

# Psyllium

## Primary Literature

McRorie JW, Daggly BP, Morel JG *et al.* Psyllium is superior to docusate sodium for treatment of chronic constipation. *Aliment Pharmacol Ther* 1998;12(5):491-7.

**Study Objectives:** The study objective was to compare psyllium hydrophilic mucilloid versus docusate sodium for their stool softening and laxative efficacy.

### Methods:

**Design:** Randomized, parallel-design study

**Allocation:** Concealed

**Blinding:** Double-blinded

**Follow-up Period:** 2 weeks

**Setting:** Multi-site

**Participants:** A total of 170 subjects with chronic idiopathic constipation were enrolled. They are between 20 and 74 years of age. Females accounted for 91.8% of the subjects, while males accounted for 8.2%.

**The Inclusion criteria** include a bowel movement (BM) frequency of less than 3 times per week during the initial 2-week baseline placebo phase prior to treatment. Moreover, only “productive” BMs (more than 4 stool pieces with each piece being more than or equal to 2 cm in diameter) were counted for the less than 3 BMs per week for inclusion in this study.

**The Exclusion criteria** include obstructive or metabolic etiology for constipation, history of regular stimulant laxative use (more than 1 dose/week) or laxative abuse (more than the recommended daily dosage on label for any laxative).

**Intervention:** Study participants had first undergone a 1-week washout period with no laxative treatment and 1-week baseline, placebo phase, followed by 2-week treatment period. Eligible subjects were then randomized into 1 of two treatment groups: psyllium (5.1 g bid + docusate placebo; n = 88), or docusate sodium (100 mg bid + psyllium placebo; n = 82).

### Outcomes:

**Objective measures** included bowel movement frequency, stool weight, total stool output, dry stool weight, stool water weight, percentage water and a rank variable for objective measures.

**Subjective measures** included patient ratings (7-point scales) of stool consistency (very soft to very hard), straining during BM (none to extreme), pain during BM (none to extreme), completeness of evacuation (complete to incomplete), and overall feeling of constipation.

**Patient follow-up:** 170 subjects were included in the intention-to-treat population

**Main Results:** Compared to baseline, psyllium had a greater increase in stool water content versus docusate (2.33% and 0.11% respectively;  $p = 0.007$ ). Psyllium also increased total stool output compared to docusate (359.9 and 271.9 g/week respectively;  $p = 0.005$ ). Bowel movement (BM) frequency was significantly greater for psyllium (3.5 BM/week) vs. docusate (2.9 BM/week) during the second week of treatment ( $p = 0.02$ ). However, significant difference in BM movement frequency was not observed between the treatment and placebo group during week 1 of the treatment (3.3 vs. 3.1 BM/week;  $p > 0.05$ ).

**Conclusions:** The authors concluded that psyllium has a superior stool softening effect compared to docusate sodium, with psyllium having significantly greater increase in stool water content, total stool output and stool frequency in subjects with chronic idiopathic constipation.

**Comments/Critical appraisal:** In assessing the internal and external validity of this study, several strengths and limitations were identified. In terms of internal validity, the study is a multi-site, randomized double-blinded, parallel-designed study which is a good methodological design. The allocation assignment of the study was concealed. It also employed a relatively large sample size to provide the study with adequate power. The subjects have also undergone a 2-week, baseline placebo phase to achieve baseline homogeneity. However, it is to note that the study duration was relatively short (2 weeks). Moreover, the study was not placebo-controlled; therefore, it is uncertain whether treatment with psyllium would demonstrate the same degree of clinical efficacy when compared to patients without treatment. Additionally, the baseline characteristics (age, ethnicity, previous laxative use, etc.) of both intervention groups were not defined which puts the comparability of the two treatment groups in question.

In terms of external validity, the study has established inclusion and exclusion criteria that are mostly well-defined. However, it did not fully explain the implication of metabolic etiology of constipation mentioned under its exclusion criteria. Overall, it appears that the study results can be applied to the general adult population with chronic constipation having a BM of less than 3 times a week. However, the efficacy and safety of psyllium was not examined in special populations such as the pregnant and pediatric populations.

Ashraf W, Park F, Lof J *et al.* Effects of psyllium therapy on stool characteristics, colon transit and anorectal function in chronic idiopathic constipation. *Aliment Pharmacol Ther* 1995;12:639-47.

**Study Objectives:** The study objective was to evaluate the effect of psyllium on stool frequency, symptoms of difficult defecation, colon transit and parameters of anorectal manometry in chronic constipation.

