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Review

Systematic review of the effectiveness of laxatives in the elderly

Mark Petticrew
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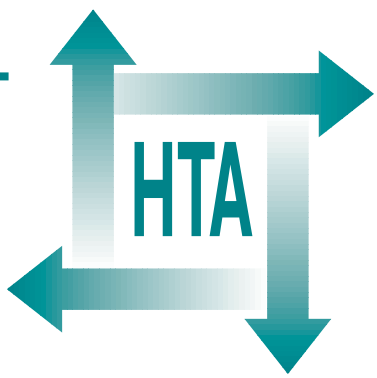
Health Technology Assessment
NHS R&D HTA Programme



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Systematic review of the effectiveness of laxatives in the elderly

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This report is one of a series covering acute care, diagnostics and imaging, methodology, pharmaceuticals, population screening, and primary and community care. It was identified as a priority by the Pharmaceutical Panel (see inside back cover).

The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health.

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Contents

List of abbreviations

BM	bowel movement*
BNF	British National Formulary
CI	confidence interval*
CRD	NHS Centre for Reviews and Dissemination
DCS	dioctyl calcium sulphosuccinate*
DSS	dioctyl sodium sulphosuccinate*
NHIS	National Health Interview Survey (USA)
NSAID	non-steroidal anti-inflammatory drug
RCT	randomised controlled trial
SD	standard deviation

* Used only in tables and figures

Executive summary

Objectives

To determine the effectiveness and cost of laxatives in the prevention and treatment of constipation in the elderly.

How the research was conducted

Study design

Randomised controlled trials (RCTs) of treatment or prevention of constipation were included in the review.

Interventions

The four classes of laxatives, bulk, osmotic, stimulant laxatives and faecal softeners, were covered by the review. The main laxatives included in the trials were bran, psyllium, prucara, cascara, dioctyl sodium, lactulose, and lactitol.

Participants

Elderly people suffering from chronic functional constipation. A trial was eligible for inclusion if all participants were aged 55 years or older and being treated for chronic constipation. The trials reviewed did not provide further subcategorisation by aetiology.

Main outcomes

Number of bowel movements per week; symptom improvement; stool consistency; abdominal pain.

Data sources

The recent systematic review by Tramonte and colleagues was used as a source of trials (*J Gen Intern Med* 1997;**12**:15–24). In addition, the following databases were searched: Embase, Psychlit, Medline, the Cochrane library, the nursing database CINAHL, International Pharmaceutical Abstracts, and the alternative therapies database, AMED. Authors and manufacturers were also asked for information. Studies in any language were eligible for inclusion. Decisions on the relevance of primary studies were made independently by two reviewers.

Economic information was searched for in Current Contents/Clinical Medicine, Medline, and the NHS Economic Evaluation Database (NEED).

Validity assessment

The quality of primary studies was summarised on a 6-item scale. This covered reporting of inclusion and exclusion criteria, randomisation method, standardised assessment of adverse effects, double-blind design, description of withdrawals, and statistical analysis. The assessment of validity of included studies was carried out independently by two reviewers. Data were extracted from studies independently by two reviewers. Authors were contacted for more information where necessary to obtain unpublished information.

Clinical trials included

Ten trials comparing single agents with placebo were identified, with a total of 367 patients who had a mean age of about 74 years. Two of these presented no information on the numbers of men and women. Just over half of the included patients were women (54%) in the remaining eight trials. The majority of patients were in an institutional setting, such as a nursing home or hospital.

Ten trials compared one laxative agent with another. The mean age of participants in these trials was estimated at 77 years. Only one trial examined patients in an outpatient setting; the other trials were carried out in nursing homes or hospitals.

Data synthesis

The studies were combined by narrative review, with quantitative summary of the results of similar trials where appropriate. This involved meta-analysis of outcome data using Cochrane Revman software. Differences between subgroups were investigated narratively.

Research findings

Four previous systematic reviews were identified, although none of these had specifically examined the effectiveness of laxatives in the elderly.

Clinical effectiveness

Most of the studies of the prevention of constipation had been observational studies. Two RCTs were identified but these were not double-blinded.

