ClinicalEvidence

Constipation in adults

Search date October 2006
Frank Frizelle and Murray Barclay

ABSTRACT

INTRODUCTION: Although there are defined criteria for the diagnosis of constipation, in practice, diagnostic criteria are less rigid, and in part depend 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, and of other interventions, in adults with idiopathic chronic constipation? We searched: Medline, Embase, The Cochrane Library and other important databases up to October 2006 (BMJ 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 42 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, glycerine suppositories, glycerol, high-fibre diet, increasing fluids, ispaghula husk, lactitol, lactulose, macrogols (polyethylene glycols), magnesium salts, methylcellulose, paraffin, phosphate enemas, seed oils, senna, sodium citrate enemas, sterculia.

QUESTIONS

INTERVENTIONS

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 in part depend 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 that examines the effects of other non-drug interventions such as increasing fluid intake or performing biofeedback, although biofeedback may be useful for constipation caused by anismus.
- Despite this lack of firm evidence, a number of poorer-quality studies have implicated these lifestyle interventions as being potentially beneficial.
- Macrogols (polyethylene glycols) improve symptoms of constipation without any serious adverse effects.
- Ispaghula husk (psyllium) seems to improve overall symptoms of constipation more effectively than lactulose.

- The osmotic laxatives lactitol and lactulose seem equally effective in improving the frequency of bowel movements.
- We don't know if other osmotic laxatives such as magnesium salts, or phosphate or sodium citrate enemas are effective.
- 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, glycerol/glycerine suppositories, or senna.
- Although generally considered beneficial, we did not find any evidence examining the use of paraffin or seed oils 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 II 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 year: straining at defecation on at least a quarter of occasions; stools that 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. [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 II 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 anismus. 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. This review does not cover interventions, such as dantron, which are recommended for use only in terminally ill people. **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 a quarter of occasions. [4] Prevalence rises in the elderly. Several surveys from around the world suggest that, in a community setting, prevalence among the elderly 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 elderly 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

Symptoms (including frequency of bowel movements, straining at defecation, hard/lumpy stools, sensation of incomplete evacuation/tenesmus); use of laxatives; cure of constipation (based on Rome II criteria or self or practitioner's report); prevalence of constipation.

METHODS

BMJ Clinical Evidence search and appraisal October 2006. The following databases were used to identify studies for this review: Medline 1966 to October 2006, Embase 1980 to October 2006, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled

Clinical Trials 2006, 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, except biofeedback, 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. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 16).

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**

Prevalence of constipation
Higher-fibre diet compared with lower-fibre diet Eating a higher-fibre diet may reduce the prevalence of constipation compared with eating a lower-fibre diet in adults with chronic constipation (very low-quality evidence).

Stool frequency
Increased fluids plus high-fibre diet compared with high-fibre diet alone Consuming a high-fibre diet with increased oral fluids increases stool frequency compared with a high-fibre diet alone (moderate-quality evidence).

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits:

We found one small RCT (43 people with constipation fulfilling the Rome II criteria) assessing the effects of physical activity on chronic constipation, in which all participants were also advised to increase mean fibre intake to greater than 30 g per day. The RCT found that there was no significant increase in fibre intake in either the intervention or control group (significance values not reported). [10] We found a second small RCT (59 women aged 18 to 57 years with self-reported constipation) that compared fibre-rich rye bread with or without *Lactobacillus* GG yoghurt versus a control diet (low-fibre bread and no *Lactobacillus* GG) for three weeks. The RCT found that fibre-rich rye bread significantly increased bowel movement frequency, softened stool and made defecation easier over 3 weeks (mean difference in bowel movement frequency: 0.3 defecations per day, 95% CI 0.1 to 0.5, P = 0.001; mean difference in consistency of stools [measured on a scale in which –1 = loose, 0 = normal, 1 = hard]: –0.3, 95% CI –0.4 to –0.2; P < 0.001; mean difference in difficulty with defecation [measured on a scale in which –1 = easy, 0 = normal, 1 = straining]: –0.4, 95% CI –0.5 to –0.2). [11] We found one prospective cohort study (3327 women aged 30 to 55 years who reported bowel movements every third day or less) that assessed the effect of a high-fibre diet on constipation. Analysis included logistic regression to control for multiple variables. Multivariate analysis found 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 a lower median daily fibre intake of 7 g/day (number of women reporting constipation: 742 with daily fibre intake of 7.1 g *v* 447 with daily fibre intake of 20 g; prevalence ratio [PR] 0.64, 95% CI 0.57 to 0.73; P for trend < 0.0001). However, the authors noted that a mean fibre intake of 20 g/day is below the recommended daily fibre intake. [12] One cross-sectional study (436 Japanese women with self-reported constipation) found that women with a higher dietary fibre intake (mean total dietary fibre 8.1 g/1000 kcal) were more likely to report constipation than women with lower fibre intake (mean total dietary fibre 4.6 g/1000 kcal), but the difference was not significant (number of women reporting constipation: 97/326 with low fibre intake *v* 120/305 with high fibre intake; P for trend = 0.07). The authors noted that this trend was probably associated with decreased rice consumption among women with a higher fibre intake (rice significantly improved constipation in this study). [13] Dukas 2003][Murakami 2006]

High fibre diet plus increasing fluids:
see the benefits of increasing fluids or advice to increase fluids, p 4 .