**Methods:**

**Design:** Randomized, placebo-controlled, parallel study

**Allocation:** Concealed

**Blinding:** Double-blinded

**Follow-up Period:** 8 weeks

**Setting:** Undefined

**Participants:** Twenty two patients with chronic idiopathic constipation confirmed by prospectively administered stool diaries were enrolled in the study (8 males, 14 females; mean age 51 years; range 40-75 years).

**Intervention:** After a 4-week baseline, placebo, run-in phase, eligible subjects with confirmed idiopathic constipation were randomly assigned to receive either psyllium 5 g bid (n=11) or placebo (n=11) for 8 weeks. Patients were instructed to stop taking laxatives at least 1 week before and throughout the study period. This was then followed by another 4-week wash-out, placebo phase.

**Outcomes:** Outcome parameters included daily stool frequency (measured as mean stool frequency calculated from records in stool diaries), ease of defecation and stool consistency (both were measured on a visual analog scale which ranged from 1 to 7; a score of 1 is indicative of soft but formed stools, no straining and no pain, whereas a score of 7 indicated hard, pellet-like stools, continuous straining effort and excruciating pain on evacuation. and stool consistency). Completeness of evacuation, mean colon transit time and anorectal manometry were also assessed.

**Patient follow-up:** 22

**Main Results:** Compared to placebo, patients who received psyllium had significantly increased stool frequency (3.8 vs. 2.9;  $p < 0.05$ ). Stool consistency, as well as the ease of defecation, was also significantly improved with the use of psyllium versus placebo (3.2 vs. 3.8;  $p < 0.05$  and 2.0 vs. 2.6;  $p < 0.05$ , respectively). Ease of stool evacuation, mean colon transit time and anorectal manometric parameters were not statistically significant between the treatment and placebo group.

**Conclusions:** The authors concluded that psyllium increases stool frequency and improves stool consistency in chronic idiopathic constipation.

**Comments/Critical appraisal:** There are a number of strengths and limitations to this study. First of all, it is to be acknowledged that this is a randomized, double-blinded, placebo controlled study. In terms of internal validity, the study employed a small sample size of 22 which may have negatively impacted the power of the study. However, the authors were specific in defining chronic constipation in the study selecting for eligible participants only. Subjects were chosen based on an objective 4-week baseline, placebo, run-in phase to confirm the diagnosis of chronic constipation. The subjects in the treatment and placebo group also share similar baseline characteristics, including age and laxative use prior to the study. This ensures comparability between the placebo and treatment group. The subjects were all instructed to stop taking laxatives during both the run-in and study periods to ensure baseline homogeneity.

In terms of external validity, the study is applicable to the general middle-aged population who experiences a passage of less than or equal to 3 times per week. However, the study did

not clearly outline the inclusion and exclusion criteria. Moreover, the authors did not state any correlation between stool frequency and constipation severity. It was only casually implied in the study that a stool frequently of 3 stools or less per week corresponds mild to moderate constipation. Also, the study did not address psyllium use in pregnancy or the pediatric population. It is also unknown whether psyllium is beneficial in individuals with obstructive symptoms as they are excluded in the studies based on the single criterion of decreased stool frequency.

Overall, this study provided credible efficacy and safety evidence in terms of psyllium use as compared to placebo. It is valid to include psyllium in the treatment algorithm based on the positive outcome from this current study.

## Systematic Review

Brandt LJ, Prather CM, Eamonn MM *et al.* Systematic review on the management of chronic constipation in North America. *Am J Gastroenterol* 2005;100:S5-22.

**Study Objectives:** The objective of this systematic review was to assess published data regarding the management of chronic constipation in order to create an evidence-based approach to treatment. This was developed to educate physicians about the epidemiology, diagnostic approach and treatment of chronic constipation.

**Scope:** The scope of this systematic review focused on the North American perspective. Only epidemiologic studies from North American populations were used and only treatments available in the US were examined.

Regarding the study selection criteria for chronic constipation therapy trials, studies that were selected include: randomized-controlled trials, a study population that involve adults with chronic constipation, comparison of chronic constipation therapy versus placebo or control therapy, evaluation of relief of chronic constipation systems, results published in English in full manuscript form, and therapies that are available in the US. All identified citations were thoroughly reviewed.