Most of the participants in the ten treatment trials were living in hospitals or nursing homes.

In most placebo-controlled trials, non-significant trends in favour of treatment were shown for the number of bowel movements per week; however, most trials were small and may have lacked statistical power. Many trials also reported non-significant improvements in stool consistency and pain.

It was not possible to determine the relative effectiveness of different types of laxative as few good quality comparative studies have been carried out. However, a combination of a bulk plus stimulant laxative (Agiolax®) was found in two good quality trials to be more effective in improving stool consistency and frequency than an osmotic laxative alone (lactulose).

Three trials of the prevention of constipation in the elderly were found, none of which found any significant benefit of laxatives in preventing constipation.

No RCTs were found that specifically examined the role of laxatives in preventing faecal impaction in the elderly.

Cost

There have been very few economic evaluations of either laxative treatment or the prevention of constipation.

The cost to the NHS of prescription laxative items is approximately £43 million per year in England. The cost of 1 week of treatment ranges widely. Stimulant laxatives are the second most commonly prescribed class of laxatives, and the total cost of this class appears to be increasing. However, there is no evidence that they are more effective than other laxatives. There is also no evidence that the widely used stimulant laxatives, co-danthramer and co-danthrusate, are more effective than cheaper alternatives.

Conclusions

There have been so few comparative studies, and the trials have been so small, that it is difficult to determine what constitutes effective treatment of constipation in the elderly.

The majority of trials have been carried out in hospitals and nursing homes so there has been no adequate assessment of the effectiveness of laxatives in elderly people living in the community who are likely to be younger and more mobile.

There have been few direct comparisons between different classes of laxatives and between different types of laxative within classes.

The cost of treatment with laxatives varies widely. Some of the most expensive laxatives, in particular, are also becoming the most widely used, without the danthron laxatives, evidence that they are more effective.

Much additional research is therefore needed to determine the most cost-effective method of treating constipation in the elderly.

Recommendations

- Laxatives may not be appropriate for all constipated elderly people. When possible, therefore, constipation should be managed by a 'stepped-care' approach, with the first step (after exclusion of co-morbidity) being advice about dietary improvement. If this fails, patients could then be prescribed the cheapest laxative treatment and, if this also fails, other laxative preparations could be given.
- There is no evidence that the expensive danthron laxatives are more effective than other laxative preparations, and they should not be used routinely in the treatment of constipation.
- Further research is required to determine the most effective ways of preventing and treating constipation in the elderly. In particular, research is needed into the non-pharmacological prevention and treatment of constipation (that is, through dietary change).
- Trials comparing the different classes of laxative are also needed (for example, comparisons of bulk laxatives with stimulant and osmotic laxatives). These studies should include assessments of the effects of treatment on symptoms and, if possible, on stool consistency. They should also involve standardised assessments of the side-effects of treatment. If appropriate, future studies should also provide stratified analyses to reflect different clinical subgroups of patients or different subcategories of constipation.

Chapter 1

Epidemiology of constipation in the general adult population

Definition of constipation

Constipation is usually regarded as a common but trivial medical problem. The term is used primarily to refer to difficulty in defecation (straining) and/or infrequency, which is not secondary to some underlying cause (Moriarty & Irving, 1992). Associated complaints include bloating and abdominal pain (Lennard-Jones, 1993). Definitions of normal bowel function vary but it has been suggested that normal defecation frequency is between three times per day and three times per week (Drossman *et al,* 1993). As an objective criteria for defining constipation, a frequency of defecation of less than three times per week has been widely used (Wolfsen *et al,* 1993; Whitehead *et al,* 1989), although patients' definitions emphasise symptoms such as pain and straining rather than frequency (Romero *et al,* 1996). The 'Rome' diagnostic criteria for constipation, devised by a working group on functional bowel disease (Thompson *et al,* 1992), define constipation as persistent symptoms of difficult, infrequent or seemingly incomplete defecation. According to the Rome criteria, a diagnosis of constipation requires two or more of the following symptoms to be present for at least 3 months:

(i) straining at defecation for at least a quarter of the time
(ii) lumpy and/or hard stools for at least a quarter of the time
(iii) a sensation of incomplete evacuation for at least a quarter of the time
(iv) two or fewer bowel movements per week.