Harms:

The RCT that compared fibre-rich bread with or without *Lactobacillus* GG yoghurt versus low-fibre bread for three weeks used a symptom score to assess the severity of gastrointestinal adverse effects. 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 < 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). Gastrointestinal symptoms were reduced by the addition of *Lactobacillus* GG. [11]

High fibre diet plus increasing fluids:
see the harms of increasing fluids or advice to increase fluids, p 4 .

Comment: **Clinical guide:** 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 reduce constipation.

OPTION EXERCISE OR ADVICE TO EXERCISE

Prevalence of constipation
Compared with sedentary lifestyle Taking daily exercise reduces the prevalence of constipation compared with a sedentary lifestyle in adults with, or without, constipation (very low-quality evidence).

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits: We found no systematic review. We found one small RCT (43 people with constipation fulfilling the Rome II criteria). [15] One group was randomised to normal lifestyle for 12 weeks, followed by a 12-week programme consisting of a brisk 30-minute walk and a daily 11-minute programme; total duration 24 weeks. The second group was randomised to the 30-minute walk plus the daily 11 minute programme, for 12 weeks' duration. The number of fulfilled Rome criteria for constipation significantly decreased from 2.7 to 1.7 after 12 weeks in the group taking regular exercise compared with the group maintaining a normal lifestyle (P < 0.05). [15] One cohort study (39,532 women in Australia) found that women who were more physically active were less likely to report having constipation “sometimes or often” compared with women who were less physically active (comparison of most active group *v* least active group by age group: 18–23 years: OR 0.58, 95% CI 0.47 to 0.73; 45–50 years: OR 0.72, 95% CI 0.63 to 0.83; 70–75 years: OR 0.72, 95% CI 0.61 to 0.85). [16] We found a second cohort study (3327 women aged 30 to 55 years with self-reported constipation, defined as two or fewer weekly bowel movements) that assessed the effects of physical activity on constipation. Analysis included logistic regression to control for multiple variables. Multivariate analysis found that women who reported daily physical activity had a significantly lower prevalence of constipation compared with those who were sedentary (prevalence ratio [PR] 0.56, 95% CI 0.44 to 0.70). [12]

Harms: The RCT gave no information on adverse effects. [15]

Comment: **Clinical guide:**
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

Stool frequency
Increased fluids plus high-fibre diet compared with high-fibre diet alone Consuming a high-fibre diet with increased oral fluids increases stool frequency compared with a high-fibre diet alone (moderate-quality evidence).

Note
We found no clinically important results about the effects of increased fluid intake alone in adults with chronic functional constipation.

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits: We found no systematic review.

Increasing fluids plus high fibre intake:
We found one RCT (117 people aged 18–50 years with chronic functional constipation [defined as < 3 bowel movements per week]) that compared a daily fibre intake of 25 g plus increased fluid intake (1.5–2 L/day) versus high-fibre diet alone. [14] The RCT found that a daily fibre intake of

25 g significantly increased stool frequency after two months (mean stool frequency increased from 2.0 per week at baseline to 3.3 per week at two months [P < 0.001]), and this effect was significantly enhanced by high fluid intake (mean stool frequency increased from 1.8 per week at baseline to 4.2 per week at 3 months with high fibre plus fluid intake [P < 0.001]; mean difference in the number of stools per week from baseline:1.3 with high fibre intake *v* 2.4 with high fibre and fluid intake; P < 0.001).

Harms: The RCT gave no information on adverse effects. [14]

Comment: None.

OPTION BIOFEEDBACK

Symptoms of constipation

Biofeedback plus balloon defecation training compared with balloon defecation training alone Adding biofeedback therapy to balloon defecation training may be no more effective at improving symptoms of constipation compared with balloon defecation training alone (very low-quality evidence).

Biofeedback compared with macrogols

Biofeedback may improve symptoms of constipation in people with anismus (severe pelvic floor dyssynergia) after 6–12 months compared with macrogols (moderate-quality evidence).

Benefits: We found one systematic review (search date 2002) that assessed the effects of biofeedback therapy in people with constipation). [17] The review included prospective studies of both adults and children (733 adults, 27 studies, of which only four studies used parallel designs). One RCT identified by the review (60 adults) compared perianal electromyographic (EMG) biofeedback plus balloon defecation training versus balloon defecation training alone. The RCT found no significant difference between the groups in symptom improvement (significance values for this RCT were not reported in the review). However, these results should be interpreted with caution because of methodological issues: the RCT included crossover to alternative treatment after only two unsuccessful treatment sessions. In some studies included in the review, up to 75–90% 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. [17] We found one subsequent RCT (109 people with chronic constipation fulfilling the Rome II criteria with severe pelvic floor dyssynergia [anismus]) that compared the effects of five weekly biofeedback sessions versus macrogol 4000 (29.2 g/day) plus advice on preventing constipation for 12 months. [18] Laxative-treated people were instructed to increase the dose of macrogol from 14.6 to 29.2 g/day 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). Satisfaction with treatment, symptoms of constipation, and pelvic floor physiology were assessed at 6 and 12 months. The biofeedback group was also assessed at 24 months. The RCT found that, at 6 months, biofeedback significantly improved symptoms of constipation compared with macrogol (major improvement was reported by 43/54 [80%] people with biofeedback *v* 12/55 [22%] with macrogol; P < 0.001). Biofeedback significantly reduced the number of bowel movements accompanied by straining at 6 months and at 12 months compared with macrogol (results presented graphically; P < 0.01). The RCT found that biofeedback therapy also significantly reduced the need for laxatives and the frequency of abdominal pain at 6 months and12 months compared with macrogol (mean weekly frequency of laxative doses: decreased from 1.72 at baseline to 0.59 at 6 months to 0.48 at 12 months with biofeedback *v* 1.54 at baseline to 1.24 at 6 months to 1.20 at 12 months with macrogol; P < 0.01; mean weekly frequency of abdominal pain: 1.06 at baseline, 0.37 at 6 months, 0.38 at 12 months with biofeedback *v* 1.13 at baseline, 1.00 at 6 months, 0.96 at 12 months with macrogol; P < 0.01). Bowel movements increased in frequency by similar amounts in both groups (mean weekly frequency of bowel movements: 3.91 at baseline, 5.87 at 6 months, 5.18 at 12 months with biofeedback *v* 3.98 at baseline, 4.91 at 6 months, 6.00 at 12 months with macrogol; P value not reported). 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. [18]

