

Constipation in adults

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Stefan Muller-Lissner and Arnold Wald

ABSTRACT

INTRODUCTION: Although there are defined criteria for the diagnosis of constipation, in practice, diagnostic criteria are less rigid, and depend in part on the perception of normal bowel habit. Constipation is highly prevalent, with approximately 12 million general practitioner prescriptions for laxatives in England in 2001. **METHODS AND OUTCOMES:** We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of non-drug interventions, bulk-forming laxatives, faecal softeners, stimulant laxatives, osmotic laxatives, prostaglandin derivatives, and 5-HT4 agonists in adults with idiopathic chronic constipation? We searched: Medline, Embase, The Cochrane Library, and other important databases up to October 2009 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). **RESULTS:** We found 51 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. **CONCLUSIONS:** In this systematic review we present information relating to the effectiveness and safety of the following interventions: arachis oil, biofeedback, bisacodyl, cascara, docusate, exercise, glycerol/glycerine suppositories, high-fibre diet, increasing fluids, ispaghula husk, lactitol, lactulose, lubiprostone, macrogols (polyethylene glycols), magnesium salts, methylcellulose, paraffin, phosphate enemas, seed oils, senna, sodium citrate enemas, prucalopride, and sterculia.

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INTERVENTIONS		
NON DRUG INTERVENTIONS		
Likely to be beneficial	Likely to be beneficial	
High-fibre diet or advice to consume a high-fibre diet	Lactitol 14	
3	Lactulose 13	
Unknown effectiveness	Unknown effectiveness	
Biofeedback 6	Salinic laxatives 14	
Exercise or advice to exercise 5	Phosphate enemas 15	
Increasing fluids or advice to increase fluids 5	Sodium citrate enemas 15	
FIBRE SUPPLEMENTS		
Likely to be beneficial	Unknown effectiveness	
Ispaghula husk (psyllium) 8	Bisacodyl 15	
Unknown effectiveness	Cascara 16	
Methylcellulose 9	Docusate 16	
Sterculia 10	Glycerol/glycerin suppositories 16	
PARAFFIN		
Unknown effectiveness	Senna 16	
Paraffin 10	PROSTAGLANDIN DERIVATIVES	
Seed oils/arachis oil 10	Likely to be beneficial	
OSMOTIC LAXATIVES		
Beneficial	Lubiprostone New 17	
Macrogols (polyethylene glycols) 10	5-HTA AGONISTS	
	Likely to be beneficial	
	Prucalopride New 18	

Covered elsewhere in Clinical Evidence

Constipation in children

Key points

- People with chronic idiopathic constipation can be divided into two main categories: those with difficulty defecating (but with normal bowel motion frequency) and those with a transit abnormality (which can present as infrequent defecation).
Although there are defined criteria for the diagnosis of constipation, in practice, diagnostic criteria are less rigid and depend in part on the perception of normal bowel habit.
Constipation is highly prevalent, with approximately 12 million general practitioner prescriptions for laxatives being written in England in 2001.
- **Increasing fibre intake** and **exercise** may improve the symptoms and prevalence of constipation.
We haven't found sufficient evidence examining the effects of other non-drug interventions, such as **increasing fluid intake** or performing **biofeedback**, although biofeedback may be useful for constipation caused by pelvic floor dyssynergia.
Despite this lack of firm evidence, a number of poorer-quality studies have implicated these lifestyle interventions as potentially beneficial.
- **Macrogols** (polyethylene glycols) improve symptoms of constipation without any serious adverse effects.
Lactitol and **lactulose** may be equally effective in improving the frequency of bowel movements.
We found no RCTs on the effects of **magnesium salts**, or **phosphate** or **sodium citrate enemas**.
- The bulk-forming laxative **ispaghula husk** (psyllium) seems more effective than lactulose at improving overall symptoms of constipation.
- **Prucalopride** and **lubiprostone** seem to be more effective than placebo at improving frequency of bowel movements and spontaneous complete bowel movements in people with chronic constipation.
- Although the efficacy of lubiprostone has been shown in RCTs, we are unsure about its role because of relatively frequent adverse events.
We don't know whether other bulk-forming laxatives, such as **methylcellulose** or **sterculia**, are effective for improving symptoms of constipation.
- We don't know the effectiveness of stimulant laxatives, such as **bisacodyl**, **cascara**, **docusate**, **glycerol/glycerine suppositories**, or **senna**.
- Although generally considered beneficial, we did not find any evidence examining the use of the faecal softeners **paraffin** and **seed oils/arachis oil** for treating constipation.

DEFINITION

Bowel habits and perception of bowel habits vary widely within and among populations, making constipation difficult to define. People with constipation can be divided into two main categories: those with difficulty defecating (but normal bowel motion frequency) and those with a transit abnormality (which can present as infrequent defecation). The Rome III criteria is a standardised tool that diagnoses chronic constipation on the basis of two or more of the following symptoms for at least 12 weeks in the preceding 6 months: straining at defecation on at least one quarter of occasions, stools that are lumpy/hard on at least one quarter of occasions, sensation of incomplete evacuation on at least one quarter of occasions, and three or fewer bowel movements a week.^[1] In practice, however, diagnostic criteria are less rigid and are in part dependent on perception of normal bowel habit. Typically, chronic constipation is diagnosed when a person has bowel actions twice a week or less for two consecutive weeks, especially in the presence of features such as straining at stool, abdominal discomfort, and sensation of incomplete evacuation. **Population:** For the purposes of this review we included all RCTs stating that all participants had chronic constipation, whether or not this diagnosis was made according to strict Rome III criteria. Where the definitions of constipation in the RCTs differ markedly from those presented here, we have made this difference explicit. In this review, we deal with chronic constipation not caused by a specific underlying disease (sometimes known as idiopathic constipation) in adults aged over 18 years, although we have included adults with pelvic floor dyssynergia. We excluded studies in pregnant women and in people with constipation associated with underlying specific organic diseases such as dehydration, autonomic neuropathy, spinal cord injury, bowel obstruction, irritable bowel syndrome, or paralytic ileus. We excluded people with Parkinson's disease and dementia, people who were post operative, or who were terminally ill. Opioid-induced constipation was also excluded. **Diagnosis:** The diagnosis of constipation is initially based on history (see above). Specific tests available for further investigation include thyroid function tests, calcium concentration, barium enema or colonoscopy, defecation proctogram, anorectal manometry, and colon transit time studies.

INCIDENCE/ PREVALENCE	Twelve million general practitioner prescriptions were written for laxatives in England in 2001. ^[2] Prevalence data are limited by small samples and problems with definition. One UK survey of 731 women found that 8.2% had constipation meeting Rome II criteria, and 8.5% defined themselves as being constipated. ^[3] A larger survey (1892 adults) found that 39% of men and 52% of women reported straining at stool on more than one quarter of occasions. ^[4] Prevalence rises in older people. Several surveys from around the world suggest that, in a community setting, prevalence among older people is about 20%. ^{[4] [5] [6] [7]}
AETIOLOGY/ RISK FACTORS	One systematic review suggested that factors associated with an increased risk of constipation included low-fibre diet, low fluid intake, reduced mobility, consumption of drugs such as opioids and anticholinergic antidepressants, and Parkinson's disease. ^[8]
PROGNOSIS	Untreated constipation can lead to faecal impaction (with resulting faecal incontinence), particularly in older and confused people. ^[9] Constipation has been suggested as a risk factor for haemorrhoids and diverticular disease; however, evidence of causality is lacking. ^[9]
AIMS OF INTERVENTION	To relieve symptoms of constipation, to restore normal bowel habit, and to improve quality of life, with minimal adverse effects.
OUTCOMES	Frequency of bowel movements, straining at defecation, hard/lumpy stools, sensation of incomplete evacuation/tenesmus; use of laxatives; cure of constipation (based on Rome III criteria or self or practitioner's report); adverse effects.
METHODS	<i>Clinical Evidence</i> search and appraisal October 2009. The following databases were used to identify studies for this review: Medline 1966 to October 2009, Embase 1980 to October 2009, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials 2009, Issue 3. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD) — for Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA), Turning Research into Practice (TRIP), and National Institute for Health and Clinical Excellence (NICE). Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the authors for additional assessment, using pre-determined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews and RCTs in any language, and containing more than 20 individuals. There was no minimum length of follow-up required to include studies. We included all studies described as "open", "open label", or not blinded as well as any blinded studies. We also did a search for cohort studies on specific harms of named interventions. For lifestyle interventions, we also included observational studies. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the review as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 22). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the <i>Clinical Evidence</i> population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of non-drug interventions in adults with idiopathic chronic constipation?

OPTION HIGH-FIBRE DIET OR ADVICE TO CONSUME A HIGH-FIBRE DIET

Frequency of bowel movement

Compared with lower-fibre diet Consuming fibre-rich bread (with or without Lactobacillus GG yoghurt) may be more effective than consuming low-fibre bread (with or without Lactobacillus GG yoghurt) at increasing frequency of bowel movement at 3 weeks (low-quality evidence).

Compared with increased fluid intake plus high-fibre diet Consuming a high-fibre diet alone seems less effective at increasing stool frequency (moderate-quality evidence).

Straining during defecation

Compared with lower-fibre diet Consuming fibre-rich bread (with or without *Lactobacillus* GG yoghurt) may be more effective than consuming low-fibre bread (with or without *Lactobacillus* GG yoghurt) at improving ease of defecation at 3 weeks (low-quality evidence).

Hard stool

Compared with lower-fibre diet Consuming fibre-rich bread (with or without *Lactobacillus* GG yoghurt) may be more effective than low-fibre bread (with or without *Lactobacillus* GG yoghurt) at improving stool softness at 3 weeks (low-quality evidence).

Laxative use

Compared with increased fluid intake plus high-fibre diet Consuming a high-fibre diet alone seems less effective at reducing laxative use (moderate-quality evidence).