Prevalence of constipation in the general population

General prevalence

Several surveys have estimated the prevalence of constipation among British adults in the general population *(Table 1).* The survey by Thompson and Heaton (1980) found a prevalence of 10% (assessed as frequent straining at the stool) in a sample of otherwise healthy British adults aged between 17 and 91 years. In a larger survey of bowel habits in the general population of the UK, Heaton and Cripps (1993) used a random stratified sample of all men aged 40–69 years and all women aged 25–69 years registered with general practitioners in Bristol; 39.0% of men and 51.1% of women reported regular straining. However, data on defecation frequency from the same study (Heaton *et al,* 1992) showed that only 0.6% of men and 3.5% of women claimed to defecate fewer than three times per week, based on bowel record forms. Once-daily defecation was the most commonly reported bowel pattern.

These findings on straining and frequency are in accord with data from the USA, in which most people (94%) were found to defecate between three times per day and three times per week (Drossman *et al,* 1982). Frequent straining was reported by 18%, and 4% reported less than three bowel movements per week. Similar results were obtained in a US study by Talley and colleagues (1992a), in which the prevalence of constipation was calculated as 17.4%.

The prevalence of constipation has been fairly consistently estimated to be higher in women than in men. For example, in the Bristol survey (Heaton & Cripps, 1993; Heaton *et al,* 1992) women were more than twice as likely to self-report constipation and more likely than men to consider that they had frequent or constant constipation. The higher prevalence in women persists after age-adjustment of data (Everhart *et al,* 1989; Johanson *et al,* 1989).

Although all of these UK and US surveys suggest that symptoms such as straining are relatively common, these symptoms may be transient. The data on self-reported frequent or constant constipation (as opposed to symptomatic) suggest that up to one in ten women may experience frequent constipation (Heaton & Cripps, 1993). This is supported by the study reporting on the prevalence of constipation according to the

TABLE 1 *Prevalence of constipation in adults in the general population: UK surveys*

Authors	Sample (age)	Symptoms	Prevalence (95% confidence interval (CI))
General population			
Connell *et al,* 1965	Factory workers n = 1055	1. Frequency (≤ 4 bowel movements per week) 2. Self-reported constipation	1. 5.1% (4–6) 2. 4% (3–5)
Thompson & Heaton, 1980	Healthy adults; 17–91 years n = 301	Often straining at stool (> 1/4 occasions)	10% (7–13)
Heaton & Cripps, 1993; Heaton *et al,* 1993	General population; 834 men (40–60 years); 1058 women (25–29 years)	1. Frequent straining (> 1/4 occasions) 2. Self-reported 'frequent' or 'constant'	1. Men: 39% (36–42); women: 51.5% (48–54) 2. Men: 2% (1–3); women: 10% (8–11)
Probert *et al,* 1995	731 women (25–69 years)	1. Symptoms (Rome criteria) 2. Self-perceived	1. 8.2% (6–10) 2. 8.5% (7–11)
Older people			
Thompson & Heaton, 1980	Healthy adults (60–91 years) n = 100	Straining at stool	20% (12–28)
Heaton & Cripps, 1993; Heaton *et al,* 1993	General population; 181 men, 84 women (60–69 years)	Straining to start	Men: 14% (7–21); women: 23% (17–29)
Donald *et al,* 1985	Elderly living at home, sampled from general practitioner register (Mean age 76 years) n = 129	1. Self-reported constipation 2. Straining	1. 23% (16–30) 2. 25% (18–33)

Rome criteria (Probert *et al,* 1995). The prevalence of self-reported frequent constipation in men appears to be much lower – about 2% (Heaton & Cripps, 1993).

Prevalence of constipation in the elderly

Constipation appears to be a greater problem in elderly people. Not only does the prevalence appear to be much higher in this age group but the impact on quality of life is greater. There have been a small number of UK surveys which have estimated the prevalence of constipation in the elderly. These surveys are categorised below according to whether the participants were living either in the community or in some form of institution (including hospitals).

