# Table of Contents

1. **HEADER** ......................................................... 1
2. **ABSTRACT** .................................................... 1
3. **PLAIN LANGUAGE SUMMARY** ................................. 2
4. **BACKGROUND** ................................................ 2
5. **OBJECTIVES** .................................................. 4
6. **METHODS** ..................................................... 4
7. **RESULTS** ....................................................... 6
   - Figure 1. .................................................. 7
   - Figure 2. .................................................. 8
8. **DISCUSSION** .................................................. 10
9. **AUTHORS’ CONCLUSIONS** .................................... 12
10. **ACKNOWLEDGEMENTS** ........................................ 12
11. **REFERENCES** ................................................ 13
12. **CHARACTERISTICS OF STUDIES** ............................ 15
13. **DATA AND ANALYSES** ........................................ 28
   - Analysis 1.1. Comparison 1 Stool Frequency per Week, Outcome 1 Stool frequency per week - all comparable data. 29
   - Analysis 1.2. Comparison 1 Stool Frequency per Week, Outcome 2 Stool frequency per week - Children. .......... 30
   - Analysis 1.3. Comparison 1 Stool Frequency per Week, Outcome 3 Stool frequency per week - Adults. ............... 30
   - Analysis 1.4. Comparison 1 Stool Frequency per Week, Outcome 4 Stool frequency per week - all comparable data excluding studies to improve heterogeneity. 31
   - Analysis 2.1. Comparison 2 Form of Stool, Outcome 1 Form of Stool - All comparable data. ....................... 31
   - Analysis 2.2. Comparison 2 Form of Stool, Outcome 2 Form of Stool - Children. ................................. 32
   - Analysis 2.3. Comparison 2 Form of Stool, Outcome 3 Form of Stool - Adults. .................................... 32
   - Analysis 3.1. Comparison 3 Relief of Abdominal Pain, Outcome 1 Relief of Abdominal Pain - all comparable data. 33
   - Analysis 3.2. Comparison 3 Relief of Abdominal Pain, Outcome 2 Relief of Abdominal Pain - Children. ......... 33
   - Analysis 3.3. Comparison 3 Relief of Abdominal Pain, Outcome 3 Relief of Abdominal Pain - Adults. ............. 34
   - Analysis 4.1. Comparison 4 Did not require additional products, Outcome 1 Did not require additional products - all comparable data. ........................................... 34
   - Analysis 4.2. Comparison 4 Did not require additional products, Outcome 2 Did not require additional products - Children. .................................................... 35
   - Analysis 4.3. Comparison 4 Did not require additional products, Outcome 3 Did not require additional products - Adults. .................................................. 35
14. **APPENDICES** .................................................. 35
15. **HISTORY** ....................................................... 37
16. **CONTRIBUTIONS OF AUTHORS** ............................. 37
17. **DECLARATIONS OF INTEREST** .............................. 37
18. **DIFFERENCES BETWEEN PROTOCOL AND REVIEW** ......... 38
19. **NOTES** .......................................................... 38

Lactulose versus Polyethylene Glycol for Chronic Constipation (Review) 
Copyright © 2010 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
Lactulose versus Polyethylene Glycol for Chronic Constipation

Heather Lee-Robichaud1, Kathryn Thomas1, Jenna Morgan1, Richard L Nelson1

1Department of General Surgery, Northern General Hospital, Sheffield, UK

Contact address: Heather Lee-Robichaud, Department of General Surgery, Northern General Hospital, Herries Road, Sheffield, England, S5 7AU, UK. docheth@tiscali.co.uk.

Editorial group: Cochrane Colorectal Cancer Group.
Review content assessed as up-to-date: 13 June 2010.


Copyright © 2010 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Background
Constipation is a common clinical problem. Lactulose and Polyethylene Glycol (PEG) are both commonly used osmotic laxatives that have been shown to be effective and safe treatments for chronic constipation. However, there is no definitive data as to which provides the best treatment.

Objectives
To identify and review all relevant data in order to determine whether Lactulose or Polyethylene Glycol is more effective at treating chronic constipation and faecal impaction.

Search strategy
We searched the MEDLINE, EMBASE and CINAHL databases, and the Cochrane Central Register of Controlled Trials for all randomised controlled trials (RCTs) comparing the use of lactulose and polyethylene glycol in the management of faecal impaction and chronic constipation.

Selection criteria
Studies were included if they were randomised controlled trials which compared lactulose with polyethylene glycol in the management of chronic constipation.

Data collection and analysis
Data on study methods, participants, interventions used and outcomes measured was extracted from each study. Data was entered into the Cochrane Review Manager software (RevMan 5.0) and analysed using Cochrane MetaView.

Main results
In the present meta-analysis, we considered for the first time all ten randomised controlled trials so far performed. The findings of our work indicate that Polyethylene glycol is better than lactulose in outcomes of stool frequency per week, form of stool, relief of abdominal pain and the need for additional products. On subgroup analysis, this is seen in both adults and children, except for relief of abdominal pain.
Authors’ conclusions

Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.

**PLAIN LANGUAGE SUMMARY**

Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.

Constipation is a common clinical problem, encompassing much more than reduced stool frequency. In this review we compared two commonly used osmotic laxatives, Lactulose and Polyethylene Glycol (PEG).

The findings of our work indicate that PEG is better than lactulose in outcomes of stool frequency per week, form of stool, relief of abdominal pain and the need for additional products. This is seen in both adults and children. Only exception is for relief of abdominal pain, where PEG is better than lactulose in children, but not in adults (no difference is seen).

We conclude that Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.

**BACKGROUND**

**Description of the condition**


Patients often consider constipation to encompass much more than reduced stool frequency alone; a range of symptoms are described, such as hard or small stool, excessive straining, feelings of incomplete evacuation, abdominal discomfort or a requirement for digital manipulation to assist defecation (Sandler 1987, Arce 2002, Drossman 1997, Velio 1996). No widely accepted clinically useful definition of chronic constipation exists, but the Rome criteria - and most recently the Rome III (Longstreth 2006) - have been created by consensus to form a framework for establishing the diagnosis (Bassotti 2003) as the presence of 2 or more of the following symptoms for at least 3 months:

- Straining in at least 25% defecations
- Lumpy or hard stool in at least 25% defecations
- Sensation of incomplete evacuation in at least 25% defecations
- Manual manoeuvres to facilitate at least 25% defecations (e.g. digital evacuation, pelvic floor support)
- Loose stools are rarely present without the use of laxatives
- Fewer than 3 defecations per week
- Insufficient criteria for irritable bowel syndrome

Chronic constipation may also be associated with further suffering in the form of faecal impaction where a firm impassable mass of faeces forms in the colon or rectum, causing additional distressing symptoms of overflow diarrhoea and faecal soiling/incontinence, as well as having a negative impact on the overall quality of life and general well-being (Glia 1997, Irvine 2002, Thompson 1999, Damon 2004, Legoretta 2006, Talley 2004, Dennison 2005).

Causes of constipation can be divided into primary (idiopathic) and secondary causes. Primary constipation is further classified in to normal-transit, slow-transit and dyssynergic constipation. Secondary causes include chronic laxative use and medications such as opioid analgesics, ferrous compounds and psychoactive drugs, as well as endocrine disorders (hypothyroidism, hyperparathyroidism, diabetes), neurological conditions (Hirschprung’s disease, multiple sclerosis, Parkinson’s disease, spinal cord injury), gastrointestinal conditions (Anal fissure, mucosal prolapse, colonic strictures or mass lesions with obstruction, idiopathic mega rectum) psychogenic conditions (anxiety, depression, eating disorders) and lifestyle factors (inadequate dietary fibre or fluid intake, extended bed rest and ignoring the urge to defecate). Despite this, the exact aetiology of chronic constipation remains largely unknown. It is postulated that patients may have reduced numbers of high-amplitude propagating contractions (Bassotti 2003).

In a bid to improve physical functioning and alleviate anxiety,
relief is often sought from the health care services, whose economic burden is substantial (Lembo 2003, Dennison 2005, Singh 2004). Treatment goals in chronic constipation aim to improve symptoms and restore bowel function by accelerating colonic transit and stimulating gut motility to ultimately facilitate defecation (Bleser 2005). Treatments include lifestyle changes, such as increased exercise, hydration and dietary fibre with the addition of simple laxatives. If these fail, the sufferers’ quality of life may continue to decline as symptoms worsen, leading to general malaise, mood changes and depression (Legoretta 2006). This can trigger increased reliance on suppositories, laxatives, enemas and manual evacuation, the latter being a particularly traumatic procedure for children and humiliating for adults.

**Description of the intervention**

A wide range of pharmacological agents have been used in attempts to treat this difficult condition, but results are limited by the poor understanding of the pathophysiological mechanisms coupled with complex central and enteric interactions. The most recognised and acceptable treatment is the use of a group of drugs commonly referred to as ‘laxatives’ which are categorised in Table 1. Other classes of drugs used include prokinetics and antibiotics.

### Table 1. Laxatives

<table>
<thead>
<tr>
<th>Category</th>
<th>Example</th>
<th>Action</th>
<th>Benefit</th>
<th>Side Effects</th>
<th>Contra-Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulk-forming</td>
<td>Isphagula</td>
<td>Increase faecal mass to stimulate peristalsis</td>
<td>Useful treatment for small hard stools. Benefit Inflammatory Bowel Disease and Irritable Bowel Syndrome patients, and colostomy and Ileostomy patients</td>
<td>Abdominal distension, flatulence, GI obstruction or impaction</td>
<td>Difficulty swallowing, intestinal obstruction, colonic atony or faecal impaction.</td>
</tr>
<tr>
<td>Stimulant</td>
<td>Bisacodyl, Docusate, Senna</td>
<td>Increase intestinal motility</td>
<td>Patients unresponsive or intolerant of fibre</td>
<td>Abdominal cramp, Hypokalaemia</td>
<td>Intestinal obstruction</td>
</tr>
<tr>
<td>Softeners</td>
<td>Mineral oils, Arachis oil</td>
<td>Faecal softeners</td>
<td>Gentle action for haemorrhoids or anal fissure</td>
<td>Granulomatous reactions, lipid pneumonia, interference with absorption of fat-soluble vitamins</td>
<td>Enemas can be painful and distressing for children</td>
</tr>
<tr>
<td>Osmotics</td>
<td>Lactulose, Polyethylene glycol (PEG), Magnesium hydroxide, Magnesium salts</td>
<td>Increase water content in large bowel. Lactulose is fermented by colonic bacteria which decrease gut pH, resulting in faecal volume expansion &amp; accelerated transit.</td>
<td>Minimal electrolyte losses. PEG activity does not increase colonic gas Laculose: altered bowel flora causing bloating, flatulence, colic, excessive diarrhoea. PEG: abdominal distension and pain, nausea, excessive diarrhoea.</td>
<td>Lactulose: galactosaemia, intestinal obstruction. PEG: intestinal perforation or obstruction, paralytic ileus, severe inflammatory conditions of the GI tract (e.g. Crohn’s, UC, toxic megacolon).</td>
<td></td>
</tr>
</tbody>
</table>
Lactulose and Polyethylene glycol (PEG) have been shown to be effective and safe treatments for chronic constipation (Candy 2006, Rendeli 2006, Dupont 2005, Brandt 2005, Voskuil 2004, Boughnik 2004, Gremse 2002, Christie 2002, Attar 1999, Freedman 1997, Fritz 2005, Mangin 2002, Guest 2004, Ferguson 1999), and are commonly used in both paediatric and adult populations. The alternative osmotic laxatives of magnesium hydroxide or magnesium salts are satisfactory for occasional use or where rapid bowel evacuation is required but tend not to be used in the long term, hence they are not included in this study dealing with the management of chronic constipation (BNF 2007).