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits:

We found one small RCT (59 women aged 18–57 years with self-reported constipation) that compared fibre-rich rye bread with or without *Lactobacillus* GG yoghurt versus low-fibre bread with or without *Lactobacillus* GG yoghurt for 3 weeks.^[10] The RCT found that the groups consuming fibre-rich rye bread had significant increases in bowel movement frequency, softened stool, and ease of defecation at 3 weeks compared with the groups consuming low-fibre bread (mean difference in bowel movement frequency: 0.3 defecations a day, 95% CI 0.1 defecations a day to 0.5 defecations a day; $P = 0.001$; mean difference in consistency of stools [measured on a scale in which $-1 = \text{loose}$, $0 = \text{normal}$, $+1 = \text{hard}$]: -0.3 , 95% CI -0.4 to -0.2 ; P less than 0.001 ; mean difference in difficulty with defecation [measured on a scale in which $-1 = \text{easy}$, $0 = \text{normal}$, $+1 = \text{straining}$]: -0.4 , 95% CI -0.5 to -0.2 ; P less than 0.001). The RCT did not carry out a direct statistical comparison for fibre-rich bread alone versus low-fibre bread alone.

High-fibre diet versus high-fibre diet plus increasing fluids:

See benefits of [increasing fluids or advice to increase fluids, p 5](#) .

Harms:

The RCT that compared fibre-rich bread with or without *Lactobacillus* GG yoghurt versus low-fibre bread with or without *Lactobacillus* GG yoghurt for 3 weeks used a symptom score to assess the severity of gastrointestinal adverse effects.^[10] The score ranked symptoms on a scale of 0 to 3, and evaluated abdominal pain, flatulence, borborygmi, abdominal bloating, and loose stools. The RCT found that, in the first week, fibre-rich bread significantly increased gastrointestinal symptoms — mainly flatulence and abdominal bloating — compared with low-fibre bread (baseline adjusted mean score: 4.7 with rye bread v 2.6 with low-fibre bread; mean difference in symptom score: 2.1, 95% CI 1.1 to 3.0; P less than 0.001). However, gastrointestinal symptoms associated with rye bread decreased by the third intervention week (baseline adjusted mean score: 3.6 with rye bread v 2.7 with low fibre bread; mean difference in symptom score: 0.9, 95% CI 0.1 to 0.9; $P = 0.039$).

High-fibre diet versus high-fibre diet plus increasing fluids:

See harms of [increasing fluids or advice to increase fluids, p 5](#) .

Comment:

Clinical guide:

One prospective cohort study (3327 women aged 30–55 years with constipation, defined as 2 or fewer weekly bowel movements) that assessed the effect of a high-fibre diet on constipation found that women with higher dietary fibre intake were significantly less likely to report constipation compared with women with a lower median daily fibre intake of 7 g daily (multivariate analysis: proportion of women reporting constipation: 742/3327 [22%] with daily fibre intake of 7.1 g v 635/3327 [19%] with daily fibre intake of 10.2 g v 959/3327 [29%] with daily fibre intake of 12.5 g v 544/3327 [16%] with daily fibre intake of 18.1 g v 447/3327 [13%] with daily fibre intake of 20.2 g; P for trend less than 0.0001).^[11] The study reported that women with the highest dietary fibre intake (median daily fibre intake of 20 g/day) were significantly less likely to report constipation compared with women with the lowest median daily fibre intake of 7 g daily (prevalence ratio [PR] 0.64, 95% CI 0.57 to 0.73). However, the authors noted that a mean fibre intake of 20 g daily is below the recommended daily fibre intake. Analysis included logistic regression to control for multiple variables (age, BMI, smoking status, postmenopausal hormone use, physical activity, aspirin use, number of medications, alcohol, coffee, and fibre).

It is thought that fibre increases the bulk and plasticity of stool, which might distend the colon and promote propulsive activity and colonic transit. The results from published studies are contradictory; however, overall, fibre intake seems to improve the symptoms and reduce the prevalence of constipation.

OPTION EXERCISE OR ADVICE TO EXERCISE**Cure rate**

Compared with normal lifestyle Regular exercise may be more effective at decreasing the number of people fulfilling Rome II criteria for constipation at 12 weeks ([low-quality evidence](#)).

Frequency of bowel movement

Compared with normal lifestyle Regular exercise may be no more effective at increasing frequency of bowel movement at 12 weeks ([very low-quality evidence](#)).

Straining during defecation

Compared with normal lifestyle Regular exercise may be more effective at decreasing straining during defecation at 12 weeks ([very low-quality evidence](#)).

Hard stool

Compared with normal lifestyle Regular exercise may be more effective at reducing the number of hard stools at 12 weeks ([very low-quality evidence](#)).

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits:

We found no systematic review. We found one small RCT (43 people aged 45 years or over and with constipation fulfilling the Rome II criteria) comparing a 12-week exercise programme consisting of a brisk 30-minute walk and a daily 11-minute programme versus a waiting list control (normal lifestyle for 12 weeks).^[12] The RCT found that, after 12 weeks, the number of fulfilled [Rome criteria](#) for constipation decreased in the group taking regular exercise but not in the group maintaining a normal lifestyle (change from baseline in number of Rome criteria: from 2.7 to 1.7 with exercise v from 2.3 to 2.6 with no exercise; significance not assessed).^[12] The RCT found larger reductions in the exercise group in the proportion of people reporting hard stools and straining at defecation at 12 weeks compared with the waiting list control group (hard stool: from 59% to 39% with exercise v from 54% to 52% with no exercise; strain at defecation: from 71% to 40% with exercise v from 66% to 69% with no exercise; absolute numbers not reported and significance not assessed for any outcome). However, the RCT found that the change in the number of defecations a week after 12 weeks was similar for the two groups (from 7.5 to 7.8 with exercise v from 7.1 to 7.5 with no exercise; significance not assessed).

Harms:

The RCT gave no information on adverse effects.^[12]

Comment:**Clinical guide:**

One prospective cohort study (3327 women aged 30–55 years with constipation, defined as 2 or fewer weekly bowel movements) that assessed the effects of physical activity on constipation found that women who reported physical activity of once a week or more were significantly less likely to report constipation compared with those who were sedentary (multivariate analysis: proportion of women reporting constipation: 1454/3327 [44%] with exercise less than once a week v 671/3327 [20%] with exercise once a week v 782/3327 [24%] with exercise 2–3 times a week v 340/3327 [10%] with exercise 4–6 times a week v 80/3327 [2%] with daily exercise; P for trend less than 0.0001).^[11] The study reported that women taking daily exercise were significantly less likely to report constipation compared with women who exercised less than once a week (prevalence ratio [PR] 0.56, 95% CI 0.44 to 0.70). Analysis included logistic regression to control for multiple variables (age, BMI, smoking status, postmenopausal hormone use, physical activity, aspirin use, number of medications, alcohol, coffee, and fibre).

Regular exercise or increasing physical activity is not often offered as a treatment option for people with chronic idiopathic constipation. However, low to moderate levels of exercise are associated with a range of health benefits for people of all ages.

OPTION INCREASING FLUIDS OR ADVICE TO INCREASE FLUIDS**Frequency of bowel movement**

Compared with high-fibre diet alone Consuming a high-fibre diet plus increased intake of oral fluid seems more effective at increasing frequency of bowel movement ([moderate-quality evidence](#)).

Laxative use

Compared with high-fibre diet alone Consuming a high-fibre diet plus increases oral fluids seems more effective at reducing laxative use ([moderate-quality evidence](#)).

Note

We found no clinically important results from RCTs comparing the effects of increased fluid intake alone versus no active treatment or no treatment in adults with constipation.

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits: **Increasing fluids or advice to increase fluids versus placebo/no treatment:**

We found no systematic review or RCTs.

Increased fluid intake plus high-fibre diet versus high-fibre diet alone:

We found one RCT (117 people aged 18–50 years with chronic functional constipation [defined as less than 3 bowel movements a week]) that compared a daily fibre intake of 25 g plus increased fluid intake (1.5–2 L/day) versus high-fibre diet alone.^[13] The RCT found that, compared with high-fibre diet alone, increased fluid intake plus high-fibre diet significantly increased frequency of bowel movement (increase in stool frequency a week [change from baseline]: +2.4 [from 1.8 to 4.2] with increased fluids plus high-fibre diet v +1.3 [from 2.0 to 3.3] with high-fibre diet alone; P less than 0.001) and significantly decreased laxative use at 2 months (decrease in laxative use in doses/week [change from baseline]: –2.2 [from 2.5 to 0.3] with increased fluids plus high-fibre diet v –0.8 [from 1.5 to 0.7] with high-fibre diet alone; P less than 0.001).

Harms: **Increasing fluids or advice to increase fluids versus placebo/no treatment:**

We found no RCTs.

Increased fluid intake plus high-fibre diet versus high-fibre diet alone:

The RCT gave no information on adverse effects.^[13]

Comment: None.

OPTION

BIOFEEDBACK

Cure rate

Compared with sham or standard treatment Biofeedback may be more effective at improving global bowel satisfaction compared with sham but not standard treatment at 3 months in people with chronic constipation (low-quality evidence).

Frequency of bowel movement

Compared with sham or standard treatment Biofeedback may be more effective at improving the rate of complete spontaneous bowel movement at 3 months in people with chronic constipation (low-quality evidence).

Compared with macrogols We don't know whether biofeedback is more effective than macrogol plus advice on prevention of constipation at increasing frequency of bowel movement in people with anismus at 6 to 12 months (very low-quality evidence).

Straining during defecation

Compared with sham or standard treatment We don't know whether biofeedback improves straining scores at 3 months in people with chronic constipation (low-quality evidence).