Prevalence of constipation in elderly people living in the community

Estimates of the prevalence of constipation in elderly people living in private households are available from several UK surveys *(Table 1)*. Some of these allow direct comparisons with the prevalence in younger age groups in the same survey. For example, in Thompson and Heaton's (1980) survey of 301 apparently healthy adults, constipation (defined as straining at stool) was reported significantly more often by elderly respondents (20% ± 8%) than by middle-aged (8%) and younger (3%) respondents. In their UK survey, Heaton and Cripps (1993) also found the prevalence of reported straining to increase

with age. Around 15% of women and 6% of men aged 30–39 years reported straining to start, compared to 23% (± 6%) and 14% (± 7%), respectively, of those aged 60–69 years. Donald and colleagues (1985) drew their sample of the elderly living at home from an Edinburgh general practitioner register and found that constipation was reported by 23% (± 7%) and straining by 25% (± 8%). Regular use of analgesics (but not diuretics or hypnotics) and depression were both associated with reported constipation.

These UK estimates of about 20% of elderly people suffering from one or more symptoms of constipation are broadly supported by several non-UK surveys. For example, Campbell and colleagues (1993) found that 22% (± 3%) of those aged over 70 years living in the community in New Zealand had symptoms of constipation (based on frequency or straining). Constipation increased with age and, in patients aged over 70 years, was associated with use of constipating drugs and with lack of physical activity. Talley and colleagues (1996b) found a prevalence of constipation, adjusted for age and sex, of 24% (± 3%) in the independent elderly (aged over 65 years) living in the community in Minnesota, USA. In addition, the use of non-steroidal anti-inflammatory drugs (NSAIDs) was significantly associated with constipation. Whitehead and colleagues (1989) found a prevalence in the USA of 34% (± 9%) in men and 29% (± 9%) in women aged 65–93 years. This was based on self-reports of constipation in a door-to-door survey of 209 people. Also in the USA, Everhart and colleagues (1989) found an increase in self-reported constipation and a decrease in bowel frequency with ageing. The US National Health Interview Survey (NHIS) of 42,375 adults (Harari *et al,* 1996) also found that self-reported constipation and laxative use increased with age.

In summary, on the basis of surveys in the UK and USA, possibly about one-fifth of older people living in the community have symptoms of constipation.

The prevalence of consultation for constipation has been estimated from the UK national survey of morbidity in general practice (McCormick *et al,* 1995). In this survey, data on general practitioner contacts in 1% of the population of England and Wales was collected during 1991–92. Consultations for constipation were found to be common in the very young and the very old *(Figure 1)* and, although