How the intervention might work

Lactulose and Polyethylene glycol (PEG) are osmotic laxatives widely used in the treatment of chronic constipation (Boughnik 2004). These are non-absorbable, non-metabolised agents which increase the amount of water in the large bowel. Lactulose is a semi-synthetic disaccharide producing an osmotic diarrhoea of low faecal pH. PEG is an inert polymer which sequesters fluid in the bowel (BNF 2007).

Why it is important to do this review

Despite the wide variety of drugs aimed at treating constipation and faecal impaction, and the large sum of healthcare budget spent on these, evidence of their effectiveness is limited, with rates of successful treatment reported by specialist centres of only 50-60% (Sondheimer 2002, Schiller 2004). Lactulose and Polyethylene glycol are both osmotic laxatives which are commonly used in the treatment of chronic constipation. However, there are no definitive data as to which provides the best treatment and economic outcome (Voskuil 2004). Approximately ten randomised studies have been reported (Candy 2006, Rendeli 2006, Dupont 2005, Brandt 2005, Voskuil 2004, Boughnik 2004, Gremse 2002, Christie 2002, Attar 1999, Freedman 1997, Fritz 2005, Mangin 2002, Guest 2004, Ferguson 1999), providing enough information for a systematic review comparing these two agents for efficacy.

OBJECTIVES

To identify and review all relevant data in order to determine whether Lactulose or Polyethylene Glycol is more effective at treating chronic constipation and faecal impaction.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) comparing the use of lactulose and polyethylene glycol in the management of faecal impaction and chronic constipation. Both monotherapy and crossover studies were reviewed.

Types of participants

Patients diagnosed with chronic constipation (Rome III criteria) or faecal impaction, including both adults and children, treated with lactulose or polyethylene glycol.

Types of interventions

The specific comparison made was: Treatment with lactulose versus polyethylene glycol in adults and children with chronic constipation and/or faecal impaction. Different treatment protocols were used.

Types of outcome measures

Primary outcomes

- Change in frequency of defecation

Secondary outcomes

- Use of additional products, e.g. alternative laxative agents, enemas
- Percentage in global improvement of symptoms
- Relief of abdominal pain

Search methods for identification of studies

We searched the MEDLINE, EMBASE and CINAHL databases, and the Cochrane Central Register of Controlled Trials (CENTRAL). There were no limitations based on language or date of publication. Bibliographies of all retrieved and relevant publications identified by these strategies were searched for further studies. All searches were carried on January 2008.

Electronic searches

We searched the MEDLINE, EMBASE and CINAHL databases, and the Cochrane Central Register of Controlled Trials as above. For comprehensive search strategy see Appendix 1.

Searching other resources

In addition, we searched additional trials by scanning reference lists in relevant papers and conference proceedings and through correspondence with experts and pharmaceutical companies.
The quality of the included trials was evaluated independently by the reviewers. It was assessed according to the four types of bias: Selection bias; Performance bias; Attrition bias and Detection bias. Criteria for quality assessment included:

(1) **Selection bias**
Allocation concealment:
- A: Adequate: Use of randomisation method that did not allow investigator and participant to know or influence the allocation of treatment before eligible participants entered the studies.
- B: Unclear: Randomization stated but no information on method used was available.
- C: Inadequate: Use of alternate medical record numbers or unsealed envelopes as randomisation method, and/or there was information in the study indicating that investigators or participants could have influenced the allocation of treatment.

(2) **Performance bias**
- C: Unclear: Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.
- B: No: Some participants (<5%, 5-10%, 10-20%,> 20%) were not received the allocated intervention.
- A: Yes: All participants were analysed in the treatment group to which they were randomised, regardless of whether or not they received the allocated intervention.

(3) **Detection bias**

(4) **Attrition bias**

**Intention-to-treat analysis**
- A: Yes: All participants were analysed in the treatment group to which they were allocated, regardless of whether or not they received the allocated intervention.
- B: No: Some participants (<5%, 5-10%, 10-20%,> 20%) were not analysed in the treatment group to which they were randomised because they did not receive study intervention; they withdrew from the study, or because of protocol violation.
- C: Unclear: Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**Completeness of follow-up**
- A: Yes: All participants were analysed in the treatment group to which they were allocated, regardless of whether or not they received the allocated intervention.
- B: No: Some participants (<5%, 5-10%, 10-20%,> 20%) were not analysed in the treatment group to which they were randomised because they did not receive study intervention; they withdrew from the study, or because of protocol violation.
- C: Unclear: Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**Care providers and participants were considered not blinded if the intervention group could be identified in >20% of participants because of the side effects of treatment.**

**Data collection and analysis**

Data from the selected studies was extracted using a paper data extraction form. Data was entered into the Cochrane Review Manager software (RevMan 5.0) and analysed using Cochrane MetaView.

**Selection of studies**
The reviewers (HLR, KT, JM) independently assessed titles and abstracts of the references identified by the search strategy according to the selection criteria. Full text copies of those articles and studies that appear to satisfy these criteria was obtained. When it was unclear from the title or abstract whether the paper fulfilled the criteria, or when there was disparity between reviewers, a full text copy was obtained. Obtained studies were individually assessed by two of the three reviewers (HLR, KT, JM) and then agreement obtained as to whether include or exclude a study. Any dispute was resolved by requesting a third independent review (HLR, KT, JM, RLN).

Studies were assessed for quality, with respect to methods of randomisation, allocation concealment, blinding of outcomes and drop-out rate.

**Data extraction and management**

Reviewers used a piloted data extraction sheet to summarise details of the studies. Data extraction was undertaken independently by the two reviewers and compared, with any dispute resolved by the third independent reviewer.

The following data was extracted from each study:
- **Study methods**
  - Definition and diagnostic criteria
- **Participants**
  - Number, source, age, gender, inclusion and exclusion criteria, duration of symptoms, previous treatments, underlying conditions
- **Interventions**
  - Run-in phase, treatment phase, follow-up
  - Or type, dose, duration, control used
- **Outcomes**
  - Change in frequency of defecation
  - Percentage global improvement, use of additional products, relief of abdominal pain

**Assessment of risk of bias in included studies**
The quality of the included trials was evaluated independently by the reviewers. It was assessed according to the four types of bias:
- Selection bias; Performance bias; Attrition bias and Detection bias. Criteria for quality assessment included:
- **(1) Selection bias**
  - Allocation concealment:
    - A: Adequate: Use of randomisation method that did not allow investigator and participant to know or influence the allocation of treatment before eligible participants entered the studies.
    - B: Unclear: Randomization stated but no information on method used was available.
    - C: Inadequate: Use of alternate medical record numbers or unsealed envelopes as randomisation method, and/or there was information in the study indicating that investigators or participants could have influenced the allocation of treatment.
- **(2) Performance bias:**
  - C: Unclear: Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.
  - B: No: Some participants (<5%, 5-10%, 10-20%,> 20%) were not received the allocated intervention.
  - A: Yes: All participants were analysed in the treatment group to which they were randomised, regardless of whether or not they received the allocated intervention.

**(3) Detection bias:**

**(4) Attrition bias:**

**Intention-to-treat analysis:**
- A: Yes: All participants were analysed in the treatment group to which they were allocated, regardless of whether or not they received the allocated intervention.
- B: No: Some participants (<5%, 5-10%, 10-20%,> 20%) were not analysed in the treatment group to which they were randomised because they did not receive study intervention; they withdrew from the study, or because of protocol violation.
- C: Unclear: Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**Completeness of follow-up:**
- A: Yes: All participants were analysed in the treatment group to which they were allocated, regardless of whether or not they received the allocated intervention.
- B: No: Some participants (<5%, 5-10%, 10-20%,> 20%) were not analysed in the treatment group to which they were randomised because they did not receive study intervention; they withdrew from the study, or because of protocol violation.
- C: Unclear: Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**C. Inadequate:** Use of alternate medical record numbers or unsealed envelopes as randomisation method, and/or there was information in the study indicating that investigators or participants could have influenced the allocation of treatment.

**D. Unclear:** Randomization stated but no information on method used was available.

**E. Inadequate:** Use of alternate medical record numbers or unsealed envelopes as randomisation method, and/or there was information in the study indicating that investigators or participants could have influenced the allocation of treatment.

**F. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**G. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**H. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**I. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**J. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**K. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**L. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**M. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**N. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**O. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**P. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**Q. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**R. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**S. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**T. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**U. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**V. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**W. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**X. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**Y. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

**Z. Unclear:** Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.
Measures of treatment effect
The primary outcome of frequency of defecation were assessed using weighted mean difference with 95% confidence intervals. The secondary outcomes were dichotomous data and were assessed by calculating the relative risks or risk ratios (RR) with 95% confidence intervals. RR less than 1.0 favoured the intervention group, indicating that PEG was superior when compared to Lactulose in the treatment of chronic constipation.

Unit of analysis issues
The primary outcome - frequency of defecation - was a continuous outcome (measured as the number of defecations per week). The analysis used the weighted mean difference + 95% confidence intervals. The secondary outcome of “use of associated products” was dichotomous (yes or no) and “assessment of improvement in abdominal pain” was analysed as a score, or dichotomised.

Dealing with missing data
The authors of included studies were contacted to supply missing data. Missing data and drop-outs/attrition was assessed for each included study, and the extent to which the result/conclusion of the review could have been altered by the missing data was assessed and discussed. When data were missing from the paper, an attempt was made to contact the authors to obtain the missing information. When significant gaps in data occurred and we were unable to obtain the missing data, we excluded these studies from review.

Assessment of heterogeneity
Clinical heterogeneity was assessed by comparing the distribution of important participant factors (age, sex) between trials and trial factors (randomisation concealment, blinding of outcome assessment, and losses to follow-up, treatment regimens). Statistical heterogeneity was assessed by examining I² (Higgins 2008) or Chi-Squared test. If significant heterogeneity was present (i.e. I² > 50%) (Higgins 2008), trials were explored to investigate for possible explanations. In the case of the absence of heterogeneity, data was analysed using fixed effects model.

Assessment of reporting biases
Where possible, we performed funnel plots to assess the chance of report bias and presented these using a table of bias.