Harms: The systematic review and RCT gave no information on adverse effects. [17] [18]

Comment: Benefit from biofeedback therapy seems limited to people with paradoxically contracting puborectalis syndrome (also called anismus or pelvic floor dyssynergia). 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 patient numbers and use of retrospective

controls. The best of these studies support the use of biofeedback for constipation caused by functional outlet obstruction. [19] [20] [21] [22]

Clinical guide: Biofeedback may have a role in people with constipation caused by obstructed defecation secondary to anismus. [23]

QUESTION What are the effects of other treatments in adults with idiopathic chronic constipation?

OPTION MACROGOLS (POLYETHYLENE GLYCOLS)

Stool frequency
Compared with placebo Macrogols (polyethylene glycols) improve stool frequency after 1–20 weeks compared with placebo in adults with idiopathic chronic constipation (moderate-quality evidence).

Compared with ispaghula husk Macrogols may improve stool frequency after 2 weeks compared with ispaghula husk (very low-quality evidence).

Compared with lactulose Macrogols increase stool frequency after 2–4 weeks compared with lactulose (high-quality evidence).

Higher doses of macrogols compared with lower doses Higher doses of macrogols do not increase stool frequency, but are more likely to lead to abnormal-consistency stool compared with lower doses (high-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 16 .

Benefits:

Macrogols versus placebo:
We found one systematic review (search date 2001, [8] 3 RCTs [24] [25] [26]) and one additional RCT. [27] The first RCT identified by the review (70 adults aged 18–73 years meeting Rome diagnostic criteria for chronic constipation who had previously received a 4-week course of macrogol 4000 14.6 g twice/day) found that continued macrogol 4000 significantly increased the proportion of people who were "asymptomatic" at 20 weeks compared with placebo (70% with macrogol 4000 *v* 20% with placebo; P < 0.001). [24] "Asymptomatic" was defined as three or more bowel movements a week, no use of laxatives, no straining at defecation, feeling of complete evacuation, and no hard/pellet-like stools. It would seem that the analysis of results was not by intention to treat; significantly more people taking macrogol 4000 completed the trial (70% with macrogol 4000 *v* 30% with placebo; P < 0.01), which may have biased the results in favour of macrogol. [24] The second 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, 144 people analysed) found that macrogol 17 g significantly increased the frequency of bowel movements and the number of satisfactory bowel movements (defined by self report) compared with dextrose placebo after 14 days (number of bowel movements in week 2: 4.5 with macrogols *v* 2.7 with placebo; P < 0.001; satisfactory bowel movements: 68% with macrogol *v* 46% with placebo; P < 0.001). [25] The third RCT identified by the review (55 people with < 2 bowel movements/week for > 12 months, mean age 42 years, 48 people analysed) compared twice-daily macrogols versus placebo. It found that macrogols significantly increased the number of bowel movements a week (4.8 with macrogols *v* 2.8 with placebo; P < 0.002), and decreased marked straining at defecation (8% with macrogols *v* 41% with placebo; P < 0.03) compared with placebo at 8 weeks. [26] The additional small crossover RCT (34 people randomised, aged 20–60 years, 31 people analysed) 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 reported for this period before crossover (13.56 bowel movements/week with macrogols *v* 5.53 bowel movements/week with placebo). [27]

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). It 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 (63 people with chronic functional constipation) that compared macrogol 3350 plus electrolytes (13.8 g/sachet twice daily) versus ispaghula husk (3.5 g/sachet twice daily) for two weeks. [28] The RCT found that macrogol significantly increased bowel movement frequency, and increased the proportion of people with normal stool consistency after 1 week and again after 2 weeks compared with ispaghula husk (mean weekly defecation rate: results depicted graphically,

P < 0.001; proportion of people with normal stool consistency: increased from 0 at baseline in both groups to 55/63 [87%] after 2 weeks with macrogol *v* 42/63 [67%] with ispaghula husk; P < 0.001).