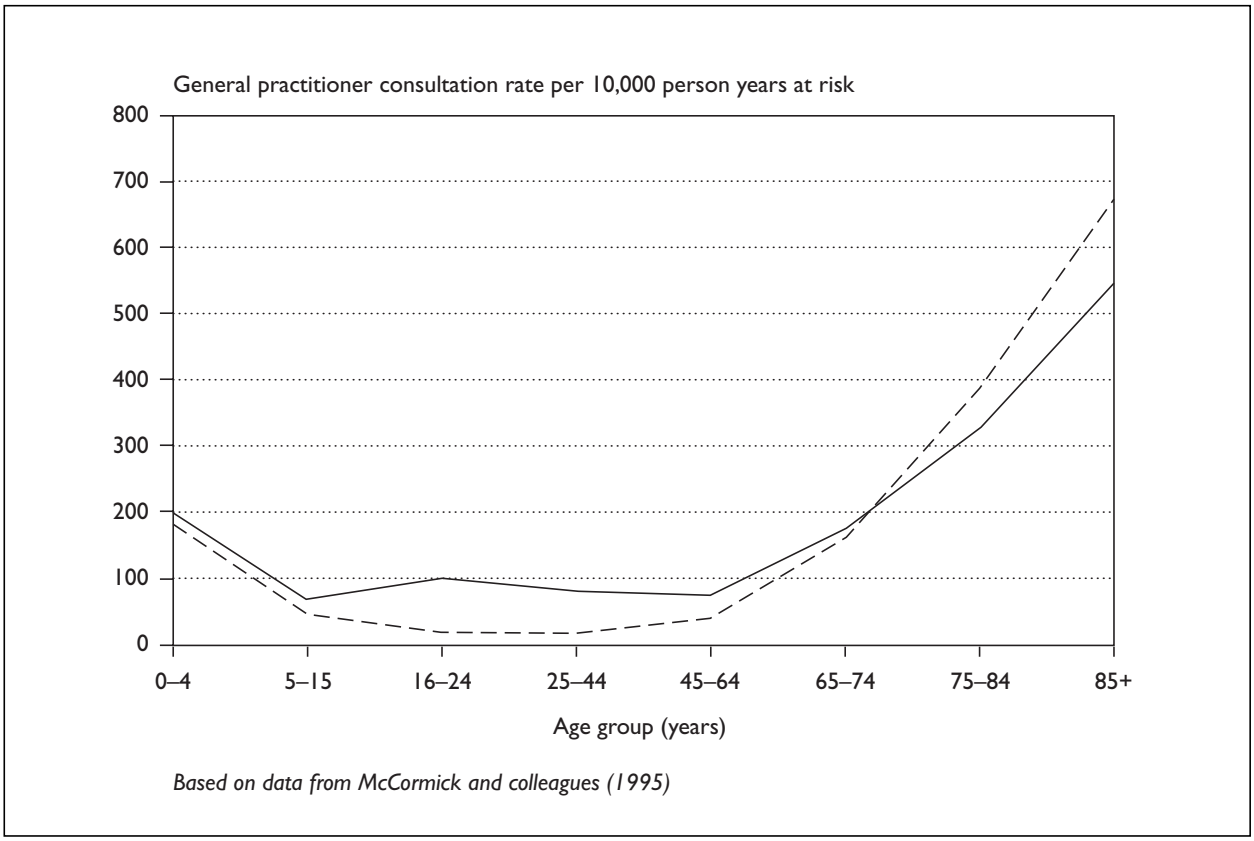

FIGURE 1 *General practitioner rate per 10,000 person years at risk (– – – –, men; ———, women)*

such consultations are more common for women overall, in the older age groups they are more common among men. This latter finding does not accord with the findings of community surveys, in which constipation tends to be found more commonly in older women. There are several possible reasons for this difference:

- older women may be more likely than men to treat themselves without recourse to a general practitioner
- they may be less likely to seek help
- they may be more likely to report less severe symptoms in surveys
- they may regard constipation as normal.

Constipation in the elderly in hospital and other institutions

Constipation in the elderly is commonly suggested to be greater in those living in nursing homes and hospitals than in those living in the community. About half of elderly patients are already constipated on admission to hospital (Read *et al,* 1985). Once admitted, additional factors may contribute to the development of constipation. For example, environmental factors may assume great importance: repression of the urge to defecate because of lack of privacy, inconvenience or lack of toilet facilities may lead to a more general reduction in rectal sensitivity and loss of the normal defecation reflex (Read & Timms, 1987). One study in an acute care hospital in the USA underlined the importance of diet and activity; these variables showed significant associations with changes in bowel patterns after adjustment for gender, illness severity and functional and cognitive status (Ross, 1995).

Impact of constipation

Quality of life

Little research has been conducted into the effect of constipation on quality of life in elderly people. However, one random sample of 704 older people (aged over 65 years) living in the community found that functional disorders of the bowel (a group of disorders which included constipation) interfered with daily living and impaired well-being. A particular feature of constipation in this sample (after controlling for age, gender and other chronic illness) was pain (O'Keefe *et al,* 1995). Wolfsen and colleagues (1993) interviewed 211 frail, community-living elderly people in the USA who were receiving in-home health-care; they found that constipation was spontaneously mentioned by 45% of those interviewed, and was considered a major problem by 11%. For 6% of these elderly people, constipation was one of their top three health concerns. In this group, 89% were using pharmacological laxatives but only 17% mentioned a healthcare professional in this context. The qualitative results of the survey also underline the influence of constipation on the quality of life of elderly people.