Compared with balloon defecation training alone Adding biofeedback therapy to balloon defecation training may be no more effective at improving straining during defecation (very low-quality evidence).

Compared with macrogols Biofeedback may be more effective than macrogol plus advice on prevention of constipation at reducing straining during defecation in people with anismus at 6 to 12 months (low-quality evidence).

Laxative use

Compared with sham or standard treatment We don't know whether biofeedback reduces the rate of laxative consumption at 3 months in people with chronic constipation (low-quality evidence).

Compared with macrogols Biofeedback may be more effective than macrogol plus advice on prevention of constipation at reducing laxative use in people with anismus at 6 to 12 months (low-quality evidence).

Note

We found no clinically important results from RCTs comparing the effects of biofeedback versus no active treatment or no treatment in adults with constipation.

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits: We found one systematic review (search date 2002) that assessed the effects of biofeedback therapy in people with constipation.^[14] The review included prospective studies of both adults and children (733 adults, 27 studies, of which only 4 studies used parallel designs).

Biofeedback versus placebo/sham treatment/no treatment/standard treatment:

The review identified no RCTs comparing biofeedback versus placebo or no treatment. ^[14]

One subsequent RCT (77 people with chronic constipation [69 women, 8 men]) compared 3 treatment groups: biofeedback versus sham (both consisting of biweekly sessions to a maximum of 6 in 3 months) versus standard treatment (including laxatives, diet, and exercise). ^[15] The RCT found that biofeedback significantly improved the rate of complete spontaneous bowel movements a week compared with sham treatment (P less than 0.05) and standard treatment ($P = 0.006$). The RCT also reported that biofeedback significantly improved global bowel satisfaction compared with sham treatment (70% with biofeedback ν 40% with sham treatment; $P = 0.04$) but not standard treatment (reported as not significant; P value not reported) at 3 months. ^[15] The RCT found that biofeedback significantly improved stool frequency compared with standard treatment (mean difference: 7.1 with biofeedback ν 4.7 with standard treatment; $P = 0.019$), but not sham treatment (mean difference: 7.1 with biofeedback ν 5.4 with sham treatment; reported as not significant; P value not reported) at 3 months. The RCT also found no significant difference for biofeedback for stool consistency (mean difference: 3.9 with biofeedback ν 3.4 with sham treatment ν 3.5 with standard treatment), stool straining score (mean difference: 1.85 with biofeedback ν 1.8 with sham treatment ν 1.9 with standard treatment), or laxative consumption (Types I-II [Type I, high-fibre diet bran and stool softeners; Type II, oral laxatives {magnesium oxide, 17 g polyethylene glycol (Miralax)}: 85% with biofeedback ν 76% with sham treatment ν 75% with standard treatment; Types III-IV [Type III, stimulants {bisacodyl}; Type IV, enemas, suppositories, magnesium citrate, 236 g polyethylene glycol solutions]: 11% with biofeedback ν 16% with sham treatment ν 21% with standard treatment) compared with either sham or standard treatment (all comparisons reported as not significant; P value not reported) at 3 months. ^[15]

Biofeedback plus balloon defecation training versus balloon defecation training alone:

One RCT identified by the review (60 adults with constipation) compared perianal electromyographic (EMG) biofeedback plus balloon defecation training versus balloon defecation training alone. ^[16]

The RCT found similar improvements between groups in the number of straining episodes a week 1 week after treatment (from 5.5 to 3 with biofeedback plus balloon ν from 3 to 3 with biofeedback alone; significance not assessed). However, these results should be interpreted with caution because of methodological issues: the analysis included people who had crossed over to alternative treatment after only two unsuccessful treatment sessions (8 people).

Biofeedback versus macrogol:

We found one subsequent RCT (109 people with severe pelvic floor dyssynergia [[anismus](#)] not responding to treatment with 20 g daily of fibre plus enema or suppository up to twice weekly) that compared the effects of five weekly biofeedback sessions versus macrogol 4000 (29.2 g/day) plus advice on preventing constipation for 12 months. ^[17] Laxative-treated people were instructed to increase the dose of macrogol from 14.6 to 29.2 g daily after 6 months. Participants kept a diary recording symptoms of constipation, and also recorded a symptoms score, measured on a scale from 0 (worse) to 4 (major improvement). The RCT found that, at 6 months, a significantly larger proportion of people reported a major improvement in their symptoms of constipation with biofeedback compared with macrogol (43/54 [80%] with biofeedback ν 12/55 [22%] with macrogol; P less than 0.001). Biofeedback significantly reduced the number of bowel movements accompanied by straining at 6 and 12 months compared with macrogol (results presented graphically; P less than 0.01 for both timeframes). The RCT found that, compared with macrogol, biofeedback therapy also significantly reduced the need for laxatives at 6 months (dose/week: 0.59 with biofeedback ν 1.24 with macrogol; P less than 0.01) and at 12 months (dose/week: 0.48 with biofeedback ν 1.20 with macrogol; P less than 0.01) and significantly reduced the frequency of abdominal pain at 6 months (0.37 with biofeedback ν 1.00 with macrogol; P less than 0.01) and at 12 months (0.38 with biofeedback ν 0.96 with macrogol; P less than 0.01). Bowel movements increased in frequency by similar amounts in both groups at 6 and 12 months (6 months: from 3.91 to 5.87 with biofeedback ν from 3.98 to 4.91 with macrogol; 12 months: from 3.91 to 5.18 with biofeedback ν from 3.98 to 6.00 with macrogol; significance not assessed). All people treated with biofeedback reporting major improvement were able to relax the pelvic floor and defecate a 50 mL balloon at 6 and 12 months. ^[17]

Harms:**Biofeedback versus placebo/sham treatment/no treatment/standard treatment:**

The review found no RCTs comparing biofeedback versus placebo or no treatment. ^[14] The subsequent RCT gave no information on adverse effects. ^[15]

Biofeedback plus balloon defecation training versus balloon defecation training alone:

The RCT identified by the review gave no information on adverse effects. ^[16]

Biofeedback versus macrogol:

The RCT gave no information on adverse effects ^[17]

Comment: Benefit from biofeedback therapy seems limited to people with paradoxically contracting puborectalis syndrome (also called **anismus** or pelvic floor dyssynergia). In some studies included in the review, up to 75% to 90% of people with anismus had a successful response to biofeedback therapy. However, the review highlights that, although most studies reported positive results using biofeedback to treat constipation, methodological flaws, such as lack of randomised trials, heterogeneity of study populations, and small samples preclude meaningful conclusions.^[14] Although most studies report positive results using biofeedback to treat constipation, quality research is lacking. A total of 48 biofeedback studies on constipation without recognised organic causes were identified. Ten of these were controlled-outcome studies. All except three of the controlled studies were in children. Two of these studies were of poor quality, owing to small numbers of patients and use of retrospective controls. The best of these studies support the use of biofeedback for constipation caused by functional outlet obstruction.^{[18] [19] [20] [21]}

Clinical guide:

Biofeedback may have a role in people with constipation caused by obstructed defecation secondary to anismus.^[22] Biofeedback has demonstrated efficacy in that small group of chronically constipated patients who do not respond to standard therapies and who exhibit evidence of pelvic floor dyssynergia on diagnostic testing.

QUESTION What are the effects of fibre supplements in adults with idiopathic chronic constipation?

OPTION ISPAGHULA HUSK (PSYLLIUM)

Frequency of bowel movement

Compared with placebo Ispaghula husk is more effective at increasing frequency of bowel movement at 2 weeks in adults with chronic idiopathic constipation (**high-quality evidence**).

Compared with lactulose We don't know whether ispaghula husk is more effective at increasing frequency of defecation at 4 weeks (**low-quality evidence**).

Compared with macrogols Ispaghula husk may be less effective at increasing stool frequency at 2 weeks (**very low-quality evidence**).

Compared with docusate Ispaghula husk may be more effective at increasing frequency of bowel movement at 2 weeks, although the difference may not be clinically important (**low-quality evidence**).

Straining during defecation

Compared with placebo Ispaghula husk seems more effective at reducing straining during defecation at 2 weeks in adults with chronic idiopathic constipation (**moderate-quality evidence**).

Compared with lactulose We don't know whether ispaghula husk is more effective at increasing frequency of defecation at 4 weeks (**low-quality evidence**).

Compared with docusate Ispaghula husk and docusate seem equally effective at reducing straining during defecation at 4 weeks (**moderate-quality evidence**).

Hard stool

Compared with macrogols Ispaghula husk may be less effective than macrogols plus electrolytes at increasing the proportion of people with normal stool consistency at 2 to 4 weeks (**very low-quality evidence**).

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits:

Ispaghula husk versus placebo:

We found one systematic review (1 RCT, search date 2001, 201 people aged 18–70 years [mean age 49 years], mean 2.3 bowel movements/week).^[8] The RCT identified by the review found that, compared with placebo, ispaghula husk 3.6 g three times daily significantly increased the frequency of bowel movements at 2 weeks (total number of bowel movements at 2 weeks: 14 with ispaghula v 9 with placebo; P less than 0.001).^[23] The RCT also found that, at 2 weeks, compared with placebo, ispaghula husk significantly increased the proportion of people rating their abdominal pain/discomfort as better (assessed using 3-point Likert scale as "better", "the same", or "worse"; rated as better: 44/101 [44%] with ispaghula v 27/95 [28%] with placebo; P = 0.035) and significantly reduced the proportion of people reporting straining on defecation (49/101 [49%] with ispaghula v 71/95 [75%] with placebo; P = 0.003). A significantly larger proportion of people rated their constipation as being "better" after treatment with ispaghula husk compared with placebo (90/101 [89%] with ispaghula v 46/95 [48%] with placebo; P less than 0.001).

Ispaghula husk versus macrogols:

See [benefits of macrogols](#), p 10 .