Macrogols versus lactulose:
We found one systematic review (search date 2001) [8] which identified one RCT, [29] and we found one subsequent RCT. [30] The RCT identified by the review (115 people passing < 3 stools/week, straining at stool, or both) found that macrogol 3350 26 g daily was significantly more effective than 20 g lactulose daily in increasing the number of weekly bowel movements (1.3 with macrogol 3350 *v* 0.9 with lactulose; P = 0.005), easing stool evacuation (scored as 0 for "easy" to 4 for "very difficult"; absolute mean score: 0.5 with macrogol 3350 *v* 1.0 with lactulose; P < 0.001), and improving global satisfaction at 1 month (satisfaction scored as 0 for "terrible" to 10 for "excellent": 7.4 with macrogol 3500 *v* 5.2 with lactulose; P < 0.001). [29] The subsequent RCT (85 elderly 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 (64% with macrogol 4000 *v* 39% with lactulose; P < 0.01) and 4 weeks (69% with macrogol 4000 *v* 42% with lactulose; P < 0.01). [30]

Macrogol regimens:
One RCT (266 ambulatory people in general practice, mean age 51 years, 85% female) compared four different macrogol regimens over 4 weeks: macrogol 3350 5.9 g daily; macrogol 3350 11.8 g daily; macrogol 4000 10 g daily, and macrogol 4000 20 g daily. [31] It found no significant difference among treatments in bowel frequency, but found that standard dose macrogol 3350 5.9 g significantly increased the proportion of people with stools of normal consistency compared with maximum dose macrogol 3350 and maximum dose macrogol 4000 (P < 0.001). [31]

Harms:

Macrogols versus placebo:
The first RCT identified by the review found no significant difference between macrogol 4000 and placebo in overall frequency of adverse effects (57 events with macrogol *v* 41 events with placebo; P reported as not significant). [24] The second RCT identified by the review found no significant difference between macrogols and placebo in adverse effects (no further data reported). [25] The third RCT in 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; P values reported as not significant). [26] The additional RCT did not report adverse effects by treatment group. [27]

Macrogols versus ispaghula husk:
The review did not report on adverse effects. [8] The RCT found no significant difference in the proportion of people with adverse effects over two weeks between macrogol 3350 plus electrolytes compared with ispaghula husk (7/60 with macrogol *v* 5/60 with ispaghula husk; P = 0.76). Adverse effects were minor and none required treatment. [28]

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. [29] It found that macrogol 3350 increased the frequency of liquid stools compared with lactulose over 4 weeks (mean number of loose stools over 4 weeks: 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; P > 0.05). [30]

Comment: None.

OPTION ISPAGHULA HUSK (PSYLLIUM)

Stool frequency
Compared with placebo Ispaghula husk increases stool frequency after 2 weeks compared with placebo in adults with chronic idiopathic constipation (high-quality evidence).

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

Compared with lactulose Ispaghula husk may improve symptoms of constipation after 4 weeks compared with lactulose (low-quality evidence).

Compared with docusate Ispaghula husk increases stool frequency after 2 weeks compared with docusate, although the difference may not be clinically important (moderate-quality evidence).

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits:

Ispaghula husk versus placebo:
We found one systematic review (1 RCT, search date 2001, 201 people, mean 2.3 bowel movements/week, mean age 49 years, 183 completed the trial). [8] The RCT found that ispaghula husk 3.6 g three times daily significantly increased the frequency of bowel movements after 2 weeks compared with placebo and improved abdominal pain/discomfort (median bowel movements/week: 7.0 with ispaghula *v* 4.5 with placebo; P < 0.05; abdominal pain/discomfort assessed using 3-point Likert scale as "better", "the same", or "worse"; abdominal pain/discomfort "better": 21/35 [60%] with ispaghula *v* 12/26 [46%] with placebo; P = 0.035). [32] It also assessed symptoms of straining and constipation as "better", "the same", or "worse" than baseline. It found that, compared with placebo, ispaghula husk significantly increased the proportion of people whose symptoms were "better" (straining "better": 59/70 [84%] with ispaghula *v* 36/63 [57%] with placebo; P = 0.003; self assessment that constipation was "better": 90/101 [89%] with ispaghula *v* 46/95 [48%] with placebo; P < 0.001).

Ispaghula husk versus macrogols:
See benefits of macrogols, p 6 .

Ispaghula husk versus lactulose:
We found two systematic reviews (search dates 1995 [33] and 2001 [8]). The first review [33] identified one RCT (112 outpatients, mean age 50 years). [34] It found that ispaghula 3.5 g twice daily significantly increased the frequency of bowel movements after 4 weeks compared with lactulose 15 mL twice daily (7.8 bowel movements/week with ispaghula *v* 6.6 bowel movements/week with lactulose; P < 0.05). [34] Fewer people had abdominal pain over 4 weeks with ispaghula than with lactulose (weeks 1–2: 32% with ispaghula *v* 41% with lactulose; weeks 3–4: 15% with ispaghula *v* 22% with lactulose; P values not reported). Similar proportions of people in both groups had straining at stool (no straining: 21/45 [47%] with ispaghula *v* 15/48 [31%] with lactulose; P value not reported) and clinical improvement (defined by practitioner's report of overall clinical impression of symptom severity; much improved on Clinical Global Improvement score: 29/45 [64%] with ispaghula *v* 33/48 [69%] with lactulose; P value not reported). [34] The second review [8] identified one RCT (see comment below). [35] The RCT (394 people presenting to their general practitioner with constipation; 90% had constipation > 7 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). [35] 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 the proportion of movements with hard stools was lower with ispaghula husk than with lactulose at 4 weeks (18% with ispaghula *v* 27% with lactulose; P value not reported).

Ispaghula husk versus docusate:
We identified one systematic review (search date 2001) [8] which identified one RCT (170 people aged 20–70 years, 90% female, mean age 37 years). [36] It found that ispaghula husk 5.1 g twice daily significantly increased the frequency of bowel movements in the second week 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 = 0.02). However, the difference in frequency of bowel movements was small, and is likely to be of little clinical importance. The RCT found no significant difference between straining at stool or pain with bowel motions (straining: P = 0.15; pain: 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 did not report on adverse effects. [8]

Ispaghula husk versus macrogols:
See harms of macrogols, p 6 .

