT (b = - 215.26; z = - 29.28; P < 0.0001) and SNDT (b = - 214.46; z = - 27.71; P < 0.0001). At 3-months, 65.5% of the total sample no longer met the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria for depression.

		Global Mental Health	Children's Global Assessment Scale	No significant difference between interventions. Mean CGAS scores posttreatment, (CBT 65.83 versus SNDT 64.30) were consistent with minimal impairment on the CGAS scale.
		HRQoL	Mean IMPACT-III	Both therapies showed an improvement in HRQoL but no significant differences were found between treatments.
Szigethy et al (2007); USA & Thompson et al (2012); USA[30,34]	Baseline T2: 12 - 14wks T3: 6mths T4: 12mths	Psychosocial - Perceived control	Perceived Control Scale for Children (PCSC)	Significant positive effect of Intervention at T2 (t=2.13, p= 0.042).
		Depressive symptoms	Kiddie-Schedule for Affective Disorders and Schizophrenia – Present Version (K-SADS-PL)	No significant. differences between groups and over time in syndromal depressive symptoms

			Children's Depression Inventory (CDI) and parent version (CDI-P)	Statistically significant. CDI-CP difference between intervention and comparison group at T2 (t = 3.18, p = 0.003) however not significant at T3 and T4. Statistically significant CDI-CP reduction in intervention from baseline to T4 (p= 0.002)
		Mental Health – General Mental functioning	Children's Global Assessment Scale (CGAS)	Global functioning significantly improved in the intervention group relative to the control group (F (3,35) = 3.70, p= .021) Significant higher scores in the intervention group at T2 and T3 (ps ≤ .05)

Figure 1. Preferred Reporting item for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram

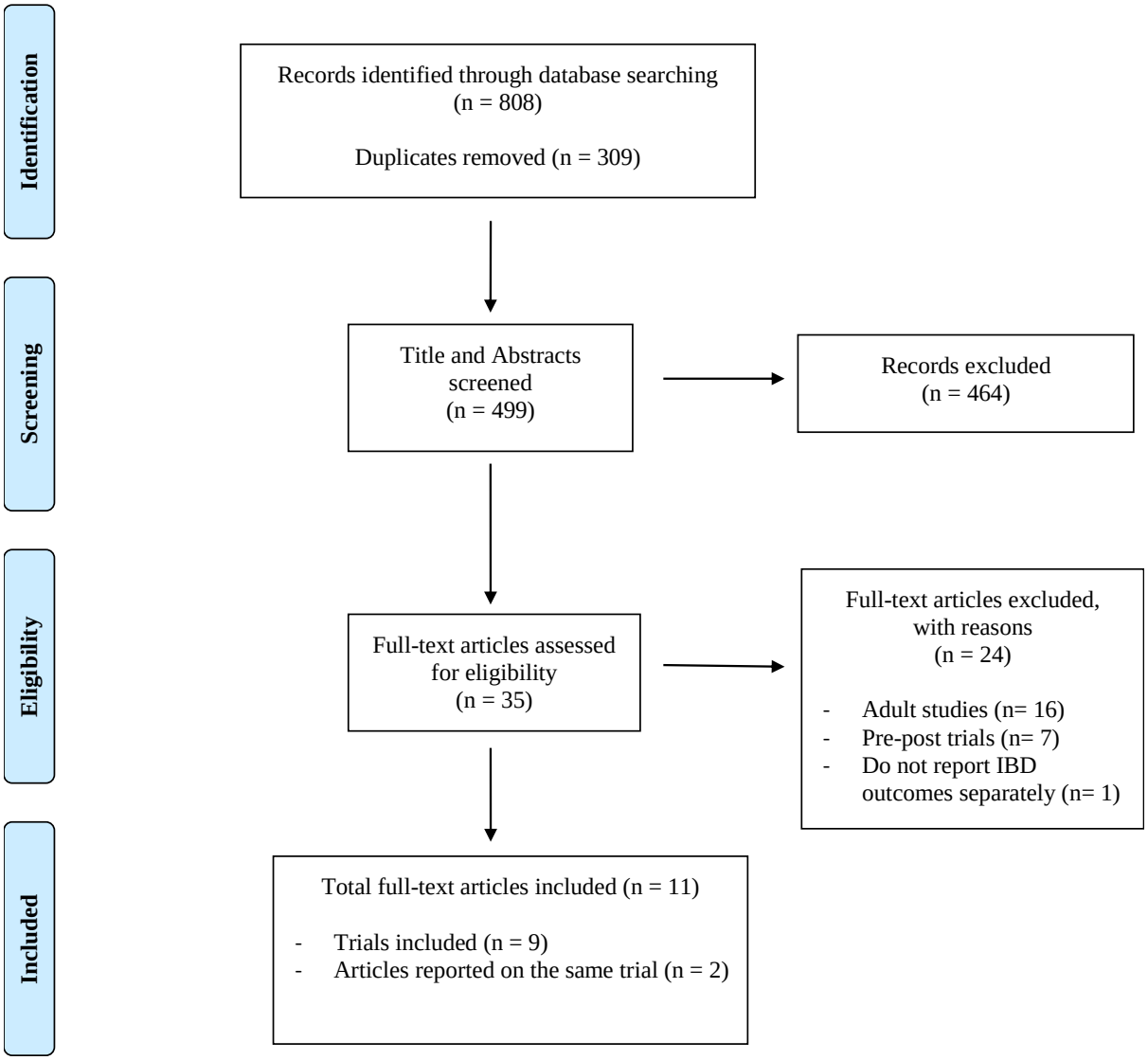
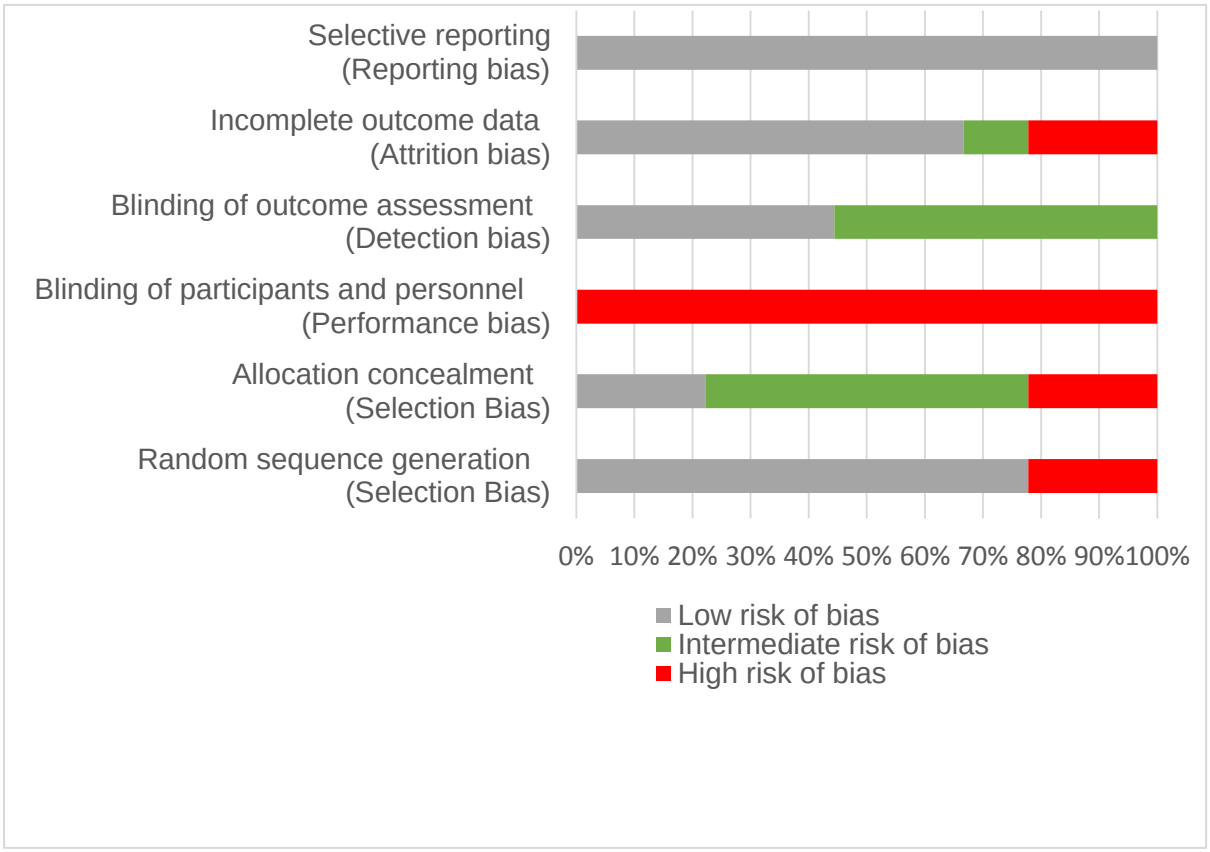


Figure 2. Risk of bias for all included trials



Supplemental file 1. Search terms

Search carried out in CINAHL. Date of search: 02.06.2016		
#	**Query**	**Results**
S25	S5 AND S9 AND S23 AND S24	33
S24	AB intervention* OR AB program* OR AB therapy	419,305
S23	S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22	420,275
S22	AB cope OR AB coping	22,126
S21	(MM "Coping")	9,812
S20	AB behavio#r* OR AB cognitive OR AB psycho*	227,807
S19	AB compliance OR AB adherence	32,408
S18	(MM "Patient Compliance")	10,075
S17	AB lifestyle	18,088
S16	(MM "Life Style")	6,212
S15	AB "health promotion"	9,890
S14	(MM "Health Promotion")	27,080
S13	AB education	108,359
S12	(MM "Patient Education")	20,015
S11	AB "self care" OR AB self manag*	13,307
S10	(MM "Self Care")	13,991
S9	S6 OR S7 OR S8	210,330
S8	AB child* OR AB adolescen* OR AB teen* OR AB young pe* OR AB	207,857

	juvenile OR AB youth	
S7	(MM "Adolescence")	1,540
S6	(MM "Child")	1,179
S5	S1 OR S2 OR S3 OR S4	8,245
S4	AB inflammatory bowel disease OR AB crohn* OR AB ulcerative colitis	3,937
S3	(MM "Colitis, Ulcerative")	1,856
S2	(MM "Crohn Disease")	2,811
S1	(MM "Inflammatory Bowel Diseases")	2,412

Supplemental file 2. PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Not registered
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3,4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Suppl file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Table 3
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5