Ispaghula husk versus lactulose:

We found two systematic reviews (search dates 1995^[24] and 2001^[8]). The first review^[24] identified one RCT (124 people with at least a 3-week history of having 3 or fewer bowel movements a week, mean age 50 years).^[25] The RCT found no significant difference between ispaghula 3.5 g twice daily and lactulose 15 mL twice daily in frequency of bowel movement at 7 days (data presented graphically; P value not reported; reported as not significant).^[25] The RCT found no significant difference between groups at 7 days in the proportion of people reporting no abdominal pain (31/54 [57%] with ispaghula v 32/53 [60%] with lactulose) or no straining at stool (16/54 [30%] with ispaghula v 16/53 [30%] with lactulose), or in the proportion assessed as having a clinical improvement (defined by practitioner's report of overall clinical impression of symptom severity; much improved on Clinical Global Improvement score: 19/54 [35%] with ispaghula v 19/53 [36%] with lactulose; P values not reported; reported as not significant for all outcomes).^[25]

The second review^[8] identified one RCT:^[26] it is not clear why the review did not include the RCT^[25] identified by the first review.^[24] The RCT identified by the second review (394 people aged over 18 years and presenting to their general practitioner with constipation; 80% had had no bowel movement for at least 2 days) compared ispaghula husk 3.5 g twice daily (224 people) versus other laxatives chosen at the discretion of the general practitioner (170 people, of whom 91 received lactulose).^[26] Constipation was defined on the basis of self-report of perceived reduction in bowel frequency or difficulty in passing stool over the previous week. Subgroup analysis found that a similar proportion of people in the ispaghula husk and lactulose groups rated their bowel function at 28 days as "much better" (33% with ispaghula husk v 27% with lactulose; absolute numbers not reported; significance not assessed).

Ispaghula husk versus docusate:

We identified one systematic review (search date 2001),^[8] which identified one RCT (170 people with constipation and aged 20–70 years, 90% female, mean age 37 years).^[27] The RCT found that ispaghula husk 5.1 g twice daily significantly increased the frequency of bowel movements at 14 days compared with docusate sodium 100 mg twice daily (3.5 bowel movements/week with ispaghula husk v 2.9 bowel movements/week with docusate; P = 0.021). The RCT found no significant difference between groups at 14 days in straining at stool or pain with bowel motions (assessed using a 7-point patient-assessed scale, where 1 = normal/no symptoms and 7 = constipated/extreme symptoms: straining: 2.82 with ispaghula v 3.05 with docusate; P = 0.15; pain: 2.04 with ispaghula v 2.27 with docusate; P = 0.12).

Harms:

Reported adverse effects of ispaghula include flatulence, abdominal distension, and a feeling of bloating. However, we were unable to reliably estimate the frequency of these effects.

Ispaghula husk versus placebo:

The review^[8] and RCT^[23] identified by the review gave no information on adverse effects.

Ispaghula husk versus macrogols:

See [harms of macrogols](#), p 10 .

Ispaghula husk versus lactulose:

The RCT^[25] identified by the first review^[24] gave no information on adverse effects. The RCT^[26] identified by the second review^[8] found that proportionately fewer people had soiling at the time of the first bowel motion with ispaghula husk than with lactulose (2% with ispaghula v 8% with lactulose; absolute numbers not reported; significance not assessed).^[26]

Ispaghula husk versus docusate:

The review^[8] and the RCT identified by the review^[27] gave no information on adverse effects.

Comment:

Clinical guide: Treatment with commercial concentrated fibre products are a good way to assess whether dietary fibre works in a particular patient. If it does work, enrichment of the diet with whole-grain products and bran should be tried. They are cheaper but may be less well tolerated.

OPTION**METHYLCELLULOSE**

We found no clinically important results from RCTs about the effects of methylcellulose in adults with idiopathic chronic constipation.

For GRADE evaluation of interventions for constipation in adults, see [table](#), p 22 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: **Clinical guide:** Methylcellulose is a bulk-forming laxative. Non-randomised, uncontrolled trials suggest that it increases stool frequency, water content, ease of stool passage, and faecal solids in adults with constipation.

OPTION STERCULIA

We found no clinically important results from RCTs about the effects of sterculia in adults with idiopathic chronic constipation.

For GRADE evaluation of interventions for constipation in adults, [see table, p 22](#).

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

QUESTION What are the effects of paraffin (or similar compounds) in adults with idiopathic chronic constipation?

OPTION PARAFFIN

We found no clinically important results from RCTs about the effects of paraffin in adults with idiopathic chronic constipation.

For GRADE evaluation of interventions for constipation in adults, [see table, p 22](#).

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs. Paraffin reduces absorption of fat-soluble vitamins (vitamins A, D, E, and K). However, we found no reliable evidence to measure the risk of vitamin deficiency with paraffin in people with chronic constipation.

Comment: **Clinical guide:** Paraffin treatment is generally considered beneficial and cost effective. However, usage is becoming less common. The use of oral paraffin should be discouraged owing to the risk of aspiration pneumonia in persons with disordered swallowing.

OPTION SEED OILS/ARACHIS OIL

We found no clinically important results from RCTs about the effects of seed oils/arachis oil in adults with idiopathic chronic constipation.

For GRADE evaluation of interventions for constipation in adults, [see table, p 22](#).

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs. Arachis oil is derived from peanuts, and is therefore contraindicated in people with peanut allergy.

Comment: None.

QUESTION What are the effects of osmotic laxatives in adults with idiopathic chronic constipation

OPTION MACROGOLS (POLYETHYLENE GLYCOLS)

Cure rate

Compared with placebo Macrogols (polyethylene glycols) seem more effective at improving rates of treatment success at 6 months in people with constipation ([moderate-quality evidence](#)).

Frequency of bowel movement

Compared with placebo Macrogols (polyethylene glycols) seem more effective at increasing frequency of bowel movement at 1 to 30 weeks in adults with idiopathic chronic constipation (moderate-quality evidence).

Compared with biofeedback We don't know whether macrogol plus advice on prevention of constipation is more effective at increasing frequency of bowel movement in people with anismus at 6 to 12 months (very low-quality evidence).

Compared with ispaghula husk Macrogols plus electrolytes may be more effective at increasing frequency of bowel movement at 2 weeks (very low-quality evidence).

Compared with lactulose Macrogols seem more effective at increasing frequency of bowel movement at 2 to 4 weeks (moderate-quality evidence).

Straining during defecation

Compared with placebo Macrogols may be more effective at reducing straining during defecation (low-quality evidence).

Compared with biofeedback Macrogol plus advice on prevention of constipation may be less effective at reducing straining during defecation in people with anismus at 6 to 12 months (low-quality evidence).

Compared with lactulose Macrogols may be more effective at improving ease of defecation at 2 to 4 weeks (low-quality evidence).

Hard stool

Compared with ispaghula husk Macrogols plus electrolytes may be more effective at increasing the proportion of people with normal stool consistency at 2 to 4 weeks (very low-quality evidence).

Laxative use

Compared with placebo We don't know whether macrogols are more effective at reducing rescue laxative use at 6 months in adults with constipation (moderate-quality evidence).

Compared with biofeedback Macrogol plus advice on prevention of constipation may be less effective at reducing laxative use in people with anismus at 6 to 12 months (low-quality evidence).

Adverse effects

Macrogols have been associated with diarrhoea and abdominal pain.

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits:

Macrogols versus placebo:

We found one systematic review (search date 2001, [8] 2 RCTs meeting our reporting criteria [28] [29]) and one additional RCT. [30] The first RCT identified by the review (151 people with no more than 2 bowel movements during the 7-day run-in period, mean age 47 years) found that macrogol 17 g significantly increased the frequency of bowel movements and the number of satisfactory bowel movements (defined by self-report) after 14 days compared with dextrose placebo (number of bowel movements: 4.5 with macrogols v 2.7 with placebo; P less than 0.001; satisfactory bowel movements: 68% with macrogol v 46% with placebo; absolute numbers and P values not reported; reported as significant). [28]

The second RCT identified by the review (55 people with fewer than 2 bowel movements/week for more than 12 months, mean age 42 years) compared twice-daily macrogols versus placebo. It found that macrogols significantly increased the frequency of bowel movements at 8 weeks (number of bowel movements a week: 4.8 with macrogols v 2.8 with placebo; P less than 0.002), and decreased marked straining at defecation (8% with macrogols v 41% with placebo; absolute numbers not reported; P less than 0.03) compared with placebo. [29] The additional small crossover RCT (34 people aged 20–60 years) found that macrogol 3350 (69.6 g/L; 500 mL/day) increased the frequency of bowel movements at 1 week compared with placebo, but significance was not assessed for this pre-crossover period (13.56 bowel movements/week with macrogols v 5.53 bowel movements/week with placebo). [30]

One subsequent RCT (304 people with constipation defined by Rome criteria) compared macrogol (polyethylene glycol; PEG) (17 g/day) (204 people) versus placebo (100 people) for 6 months. [31] The RCT found that PEG significantly increased treatment success (defined as relief from modified Rome criteria for at least 50% of the treatment weeks) (52% with PEG v 11% with placebo; P less than 0.001) at 6 months. A subgroup analysis of 75 older people (parameters undefined) had similar results (no data reported). The RCT found that PEG significantly improved bowel movements a week, complete spontaneous bowel movements a week, and global assessment scores compared with placebo at 6 months (bowel movements a week; mean difference: 7.9 with PEG v 5.6 with

placebo; P less than 0.001; complete spontaneous bowel movements a week; mean difference: 5.4 with PEG v 2.7 with placebo; P less than 0.001; global assessment scores; mean difference: 12.5 with PEG v 5.2 with placebo; P less than 0.001). However there was no significant difference between groups for the rate of rescue laxative use (mean difference: 2.8 with PEG v 3.9 with placebo; P less than 0.138).^[31]

Macrogols versus ispaghula husk:

We found one systematic review (search date 2001),^[8] which identified one RCT published only as an abstract (120 people in hospital, mean age 50 years). The review found that macrogol 3350 13.7 g plus electrolytes twice daily significantly increased "overall effectiveness" compared with ispaghula 3.5 g twice daily at 2 weeks (92% with macrogol 3350 v 73% with ispaghula; P = 0.005). "Overall effectiveness" was not defined in the review, and no further details were available.^[8]

We found one subsequent RCT (126 people aged 18–75 years with chronic functional constipation), which compared macrogol 3350 plus electrolytes (13.8 g/sachet twice daily) versus ispaghula husk (3.5 g/sachet twice daily) for 2 weeks.^[32] The RCT found that, at 14 days, macrogol significantly increased bowel movement frequency and the proportion of people with normal stool consistency compared with ispaghula husk (bowel movement frequency; mean weekly defecation rate: 8.48 with macrogol v 5.71 with ispaghula husk; P less than 0.001; proportion of people with normal stool consistency: 55/63 [87%] with macrogol v 42/63 [67%] with ispaghula husk; P less than 0.001).