Data synthesis
The analyses were performed in RevMan version 5.0. Results were shown using the approach recommended in the Cochrane Handbook (Higgins 2008). Dichotomous data were presented as relative risks (RR) with 95% confidence intervals. All randomised patients included were analysed using the intention-to-treat principle. We assessed heterogeneity between the trials using I². Where the interventions were the same or similar enough, we synthesized results in meta-analysis if there was no important clinical heterogeneity. In the case of the absence of heterogeneity, data were analysed using fixed-effects model. Random-effects models were used if there was heterogeneity. We performed subgroup analyses to assess the impact of these possible sources of heterogeneity, where appropriate. The authors of included studies were contacted to supply missing data. Funnel plots were drawn if sufficient studies were found.

Subgroup analysis and investigation of heterogeneity
If data permitted, we conducted subgroup analyses for studies using children compared with adults, and also endpoints if there were many different endpoints used between studies. As trials were conducted by different groups of investigators at different periods of time, some were heterogeneous. We explored heterogeneity between trial results using multi-step process including: (1) Forest plots were examined and the presence or absence of overlap in the confidence intervals noted. Lack of overlap of confidence intervals indicated heterogeneity. (2): We looked at the I² statistic to describe the proportion of the variability in the results that was due to heterogeneity (Higgins 2008). (3): Chi-Squared test for heterogeneity was performed and data considered heterogeneous if p<0.1. (4) If significant heterogeneity was detected, possible explanations were sought.

Sensitivity analysis
If a sufficient number of randomised trials were identified, we performed sensitivity analysis to explore the impact of study quality. Studies with clearly inadequate allocation of concealment were excluded. A second sensitivity analysis would be based on excluding outlying results.

RESULTS

Description of studies
See: Characteristics of included studies; Characteristics of excluded studies.
See Characteristics of included studies and Characteristics of excluded studies

Results of the search
We assessed 103 references from the primary search and additional search methods described, until 24/01/2008. From their abstracts, 16 of these potentially meet our inclusion criteria and the full papers were obtained. Following this review, we excluded 6 of these
trials (see Characteristics of excluded studies). A total of ten trials were included in the review. The ten trials enrolled a total of 868 participants (range 37 - 191), of which 322 were adults and 546 were children. All trials were reported in English, except for Zhang 2003, Wang 2007. The trials included in the review were published between 1997 and 2007. Location: The trials were conducted in six different countries. The trials were conducted in a variety of different settings, including hospital inpatients, outpatients, local community. Funding: Six trials did not state their source of funding. One trial stated it had no funding. Three trials reported a pharmaceutical company provided funding Dupont 2005, Bouhnik 2004, Candy 2006 Patient Symptoms: Trials used different inclusion criteria for the participants. Four studies used the Rome Diagnostic Criteria. The remaining six studies used a range of definitions of chronic constipation. Participant Age: Participant age ranged from 3 months to 70 years. Adults only were recruited for 4 studies.

**Included studies**
From 1997 to 2007, 10 randomised controlled trials were conducted that compared lactulose with polyethylene glycol (+/- placebo) for the treatment of chronic constipation.

**Excluded studies**
Four studies were excluded because they were not randomised controlled trials (Brandt 2005, Christie 2002, Fritz 2005, Guest 2004), one was an abstract with no data available to be obtained from the authors at this time (Ferguson 1999), and one only included patients with acute constipation (Van der Spoel 2007).

**Risk of bias in included studies**
See Figure 1, Figure 2.
Figure 2. Methodological quality summary: review authors' judgments about each methodological quality item for each included study.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Attar 1999</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Bouhnik 2004</td>
<td>+</td>
<td>?</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Candy 2006</td>
<td>?</td>
<td>+</td>
<td>?</td>
<td>?</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Dupont 2005</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Freedman 1997</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Gremse 2002</td>
<td>?</td>
<td>?</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Voskuijl 2004</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Wang 2007</td>
<td>?</td>
<td>+</td>
<td>-</td>
<td>?</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Zhang 2003</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
Allocation
Three of the ten included trials reported adequate generation of the allocation sequence. Attar 1999 and Dupont 2005 used a randomised list. Freedman 1997 employed a Latin square design.

Blinding
Five trials Candy 2006, Dupont 2005, Freedman 1997, Voskuil 2004, Wang 2007 reported to be double-blind studies with blinding of the participants, care providers and outcome assessors. Two trials Attar 1999, Bouhnik 2004 reported single-blinding with blinding of the assessors but not the participants or care providers. One trial Gremse 2002 reported that the study was undertaken unblinded with a cross-over design. Two trials Rendeli 2006, Zhang 2003 were unclear regarding blinding.

Incomplete outcome data
The following studies reported the outcomes below, however due to the use of incomparable scales or incomplete raw data, they could not be included in the meta-analysis.

**Stool frequency per week:**
- Dupont 2005 reported his data using medians and Interquartile ranges which we were unable to analyse in this meta analysis.
- Freedman 1997 reported form of stool motions per week as hard, soft or loose.
- There was incomplete data for analysis by Rendeli 2006, data was only reported in Chart form with no raw data.
- There was incomplete data for analysis by Wang 2007.

**Form of stool (Bristol Stool Score):**
- There was incomplete data for analysis by Candy 2006, only giving a p value which we were unable to analyse in this meta analysis.
- Freedman 1997, Gremse 2002 and Dupont 2005 reported form of stool using their own qualitative scale, not the Bristol Stool Score.

Relief of abdominal pain:
Attar 1999 reported his data using his own scale of 1-3 using the median, which we were unable to analyse in this meta analysis.

Selective reporting
Our primary outcome of stool frequency per week was reported by all authors except for Zhang 2003. Unusually, they reported the time to pass stool.

Other potential sources of bias
None identified.

Effects of interventions
All trials compared the used of lactulose and Polyethylene glycol using a combination of outcomes to assess this.

**Stool frequency per week:**
Five trials Attar 1999, Bouhnik 2004, Candy 2006, Gremse 2002, Voskuil 2004 reported stool frequency per week. Singularly taken, all showed that PEG resulted in a higher stool frequency per week when compared with Lactulose Analysis 1.1.

Data for Attar 1999: There were 60 patients in the Polyethylene glycol group, with a mean stool frequency of 1.3 per week (S.D. 0.7) compared with 55 patients in the Lactulose group, with a mean stool frequency of 0.9 per week (S.D. 0.6).

Data for Bouhnik 2004: There were 32 patients in the Polyethylene glycol group, with a mean stool frequency of 1.26 per week (S.D. 0.65) compared with 33 patients in the Lactulose group, with a mean stool frequency of 1.12 per week (S.D. 0.33).

Data for Candy 2006: There were 27 patients in the Polyethylene glycol group, with a mean stool frequency of 9.4 per week (S.D. 4.56) compared with 26 patients in the Lactulose group, with a mean stool frequency of 5.9 per week (S.D. 4.29).

Data for Gremse 2002: There were 37 patients in the Polyethylene glycol group, with a mean stool frequency of 14.8 per week (S.D. 1.4) compared with 37 patients in the Lactulose group, with a mean stool frequency of 13.5 per week (S.D. 1.5).

Data for Voskuil 2004: There were 50 patients in the Polyethylene glycol group, with a mean stool frequency of 7.12 per week (S.D. 5.14) compared with 50 patients in the Lactulose group, with a mean stool frequency of 6.43 per week (S.D. 5.18).

We found there to be significant heterogeneity with this outcome (Heterogeneity: Chi² = 17.58, df = 4 (P = 0.001); I² = 77%). On removing both Candy 2006 and Gremse 2002 from the analysis this greatly reduces (Heterogeneity: Tau² = 0.10; Chi² = 10.88, df = 3 (P = 0.01); I² = 72% on removing Candy 2006 alone. Heterogeneity: Tau² = 0.09; Chi² = 9.30, df = 3 (P = 0.03); I² = 68% on removing Gremse 2002 alone. Heterogeneity: Tau² = 0.00; Chi² = 2.32, df = 2 (P = 0.31); I² = 14% on removing both studies from the analysis). When looking at these studies we found that one possible source could be that in the Candy 2006 study, the participants had already undergone a prior phase of the study where participants had been successfully disimpacted prior to the comparative stage of the trial. Both studies, especially Gremse 2002, had a small number of participants (Candy 2006: 58 participants, Gremse 2002: 37 participants). The only other interesting point is that both of these studies were the only crossover trials analysed in this outcome. No other source of heterogeneity could be found.
Form of Stool (Bristol Stool Score):
Two trials [Wang 2007, Zhang 2003] reported form of stool on the Bristol Stool Scale. Singularly taken, both studies reported a higher Bristol Stool Score when using PEG compared with lactulose (softer stool) Analysis 2.1.

Data for [Wang 2007]: There were 105 patients in the Polyethylene glycol group, with a mean Bristol stool score of 4.26 (S.D. 0.89), compared with 111 patients in the Lactulose group, with a mean Bristol stool score of 3.63 (S.D. 1.33).

Data for [Zhang 2003]: There were 41 patients in the Polyethylene glycol group, with a mean Bristol stool score of 4.0 (S.D. 0.3), compared with 44 patients in the Lactulose group, with a mean Bristol stool score of 2.9 (S.D. 0.2).

We found there to be significant heterogeneity with this outcome (Heterogeneity: \( \chi^2 = 8.31, df = 1 (P = 0.004); I^2 = 88\%\)). However, owing to there only being two studies comparable we were unable to remove either study to investigate which was the possible source of this. Differences between the studies include the following: [Wang 2007] had over twice the number of patients compared with [Zhang 2003] (191 compared with 81) and [Wang 2007] was a paediatric study whereas [Zhang 2003] was an adult study. [Wang 2007] was also double-blinded compared with [Zhang 2003].

Relief of Abdominal Pain:
Three trials [Bouhnik 2004, Dupont 2005, Wang 2007] reported relief of abdominal pain. Singularly taken, two trials favour PEG in this outcome; Dupont 2005 and Wang 2007. Bouhnik 2004 found Lactulose and PEG to be comparable in this outcome. This study included only 65 patients, the other two studies included 235 patients Analysis 3.1. (PEG lac - events total)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>PEG</th>
<th>Lactulose</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>33</td>
<td>26</td>
<td>32</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>79</td>
<td>105</td>
<td>63</td>
<td>111</td>
</tr>
</tbody>
</table>
Summary of main results

In the present meta-analysis, we considered for the first time all ten randomised controlled trials so far performed. The findings of our work indicate that Polyethylene glycol is better than lactulose in outcomes of stool frequency per week, form of stool, relief of abdominal pain and the need for additional products. On subgroup analysis, this is seen in both adults and children, except for relief of abdominal pain. The single paper by Bouhnik 2004 favours Lactulose over PEG on this outcome alone, but subgroup analysis on this outcome is limited by only a single paper reporting this outcome for adults.