Faecal impaction and faecal incontinence

The impact of constipation is not limited to its immediate physical symptoms. One of the possible consequences of untreated constipation is faecal impaction, particularly in the old and confused patient. This complication has been found in a high proportion (> 40%) of such patients admitted to UK hospitals (Read *et al,* 1995). There is no information as to the prevalence of this condition in the community.

It has been widely suggested that faecal impaction, by impairment of anorectal sensation, eventually results in the development of faecal incontinence (Read & Abouzekry, 1986), although little evidence is generally provided to support this assumption. The prevalence of faecal incontinence has been estimated at 3% in a random community sample of 559 people aged 65 years or over (Campbell *et al,* 1985). This is similar to the prevalence estimated in a survey of all adults aged over 75 years in Melton Mowbray: 2% were incontinent of faeces once or twice per week (Jagger *et al,* 1986). A survey of 2000 elderly people living at home in East Anglia produced a slightly higher estimate, with 5% of those aged between 65 and 74 years found to be occasionally or frequently faecally incontinent, rising to 11% in those over 75 years of age (Kemp & Acheson, 1989). However, it is unclear from these surveys whether constipation was a contributory factor. In a study of an older, hospitalised population, for example, it was reported that faecal incontinence was found in patients who showed no evidence of faecal impaction on rectal examination (Mantle, 1992).

The scale of the problem of faecal incontinence is greater among those in residential care: one UK survey of 30 residential homes for the elderly found 10% of residents to be faecally incontinent at least weekly (Tobin & Brocklehurst, 1986),

while a survey of all eight residential homes for the elderly in Harrow found that 16% of men and 17% of women were faecally incontinent at least twice per month (Thomas *et al,* 1987).

More recently, Peet and colleagues (1995) estimated the prevalence of faecal incontinence, based on a census of all those aged over 65 years in long-term care in Leicestershire. Data on incontinence were recorded for 95% of residents. Overall, 3% of residents were incontinent of faeces on a weekly basis. The prevalence was highest in NHS acute hospitals, private nursing homes and other hospitals and hostels (about 4–5%), but there was relatively little variation in prevalence by type of establishment.

It is not possible to estimate from these studies what proportion of cases of faecal incontinence are due to previous faecal impaction. Although constipation is associated with faecal incontinence (Romero *et al,* 1996), this may be simply because those at high risk of incontinence are also at high risk of constipation.

Other complications of constipation

Haemorrhoids in the elderly are believed to be caused by chronic constipation (Read *et al,* 1995; Stewart *et al,* 1992). However, Johanson and Sonnenberg (1990) questioned this association by analysing data from four sources in the USA and UK: in the USA, the NHIS, the National Hospital Discharge Survey, and the National Disease and Therapeutic Index; and in the UK, *Morbidity Statistics from General Practice* (McCormick *et al,* 1995). Differences in the epidemiology of haemorrhoids and constipation were considered by the authors to undermine any presumption of causality.

Constipation has also been reported to be a risk factor for colorectal cancer, the incidence of which increases with age. A recent meta-analysis of 14 case-control studies found significant risks for colorectal cancer associated with both constipation and use of laxatives (Sonnenberg & Müller, 1993). However, this association is likely to be confounded by the effects of various dietary factors including fibre, fat and vegetable consumption, and even by age, which was not adjusted for in the analysis. In addition, the direction of causality may be the opposite to that implied by the analysis; that is, increased constipation and need for laxatives may be a result of colorectal cancer rather than vice versa.

Risk factors for constipation

Although many studies have found that constipation is a greater problem for the elderly, it has also been emphasised that there is nothing about ageing *per se* that causes constipation. Old people who are healthy and active often have normal defecation (Merkus, 1984). Rather, the association between age and constipation may be confounded by other known risk factors, in particular, fluid intake, diet and mobility.