Macrogols versus lactulose:

We found one systematic review (search date 2001),^[8] which identified one RCT,^[33] and one subsequent RCT.^[34] The RCT identified by the review (115 people aged 18 years or over and passing fewer than 3 stools/week, straining at stool, or both) found that, compared with lactulose 20 g daily at 4 weeks, macrogol 3350 26 g daily significantly increased the number of weekly bowel movements (1.3 with macrogol 3350 v 0.9 with lactulose; P = 0.005), and significantly improved ease of stool evacuation (scored as 0 for "easy" to 4 for "very difficult"; absolute mean score: 0.5 with macrogol 3350 v 1.2 with lactulose; P = 0.001) and global satisfaction (satisfaction scored as 0 for "terrible" to 10 for "excellent": 7.4 with macrogol 3500 v 5.2 with lactulose; P less than 0.001).^[33]

The subsequent RCT (85 older people) found that macrogol 4000 10 g daily significantly increased the proportion of people with complete remission of constipation compared with lactulose 15 mL daily at 2 and 4 weeks (2 weeks: 64% with macrogol 4000 v 39% with lactulose; P less than 0.01; 4 weeks: 69% with macrogol 4000 v 42% with lactulose; P less than 0.01; absolute numbers not reported).^[34] The data reported from this RCT are taken from only the abstract; we are currently awaiting translation of this reference.

Macrogols versus biofeedback:

See [benefits of biofeedback](#), p 6 .

Harms:

Macrogols versus placebo:

The first RCT identified by the review found no significant difference between macrogols and placebo in adverse effects (no further data reported).^[28] The second RCT identified by the review found no significant difference in abdominal symptoms at 8 weeks between macrogols and placebo (abdominal pain: 24% with macrogols v 35% with placebo; abdominal bloating: 48% with macrogols v 70% with placebo; flatulence: 20% with macrogols v 39% with placebo; borborygmi: 32% with macrogols v 13% with placebo; absolute numbers not reported; P values not reported; reported as not significant).^[29] The additional RCT gave no information on adverse effects by treatment group.^[30]

Macrogols versus ispaghula husk:

The review gave no information on adverse effects.^[8] The RCT found no significant difference in the proportion of people with adverse effects over 14 days between macrogol 3350 plus electrolytes and ispaghula husk (7/60 [12%] with macrogol v 5/60 [8%] with ispaghula husk; P = 0.76). Adverse effects were minor and none required treatment.^[32]

Macrogols versus lactulose:

The RCT identified by the review found two adverse effects (acute diarrhoea and abdominal pain) leading to withdrawal with macrogols 3350 compared with one adverse effect (depression) with lactulose.^[33] It found that macrogol 3350 significantly increased the frequency of liquid stools compared with lactulose over 4 weeks (mean number of loose stools: 2.4 with macrogol 3350 v 0.6 with lactulose; P = 0.001). The subsequent RCT found no significant difference in adverse effects between macrogol and lactulose (12% with macrogol 4000 v 16% with lactulose; absolute numbers not reported; P greater than 0.05).^[34]

Macrogols versus biofeedback:

See harms of biofeedback, p 6 .

Comment: The data reported from the subsequent RCT are taken from the abstract; we are currently awaiting translation of this reference, and additional data may be added after further assessment. ^[34]

OPTION**LACTULOSE****Frequency of bowel movement**

Compared with placebo High-dose lactulose (60 mL 4 times/day) may be more effective at increasing frequency of bowel movement at 1 week in adults with chronic idiopathic constipation ([low-quality evidence](#)).

Compared with macrogols Lactulose seems less effective at increasing frequency of bowel movement at 2 to 4 weeks ([moderate-quality evidence](#)).

Compared with ispaghula husk We don't know whether lactulose is more effective at increasing frequency of defecation at 4 weeks (low-quality evidence).

Compared with lactitol We don't know whether lactulose is more effective at increasing frequency of bowel movement at 2 to 4 weeks (low-quality evidence).

Straining during defecation

Compared with macrogols Lactulose may be less effective at improving ease of defecation at 2 to 4 weeks (low-quality evidence).

Compared with ispaghula husk We don't know whether lactulose is more effective at increasing frequency of defecation at 4 weeks (low-quality evidence).

Hard stool

Compared with placebo Lactulose may be more effective at increasing the proportion of people reporting complete or partial treatment success, as assessed by improvement in stool consistency score at 4 weeks ([very low-quality evidence](#)).

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits: We found three systematic reviews that included trials of lactulose (search dates 1995, ^[24] 1996, ^[9] and 2001 ^[8]).

Lactulose versus placebo:

The reviews identified two RCTs that met *Clinical Evidence* reporting criteria. One RCT (24 outpatients, mean age 28 years) identified by the first review ^[24] found that high-dose lactulose (60 mL 4 times/day) significantly increased the frequency of bowel movements compared with placebo at 1 week (4.5 bowel movements/week with lactulose v 2.8 bowel movements/week with placebo; P less than 0.05). ^[35] The review with the most recent search date ^[8] identified one RCT ^[36] that compared lactulose versus placebo in a crossover design, with 4-week treatment periods and a 2-week washout. The RCT (30 adults; age range not specified) found that lactulose 30 mL significantly increased the proportion of people reporting complete or partial treatment success (measured by mean Bristol score of stool consistency) compared with placebo (23/29 [79%] with lactulose v 17/26 [65%] with placebo; P less than 0.01). Pre-crossover results were not reported.

Lactulose versus macrogols:

See benefits of macrogols, p 10 .

Lactulose versus ispaghula husk:

See benefits of ispaghula husk, p 8 .

Lactulose versus lactitol:

See benefits of lactitol, p 14 .

Harms:**Lactulose versus placebo:**

The reviews gave no information on adverse effects. ^[24] ^[9] ^[8]

Lactulose versus macrogols:

See harms of macrogols, p 10 .

Lactulose versus ispaghula husk:

See harms of ispaghula husk, p 8 .

Lactulose versus lactitol:

See harms of lactitol, p 14 .

Comment:**Clinical guide:**

Owing to the identical mode of action of lactulose, lactitol, sorbitol, and lactose (as far as not digested) no difference in efficacy and adverse effects between these sugars would be expected.

OPTION**LACTITOL****Frequency of bowel movement***Compared with placebo* Lactitol may be more effective at increasing frequency of bowel movement at 4 weeks in older adults with chronic constipation ([very low-quality evidence](#)).*Compared with lactulose* We don't know whether lactitol is more effective at increasing frequency of bowel movement at 2 to 4 weeks ([low-quality evidence](#)).**For GRADE evaluation of interventions for constipation in adults, see table, p 22 .****Benefits:****Lactitol versus placebo:**We found one systematic review (search date 1996, ^[9] 1 crossover RCT, ^[37] 43 people recruited in nursing homes and passing no more than 3 bowel movements/week, mean age 84 years). The RCT found that lactitol 20 g four times daily significantly increased the number of bowel movements compared with placebo at 21 and 28 days of treatment before crossover (absolute numbers presented graphically; P less than 0.001 for both timeframes). ^[37]**Lactitol versus lactulose:**We found two systematic reviews (search dates 1996 ^[9] and 2001 ^[8]), which between them identified three RCTs. ^[38] ^[39] ^[40] The first RCT (60 people in nursing homes, mean age 79 years, most not independent) found no significant difference between lactitol 15 g daily and lactulose 15 mL daily in the mean number of bowel movements over 12 days (mean: 9.4 bowel movements/person with lactitol v 8.4 bowel movements/person with lactulose; P = 0.053). ^[38]The second RCT (61 people, mean age 54 years) found no significant difference between lactitol (20 g/day for 3 days then 10 g/day) and lactulose (30 mL syrup [20.1 g]/day for 3 days then 20 mL syrup [13.4 g]/day) in frequency of bowel movements over 4 weeks (6.7 bowel movements/week with lactitol v 7.4 bowel movements/week with lactulose; P value not reported; reported as not significant). ^[39]The third RCT (60 people taking laxatives, mean age 60 years) found no significant difference between lactitol (mean dose 20 g/day) and lactulose 20 mL syrup daily in frequency of bowel movement at 2 weeks (6.1 bowel movements/week with lactitol v 5.5 bowel movements/week with lactulose; P greater than 0.05). ^[40]**Harms:****Lactitol versus placebo:**The review ^[9] and RCT ^[37] identified by the review gave no information on adverse effects.**Lactitol versus lactulose:**The first RCT gave no information on adverse effects. ^[38] The second RCT found that lactitol significantly reduced the proportion of people with adverse effects compared with lactulose (10/32 [31%] with lactitol v 16/26 [62%] with lactulose; P = 0.02). ^[39] The third RCT found no significant difference between lactitol and lactulose in adverse events or other symptoms (bloating, flatulence, nausea, cramping, or diarrhoea; no further data reported). ^[40]**Comment:****Clinical guide:**

Owing to the identical mode of action of lactulose, lactitol, sorbitol, and lactose (as far as not digested) no difference in efficacy and adverse effects between these sugars would be expected.