Overall completeness and applicability of evidence

In the light of the improved efficacy of Polyethylene glycol, the findings of the present meta-analysis must be taken into consideration in the therapeutic management of patients with chronic constipation.

Quality of the evidence

Overall, we feel there is sufficient evidence, looking at all the outcomes across all of the randomised controlled trials, that Polyethylene Glycol is superior to Lactulose in the management of chronic constipation.

When analysing the outcome of stool frequency we found significant heterogeneity and all studies were reviewed for potential sources. We assessed each study individually for quality. Attar 1999 appeared to be a well-designed and carried-out study. They gave an adequate definition of chronic constipation. The generation of their allocation sequence was adequate and the study was performed blind. They performed a priory calculation of sample size and their population sample was 115, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. A good comparison was made between the two products with assessed outcomes including stool frequency, relief of abdominal pain, use of additional products, ease of passage, adverse events.

Bouhnik 2004 appeared to be a well-designed and carried-out study. They gave an adequate definition of chronic constipation. The generation of their allocation sequence seemed adequate, however the study was not blinded to the participants or the physicians. They performed a priory calculation of sample size and their population sample was 65, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. A good comparison was made between the two products with assessed outcomes including stool frequency, relief of abdominal pain, ease of passage, adverse events.

Candy 2006 appeared to be a well-designed and carried-out study on the whole but it is important to note that this was a two-stage trial with the second phase only being relevant to our analysis, hence providing a possible source of heterogeneity. A definition of chronic constipation was given in this study, however it was felt to be inadequate, with no mention of Rome criteria. The generation of their allocation sequence was felt to be inadequate, however the study was performed blind. They performed a priory calculation of sample size and their population sample was 65, with both groups comparable at baseline. The treatment phase was explained although in comparison with some other studies, no adjustment of dosage was made depending on tolerance and symptoms as this was a two phase trial with the comparison between the two interventions being made after disimpaction, more as a maintenance therapy. This paper differed significantly from the rest in this respect. Outcomes assessed included only stool frequency and use of additional products.

Dupont 2005 appeared to be a well-designed and carried-out study. They gave an adequate definition of chronic constipation. The generation of their allocation sequence was adequate and the study was performed blind. They performed a priory calculation of sample size and their population sample was 101, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. A good comparison was made between the two products with assessed outcomes including stool frequency, form of stool, relief of abdominal pain, use of additional products.

Gremse 2002 appeared to be a well-designed study although there was a lot of missing data and so it is difficult to comment with much certainty. A definition of chronic constipation was not given. The generation of their allocation sequence was not stated and the study was performed unblinded. It was not stated whether they performed a priory calculation of sample size and their population sample was small at 44, however this was a cross-over design. The treatment phase was explained although in comparison with some other studies, no adjustment of dosage was made depending on tolerance and symptoms. A good comparison was made between the two products with assessed outcomes including stool frequency, form of stool, ease of passage, transit time.

Freedman 1997 appeared to be a well-designed study although there was a lot of missing data and so it is difficult to comment with much certainty. A definition of chronic constipation was given in this study, however it was felt to be inadequate with no quantifiable statement. The generation of their allocation sequence was adequate and the study was performed blind. No priory calculation of sample size was performed, however their population sample was 57 with a cross-over design. The treatment phase was not explained. A good comparison was made between the two products with assessed outcomes including stool frequency, form of stool, relief of abdominal pain and use of additional products, however none of these were analysed in the meta analysis due to incomparable scales used.

Rendeli 2006 appeared to be an adequately designed and carried-out study. They gave an adequate definition of chronic constipation. The generation of their allocation sequence was not...
stated and the study was performed unblinded. They did not state whether they performed a priory calculation of sample size. Their population sample was 80, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. The comparison between the two products with assessed using only stool frequency. Voskuil 2004 appeared to be a well-designed and carried-out study. They gave an adequate definition of chronic constipation. The generation of their allocation sequence was not stated. The study was performed blind. They performed a priory calculation of sample size and their population sample was 100, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. The comparison between the two products with assessed using only stool frequency. Wang 2007 appeared to be a well-designed and carried-out study. No adequate definition of chronic constipation was given. The generation of their allocation sequence was not stated. The study was performed blind. They did not state whether they performed a priory calculation of sample size and their population sample was 227. It was unclear whether groups were comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. A good comparison was made between the two products with assessed outcomes including stool frequency, form of stool, relief of abdominal pain, adverse events. Zhang 2003 appeared to be the least well designed and carried-out study of those used in the meta-analysis although it is important to mention that the review was translated from Mandarin and some information may have been lost at this point. They gave an adequate definition of chronic constipation. The generation of their allocation sequence was not stated. It was unclear whether the study was performed blind. They did not state whether they performed a priory calculation of sample size and their population sample was 85, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. The comparison between the two products with assessed using only form of stool and adverse events.

Agreements and disagreements with other studies or reviews

The American College of Gastroenterology 2005 recommended that both PEG and lactulose are effective at improving stool frequency and stool consistency in patients with chronic constipation. However, they only found two randomised controlled trials comparing these and did not provide reference or describe their search strategy. This paper is expert opinion considering the evidence available. Ramkumar 2005 used Attar 1999 and Freedman 1997 to conclude that lactulose is less efficacious and has more side effects than PEG. They quote Christie 2002, suggesting that PEG is more cost-effective than lactulose for treating chronic constipation, particularly in the National Health Service.

Authors’ Conclusions

Implications for practice
Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.

Implications for research
A standardised validated scale should be used for form of stool - e.g. Bristol Stool Score.
A standard definition of chronic constipation to be used - e.g. Rome II criteria.
Further information on subgroups, such as the elderly population would provide greater strength to this evidence.
Studies involving a chronic condition should consider long-term outcomes and therefore a cross-over design may not be the most appropriate way to look at these conditions.

Potential biases in the review process
Some included trials were drug company sponsored studies. Bouhnik 2004 sponsored by Solvay Pharma who supplied the PEG 4000 used in the study, however Solvay Duphar B.V. supplied the Lactulose. Norgine Pharmaceuticals sponsored Candy 2006, it was not declared whether they supplied or produce either drug. Dupont 2005 were supported by Ipsen who packaged both Lactulose and PEG used in this trial.

Acknowledgements

Thanks to Dr Zhenyi Wang, Shanghai, China, for his assistance in translation and data extraction of the two papers published in Mandarin Wang 2007 and Zhang 2003.
References to studies included in this review

Attar 1999 [published data only]

Bouhnik 2004 [published data only]

Dupont 2005 [published data only]

Freedman 1997 [published data only]

Greense 2002 [published data only]

Rendeli 2006 [published data only]

Voskuijl 2004 [published data only]

Wang 2007 [published data only]

Zhang 2003 [published data only]

References to studies excluded from this review

Brandt 2005 [published data only]

Christie 2002 [published data only]

Ferguson 1999 [published data only]

Fritz 2005 [published data only]

Guest 2004 [published data only]

Van der Spoel 2007 [published data only]

Additional references

American College of Gastroenterology 2005

Arce 2002
Bassotti 2003

Bassotti 2004

Bleser 2005

BNF 2007

Damon 2004

Dennison 2005
Dennison C, Prasad M, Lloyd A, Bhattacharyya SK, Dhawan R, Coney K. The health-related quality of life and economic burden of constipation. Pharmacoeconomics 2005;23:461–476.

Drossman 1997

Drossman 1998

Frexinos 1998

Glia 1997

Higgins 2004

Higgins 2008

Irvine 2002

Johanson 1989

Legoreta 2006

Lembo 2003

Loening-Baucke 1993

Longstreth 2006

Mangin 2002

Peppas 2008
George Peppas, Vangelis G. Alexiou1, Eleni Mourtzoukou, Matthew E. Falagas. Epidemiology of constipation in Europe and Oceania: a systematic review. BMC Gastroenterology 2008 2008;8:5.

Ramkumar 2005

Rao 2003

Sandler 1987

Schiller 2004

Singh 2004

Sondheimer 2002

Talley 1993
Talley 2003

Talley 2004

Thompson 1999

Velio 1996

* Indicates the major publication for the study
### Characteristics of included studies

**Attar 1999**

| **Methods** | Generation of allocation sequence: a randomised list was established by the statistician. Allocation concealment: was not described. Blinding: As the two treatments differed in appearance and taste, the study was not conducted double blind. Investigators were unaware of the allocation of treatments. Inclusion of all randomised patients: All randomised patients were included in data analysis. |
| **Participants** | Number: 115
Age: 55 +/- 23 years (mean +/- S.D.)
Source: Ten centres in France and Scotland. Patients were recruited from both general and geriatric hospitals, mainly from outpatient departments.
Inclusion criteria: At least 18 years of age. The diagnosis of chronic idiopathic constipation was based on presence for at least three months of less than three stools per week and/or straining at stool. Patients older than 45 years required exclusion of constipation secondary to colonic disease, verified by colonoscopy or barium enema performed within the last 5 years.
Exclusion criteria: Patients taking concomitant medications which could modify bowel habit and those suffering from severe liver, renal or cardiac diseases. Pregnant and breastfeeding women. |
| **Interventions** | 10g Lactulose diluted in 15mls water or 13.12g PEG 3350, 0.18g sodium bicarbonate, 0.35g sodium chloride, 0.05g potassium chloride, 0.01g acesulfame-K and J2076 lemon flavours. Patients were instructed to take two sachets per day of the medications, in two divided doses, each sachet being diluted in 125mls water. If stools became liquid, participants could reduce the dosage. After two weeks patients were given the option to change the dosage based on efficacy and tolerance. No other treatments for constipation were allowed in this study, except for suppositories and micro-enemas. |
| **Outcomes** | Included in review: Number of stools per week, Use of additional products
Excluded from review: Straining at stool, Liquid stools, Abdominal pain, Bloating/flatus/rumbling. All of these used a non-comparable symptom score scale. |
| **Notes** | Location: Scotland and France
Source of funding: Not stated
Attempts to clarify information: not required
Language of Publication: English |

#### Risk of bias

<table>
<thead>
<tr>
<th><strong>Item</strong></th>
<th><strong>Authors’ judgement</strong></th>
<th><strong>Description</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>Yes</td>
<td>A randomised list was established by the statistician. Inclusion of all randomised patients: All</td>
</tr>
</tbody>
</table>
### Attar 1999 (Continued)

<table>
<thead>
<tr>
<th>Allocation concealment?</th>
<th>Unclear</th>
<th>Allocation concealment was not described.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding?</td>
<td>No</td>
<td>As the two treatments differed in appear-</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td>ance and taste, the study was not conducted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>double blind. Investigators were unaware</td>
</tr>
<tr>
<td></td>
<td></td>
<td>of the allocation of treatments.</td>
</tr>
<tr>
<td>Incomplete outcome data addressed?</td>
<td>Yes</td>
<td>All randomised patients were included in</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td>data analysis.</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>No</td>
<td>Did not report data on Form of stool</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