**Methods:** In order to identify chronic constipation therapy trials, separate PUBMED and MEDLINE searches of articles in English from 1966 to 2003 were performed using different combinations of search terms related to constipation and available treatment therapies. Examples of search terms included "constipation", "laxative stimulants", "laxatives, bulk", "psyllium", etc. Exploded terms were also reviewed and included in the search if deemed appropriate. Manual searches of reference lists from relevant articles were also performed to identify additional studies that may have been missed during the online search.

In performing the systematic review of literature, data about study methodology and results were abstracted onto standard forms for performance of systematic reviews. Data that were extracted include study type, intervention, dosage and schedule of treatment versus placebo or control therapy, sample size, randomization, blinding and follow-up, study duration, outcome measures. The outcome measures included global improvements in symptoms based on the Rome Committee recommendations, as well as stool frequency and stool

consistency. Data were not combined into meta-analyses as variations exist between study design, treatment interventions, as well as treatment endpoints.

In terms of assessing the evidence for use of a specific therapeutic agent used in chronic constipation, a quality score was assigned to each of the studies being reviewed pertaining to the specific agent. The quality score was determined by a single grading system that has been validated for appropriate study design of therapy trials examined in a systematic review. Moreover, regarding the grading of recommendations, the therapy is either listed as Grade A, Grade B or Grade C based on the level of evidence presented by the trials. Grade A recommendations are supported by the strongest (Level I) evidence, while Grade B recommendations are supported by intermediate quality evidence (Level II) with important limitations. Lastly, Grade C recommendations are supported by observational studies (Level III-V).

**Main Results:** In performing the systematic review of literature on psyllium, 5 randomized-controlled trials were identified, 3 of which are placebo-controlled. The authors reported only one of these trials was of high quality lasting more than 4 weeks. However, it only included a sample size of 22, and only met 5 out of 14 Rome criteria for the recommended study design techniques to minimize bias (Quality score = 4). The three largest identified trials were placebo-controlled studies but are identified to be of low quality (Quality scores = 2-3). Psyllium overall was found to increase stool frequency, improve stool consistency and ease of defecation in these trials. However, one reported no significant increase in stool frequency, consistency and stool weights compared to placebo. When compared with “other laxatives”, psyllium produced more well-formed stools and fewer hard stools compared to baseline. When compared to lactulose, psyllium did not demonstrate significant differences in the magnitude of improvement of constipation symptoms.

**Conclusions:** The authors concluded that overall, the trials identified regarding psyllium use in chronic constipation display a weak study design. Based on the low-intermediate quality RCTs, psyllium appears to improve stool frequency and consistency. There were no statistically significant differences in side effects among psyllium, placebo and lactulose use. As a result, a Grade B recommendation was given for the use of psyllium in the treatment of chronic constipation.

**Comments/Critical appraisal:** In considering the internal validity of this systematic review, the authors clearly outlined the scope of the review, defining its selection criteria, as well as explaining how the quality score and final grading recommendation for the trials are assigned. The authors also justified why the results were not combined into meta-analyses, as there exists a wide variation in study design, study endpoints and dosages of study medications. It is to be noted that the authors of the study expanded the study endpoints to include stool frequency and consistency in addition to improvement in global chronic constipation symptoms recommended by the Rome committee as ideal primary outcomes.

Regarding the external validity of the systematic review, the authors clearly stated the studies being assessed involved the adult population. Inclusion criteria for chronic constipation were clearly defined as well as per the Rome criteria. However, there was no age specified and it is uncertain whether the results are applicable to the senior population. Moreover, the use of Rome criteria to identify patients with chronic constipation was recognized to be impractical as many patients reported to have constipation symptoms do

not fit into the Rome criteria. Lastly, exclusion criteria and any contraindication of use were not defined. The safety of psyllium use was only address for the adult population.

## Clinical Practice Guidelines/recommendations

Pare P, Bridges R, Champion M *et al.* Recommendations on chronic constipation (including constipation associated with irritable bowel syndrome) treatment. *Can J Gastroenterol* 2007;21(Suppl B):3B-22B

**Study objectives:** The objective of this article was to develop a set of treatment recommendations along with a treatment algorithm for the management of chronic constipation, including constipation associated with irritable syndrome, in the setting of primary care.

**Scope:** Literature identified that was used in the compilation of the recommendation document included publications of research in adults. No information was provided regarding study intervention, outcomes and duration.