OPTION**SALINIC LAXATIVES (E.G., MAGNESIUM SALTS, SODIUM SULPHATE)****We found no clinically important results from RCTs about the effects of magnesium salts or sodium sulphate in adults with idiopathic chronic constipation.****For GRADE evaluation of interventions for constipation in adults, see table, p 22 .****Benefits:**

We found no systematic review or RCTs.

Harms:

We found no RCTs.

Comment: **Clinical guide:**
On the basis of clinical experience, the clinical efficacy of salinic laxatives in constipation is beyond any doubt. However, case reports show that salinic laxatives might be dangerous in patients with cardiac or kidney failure.

OPTION PHOSPHATE ENEMAS (RECTAL PHOSPHATES)

We found no clinically important results from RCTs about the effects of phosphate enemas in adults with idiopathic chronic constipation.

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: **Clinical guide:**
Phosphate enemas are commonly used in clinical practice, especially for symptoms of incomplete rectal emptying; however, there are no data to support their use.

OPTION SODIUM CITRATE ENEMAS (RECTAL SODIUM CITRATE)

We found no clinically important results from RCTs about the effects of sodium citrate enemas in adults with idiopathic chronic constipation.

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

QUESTION What are the effects of stimulant laxatives in adults with idiopathic chronic constipation?

OPTION BISACODYL

Frequency of bowel movement

Compared with placebo Bisacodyl may be more effective at increasing frequency of bowel movement at 3 days (low-quality evidence).

Hard stool

Compared with placebo Bisacodyl may be more effective at improving stool consistency at 3 days (low-quality evidence).

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits: We found no systematic review. We found one small RCT (55 people aged 19–89 years with idiopathic constipation) that compared bisacodyl 10 mg once daily versus placebo for 3 successive days.^[41] The RCT found that, compared with placebo, bisacodyl significantly increased frequency of bowel movements at 3 days (mean number of stools: 1.8 a day with bisacodyl v 0.95 a day with placebo; difference between groups 0.86, 95% CI 0.26 to 1.5; P = 0.006) and significantly improved mean stool consistency score (2.8 with bisacodyl v 4.2 with placebo; difference between groups –1.4, 95% CI –2.0 to –0.75; P less than 0.0001). Stool consistency was scored on a 5-point rating scale, where 1 = liquid and 5 = hard.^[41] It is important to consider the short duration and follow-up period of this study when evaluating its results.

Harms: The RCT found that the proportion of people reporting an adverse effect, including eosinophilia, monocytosis, and raised blood urea nitrogen, was similar for the two treatment groups (15/27 [56%] with bisacodyl v 18/27 [67%] with placebo; significance not assessed).^[41] None of the adverse events, in either the bisacodyl or placebo groups, was considered to be of clinical significance.^[41]

Comment: Stimulant laxatives have been implicated as a cause of cathartic colon in the past, but the evidence for this was found to be lacking in two reviews.^{[42] [43]} Recently completed RCTs show that both bisacodyl and its derivative sodium picosulphate increase stool frequency, decrease use of rescue

medication, and improve quality of life in patients with chronic constipation, thus reinforcing clinical experience. ^[44] ^[45]

OPTION DOCUSATE

Frequency of bowel movement

Compared with ispaghula husk Docusate may be less effective at increasing stool frequency at 2 weeks, although the difference may not be clinically important ([low-quality evidence](#)).

Straining during defecation

Compared with ispaghula husk Docusate and ispaghula husk seem equally effective at reducing straining during defecation at 4 weeks ([moderate-quality evidence](#)).

Note

We found no direct information from RCTs comparing docusate versus no active treatment in adults with chronic idiopathic constipation.

For GRADE evaluation of interventions for constipation in adults, [see table, p 22](#) .

Benefits: **Docusate versus placebo:**
We found one systematic review (search date 1995), which identified no RCTs of sufficient quality. ^[24]

Docusate versus ispaghula husk:
[See benefits of ispaghula husk, p 8](#) .

Harms: **Docusate versus placebo:**
The review gave no information on adverse effects. ^[24]

Docusate versus ispaghula husk:
[See harms of ispaghula husk, p 8](#) .

Comment: None.

OPTION GLYCEROL/GLYCERIN SUPPOSITORIES

We found no clinically important results from RCTs about the effects of glycerol/glycerin suppositories in adults with idiopathic chronic constipation.

For GRADE evaluation of interventions for constipation in adults, [see table, p 22](#) .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION SENNA

We found no clinically important results from RCTs about the effects of senna in adults with idiopathic chronic constipation.

For GRADE evaluation of interventions for constipation in adults, [see table, p 22](#) .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION CASCARA

We found no clinically important results from RCTs about the effects of cascara in adults with idiopathic chronic constipation.

For GRADE evaluation of interventions for constipation in adults, [see table, p 22](#) .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

QUESTION What are the effects of prostaglandin derivatives in people with idiopathic chronic constipation?

OPTION LUBIPROSTONE New

Cure rate

Compared with placebo Lubiprostone seems more effective at increasing response rates at 1 to 4 weeks in adults with idiopathic chronic constipation ([moderate-quality evidence](#)).

Frequency of bowel movement

Compared with placebo Lubiprostone seems to be more effective at increasing frequency of bowel movements at 1 to 4 weeks in adults with idiopathic chronic constipation ([moderate-quality evidence](#)).

Straining during defecation

Compared with placebo Lubiprostone seems more effective at reducing straining during defecation in adults with idiopathic chronic constipation ([moderate-quality evidence](#)).

Laxative use

Compared with placebo Lubiprostone seems more effective at reducing laxative use in people with chronic constipation at 4 weeks ([moderate-quality evidence](#)).

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .

Benefits: We found two RCTs comparing lubiprostone versus placebo. ^[46] ^[47]

The first RCT (129 people with chronic constipation who met Rome II criteria, 90% female, 109 people completed the study) compared lubiprostone (24, 48, or 72 micrograms/day) versus placebo for 3 weeks. ^[46] The RCT found that all three doses of lubiprostone significantly increased the number of spontaneous bowel movements (SBMs) compared with placebo (P = 0.046, absolute data not reported). ^[46] During week 1 of the study, the RCT found that 48 and 72 micrograms daily lubiprostone significantly increased SBMs (P less than 0.007 for both comparisons) compared with placebo, but there was no significant difference between 25 micrograms daily lubiprostone and placebo. During week 2 of the study, the RCT found that all three doses of lubiprostone significantly increased SBMs compared with placebo (24 and 48 micrograms/day: P less than 0.02; 72 micrograms/day: P less than 0.007); however, there were no significant differences between groups at week 3 (reported as not significant; P values not reported). ^[46] The RCT found that all doses of lubiprostone significantly improved degree of straining (P = 0.005), stool consistency (P less than 0.0001), severity of constipation (P = 0.010), and rating of treatment effectiveness (P = 0.045) when assessed subjectively by the participants. It also found no significant differences in the proportion of people who used rescue laxatives between groups for week 1 (10/29 [34%] with 24 micrograms/day v 10/32 [31%] with 48 micrograms/day v 10/33 [30%] with 72 micrograms/day v 13/33 [39%] with placebo; P = 0.6), week 2 (11/29 [39%] with 24 micrograms/day v 7/32 [25%] with 48 micrograms/day v 14/33 [47%] with 72 micrograms/day; P = 0.4 v 9/33 [30%] with placebo), and week 3 (10/29 [37%] with 24 micrograms/day v 8/32 [30%] with 48 micrograms/day v 12/33 [40%] with 72 micrograms/day; P = 0.715 v 13/33 [45%] with placebo). ^[46]

The second RCT (242 people with constipation) compared oral lubiprostone (24 micrograms twice daily) versus placebo for 4 weeks. ^[47] The RCT found that lubiprostone significantly increased the mean number of SBMs a week at week 1 (mean difference: 5.69 with lubiprostone v 3.46 with placebo; P = 0.0001), week 2 (mean difference: 5.06 with lubiprostone v 3.18 with placebo; P less than 0.02), week 3 (mean difference: 5.25 with lubiprostone v 2.84 with placebo; P less than 0.02) and week 4 (mean difference: 5.30 with lubiprostone v 2.91 with placebo; P less than 0.02) compared with placebo. ^[47] The RCT also found that lubiprostone significantly reduced the proportion of people who used rescue laxatives at week 4 (36% with lubiprostone v 51% with placebo; P = 0.03), and increased the proportion of people who were full responders (SBM frequency of more than 3 a week) at weeks 1 to 4 compared with placebo (week 1: 64% with lubiprostone v 43% with placebo; P less than 0.004; week 2: 58% with lubiprostone v 36% with placebo; P less than 0.004; week 3: 56% with lubiprostone v 29% with placebo; P less than 0.004; week 4: 59% with lubiprostone v 28% with placebo; P less than 0.004). The RCT reported that lubiprostone significantly improved

stool consistency (weeks 1 to 4: P less than 0.001), straining (weeks 1 to 4: P less than 0.001), and constipation severity (weeks 1 to 4: P less than 0.0003) compared with placebo. ^[47]

Harms:

The first RCT reported that lubiprostone significantly increased the risk of abdominal bloating (P = 0.035, absolute figures not reported), but not abdominal discomfort (P = 0.136, absolute figures not reported) compared with placebo. ^[46] It also found that 44% of people taking lubiprostone 48 micrograms daily and 36% taking 72 micrograms daily experienced nausea, but made no direct comparison between groups. ^[46]

The second RCT reported that lubiprostone significantly increased the risk of abdominal bloating (P less than 0.031), abdominal discomfort (P less than 0.045), nausea (P less than 0.001), flatulence (P = 0.035), and dizziness (P = 0.035) compared with placebo (absolute figures not reported for any comparison). ^[47] The RCT found no significant differences between groups for headache, abdominal pain, diarrhoea, loose stools, fatigue, abdominal distension, or dyspepsia. ^[47]

Comment:

None.