### Bouhnik 2004

<table>
<thead>
<tr>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generation of allocation sequence: Sealed envelopes containing individual randomisation</td>
</tr>
<tr>
<td>Allocation concealment: Unclear.</td>
</tr>
<tr>
<td>Blinding: As the two treatments varied in appearance and taste, the study was blind only to the bacteriologists and biochemists, but not for the physicians and patients.</td>
</tr>
<tr>
<td>Inclusion of all randomised: All analyses were performed as intention to treat procedures.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number: 65</td>
</tr>
<tr>
<td>Age of patients: 57 +/- 18 years (mean +/- S.D.)</td>
</tr>
<tr>
<td>Source: Patients in primary care.</td>
</tr>
<tr>
<td>Inclusion criteria: Chronic idiopathic constipation diagnosed based on Rome I diagnostic criteria. An organic cause of constipation was excluded by the General Practitioner.</td>
</tr>
<tr>
<td>Exclusion criteria: Patients taking concomitant medications which may modify bowel habit, severe liver disease, renal or cardiac diseases and pregnant or breast-feeding women.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients were treated with either PEG 4000 electrolyte solution or lactulose for four weeks. In the first week 2 sachets of medication were taken per day. In the second week patients were given an option to change the dosage depending on efficacy and tolerance. For the third and fourth weeks the investigator changed the treatment dose based on the results of the second week.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Included in review: Stool frequency. Relief of abdominal pain.</td>
</tr>
<tr>
<td>Excluded from review: Difficulty in defecation, straining on passage, borborygmi, bloating, fresh stool analysis, frozen stool analysis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location: Paris, Lille and Nantes, France</td>
</tr>
<tr>
<td>Date: March-December 1998</td>
</tr>
<tr>
<td>Source of funding: Solvay Pharma, 42 rue Rouger de Lisle, F-92151, Suresnes Cedex, France</td>
</tr>
<tr>
<td>Attempts to clarify information: not required.</td>
</tr>
<tr>
<td>Item</td>
</tr>
<tr>
<td>----------------------------------</td>
</tr>
<tr>
<td>Adequate sequence generation?</td>
</tr>
<tr>
<td>Allocation concealment?</td>
</tr>
<tr>
<td>Blinding? All outcomes</td>
</tr>
<tr>
<td>Incomplete outcome data addressed? All outcomes</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
</tr>
<tr>
<td>Free of other bias?</td>
</tr>
</tbody>
</table>

**Candy 2006**

**Methods**

- Generation of allocation sequence: Not described.
- Allocation concealment: was not described.
- Blinding: Children and investigators were blinded as to the medication dispensed.
- Inclusion of all randomised: Data was summarised by randomised treatment group for the intent-to-treat and per protocol overall populations.

**Participants**

- Number: 58
- Age: 2-11 years
- Source: Children who were successfully disimpacted during Phase I of the study (oral PEG+E as inpatient).
- Inclusion criteria: Intractable constipation that had failed to respond to conventional treatment.
- Exclusion criteria: Conditions contra-indicating the use of PEG-E or lactulose, including intestinal perforation or obstruction, allergy, paralytic ileus, toxic megacolon, Hirschsprung disease, severe inflammatory bowel disease, uncontrolled renal/hepatic/cardiac disease, uncontrolled endocrine disorder or any neuromuscular disorder affecting bowel function.

**Interventions**

The children received oral maintenance doses of PEG-E or lactulose commencing with one half of the number of sachets required for disimpaction in Phase I, for twelve weeks.
Outcomes

Included in review: Stool frequency. Use of additional products.
Excluded from review: Predominant bowel movement form, pain, straining, rectal bleeding, abdominal pain, soiling, overall rating of treatment. All of these outcomes used non-comparable scales. Adverse effects were also discussed.

Notes

Location: Paediatric Gastroenterology Service, Royal West Sussex NHS Trust, Chichester, UK
Source of funding: Norgine Pharmaceuticals Ltd, Harefield, Middlesex, UK
Attempts to clarify information: not required
Language of Publication: English

Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>Unclear</td>
<td>Not described.</td>
</tr>
<tr>
<td>Allocation concealment?</td>
<td>Unclear</td>
<td>Not described.</td>
</tr>
<tr>
<td>Blinding? All outcomes</td>
<td>Yes</td>
<td>Children and investigators were blinded as to the medication dispensed.</td>
</tr>
<tr>
<td>Incomplete outcome data addressed?</td>
<td>Unclear</td>
<td>Data was summarised by randomised treatment group for the intent-to-treat and per protocol overall populations</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>Yes</td>
<td>Reported data on all outcomes however, for form of stool and relief of abdominal pain he only gave p values.</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

Dupont 2005

Methods

Generation of allocation sequence: randomisation list
Allocation concealment: double-dummy design with patients receiving paired sachets
Blinding: double-blind
Inclusion of all randomised: 98 patients were randomised but 2 dropped out before study drug intake: one withdrew their consent and one was found not to meet the inclusion criteria. Efficacy and tolerance were assessed on an intention to treat basis.

Participants

Number: 96
Source: 3 hospital centres in France
Inclusion criteria: Ambulatory children aged 6 months to 3 years with constipation despite dietary treatment for at least one month. Constipation defined as less than one stool per day for more than one month in children aged 6 to 12 months and less than 3 stools per week for more than 3 months in children aged 13 months to 3 years.
Exclusion criteria: History of intractable faecoma or organic gastrointestinal disease, neurological, endocrine or metabolic disorders, allergic disease or allergies.

Interventions

Patients received either one 3.33g sachet of lactulose and one 4g sachet of placebo or one 4g sachet of PEG4000 and one 3.33g sachet of placebo at breakfast. In children aged 13 months to 3 years the dose could be doubled if ineffective. If this dose was unsuccessful, one glycerol enema could be used for a maximum of three consecutive days. If liquid stools were produced for more than one day or more than two or three stools per day the dose could be reduced by one pair of sachets per day.

Outcomes

Included in review: Relief of abdominal pain, Use of additional products
Excluded from review: Stool frequency, Form of stools. Non-comparable scales were used. Adverse effects were also discussed.

Notes

Location: France
Date: From July 2000
Source of funding: Ipsen, Paris, France
Attempts to clarify information: not required
Language of Publication: English

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors' judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>Yes</td>
<td>Randomisation list</td>
</tr>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>Double-dummy design with patients receiving paired sachets</td>
</tr>
<tr>
<td>Blinding? All outcomes</td>
<td>Yes</td>
<td>Double-blind</td>
</tr>
<tr>
<td>Incomplete outcome data addressed? All outcomes</td>
<td>Yes</td>
<td>Efficacy and tolerance were assessed on an intention to treat basis.</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>Yes</td>
<td>All outcomes were reported.</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

### Freedman 1997

<table>
<thead>
<tr>
<th>Methods</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Generation of allocation sequence: not described</td>
<td></td>
</tr>
<tr>
<td>Allocation concealment: prospective, randomised, double-blind, cross-over design utilising latin-square assignment.</td>
<td></td>
</tr>
<tr>
<td>Blinding: double blind</td>
<td></td>
</tr>
<tr>
<td>Inclusion of all randomised: 57 patients were recruited and 57 completed the protocol.</td>
<td></td>
</tr>
</tbody>
</table>
Participants

Number: 57
Source: the Sinai Hospital Drug Dependency Program.
Inclusion criteria: Drug-dependent men and women involved in a methadone maintenance programme, who complained of constipation and had previously sought the use of laxatives, aged 18-50 years.
Exclusion criteria: Women were required to be neither pregnant nor lactating. A history of colonic surgery, childhood constipation requiring more than one bowel-purging procedure per month, adult onset constipation predating methadone use, haem-positive stool of unknown aetiology, those deemed unreliable for a seven week follow-up period, and those who had a history of rectal bleeding within the last month.

Interventions

After one week control period during which patients received no treatment, a latin square assignment was used to evaluate three regimens in random order. Treatments included 240mls of identically flavoured 1) placebo (water), 2) lactulose (30mls diluted in water to 240mls), 3) Go-Lytely Lax (polyethylene glycol/electrolyte solution).

Outcomes

Included in review: None
Excluded from review: Number of hard stools, number of soft stools and number of loose stools per week. Frequency of excessive gas per week, frequency of severe abdominal cramping. Additional product requirements were also discussed.

Notes

Location: Sinai Hospital, Baltimore, Maryland, USA.
Source of funding: None stated
Attempts to clarify information: attempted to contact authors via e-mail to obtain raw data for outcomes with incomparable scales/no data.
Language of Publication: English

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors' judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>Unclear</td>
<td>Not described</td>
</tr>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>Cross-over design utilising latin-square assignment.</td>
</tr>
<tr>
<td>Blinding? All outcomes</td>
<td>Yes</td>
<td>Double-blind</td>
</tr>
<tr>
<td>Incomplete outcome data addressed? All outcomes</td>
<td>Yes</td>
<td>All randomised patients completed the study and were included in the analysis</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>Yes</td>
<td>All outcomes were reported.</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias
### Methods

- **Generation of allocation sequence:** not stated
- **Allocation concealment:** not applicable as unblinded
- **Blinding:** Unblinded, randomised, cross-over design
- **Inclusion of all randomised:** 44 patients were enrolled in the study, 7 patients withdrew in the first two weeks due to lack of efficacy. These 7 were not included in analysis.

### Participants

- **Number:** 37
- **Source:** patients referred for subspeciality evaluation of constipation
- **Inclusion criteria:** Aged 2 to 16 years, suffering from constipation.
- **Exclusion criteria:** Patients with organic disease of the large or small bowel, known allergy to PEG or lactulose, previous GI surgery, renal or heart failure, bowel obstruction, ileus, pregnancy, lactation, galactosaemia, or diabetes mellitus.

### Interventions

Patients received either PEG 3350 (10g/m$^2$/day) or lactulose (1.3g/kg/day) orally for two weeks, followed by the other agent for two weeks.

### Outcomes

Included in review: stool frequency per week.
Excluded from review: total and segmental colonic transit time, global assessment by parent, score for stool form, ease of passage.