Ispaghula husk versus lactulose:
The RCT identified by the first review [33] found that 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; P value not reported). [34]

Ispaghula husk versus docusate:
The review [8] and included RCT [36] did not report on adverse effects.

Comment:

Ispaghula husk versus lactulose:
It is not clear why the second review [8] did not include the RCT [34] that was identified by the first review. [33]

OPTION LACTITOL

Stool frequency
Compared with placebo Lactitol may increase stool frequency after 4 weeks compared with placebo in elderly adults with chronic constipation (very low-quality evidence).

Compared with lactulose Lactitol may be as effective as lactulose at increasing stool frequency after 2–4 weeks (low-quality evidence).

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits:

Lactitol versus placebo:
We found one systematic review (search date 1996, [9] 1 crossover RCT, [37] 43 people recruited in nursing homes 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 in the third and fourth week of treatment before crossover (absolute numbers presented graphically; P < 0.001). [37]

Lactitol versus lactulose:
We found two systematic reviews (search date 1996, [9] search date 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, 57 people analysed) 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 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 > 0.05). [40]

Harms:

Lactitol versus placebo:
The review did not report on adverse effects. [9]

Lactitol versus lactulose:
The first review did not report on adverse effects in the first RCT. [9] The second RCT [39] 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). The third RCT [40] found no significant difference between lactitol and lactulose in adverse events or other symptoms (bloating, flatulence, nausea, cramping, or diarrhoea; no further data reported by the review).

Comment: None.

OPTION LACTULOSE

Severity of constipation
Compared with placebo Lactulose may increase stool frequency and improve symptoms of constipation compared with placebo in adults with chronic idiopathic constipation (very low-quality evidence).

Compared wtih macrogols Lactulose is less effective than macrogols at increasing stool frequency after 2–4 weeks (high-quality evidence).

Compared with ispaghula husk Lactulose may be less effective than iIspaghula husk at improving symptoms of constipation after 4 weeks (low-quality evidence).

Compared with lactitol Lactulose may be as effective as lactitol at increasing stool frequency after 2–4 weeks (low-quality evidence).

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits: We found three systematic reviews that included trials of lactulose (search dates 1995, [33] 1996, [9] and 2001 [8]).

Lactulose versus placebo:
Between them the reviews identified three RCTs. The first RCT (24 outpatients, mean age 28 years) found that high-dose lactulose (60 mL 4 times/day) significantly increased the frequency of bowel movements compared with placebo after 1 week (4.5 bowel movements/week with lactulose *v* 2.8 bowel movements/week with placebo; P < 0.05). [33] The second RCT (47 people in a nursing home, mean age 85 years, 42 analysed) found that lactulose (30 mL 4 times/day) significantly reduced five symptoms (cramping, griping, flatulence, tenesmus, and bloating) compared with placebo at 12 weeks (P = 0.04). [9] It found no significant difference in the number of bowel movements (4.9 bowel movements/week with lactulose *v* 3.6 bowel movements/week with placebo; P = 0.10). The most recent review [8] also identified one crossover RCT, [41] but it was not clear whether results were reported before the crossover. The RCT (55 people) compared lactulose versus placebo in a crossover design with 4-week treatment periods and a 2-week washout. It found that 30 mL lactulose significantly improved 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 < 0.01).

Lactulose versus macrogols:
See benefits of macrogols, p 6 .

Lactulose versus ispaghula husk:
See benefits of ispaghula husk, p 7 .

Lactulose versus lactitol:
See benefits of lactitol, p 9 .

Harms:

Lactulose versus placebo:
The reviews gave no information on adverse effects. [33] [9]

Lactulose versus macrogols:
See harms of macrogols, p 6 .

Lactulose versus ispaghula husk:
See harms of ispaghula husk, p 7 .

Lactulose versus lactitol:
See harms of lactitol, p 9 .

Comment: None.

OPTION BISACODYL

Stool frequency
Compared with placebo Bisacodyl may increase stool frequency after 3 days compared with placebo (low-quality evidence).

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits: We found no systematic review. We found one small RCT (55 people aged 19 to 89 years with idiopathic constipation) that compared 10 mg of bisacodyl once daily versus placebo for three successive days). [42] The RCT found that bisacodyl significantly increased frequency of bowel movements compared with placebo (mean number of stools: 1.8 per day with bisacodyl *v* 0.95 per day with placebo; P = 0.006). The mean stool consistency score improved from 'hard' (run-in) to between 'soft' and 'well-formed' during bisacodyl treatment, remaining between 'moderately hard' and 'hard' for placebo treatment (P < 0.0001). [42] It is important to consider the short duration and follow-up period of this study when evaluating its results.

Harms: The RCT found that adverse effects, including eosinophilia, monocytosis, and raised blood urea nitrogen, were comparable between treatment groups, and were mild (number of people with adverse effects: 15/27 [56%] with bisacodyl *v* 18/27 [67%] with placebo; reported as non significant; P value not reported) [42]

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. [43] [44]

OPTION CASCARA

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

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION DOCUSATE

Stool frequency
Compared with ispaghula husk Docusate is less effective than ispaghula husk at increasing stool frequency after 2 weeks, although the difference may not be clinically important (moderate-quality evidence).

Note
We found no direct information on whether docusate is better than no active treatment in adults with chronic idiopathic constipation.

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits:

Docusate versus placebo:
We found one systematic review (search date 1995), which identified no RCTs of sufficient quality. [33]

Docusate versus ispaghula husk:
See benefits of ispaghula husk, p 7 .