Clinical guide: Lubiprostone is available in the US but not in the EU.

QUESTION	What are the effects of 5-HTA agonists in people with idiopathic chronic constipation?
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OPTION	PRUCALOPRIDE	New
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Cure rate

Compared with placebo Prucalopride may be more effective at increasing response rate when subjectively assessed by people with chronic idiopathic constipation at 4 weeks. (low-quality evidence)

Frequency of bowel movement

Compared with placebo Prucalopride (1–4 mg) is more effective at increasing frequency of bowel movement at up to 12 weeks in people with chronic idiopathic constipation (high-quality evidence).

Hard stool

Compared with placebo Prucalopride is more effective at improving stool consistency up to 12 weeks in people with chronic idiopathic constipation (high-quality evidence).

Straining during defecation

Compared with placebo Prucalopride is more effective at reducing straining at up to 12 weeks in people with chronic idiopathic constipation (high quality evidence).

For GRADE evaluation of interventions for constipation in adults, see table, p 22 .**Benefits:**

We found no systematic review. We found three large RCTs ^[48] ^[49] ^[50] and two small RCTs ^[51] ^[52] that compared 1, 2, and 4 mg of prucalopride once daily versus placebo for 1 to 12 weeks.

The first RCT (628 people with severe chronic constipation; 75 males [12%]) found that prucalopride 2 and 4 mg significantly increased normal bowel function compared with placebo over 12 weeks (proportion with at least 3 complete bowel movements a week: 64/207 [31%] with prucalopride 2 mg v 58/204 [28%] with prucalopride 4 mg v 25/209 [12%] with placebo; P less than 0.001 for both doses prucalopride v placebo). ^[48]

The second RCT (713 people with chronic constipation; 66 males [9%]) found that prucalopride 2 and 4 mg significantly increased normal bowel function and complete evacuation compared with placebo over 12 weeks (proportion with at least 3 complete bowel movements a week: 46/236 [20%] with prucalopride 2 mg v 56/237 [24%] with prucalopride 4 mg v 23/240 [10%] with placebo; P less than 0.01 for 2 mg v placebo; P less than 0.001 for 4 mg v placebo; mean proportion of bowel movements said to be complete: 26% with prucalopride 2 mg v 36% with prucalopride 4 mg v 24% with placebo; P less than 0.05 for 2 mg v placebo; P less than 0.001 for 4 mg v placebo). ^[49] The RCT found that both doses of prucalopride reduced straining, but that the difference was significant only with prucalopride 4 mg (proportion of bowel movements without straining: 16% with prucalopride 2 mg v 20% with prucalopride 4 mg v 15% with placebo; P less than 0.05 for 4 mg v placebo; P value reported as not significant for 2 mg v placebo). ^[52]

The third RCT (641 people with chronic constipation; 86 males [13%]) found that prucalopride 2 and 4 mg significantly increased normal bowel function and complete evacuation compared with placebo over 12 weeks (proportion with at least 3 complete bowel movements a week: 50/209 [24%] with prucalopride 2 mg v 48/204 [24%] with prucalopride 4 mg v 25/207 [12%] with placebo; P less than 0.01 for 2 mg v placebo; P less than 0.001 for 4 mg v placebo; Mean proportion of

bowel movements said to have normal consistency: 42% with prucalopride 2 mg v 46% with prucalopride 4 mg v 36% with placebo; P less than 0.01 for 2 mg v placebo; P less than 0.001 for 4 mg v placebo).^[50] The RCT found that both doses of prucalopride reduced straining (proportion of bowel movements without straining: 27% with prucalopride 2 mg v 27% with prucalopride 4 mg v 19% with placebo; both doses P less than 0.01 v placebo).^[50]

The fourth RCT (74 women with constipation) found that prucalopride 1 mg significantly increased spontaneous stool frequency (7.6 stools/week for prucalopride v 5.0 stools/week on placebo; P less than 0.02). Prucalopride reduced the perceived severity of constipation compared with placebo at 4 weeks (mean visual analogue scale [VAS] scores: 65 with prucalopride v 21 with placebo; P less than 0.001).^[51]

The fifth RCT (53 people with chronic constipation, only one man in the placebo group) compared prucalopride 4 mg with placebo for 4 weeks.^[52] The RCT found that prucalopride was considered by participants to be significantly more effective than placebo at 4 weeks (VAS scores: 54 with prucalopride v 25 with placebo; P less than 0.01). The RCT also found that prucalopride significantly reduced the degree of straining compared with placebo (mean difference: 1.2 with prucalopride v 1.4 with placebo; P less than 0.05; based on: straining score per stool: 0 = none, 1 = a little, 2 = much).

Harms: The RCTs found that the proportion of people reporting an adverse effect was similar for the treatment groups. The most frequently reported adverse events were headache, nausea, abdominal pain, and diarrhoea. These adverse events were more prevalent in the prucalopride groups than in the placebo groups, mainly on day 1 of treatment; however, the RCTs did not make comparisons between groups.^{[48] [49] [50] [51] [52]}

Comment: Particular attention has been paid to potential prolongation of the QTc interval since this was an issue with the "precursor" drug, cisapride. No concerns have emerged so far regarding cardiac safety. The standard dose of 2 mg once daily may be too high for some patients, particularly in the higher age group. However, some patients may also need 4 mg in order to obtain an optimal effect.

Clinical guide:

Prucalopride is a 5-HT₄ receptor agonist. Its receptor specificity seems much higher than that of the previously developed compounds of this class.^[53] As prucalopride seems to stimulate propulsive motility in the entire GI tract, efficacy in conditions other than constipation is to be expected. Currently, prucalopride is approved by the European Medicines Agency (EMA) for women only as the small numbers of men included in the trials lead to borderline statistical significance in the male subgroups. However, the numerical data are nearly identical for the sexes.

GLOSSARY

Biofeedback therapy involves training the person to relax pelvic floor and anal sphincter muscles using different types of equipment, from balloons for inserting into the rectum to electrical devices to determine muscle contraction.

Rome II criteria (updated 1999) Rome criteria for constipation require two or more of the following symptoms to be present for at least 12 weeks out of the preceding 12 months: straining at defecation on at least a quarter of occasions; stools are lumpy/hard on at least a quarter of occasions; sensation of incomplete evacuation on at least a quarter of occasions; and three or fewer bowel movements a week.^[54]

Tenesmus A continual inclination to evacuate the bowels with a feeling of incomplete rectal emptying.

Anismus Paradoxical contraction of the puborectalis, anal sphincter muscles, or both, resulting in difficulty defecating.

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Lubiprostone: New option. Two RCTs identified comparing lubiprostone versus placebo.^{[46] [47]} The first RCT compared lubiprostone (24, 48, or 72 micrograms/day) versus placebo for 3 weeks.^[46] The RCT found that all three doses of lubiprostone increased the number of spontaneous bowel movements (SBMs) compared with placebo. During week 1 of the study, the RCT found that 48 and 72 micrograms daily lubiprostone increased SBMs compared with placebo, but there was no significant difference between 25 micrograms daily lubiprostone and placebo. During week 2 of the study, the RCT found that all three doses of lubiprostone increased SBMs compared with placebo;

however, there was no significant difference between groups at week 3. The RCT found that all doses of lubiprostone improved degree of straining, stool consistency, severity of constipation, and rating of treatment effectiveness, when assessed subjectively by the participants. It also found no significant difference in the proportion of people who used rescue laxatives between groups for weeks 1 to 4.^[46] The second RCT compared oral lubiprostone versus placebo for 4 weeks.^[47] The RCT found that lubiprostone increased the mean number of SBMs a week at weeks 1, 2, 3, and 4 compared with placebo.^[47] The RCT also found that lubiprostone reduced the proportion of people who used rescue laxatives at week 4, and increased the proportion of people who were full responders at weeks 1 to 4. The RCT reported that lubiprostone improved stool consistency, straining, and constipation severity compared with placebo at weeks 1 to 4.^[47] Categorized as Likely to be beneficial.

Prucalopride: Five RCTs added comparing prucalopride versus placebo.^{[48] [49] [50] [51] [52]} The RCTs unanimously found that, compared with placebo, prucalopride increased frequency of spontaneous bowel movements (i.e., not induced by a rescue laxative) and of spontaneous complete (as experienced by the patient) bowel movements irrespective of the duration of the respective trial. Likewise, prucalopride in comparison to placebo improved stool consistency and reduced the need to strain, the feeling of incomplete evacuation, and overall severity of constipation. Categorized as Likely to be beneficial.

Biofeedback: One RCT added comparing biofeedback versus either sham treatment or standard treatment.^[15] The RCT found that biofeedback improved the rate of complete spontaneous bowel movements compared with sham and standard treatment at 3 months. It also found that biofeedback increased global bowel satisfaction compared with sham but not standard treatment at 3 months. The RCT found no significant difference between groups in stool consistency, straining, or laxative consumption at 3 months.^[15] Categorisation unchanged (Unknown effectiveness), as there remains insufficient good-quality evidence to assess biofeedback.

Macrogols (polyethylene glycols): One RCT added comparing macrogols versus placebo.^[31] The RCT found that macrogols improved overall treatment success, complete spontaneous and satisfactory bowel movements a week, and global assessment scores compared with placebo at 6 months. However, there was no significant difference between groups in rate of rescue laxative use at 6 months.^[31] Categorisation unchanged (Beneficial).