### Notes

- **Location:** Division of Pediatric Gastroenterology and Nutrition, University of South Alabama, USA
- **Source of funding:** not stated
- **Attempts to clarify information:** not required
- **Language of Publication:** English

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors' judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>Unclear</td>
<td>Not stated</td>
</tr>
<tr>
<td>Allocation concealment?</td>
<td>Unclear</td>
<td>Not applicable as unblinded</td>
</tr>
<tr>
<td>Blinding? All outcomes</td>
<td>No</td>
<td>Unblinded</td>
</tr>
<tr>
<td>Incomplete outcome data addressed? All outcomes</td>
<td>Yes</td>
<td>44 patients were enrolled in the study, 7 patients withdrew in the first two weeks due to lack of efficacy. These 7 were not included in analysis.</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>Yes</td>
<td>Did not report on relief of abdominal pain or use of additional products</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>
| Methods       | Generation of allocation sequence: This is a randomised controlled clinical trial with parallel group design.  
Allocation concealment: Not stated  
Blinding: Not stated  
Inclusion of all randomised: 70 patients were randomised, 2 patients did not enter the study as they refused therapy and 4 did not complete it. These 6 patients were not included in the analysis. |
|---------------|-------------------------------------------------------------------------------------------------|
| Participants  | Number: 64  
Source: Patients referred to the spina bifida centre of the paediatric department “Policlinici Gemelli” of Rome with neural tube defect  
Inclusion criteria: Spina bifida children with chronic neurogenic constipation aged 3-14 years, defined according to Rome diagnostic criteria.  
Exclusion criteria: Not stated |
| Interventions | After initial enema or manual extraction to clean the bowel, patients were randomly assigned to receive either PEG 4000 (0.5g/kg/day) or lactulose (1.5g/kg/day). They were monitored for 6 months and during the trial, doses could only be reduced by the physician if deemed necessary, not increased. |
| Outcomes      | Included in review: None  
Excluded from review: Bowel frequency as no comparable data available, frequency of encopresis, resolution of constipation |
| Notes         | Location: “Policlinici Gemelli” Paediatric Department, Rome, Italy  
Source of funding: No external funding received  
Attempts to clarify information: attempted to contact authors via email to obtain raw data for comparison.  
Language of Publication: English |

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>Unclear</td>
<td>Not stated</td>
</tr>
<tr>
<td>Allocation concealment?</td>
<td>Unclear</td>
<td>Not stated</td>
</tr>
<tr>
<td>Blinding?</td>
<td>Unclear</td>
<td>Not stated</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data addressed?</td>
<td>No</td>
<td>70 patients were randomised, 2 patients did not enter the study as they refused therapy and 4 did not complete it. These 6 patients were not included in the analysis.</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>Unclear</td>
<td>Did not report on form of stool, relief of abdominal pain or use of additional products</td>
</tr>
</tbody>
</table>
### Voskuil 2004

**Methods**
- **Generation of allocation sequence:** Patients were randomly assigned either lactulose or PEG.
- **Allocation concealment:** Unlabelled numbered boxes with unlabelled sachets prepared by the academic medical centre pharmacy.
- **Blinding:** Double blinding
- **Inclusion of all randomised:** Yes

**Participants**
- **Number:** 100
- **Source:** Patients referred by school doctors, GPs and paediatricians to the Department of Paediatric Gastroenterology and Nutrition, Academic Medical Centre, Emma Children's Hospital, Amsterdam, The Netherlands.
- **Inclusion criteria:** Children with constipation referred by school doctors, GPs and paediatricians, aged 6 months to 15 years. Childhood constipation was defined as having at least two of the following symptoms for the last three months: less than 3 bowel movements per week, encopresis more than once a week, large amounts of stool every 7 to 30 days, palpable abdominal or rectal mass.
- **Exclusion criteria:** Children with organic causes for defecation disorders.

**Interventions**
- **Run-in phase:** no oral laxatives then one enema per day for three consecutive days.
- **Treatment phase:** patients aged between 6 months and 6 years began treatment with one sachet of PEG 3350 (2.95g) or lactulose (6g) per day. Those older than six years were given two sachets of each per day. After one week doses were altered if necessary, or a stimulant laxative added. Patients were followed up for eight weeks.

**Outcomes**
- **Included in review:** stool frequency
- **Excluded from review:** frequency of encopresis, overall treatment success, adverse events.

**Notes**
- **Location:** Department of Paediatric Gastroenterology and Nutrition, Academic Medical Centre, Emma Children's Hospital, Amsterdam, The Netherlands.
- **Date:** not stated
- **Source of funding:** Mediserv BV / Clinical research facilities BV, Schaijk, The Netherlands
- **Attempts to clarify information:** None required.
- **Language of publication:** English

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors' judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>Unclear</td>
<td>Patients were ‘randomly assigned’ either lactulose or PEG</td>
</tr>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>Unlabelled numbered boxes with unlabelled sachets prepared by the academic medical centre pharmacy</td>
</tr>
</tbody>
</table>
### Voskuil 2004 (Continued)

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors' judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding? All outcomes</td>
<td>Yes</td>
<td>Double blinded</td>
</tr>
<tr>
<td>Incomplete outcome data addressed? All outcomes</td>
<td>Yes</td>
<td>None identified</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>Unclear</td>
<td>Did not report on form of stool, relief of abdominal pain and use of additional products</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

### Wang 2007

| Methods                                   | Generation of allocation sequence: Randomised Allocation concealment: Active contract method Blinding: Double-dummy Inclusion of all randomised: 113 cases were randomised, 11 were excluded following randomisation, 5 did not take the medications and 6 were lost to follow-up. 25 children withdrew during the trial, which were not calculated into the PPT |
|-------------------------------------------|--------------------|-----------------------------------------------------------------------------|
| Participants                              | Number: 191 Source: 7 hospitals across China Inclusion criteria: Bristol Stool Standard aged 8-18 years Exclusion criteria: Children having organic digestive disease or systemic disease |
| Interventions                             | Run-in Phase: no other medication for treatment of constipation or other medications affecting GI motion for one week. Treatment Phase: Forlax group - 2 bags (20g/bag) in the morning of for fourteen days. Lactulose group - 15mls per day in the first three days, in the fourth to the fourteenth days, 10mls were taken. |
| Outcomes                                  | Included in review: Form of stool, relief of abdominal pain Excluded from review: Stool frequency per week, safety evaluation |

| Notes                                      | Location: Department of Paediatrics, Tangdu Hospital, 4th Military Medical University, Xi-An, China Date: July 2004-March 2005 Source of funding: Not stated Attempts to clarify information: Not required. Language of Publication: Mandarin - Translated to English. |

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors' judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>Unclear</td>
<td>Not stated</td>
</tr>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>Active contract method</td>
</tr>
</tbody>
</table>
### Wang 2007 (Continued)

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding?</td>
<td>Yes</td>
<td>Double dummy</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data addressed?</td>
<td>No</td>
<td>113 cases were randomised, 11 were excluded following randomisation, 5 did not take the medication and 6 were lost to follow-up. 25 children withdrew during the trial, which were not calculated into the PPT</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>Unclear</td>
<td>Did not report on use of additional products</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

### Zhang 2003

<table>
<thead>
<tr>
<th>Item</th>
<th>Generation of allocation sequence: Randomised, comparative trial. Allocation concealment: Not stated Blinding: Not stated Inclusion of all randomised: 85 patients were recruited but 5 withdrew during treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Number: 85 Source: Department of Gastroenterology, The First Hospital of Quanzhou, Fujian Province, China Inclusion criteria: Aged 60-70 years with constipation for more than three months who, without medicine, pass stool less than or equal to once a week and at least 25% of the time find it difficult to pass stool or pass hard stool and/or strain to pass stool. Exclusion criteria: Colorectal organic disease, faecal occult blood test positive.</td>
</tr>
<tr>
<td>Participants</td>
<td>15mls bd of lactulose or 10g of PEG 4000, into 200mls of water bd, for four weeks. No other medicine for constipation was taken during the trial.</td>
</tr>
<tr>
<td>Interventions</td>
<td>Included in review: Form of Stool Excluded from review: Pass stool times, side effects</td>
</tr>
<tr>
<td>Risk of bias</td>
<td>Location: Department of Gastroenterology, The First Hospital of Quanzhou, Fujian Province, China Source of funding: Not stated Attempts to clarify information: None required Language of publication: Mandarin, translated to English.</td>
</tr>
</tbody>
</table>
**Zhang 2003**  *(Continued)*

<table>
<thead>
<tr>
<th></th>
<th>Unclear</th>
<th>Not stated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinding?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data addressed?</td>
<td>No</td>
<td>85 patients were recruited but 5 withdrew during treatment</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>No</td>
<td>Did not report on stool frequency, relief of abdominal pain and use of additional products</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

**Characteristics of excluded studies**  *[ordered by study ID]*

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brandt 2005</td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td>Christie 2002</td>
<td>Not a randomised controlled trial. Used data already presented by Attar 1999 (included in the review) to analyse the economic impact.</td>
</tr>
<tr>
<td>Ferguson 1999</td>
<td>Abstract only available. Unsuccessful attempts made to contact authors.</td>
</tr>
<tr>
<td>Fritz 2005</td>
<td>Not a randomised study.</td>
</tr>
<tr>
<td>Guest 2004</td>
<td>Not a randomised study, this was an economic analysis.</td>
</tr>
<tr>
<td>Van der Spoel 2007</td>
<td>Included only patients with acute constipation.</td>
</tr>
</tbody>
</table>
## DATA AND ANALYSES

### Comparison 1. Stool Frequency per Week

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Stool frequency per week - all comparable data</td>
<td>5</td>
<td>407</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>0.65 [0.15, 1.15]</td>
</tr>
<tr>
<td>2 Stool frequency per week - Children</td>
<td>3</td>
<td>227</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>1.57 [0.36, 2.77]</td>
</tr>
<tr>
<td>3 Stool frequency per week - Adults</td>
<td>2</td>
<td>180</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.28 [0.10, 0.45]</td>
</tr>
<tr>
<td>4 Stool frequency per week - all comparable data excluding studies to improve heterogeneity</td>
<td>3</td>
<td>280</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.28 [0.11, 0.45]</td>
</tr>
</tbody>
</table>

### Comparison 2. Form of Stool

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Form of Stool - All comparable data</td>
<td>2</td>
<td>301</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>0.89 [0.43, 1.35]</td>
</tr>
<tr>
<td>2 Form of Stool - Children</td>
<td>1</td>
<td>216</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.63 [0.33, 0.93]</td>
</tr>
<tr>
<td>3 Form of Stool - Adults</td>
<td>1</td>
<td>85</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>1.1 [0.99, 1.21]</td>
</tr>
</tbody>
</table>

### Comparison 3. Relief of Abdominal Pain

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Relief of Abdominal Pain - all comparable data</td>
<td>3</td>
<td>300</td>
<td>Odds Ratio (M-H, Fixed, 95% CI)</td>
<td>2.09 [1.26, 3.44]</td>
</tr>
<tr>
<td>2 Relief of Abdominal Pain - Children</td>
<td>2</td>
<td>235</td>
<td>Odds Ratio (M-H, Fixed, 95% CI)</td>
<td>2.52 [1.45, 4.40]</td>
</tr>
<tr>
<td>3 Relief of Abdominal Pain - Adults</td>
<td>1</td>
<td>65</td>
<td>Odds Ratio (M-H, Fixed, 95% CI)</td>
<td>0.86 [0.25, 2.90]</td>
</tr>
</tbody>
</table>
Comparison 4. Did not require additional products