Harms:

Docusate versus placebo:
The review gave no information on adverse effects. [33]

Docusate versus ispaghula husk:
See harms of ispaghula husk, p 7 .

Comment: None.

OPTION GLYCEROL/GLYCERIN SUPPOSITORIES

We found no clinically important results 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 16 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION MAGNESIUM SALTS

We found no clinically important results about the effects of magnesium salts in adults with idiopathic chronic constipation.

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION METHYLCELLULOSE

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

For GRADE evaluation of interventions for constipation in adults, **see table, p 16 .**

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 PARAFFIN

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

For GRADE evaluation of interventions for constipation in adults, **see table, p 16 .**

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 to be beneficial and cost effective. However usage is becoming less common.

OPTION PHOSPHATE ENEMAS (RECTAL PHOSPHATES)

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

For GRADE evaluation of interventions for constipation in adults, **see table, p 16 .**

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 SEED OILS/ARACHIS OIL

We found no clinically important results 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 16 .**

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.

OPTION SENNA

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

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION SODIUM CITRATE ENEMAS (RECTAL SODIUM CITRATE)

We found no clinically important results 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 16 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION STERCULIA

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

For GRADE evaluation of interventions for constipation in adults, see table, p 16 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

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. [1]
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

Biofeedback: One systematic review and one RCT added; [17] [18] categorisation unchanged (Unknown effectiveness).
Bisacodyl: one RCT added; [42] categorisation unchanged (Unknown effectiveness).
Increasing fluids or advice to increase fluids: One RCT added; [14] categorisation unchanged (Unknown effectiveness)
Macrogols: One RCT added; [28] categorisation unchanged (Beneficial)
Exercise or advice to exercise: One observational study added; [12] categorisation changed (Unknown effectiveness to Likely to be beneficial)
High-fibre diet or advice to consume a high-fibre diet: Three RCTs, two observational studies added [14] [13] [12] [10] [11] ; categorisation changed (Unknown effectiveness to Likely to be beneficial).

REFERENCES

1. Thompson WG, Longstreth GF, Drossman DA, et al. Functional bowel disorders and functional abdominal pain. *Gut* 1999;45;43–47.
2. Prescription cost analysis. Department of Health. 2001. http://www.dh.gov.uk/AdvancedSearch/SearchResults/fs/en?NP=1&PO1=C&PI1=W&PF1=A&PG=1&RP=20&PT1=cost+analysis&SC=__dh_site&Z=1 (last accessed 14 March 2006).
3. Probert CS, Emmett PM, Heaton KW. Some determinants of whole-gut transit time: a population-based study. *QJM* 1995;88:311–315.[PubMed]
4. Heaton KW. Cleave and the fibre story. *J R Nav Med Serv* 1980;66:5–10.[PubMed]
5. Donald IP, Smith RG, Cruikshank JG, et al. A study of constipation in the elderly living at home. *Gerontology* 1985;31:112–118.[PubMed]