Exercise or advice to exercise: Evidence reassessed. Recategorized from Likely to be beneficial to Unknown effectiveness as there remains insufficient good-quality evidence to assess the effects of exercise or advice to exercise on constipation in adults.

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Stefan A Mueller-Lissner

Dr
Park-Klinik Weissensee Berlin
Berlin
Germany

Arnold Wald

Professor
University of Wisconsin
Madison, WI
USA

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TABLE GRADE evaluation of interventions for constipation in adults

Important outcomes	Frequency of bowel movement, straining during defecation, hard stool, laxative use, cure of constipation, adverse effects								Comment
	Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	
What are the effects of non-drug interventions in adults with idiopathic chronic constipation?									
1 (59) ^[10]	Frequency of bowel movement	Fibre-rich diet v lower-fibre diet	4	-1	0	-1	0	Low	Quality point deducted for sparse data. Directness point deducted for inclusion of co-intervention in statistical analysis
1 (59) ^[10]	Straining during defecation	Fibre-rich diet v lower-fibre diet	4	-1	0	-1	0	Low	Quality point deducted for sparse data. Directness point deducted for inclusion of co-intervention in statistical analysis
1 (59) ^[10]	Hard stool	Fibre-rich diet v lower-fibre diet	4	-1	0	-1	0	Low	Quality point deducted for sparse data. Directness point deducted for inclusion of co-intervention in statistical analysis
1 (43) ^[12]	Cure of constipation	Exercise v normal lifestyle	4	-2	0	0	0	Low	Quality points deducted for sparse data and for not assessing statistical significance
1 (43) ^[12]	Frequency of bowel movement	Exercise v normal lifestyle	4	-3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results (absolute numbers not reported), and for not assessing statistical significance
1 (43) ^[12]	Straining during defecation	Exercise v normal lifestyle	4	-3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results (absolute numbers not reported), and for not assessing statistical significance
1 (43) ^[12]	Hard stool	Exercise v normal lifestyle	4	-3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results (absolute numbers not reported), and for not assessing statistical significance
1 (117) ^[13]	Frequency of bowel movement	Increased fluid intake plus high-fibre diet v high-fibre diet alone	4	-1	0	0	0	Moderate	Quality point deducted for sparse data
1 (117) ^[13]	Laxative use	Increased fluid intake plus high-fibre diet v high-fibre diet alone	4	-1	0	0	0	Moderate	Quality point deducted for sparse data
1 (60) ^[14]	Straining during defecation	Biofeedback plus balloon defecation training v balloon defecation training alone	4	-3	0	0	0	Very low	Quality point deducted for sparse data, incomplete reporting of results (significance not assessed), and other methodological flaws
1 (77) ^[15]	Cure rate	Biofeedback v sham/standard treatment	4	-2	0	0	0	Low	Quality points deducted for sparse data and for incomplete reporting (data presented graphically).
1 (109) ^[17]	Frequency of bowel movement	Biofeedback v macrogols	4	-2	0	-1	0	Very low	Quality points deducted for sparse data and for incomplete reporting (data presented graphically). Directness point deducted for co-intervention (advice on prevention of constipation) in only one arm
1 (77) ^[15]	Frequency of bowel movement	Biofeedback v sham/standard treatment	4	-2	0	0	0	Low	Quality points deducted for sparse data and for incomplete reporting (data presented graphically)

Important outcomes	Frequency of bowel movement, straining during defecation, hard stool, laxative use, cure of constipation, adverse effects									
	Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
	1 (109) ^[17]	Straining during defecation	Biofeedback v macrogols	4	-1	0	-1	0	Low	Quality point deducted for sparse data. Directness point deducted for co-intervention (advice on prevention of constipation) in only one arm
	1 (77) ^[15]	Straining during defecation	Biofeedback v sham/standard treatment	4	-2	0	0	0	Low	Quality points deducted for sparse data and for incomplete reporting (data presented graphically)
	1 (109) ^[17]	Laxative use	Biofeedback v macrogols	4	-1	0	-1	0	Low	Quality point deducted for sparse data. Directness point deducted for co-intervention (advice on prevention of constipation) in only one arm
	1 (77) ^[15]	Laxative use	Biofeedback v sham/standard treatment	4	-2	0	0	0	Low	Quality points deducted for sparse data and for incomplete reporting (data presented graphically)
What are the effects of bulk-forming laxatives in adults with idiopathic chronic constipation?										
	1 (201) ^[23]	Frequency of bowel movement	Ispaghula husk v placebo	4	0	0	0	0	High	
	1 (196) ^[23]	Straining during defecation	Ispaghula husk v placebo	4	-1	0	0	0	Moderate	Quality point deducted for sparse data
	1 (124) ^[25]	Frequency of bowel movement	Ispaghula husk v lactulose	4	-2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results (data presented graphically and statistical data not reported)
	1 (124) ^[25]	Straining during defecation	Ispaghula husk v lactulose	4	-2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results (statistical data not reported)
	1 (170) ^[27]	Frequency of bowel movement	Ispaghula husk v docusate	4	-1	0	-1	0	Low	Quality point deducted for sparse data. Directness point deducted for uncertainty of clinical benefit
	1 (170) ^[27]	Straining during defecation	Ispaghula husk v docusate	4	-1	0	0	0	Moderate	Quality point deducted for sparse data
What are the effects of faecal softeners in adults with idiopathic chronic constipation?										
We found no studies on the effects of faecal softeners										
What are the effects of osmotic laxatives in adults with idiopathic chronic constipation?										
	1 (304) ^[31]	Cure rate	Macrogols v placebo	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
	4 (544) ^{[28] [29] [30] [31]}	Frequency of bowel movement	Macrogols v placebo	4	-2	0	0	0	Low	Quality point deducted for non-assessment of significance in one RCT, and incomplete reporting of results in one RCT
	1 (55) ^[29]	Straining during defecation	Macrogols v placebo	4	-2	0	0	0	Low	Quality point deducted for sparse data and for incomplete reporting (absolute numbers not reported)
	1 (304) ^[31]	Laxative use	Macrogols v placebo	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results

Important outcomes		Frequency of bowel movement, straining during defecation, hard stool, laxative use, cure of constipation, adverse effects							
Number of studies (participants)	Outcome	Comparison	Type of evidence		Consistency	Directness	Effect size	GRADE	Comment
			Number of studies	Quality					
2 (183) ^[8] ^[32]	Frequency of bowel movement	Macrogols v ispaghula husk	4	-2	0	-2	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Directness points deducted for unclear outcomes and inclusion of a co-intervention (electrolytes)
1 (120) ^[32]	Hard stool	Macrogols v ispaghula husk	4	-1	0	-2	0	Very low	Quality point deducted for sparse data. Directness points deducted for unclear outcomes and inclusion of a co-intervention (electrolytes)
1 (115) ^[33]	Frequency of bowel movement	Macrogols v lactulose	4	-1	0	0	0	Moderate	Quality point deducted for sparse data
1 (115) ^[33]	Straining during defecation	Macrogols v lactulose	4	-1	0	-1	0	Low	Quality point deducted for sparse data. Directness point deducted for unclear definition of outcome
1 (24) ^[35]	Frequency of bowel movement	Lactulose v placebo	4	-1	0	-1	0	Low	Quality point deducted for sparse data. Directness point deducted for using high-dose of intervention
1 (30) ^[36]	Hard stool	Lactulose v placebo	4	-2	0	-1	0	Very low	Quality points deducted for sparse data and for not reporting pre-cross-over results. Directness point deducted for unclear definition of outcome
1 (43) ^[37]	Frequency of bowel movement	Lactitol v placebo	4	-2	0	-1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Directness point deducted for including only people in nursing homes
3 (181) ^[38] ^[39] ^[40]	Frequency of bowel movement	Lactitol v lactulose	4	-2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
What are the effects of stimulant laxatives in adults with idiopathic chronic constipation?									
1 (55) ^[55]	Frequency of bowel movement	Bisacodyl v placebo	4	-2	0	0	0	Low	Quality points deducted for sparse data and short follow-up
1 (55) ^[55]	Hard stool	Bisacodyl v placebo	4	-2	0	0	0	Low	Quality points deducted for sparse data and short follow-up
What are the effects of prostaglandin derivatives in people with idiopathic chronic constipation?									
2 (371) ^[46] ^[47]	Cure rate	Lubiprostone v placebo	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
2 (371) ^[46] ^[47]	Frequency of bowel movement	Lubiprostone v placebo	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
2 (371) ^[46] ^[47]	Straining during defecation	Lubiprostone v placebo	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
2 (371) ^[46] ^[47]	Hard stools	Lubiprostone v placebo	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
2 (371) ^[46] ^[47]	Laxative use	Lubiprostone v placebo	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
What are the effects of 5-HTA agonists in people with idiopathic chronic constipation?									

Important outcomes		Frequency of bowel movement, straining during defecation, hard stool, laxative use, cure of constipation, adverse effects							
Number of studies (participants)	Outcome	Comparison	Type of evidence		Consistency	Directness	Effect size	GRADE	Comment
			Quality						
1 (53) ^[52]	Cure rate	Prucalopride v placebo	4	-2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
4 (2056) ^{[48] [49] [50] [51]}	Frequency of bowel movement	Prucalopride v placebo	4	0	0	0	0	High	
1 (641) ^[50]	Hard stool	Prucalopride v placebo	4	0	0	0	0	High	
3 (1885) ^{[49] [50] [52]}	Straining during defecation	Prucalopride v placebo	4	0	0	0	0	High	

Type of evidence: 4 = RCT; 2 = Observational.
 Consistency: similarity of results across studies
 Directness: generalisability of population or outcomes
 Effect size: based on relative risk or odds ratio