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Did not require additional products - all comparable data</td>
<td>3</td>
<td>225</td>
<td>Odds Ratio (M-H, Fixed, 95% CI)</td>
<td>4.00 [2.01, 7.95]</td>
</tr>
<tr>
<td>2 Did not require additional products - Children</td>
<td>2</td>
<td>126</td>
<td>Odds Ratio (M-H, Fixed, 95% CI)</td>
<td>5.69 [2.06, 15.68]</td>
</tr>
<tr>
<td>3 Did not require additional products - Adults</td>
<td>1</td>
<td>99</td>
<td>Odds Ratio (M-H, Fixed, 95% CI)</td>
<td>2.79 [1.07, 7.27]</td>
</tr>
</tbody>
</table>

Analysis 1.1. Comparison 1 Stool Frequency per Week, Outcome 1 Stool frequency per week - all comparable data.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 1 Stool Frequency per Week

Outcome: 1 Stool frequency per week - all comparable data

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG N</th>
<th>PEG Mean(SD)</th>
<th>Lactulose N</th>
<th>Lactulose Mean(SD)</th>
<th>Mean Difference IV,Random,95% CI</th>
<th>Weight IV,Random,95% CI</th>
<th>Mean Difference IV,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attar 1999</td>
<td>60</td>
<td>1.3 (0.7)</td>
<td>55</td>
<td>0.9 (0.6)</td>
<td>34.4 %</td>
<td>0.40 [0.16, 0.64]</td>
<td></td>
</tr>
<tr>
<td>Bouhnik 2004</td>
<td>32</td>
<td>1.26 (0.65)</td>
<td>33</td>
<td>1.12 (0.33)</td>
<td>34.0 %</td>
<td>0.14 [0.01, 0.39]</td>
<td></td>
</tr>
<tr>
<td>Candy 2006</td>
<td>27</td>
<td>9.4 (4.56)</td>
<td>26</td>
<td>5.9 (4.29)</td>
<td>3.9 %</td>
<td>3.50 [1.12, 5.88]</td>
<td></td>
</tr>
<tr>
<td>Gremse 2002</td>
<td>37</td>
<td>14.8 (1.4)</td>
<td>37</td>
<td>13.5 (1.5)</td>
<td>22.5 %</td>
<td>1.30 [0.64, 1.96]</td>
<td></td>
</tr>
<tr>
<td>Voskuil 2004</td>
<td>50</td>
<td>7.12 (5.14)</td>
<td>50</td>
<td>6.43 (5.18)</td>
<td>5.2 %</td>
<td>0.69 [-1.33, 2.71]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>206</td>
<td></td>
<td>201</td>
<td></td>
<td>100.0 %</td>
<td>0.65 [0.15, 1.15]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.17; Chi² = 17.58, df = 4 (P = 0.001); I² = 77%
Test for overall effect: Z = 2.56 (P = 0.010)
### Analysis 1.2. Comparison 1 Stool Frequency per Week, Outcome 2 Stool frequency per week - Children.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 1 Stool Frequency per Week

Outcome: 2 Stool frequency per week - Children

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG N Mean(SD)</th>
<th>Lactulose N Mean(SD)</th>
<th>Mean Difference IV,Random,95% CI</th>
<th>Weight IV,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candy 2006</td>
<td>27 9.4 (4.56)</td>
<td>26 5.9 (4.29)</td>
<td>-18.7 % 3.50 [1.12, 5.88]</td>
<td></td>
</tr>
<tr>
<td>Gremse 2002</td>
<td>37 14.8 (1.4)</td>
<td>37 13.5 (1.5)</td>
<td>-57.7 % 1.30 [0.64, 1.96]</td>
<td></td>
</tr>
<tr>
<td>Voskuil 2004</td>
<td>50 7.12 (5.14)</td>
<td>50 6.43 (5.18)</td>
<td>-23.5 % 0.69 [-1.33, 2.71]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 114 113 100.0 % 1.57 [0.36, 2.77]

Heterogeneity: $\tau^2 = 0.54$; $\chi^2 = 3.54$, df = 2 (P = 0.17); $\eta^2$ = 44%

Test for overall effect: $Z = 2.55$ (P = 0.011)

### Analysis 1.3. Comparison 1 Stool Frequency per Week, Outcome 3 Stool frequency per week - Adults.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 1 Stool Frequency per Week

Outcome: 3 Stool frequency per week - Adults

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG N Mean(SD)</th>
<th>Lactulose N Mean(SD)</th>
<th>Mean Difference IV,Fixed,95% CI</th>
<th>Weight IV,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attar 1999</td>
<td>60 1.3 (0.7)</td>
<td>55 0.9 (0.6)</td>
<td>-52.9 % 0.40 [0.16, 0.64]</td>
<td></td>
</tr>
<tr>
<td>Bouhnik 2004</td>
<td>32 1.26 (0.65)</td>
<td>33 1.12 (0.33)</td>
<td>-47.1 % 0.14 [-0.11, 0.39]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 92 88 100.0 % 0.28 [0.10, 0.45]

Heterogeneity: $\chi^2 = 2.17$, df = 1 (P = 0.14); $\eta^2$ = 54%

Test for overall effect: $Z = 3.15$ (P = 0.0017)
**Analysis 1.4. Comparison 1 Stool Frequency per Week, Outcome 4 Stool frequency per week - all comparable data excluding studies to improve heterogeneity.**

**Review:** Lactulose versus Polyethylene Glycol for Chronic Constipation

**Comparison:** 1 Stool Frequency per Week

**Outcome:** 4 Stool frequency per week - all comparable data excluding studies to improve heterogeneity

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG</th>
<th>Lactulose</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Attar 1999</td>
<td>60</td>
<td>1.3 (0.7)</td>
<td>55</td>
<td>0.9 (0.6)</td>
<td>-</td>
</tr>
<tr>
<td>Bouhnik 2004</td>
<td>32</td>
<td>1.26 (0.65)</td>
<td>33</td>
<td>1.12 (0.33)</td>
<td>-</td>
</tr>
<tr>
<td>Voskuil 2004</td>
<td>50</td>
<td>7.12 (5.14)</td>
<td>50</td>
<td>6.43 (5.18)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>142</td>
<td>138</td>
<td>-</td>
<td>100.0 %</td>
<td>0.28 [ 0.11, 0.45 ]</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 2.32, df = 2 (P = 0.31); I² = 14%

Test for overall effect: Z = 3.19 (P = 0.0014)

---

**Analysis 2.1. Comparison 2 Form of Stool, Outcome 1 Form of Stool - All comparable data.**

**Review:** Lactulose versus Polyethylene Glycol for Chronic Constipation

**Comparison:** 2 Form of Stool

**Outcome:** 1 Form of Stool - All comparable data

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG</th>
<th>Lactulose</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Random,95% CI</td>
</tr>
<tr>
<td>Wang 2007</td>
<td>105</td>
<td>4.26 (0.89)</td>
<td>111</td>
<td>3.63 (1.33)</td>
<td>-</td>
</tr>
<tr>
<td>Zhang 2003</td>
<td>41</td>
<td>4 (0.3)</td>
<td>44</td>
<td>2.9 (0.2)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>146</td>
<td>155</td>
<td>-</td>
<td>100.0 %</td>
<td>0.89 [ 0.43, 1.35 ]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.10; Chi² = 8.31, df = 1 (P = 0.004); I² = 88%

Test for overall effect: Z = 3.79 (P = 0.00015)
### Analysis 2.2. Comparison 2 Form of Stool, Outcome 2 Form of Stool - Children.

**Review:** Lactulose versus Polyethylene Glycol for Chronic Constipation  
**Comparison:** 2 Form of Stool  
**Outcome:** 2 Form of Stool - Children

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG</th>
<th>Lactulose</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV ,Fixed,95% CI</td>
</tr>
<tr>
<td>Wang 2007</td>
<td>105</td>
<td>4.26 (0.89)</td>
<td>111</td>
<td>3.63 (1.33)</td>
<td>100.0 %</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>105</strong></td>
<td><strong>111</strong></td>
<td></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.63 [0.33, 0.93]</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable  
Test for overall effect: Z = 4.11 (P = 0.000039)

![Graph showing results]

#### Analysis 2.3. Comparison 2 Form of Stool, Outcome 3 Form of Stool - Adults.

**Review:** Lactulose versus Polyethylene Glycol for Chronic Constipation  
**Comparison:** 2 Form of Stool  
**Outcome:** 3 Form of Stool - Adults

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG</th>
<th>Lactulose</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV ,Fixed,95% CI</td>
</tr>
<tr>
<td>Zhang 2003</td>
<td>41</td>
<td>4 (0.3)</td>
<td>44</td>
<td>2.9 (0.2)</td>
<td>*</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>41</strong></td>
<td><strong>44</strong></td>
<td></td>
<td><strong>100.0 %</strong></td>
<td><strong>1.10 [0.99, 1.21]</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable  
Test for overall effect: Z = 19.74 (P < 0.00001)

![Graph showing results]
### Analysis 3.1. Comparison 3 Relief of Abdominal Pain, Outcome 1 Relief of Abdominal Pain - all comparable data.

**Review:** Lactulose versus Polyethylene Glycol for Chronic Constipation  
**Comparison:** 3 Relief of Abdominal Pain  
**Outcome:** 1 Relief of Abdominal Pain - all comparable data

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG n/N</th>
<th>Lactulose n/N</th>
<th>Odds Ratio M-H, Fixed 95% CI</th>
<th>Weight %</th>
<th>Odds Ratio M-H, Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bouhnik 2004</td>
<td>26/33</td>
<td>26/32</td>
<td>26.2% 0.86 [0.25, 2.90]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dupont 2005</td>
<td>9/11</td>
<td>3/8</td>
<td>3.0% 7.50 [0.92, 61.05]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang 2007</td>
<td>79/105</td>
<td>63/111</td>
<td>70.9% 2.32 [1.30, 4.14]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>149</strong></td>
<td><strong>151</strong></td>
<td><strong>100.0% 2.09 [1.26, 3.44]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 114 (PEG), 92 (Lactulose)  
Heterogeneity: Chi² = 3.60, df = 2 (P = 0.17); I² = 44%  
Test for overall effect: Z = 2.88 (P = 0.0040)  

### Analysis 3.2. Comparison 3 Relief of Abdominal Pain, Outcome 2 Relief of Abdominal Pain - Children.

**Review:** Lactulose versus Polyethylene Glycol for Chronic Constipation  
**Comparison:** 3 Relief of Abdominal Pain  
**Outcome:** 2 Relief of Abdominal Pain - Children

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG n/N</th>
<th>Lactulose n/N</th>
<th>Odds Ratio M-H, Fixed 95% CI</th>
<th>Weight %</th>
<th>Odds Ratio M-H, Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dupont 2005</td>
<td>9/11</td>
<td>3/8</td>
<td>4.0% 7.50 [0.92, 61.05]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang 2007</td>
<td>79/105</td>
<td>63/111</td>
<td>96.0% 2.32 [1.30, 4.14]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>116</strong></td>
<td><strong>119</strong></td>
<td><strong>100.0% 2.52 [1.45, 4.40]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 88 (PEG), 66 (Lactulose)  
Heterogeneity: Chi² = 1.12, df = 1 (P = 0.29); I² = 11%  
Test for overall effect: Z = 3.26 (P = 0.001)
### Analysis 3.3. Comparison 3 Relief of Abdominal Pain, Outcome 3 Relief of Abdominal Pain - Adults.