6. Campbell AJ, Busby WJ, Horwath CC. Factors associated with constipation in a community based sample of people aged 70 years and over. *J Epidemiol Community Health* 1993;47:23–26.[PubMed]
7. Talley NJ, Fleming KC, Evans JM, et al. Constipation in an elderly community: a study of prevalence and potential risk factors. *Am J Gastroenterol* 1996;91:19–25.[PubMed]
8. NHS Centre for Reviews and Dissemination. Effectiveness of laxatives in adults. *Effective Health Care* 2001;7. Search date 2001; primary sources Medline, Embase, Psychinfo, The Cochrane Library, Cinahl, International Pharmaceutical Abstracts, Amed, and contact with manufacturers and relevant experts.
9. Petticrew M, Watt I, Sheldon T. Systematic review of the effectiveness of laxatives in the elderly. *Health Technol Assess* 1997;1:1–52. Search date 1996; primary sources recent systematic review by Tramonte et al 1997, Medline, Biological Abstracts, Microdex, bibliographies, text books, contact with manufacturers of laxatives, Embase, Psychlit, The Cochrane Library, Cinahl, International Pharmaceutical Abstracts, and Amed.
10. De Schryver AM, Keulemans YC, Peters HP, et al. Effects of regular physical activity on defecation pattern in middle-aged patients complaining of chronic constipation. *Scand J Gastroenterol* 2005;40:422–429.
11. Hongisto S-M, Paajanen L, Saxelin M, et al. A combination of fibre-rich rye bread and yoghurt containing Lactobacillus GG improves bowel function in women with self-reported constipation. *Eur J Clin Nutrition* 2006;60:319–324.
12. Dukas L, Willett WC, Giovannucci EL. Association between physical activity, fiber intake, and other lifestyle variables and constipation in a study of women. *Am J Gastroenterol* 2003;98:1790–1796.
13. Murakami K, Okubo H, Sasaki S. Dietary intake in relation to self-reported constipation among Japanese women aged 18-20 years. *Eur J Clin Nutrition* 2006;60:650–657.
14. Anti M, Pignataro G, Armuzzi A, et al. Water supplementation enhances the effect of high-fiber diet on stool frequency and laxative consumption in adult patients with functional constipation. *Hepato-Gastroenterol* 1998;45:727–732.
15. De Schryver AM, Keulemans YC, Peters HP, et al. Effects of regular physical activity on defecation pattern in middle-aged patients complaining of chronic constipation. *Scand J Gastroenterol* 2005;40:422–429.[PubMed]
16. Brown WJ, Mishra G, Lee C, et al. Leisure time physical activity in Australian women: relationship with well being and symptoms. *Res Q Exerc Sport* 2000;71:206–216.[PubMed]
17. Heymen S, Jones KR, Scarlett Y, et al. Biofeedback treatment of constipation: A critical review. *Dis Col Rectum* 2003;46:1208–1217.
18. Chiarioni G, Whitehead WE, Pezza V, et al. Biofeedback is superior to laxatives for normal transit constipation due to pelvic floor dyssynergia. *Gastroenterol* 2006;130:657–664.
19. Weber J, Ducrotte P, Touchais JY, et al. Biofeedback training for constipation in adults and children. *Dis Col Rectum* 1987;30:844–846.
20. Ho YH, Tan M, Goh HS, et al. Clinical and physiologic effects of biofeedback in outlet obstruction constipation. *Dis Col Rectum* 1996;39:520–524.
21. Glia A, Gylin M, Akerlund JE, et al. Biofeedback training in patients with fecal incontinence. *Dis Col Rectum* 1998;41:359–364.
22. Bleijenberg G, Kuijpers JHC. Treatment of the spastic pelvic floor syndrome by means of biofeedback. *Nederlands Tijdschrift voor Geneeskunde* 1987;131:446–449.
23. Brown SR, Donati D, Seow-Choen F, et al. Biofeedback avoids surgery in patients with slow-transit constipation: Report of four cases. *Dis Col Rect* 2001;44:737–740.
24. Corazziari E, Badiali D, Bazzocchi G, et al. Long term efficacy, safety, and tolerability of low daily doses of isosmotic polyethylene glycol electrolyte balanced solution (PMF-100) in the treatment of functional chronic constipation. *Gut* 2000;46:522–526.[PubMed]
25. DiPalma JA, DeRidder PH, Orlando RC, et al. A randomized, placebo-controlled, multicenter study of the safety and efficacy of a new polyethylene glycol laxative. *Am J Gastroenterol* 2000;95:446–450.[PubMed]
26. Corazziari E, Badiali D, Habib FI, et al. Small volume isosmotic polyethylene glycol electrolyte balanced solution (PMF-100) in treatment of chronic nonorganic constipation. *Dig Dis Sci* 1996;41:1636–1642.[PubMed]
27. Baldonedo YC, Lugo E, Uzcategui AA, et al. Evaluation and use of polyethylene glycol in patients with constipation. *J Ven Soc Gastroenterol* 1991;45:294–297. [In Spanish]
28. Wang H-J, Liang X-M, Yu Z-L, et al. A randomised, controlled comparison of low-dose polyethylene glycol 3350 plus electrolytes with ispaghula husk in the treatment of adults with chronic functional constipation. *Clin Drug Invest* 2004;24:569–576.
29. Attar A, Lemann M, Ferguson A, et al. Comparison of a low dose polyethylene glycol electrolyte solution with lactulose for treatment of chronic constipation. *Gut* 1999;44:226–230. [PubMed]
30. Zhang CQ, Zhang GW, Zhang KL, et al. Clinical evaluation of polyethylene glycol 4000 in treatment of functional constipation in elderly patients. *World Chin J Digesto* 2003;11:1399–1401.
31. Chaussade S, Minic M, Chaussade S, et al. Comparison of efficacy and safety of two doses of two different polyethylene glycol-based laxatives in the treatment of constipation.[see comment]. *Aliment Pharmacol Ther* 2003;17:165–172.
32. Fenn GC, Wilkinson PD, Lee CE, et al. A general practice study of the efficacy of Regulan in functional constipation. *Br J Clin Pract* 1986;40:192–197.[PubMed]
33. Tramonte SM, Brand MB, Mulrow CD, et al. The treatment of chronic constipation in adults: A systematic review. *J Gen Internal Med* 1997;12:15–24.
34. Rouse M, Chapman N, Mahapatra M, et al. An open, randomised, parallel group study of lactulose versus ispaghula in the treatment of chronic constipation in adults. *Br J Clin Pract* 1991;45:28–30.[PubMed]
35. Dettmar PW, Sykes J. A multi-centre, general practice comparison of ispaghula husk with lactulose and other laxatives in the treatment of simple constipation. *Curr Med Res Opin* 1998;14:227–233.[PubMed]
36. McRorie JW, Daggy BP, Morel JG, et al. Psyllium is superior to docusate sodium for treatment of chronic constipation. *Aliment Pharmacol Ther* 1998;12:491–497.[PubMed]
37. Vanderdonckt J, Coulon J, Denys W, et al. Study of the laxative effect of lactitol (Importal) in an elderly institutionalized but not bedridden, population suffering from constipation. *J Clin Exp Gerontol* 1990;21:171–189.
38. Doffoel M, Berthel M, Bockel R, et al. Comparative study of lactitol and lactulose in the treatment of functional constipation in elderly subjects. *Med Chir Dig* 1990;19:257–259. [In French]
39. Hammer B, Ravelli GP. Chronic functional constipation lactitol maintenance dose, a multicentre comparative study with lactulose. *Ther Schweiz* 1992;8:328–335. [In German]
40. Heitland W, Mauersberger H. Study of the laxative effect of lactitol as opposed to lactulose in an open, randomized comparative study. *Schweiz Rundsch Med Prax* 1988;77:493–495. [In German][PubMed]
41. Castillo R, Nardi G, Simhan D. Lactulose in the treatment of chronic idiopathic constipation. *Pren Med Argent* 1995;82:173–176. [In Spanish]
42. Kienzle-Horn S, Vix J-M, Schuijt C, et al. Efficacy and safety of bisacodyl in the acute treatment of constipation: A double-blind, randomized, placebo-controlled study. *Aliment Pharmacol Ther* 2006;23:1479–1488.
43. Wald A. Is chronic use of stimulant laxatives harmful to the colon? *J Clin Gastroenterol* 2003;36:386–389.[PubMed]
44. Müller-Lissner S. What has happened to the cathartic colon? *Gut* 1996;39:486–488.
45. Zhang C-Q, Zhang G-W, Zhang K-L, et al. Clinical evaluation of polyethylene glycol 4000 in treatment of functional constipation in elderly patients. *World Chinese Journal of Digestology* 2003;11:1399–1401
46. Tramonte SM, Brand MB, Mulrow CD, et al. The treatment of chronic constipation in adults: a systematic review. *J Gen Intern Med* 1997;12:15–24. Search date 1995; primary sources Medline, Biological Abstracts, Micromedex (a drug information service), hand searches of bibliographies of identified articles and textbooks, and personal contact with laxative manufacturers in North America and authors.[PubMed]
47. Kienzle-Horn S, Vix J-M, Schuijt C, et al. Efficacy and safety of bisacodyl in the acute treatment of constipation: A double-blind, randomized, placebo-controlled study. *Aliment Pharmacol Ther* 2006;23:1479–1488.