**Methods:** Recommendations for the treatment of constipation are made based on evidence-based literature when available. Literature used was retrieved through MEDLINE, PubMed or EMBASE, or available Cochrane reviews. Examples of search terms pertaining to efficacy of psyllium use include “laxatives”, “psyllium”, “bulk agents” and “chronic constipation”. Articles were restricted to English-language full publications of research in adults between 1966 and 2006. Evidence from abstracts was not used to formulate recommendations. The evidence and recommendations compiled by individual consensus were then presented to the group for discussion. The statements of recommendation were finalized prior to the discussion with a summary of supporting evidence. During the discussion, a series of statements were voted using a five-point Likert scale. The grade of evidence was also voted according to the quality of data available. Recommendations were accepted only if 80% of participants voted for “accept completely” or “accept with some reservations”. Regarding the voting procedure, all 10 gastroenterologist members of the consensus group, excluding the Chair and the general practitioner, participated in an anonymous voting system was used for all proposed statements. If less than 80% of participants voted for these 2 categories, the objections were discussed to have either the conflict resolved or recommendation revised. All recommendations that achieved a voting consensus by the group were used in the development of the treatment algorithm for chronic constipation.

**Main results:** In support of psyllium’s efficacy for the treatment of chronic constipation in the short-term, the consensus group agreed that psyllium was more effective than placebo or docusate at increasing stool output. Constipation symptoms, such as abdominal pain, defecation effort, painful defecation and evacuation completeness were also improved with psyllium. Although no studies had been conducted on psyllium that has lasted for longer than 8 weeks, clinical experience suggested that the therapeutic effects of psyllium can be maintained for a long time (Level B; vote – 80% accepted completely, 20% accept with some reservation).

**Conclusions:** Recommendation: Psyllium is effective in the short-term treatment of chronic constipation. Studies of longer duration are lacking.

**Comments/critical appraisal:** In terms of internal validity of the recommendations compiled by the consensus group, there are a few limitations identified. First of all, some of the recommendations were made based on expert opinions when supporting evidence was not available. This could introduce bias to the consensus group during the discussion in determining the validity of the recommendations. Moreover, some of the recommendations were not accepted by all members of the consensus group. For example, the recommendation provided regarding psyllium was not definite given that 20% of the members accepted it with some reservation. Additionally, the supporting evidence that was used to formulate the recommendation did not outline the study type that were used, the patient population involved, interventions that were assigned and the duration of treatment, etc.

In considering the external validity, the only information provided for the use of psyllium was its applicability to the adult population. Exclusion criteria or red flags that suggest the need for referral were determined based on expert opinion and observational data which was graded a level E, with 80% of the consensus group completely accepting, and 20% accepting the recommendation with reservation. Despite of the number of limitations associated with the methodology of the document, the recommendation made on the use of psyllium is in agreement with most of the literature, in that psyllium use is supported in the management of chronic constipation.

## Textbooks

Bowles-Jordan, J. Constipation. In: Canadian Pharmacists Association. Patient Self-Care, 2<sup>nd</sup> ed. Ottawa, ON: Canadian Pharmacist Association, 2010:262-80.

**Source Description:** Patient Self-Care, 2<sup>nd</sup> edition (2010) is a reference text written by an expert author. The information provided is based on the best available evidence. The content of the reference text is extensively validated under a vigorous review process employed by the Canadian Pharmacists Association (CPhA). Each therapeutic topic section is reviewed by skilled CPhA pharmacist editors and two other expert reviewers who are specialized in the particular clinical area. References of new and controversial statements are provided within the text for further information.

**Summary:** Psyllium is a bulk-forming laxative that should be used initially in the management of chronic constipation, as defined by the ROME III Diagnostic Criteria. In terms of its efficacy in the management of constipation, psyllium is shown to improve stool frequency and consistency. In terms of safety, it is considered to be one of the safest laxative agents suitable for long-term use. Some flatulence or bloating may be experienced at the start of therapy. Anaphylaxis, asthma and other allergic reactions have been reported. Psyllium use is contraindicated if the patient is experiencing partial mechanical obstruction of the gastrointestinal tract, or if the patient is fluid-restricted. When used for chronic functional constipation, psyllium may take up to 2 or 3 months for maximum effect.

**Comments/Critical appraisal:** In terms of internal validity of the reference text, a major limitation being recognized is the fact that some information provided were based on expert opinions and experiences of individual authors. Regarding external validity, in



addition to the adult population, the text provided information of use for special population such as the paediatrics, pregnant and senior populations. Information on patient referral, contraindications and adverse effects of the medication were comprehensive.