**Review:** Lactulose versus Polyethylene Glycol for Chronic Constipation

**Comparison:** 3 Relief of Abdominal Pain

**Outcome:** 3 Relief of Abdominal Pain - Adults

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG (n/N)</th>
<th>Lactulose (n/N)</th>
<th>Odds Ratio M-H,Fixed 95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bouhnik 2004</td>
<td>26/33</td>
<td>26/32</td>
<td></td>
<td>100.0 %</td>
<td>0.86 [0.25, 2.90]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>33</strong></td>
<td><strong>32</strong></td>
<td></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.86 [0.25, 2.90]</strong></td>
</tr>
</tbody>
</table>

Total events: 26 (PEG), 26 (Lactulose)

Heterogeneity: not applicable

Test for overall effect: Z = 0.25 (P = 0.80)

---

### Analysis 4.1. Comparison 4 Did not require additional products, Outcome 1 Did not require additional products - all comparable data.

**Review:** Lactulose versus Polyethylene Glycol for Chronic Constipation

**Comparison:** 4 Did not require additional products

**Outcome:** 1 Did not require additional products - all comparable data

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG (n/N)</th>
<th>Lactulose (n/N)</th>
<th>Odds Ratio M-H,Fixed 95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attar 1999</td>
<td>42/50</td>
<td>32/49</td>
<td></td>
<td>58.3 %</td>
<td>2.79 [1.07, 7.27]</td>
</tr>
<tr>
<td>Candy 2006</td>
<td>27/27</td>
<td>17/25</td>
<td></td>
<td>3.7 %</td>
<td>26.71 [1.45, 492.58]</td>
</tr>
<tr>
<td>Dupont 2005</td>
<td>27/32</td>
<td>25/42</td>
<td></td>
<td>38.1 %</td>
<td>3.67 [1.18, 11.43]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>109</strong></td>
<td><strong>116</strong></td>
<td></td>
<td><strong>100.0 %</strong></td>
<td><strong>4.00 [2.01, 7.95]</strong></td>
</tr>
</tbody>
</table>

Total events: 96 (PEG), 74 (Lactulose)

Heterogeneity: Chi² = 2.20, df = 2 (P = 0.33), I² = 9%

Test for overall effect: Z = 3.95 (P = 0.000078)
**Analysis 4.2. Comparison 4 Did not require additional products, Outcome 2 Did not require additional products - Children.**

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 4 Did not require additional products

Outcome: 2 Did not require additional products - Children

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG n/N</th>
<th>Lactulose n/N</th>
<th>Odds Ratio M-H,Fixed 95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candy 2006</td>
<td>27/27</td>
<td>17/25</td>
<td>8.8 % 26.71 [1.45, 492.58]</td>
<td></td>
</tr>
<tr>
<td>Dupont 2005</td>
<td>27/32</td>
<td>25/42</td>
<td>91.2 % 3.67 [1.18, 11.43]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>59</strong></td>
<td><strong>67</strong></td>
<td><strong>100.0 % 5.69 [2.06, 15.68]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 54 (PEG), 42 (Lactulose)

Heterogeneity: Chi^2 = 1.65, df = 1 (P = 0.20); I^2 =39%

Test for overall effect: Z = 3.36 (P = 0.00077)

---

**Analysis 4.3. Comparison 4 Did not require additional products, Outcome 3 Did not require additional products - Adults.**

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 4 Did not require additional products

Outcome: 3 Did not require additional products - Adults

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>PEG n/N</th>
<th>Lactulose n/N</th>
<th>Odds Ratio M-H,Fixed 95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attar 1999</td>
<td>42/50</td>
<td>32/49</td>
<td>100.0 % 2.79 [1.07, 7.27]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>50</strong></td>
<td><strong>49</strong></td>
<td><strong>100.0 % 2.79 [1.07, 7.27]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 42 (PEG), 32 (Lactulose)

Heterogeneity: not applicable

Test for overall effect: Z = 2.10 (P = 0.036)
Appendix 1. Comprehensive Search Strategy

Search strategy for review HLR 057

(‘Polyethylene glycol versus Lactulose for faecal impaction in patients with chronic constipation’)

**The Cochrane Library (24.01.08) (41 hits in Clinical trials):**

#1 (faecal impaction) or (chronic constipation) or (retention) or (delayed bowel movement) or (obstipation) or (costiveness) or (irregularity) or (feeces) or (egoest) 8483

#2 MeSH descriptor Constipation explode all trees 544

#3 (#1 OR #2) 8809

#4 4 (Polyethylene glycol) or (ethylene glycol) or (PEG) or (ethylene oxide) or (PEO) or (polyethers) or (laxatives) or (Movicol) or (polyethylene glycol 3350) or (MiraLax) or (GlycoLax) or (GoLYTELY) or (GlycoLax) or (Fortrans) or (TriLyte) or (Colyte) 1644

#5 MeSH descriptor Polyethylene Glycols explode all trees 991

#6 (#4 OR #5) 2124

#7 (lactulose) or (disaccharide) or (Generlac) or (Cephulac) or (Cholac) or (Constilac) or (Enulose) or (cilac) or (Heptalac) or (Actilax) or (Dulphalac) or (Kristalose) or (Apo-Lactulose) 677

#8 MeSH descriptor Lactulose explode all trees 230

#9 (#7 OR #8) 677

#10 (#3 AND #6 AND #9) 56 (9 reviews 41 clinical trials)

**EMBASE (Webspir 5.1, Silver Platter version 2.0) (24.01.08) (81 hits)**

#28 #10 and #27 81

#27 #22 not #26 1743633

#26 #24 not #25 2733327

#25 #23 and #24 498650

#24 (ANIMAL or NONHUMAN) in DER 3231977

#23 HUMAN in DER 6017497

#22 #19 or #20 or #21 2783097

#21 (SINGL* or DOUBL* or TREBL* or TRIPL*) near ((BLIND* or MASK*) in TLAB) 88453

#20 (RANDOM* or CROSSOVER* or FACTORIAL* or PLACEBO* or VOLUNTEER*) in TLAB 488225

#19 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 2583416

#18 “SINGLE-BLIND-PROCEDURE”/ all subheadings 7024

#17 “DOUBLE-BLIND-PROCEDURE”/ all subheadings 66374

#16 “PHASE-4-CLINICAL-TRIAL”/ all subheadings 619

#15 “PHASE-3-CLINICAL-TRIAL”/ all subheadings 7693

#14 “MULTICENTER-STUDY”/ all subheadings 40641

#13 “CONTROLLED-STUDY”/ all subheadings 2552498

#12 “RANDOMIZATION”/ all subheadings 24156

#11 “RANDOMIZED-CONTROLLED-TRIAL”/ all subheadings 148911

#10 #3 and #6 and #9 367

#9 #7 or #8 8788

#8 explode "lactulose-" / all SUBHEADINGS in DEM,DER,DRM,DRR 3294

#7 (lactulose) or (disaccharide) or (Generlac) or (Cephulac) or (Cholac) or (Constilac) or (Enulose) or (cilac) or (Heptalac) or (Actilax) or (Dulphalac) or (Kristalose) or (Apo-Lactulose) 8788

#6 #4 or #5 44699

#5 (explode "macrogol-" / all SUBHEADINGS in DEM,DER,DRM,DRR) or (explode "polyethylene-" / all SUBHEADINGS in DEM,DER,DRM,DRR) 19335

#4 (Polyethylene glycol) or (ethylene glycol) or (PEG) or (ethylene oxide) or (PEO) or (polyethers) or (laxatives) or (Movicol) or (polyethylene glycol 3350) or (MiraLax) or (GlycoLax) or (GoLYTELY) or (GlycoLax) or (Fortrans) or (TriLyte) or (Colyte) or (macrogol) 38651

#3 #1 or #2 132111

#2 explode "constipation-" / all SUBHEADINGS in DEM,DER,DRM,DRR 23107
#1 (faecal impaction) or (chronic constipation) or (retention) or (delayed bowel movement) or (obstipation) or (costiveness) or (irregularity) or (feces) or (egest)

**Medline (Webspirs 5.1, Silver Platter version 2.0) (24.01.08) (32 hits)**

#10 and #21 32
#21 #17 not #20 711841
#20 #18 not ( #18 and #19) 119606
#19 (humans) in MESH 143
#18 (animals) in MESH 119607
#17 #11 or #12 or #13 or #14 or #15 or #16 713797
#16 trial in TI 74142
#15 randomly in AB 132363
#14 (clinical trials) in MESH 143440
#13 placebo in AB 108575
#12 randomized in AB 173365
#11 clinical-trial in pt 439025
#10 #3 and #6 and #9 79
#9 #7 or #8 7021
#8 explode "Lactulose-" / all SUBHEADINGS in MIME,MJME,PT 1365
#7 (lactulose) or (disaccharide) or (Generlac) or (Cephulac) or (Cholac) or (Constitlac) or (Enulose) or (cilac) or (Heptalac) or (Actilax) or (Duphalac) or (Kristalose) or (Apo-Lactulose) 7021
#6 #4 or #5 51704
#5 explode "Polyethylene-Glycols" / all SUBHEADINGS in MIME,MJME,PT 28236
#4 (Polyethylene glycol) or (ethylene glycol) or (PEG) or (ethylene oxide) or (PEO) or (polylethers) or (laxatives) or (Movicol) or (polyethylene glycol 3350) or (MiraLax) or (GlycoLax) or (GlycoLax) or (GolyteLY) or (GlycoLax) or (Fortrans) or (TriLyte) or (Colyte) or (macrogol) 33579
#3 #1 or #2 159498
#2 explode "Constipation-" / all SUBHEADINGS in MIME,MJME,PT 7121
#1 (faecal impaction) or (chronic constipation) or (retention) or (delayed bowel movement) or (obstipation) or (costiveness) or (irregularity) or (feces) or (egest)

**HISTORY**

Protocol first published: Issue 1, 2009
Review first published: Issue 7, 2010

**CONTRIBUTIONS OF AUTHORS**

Draft the protocol (HLR, KT, JM, RLN)
Develop the search strategy (HLR, KT, JM, RLN)
Extract data (HLR, KT, JM)
Data Analysis (HLR, KT, JM, RLN)
Construction of review (HLR, JKT, JM, RLN)
DECLARATIONS OF INTEREST

None

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

N/A

NOTES

Poster presentation at European Society of Coloproctology 4th Annual Meeting, Prague, Czech Republic. 23-26 September 2009. Colorectal Disease, September 2009; 11 (suppl 2), 29 [Abstract only]