Frank Frizelle
Professor of Colorectal Surgery
Christchurch Hospital and School of Medicine
Christchurch
New Zealand

Murray Barclay
Gastroenterologist and Clinical Pharmacologist
Christchurch Hospital and School of Medicine
Christchurch
New Zealand

Competing interests: FF and MB declare that they have no competing interests.
We would like to acknowledge the previous contributors of this review, including Bazian Ltd.

Disclaimer

The information contained in this publication is intended for medical professionals. Categories presented in Clinical Evidence indicate a judgement about the strength of the evidence available to our contributors prior to publication and the relevant importance of benefit and harms. We rely on our contributors to confirm the accuracy of the information presented and to adhere to describe accepted practices. Readers should be aware that professionals in the field may have different opinions. Because of this and regular advances in medical research we strongly recommend that readers' independently verify specified treatments and drugs including manufacturers' guidance. Also, the categories do not indicate whether a particular treatment is generally appropriate or whether it is suitable for a particular individual. Ultimately it is the readers' responsibility to make their own professional judgements, so to appropriately advise and treat their patients. To the fullest extent permitted by law, BMJ Publishing Group Limited and its editors are not responsible for any losses, injury or damage caused to any person or property (including under contract, by negligence, products liability or otherwise) whether they be direct or indirect, special, incidental or consequential, resulting from the application of the information in this publication.

TABLE **GRADE evaluation of interventions for constipation in adults**

Important outcomes	Symptoms of constipation, cure of constipation, use of laxatives, adverse effects								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consis-tency**	**Direct-ness**	**Effect size**	**GRADE**	**Comment**
What are the effects of non-drug interventions in adults with idiopathic chronic constipation?									
3 (3822) [11]	Prevalence of constipation	Higher-fibre diet *v* lower-fibre diet	2	0	–1	0	0	Very low	Consistency point deducted for conflicting results
1 (117) [14]	Stool frequency	High-fibre diet plus increased fluids *v* high-fibre diet alone	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
3 (42902) [10] [16] [12]	Prevalence of constipation	Daily exercise *v* sedentary lifestyle	2	0	0	–1	0	Very low	Directness point deducted for inclusion of adults without constipation
1 (109) [18]	Symptoms of constipation	Biofeedback *v* macrogols	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (60) [17]	Symptoms of constipation	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, and other methodological flaws
What are the effects of other treatments in adults with idiopathic chronic constipation?									
4 (310) [24] [25] [26] [27]	Stool frequency	Macrogols *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for some methodological flaws
2 (183) [8] [28]	Stool frequency	Macrogols *v* ispaghula husk	4	–2	0	–1	0	Very low	Quality point deducted for sparse data and incomplete reporting of results. Directness point deducted for unclear outcomes
2 (200) [29] [45]	Stool frequency	Macrogols *v* lactulose	4	0	0	0	0	High	
1 (266) [31]	Bowel frequency	Higher doses of macrogols *v* lower doses	4	0	0	0	0	High	
1 (201) [32]	Stool frequency	Ispaghula husk *v* placebo	4	0	0	0	0	High	
2 (506) [34] [35]	Severity of constipation	Ispaghula husk *v* lactulose	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for differences in outcomes
1 (170) [36]	Stool frequency	Ispaghula husk *v* docusate	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (43) [37]	Stool frequency	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]	Stool frequency	Lactitol *v* lactulose	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
3 (126) [46] [9] [41]	Severity of constipation	Lactulose *v* placebo	4	–2	–1	0	0	Very low	Quality points deducted for sparse data and uncertain crossover methodology. Consistency point deducted for conflicting results
1 (55) [47]	Stool frequency	Bisacodyl *v* placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and short follow-up

Important outcomes	Symptoms of constipation, cure of constipation, use of laxatives, adverse effects								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consis-tency**	**Direct-ness**	**Effect size**	**GRADE**	**Comment**

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion. Consistency: similarity of results across studies
Directness: generalisability of population or outcomes
Effect size: based on relative risk or odds ratio