Dietary factors

It has been hypothesised that the prevalence of digestive diseases, including constipation, is increasing because modern food processing methods in this century have produced a refined roughage-free modern diet (Taylor, 1990; Heaton, 1980). Numerous studies support the theory that diet has a direct influence on constipation and show that dietary fibre intake is associated variously with increased bowel transit time, faecal weight, bowel movement frequency and symptoms (for recent overviews, see Spiller, 1994; Bennett & Cerda, 1996); there are also studies showing a lower incidence of constipation in vegetarians (Nair & Mayberry, 1994; Gear *et al,* 1981). One large population survey (Sandler *et al,* 1990) has also found that constipated adults reported lower consumption of beans, peas, fruit and vegetables.

Müller-Lissner's (1988) meta-analysis of the effects of wheat bran incorporated 20 comparative studies (non-randomised controlled trials (RCT)) of the association between stool weight and gastro-intestinal transit time. Bran supplementation resulted in increased stool weight and decreased transit time in both healthy and constipated adults. However, in constipated patients receiving bran, stool weight remained lower than in controls, suggesting that low dietary fibre intake may not be the only factor influencing constipation.

The *Health Survey for England 1993* (Bennett *et al,* 1995) indicates that frequency of consumption of fruit, vegetables and bread declines significantly with age in UK adults. This may partly be due to gastrointestinal intolerance of certain of these food types (Zimmerman & Krondl, 1986). It has also been suggested that lower consumption of these food groups is a result of chewing difficulties and/or denture problems in older people; however, the evidence is limited. A UK longitudinal dietary survey did not find these factors to significantly affect dietary fibre intake (Davies *et al,* 1986), although respondents were only followed for

4 years from retirement age. Lower caloric intake in the elderly (adjusted for fibre consumption) has also been implicated in the aetiology of constipation (Towers *et al,* 1994).

Fluid intake

Lack of fluid has been cited as a risk factor for constipation (Richards-Hall *et al,* 1995; Maestri-Banks & Burns, 1996). It has been suggested that the elderly may drink less in an attempt to control incontinence (Richards-Hall *et al,* 1995), thus increasing the risk of constipation. However, there have been few studies which have examined the effects of low fluid intake on constipation while controlling adequately for other factors. One such study has shown low fluid intake to be related to slow colonic transit (Towers *et al,* 1994), and another found it to be related to low stool output in healthy adults (Klauser *et al,* 1990). Constipated adults in Sandler and colleagues' (1990) large US survey also reported less consumption of beverages (sweetened, carbonated and non-carbonated) in constipated adults. However, in a community survey in New Zealand, no association with constipation was found (Campbell *et al,* 1993).

Mobility

Physical mobility problems are more likely in the elderly, and constipation has been found to be more prevalent in those who take little exercise or are relatively inactive (Sandler *et al,* 1990). This association persisted after controlling for age. Kinnunen (1991) has calculated that the risk of constipation is significantly increased with decreased physical mobility, the highest risks being associated with being chairbound or bedbound. Several studies have described bowel management programmes in institutionalised patients in which exercise has been recommended in the treatment of constipation (see, for example, Karam & Nies, 1994; Kligman & Pepin, 1992). Exercise has also been recommended in several reviews (Romero *et al,* 1996; Lederle, 1995). However, as Klauser and Müller-Lissner (1993) point out, these treatments have not been formally evaluated in constipated patients. This has been confirmed by a Medline search (1966–96) (see Appendix 1).

Other risk factors

Other variables which have been implicated in the development of constipation, such as anxiety, depression and impaired cognitive function, are also more prevalent in older age groups. Increased use of constipating drugs may also become important and anticholinergic anti-depressants, opioid analgesics and NSAIDs, including, in particular, aspirin, seem to have a role to play (Monane *et al,* 1993; Canty, 1994; Jones & Tait, 1995). A more extensive list of other risk factors for constipation has been given by Moriarty and Irving (1992).

Finally, Harari and colleagues (1993) systematically reviewed the pathophysiology, symptoms, diagnosis, causes and treatment of constipation in older people and concluded that while the prevalence of self-reported constipation increased with age, a similar increase in the prevalence of 'true clinical constipation' is not shown. They also questioned the validity of many suspected risk factors. However, the inclusion and exclusion criteria for the review are unclear and there is no assessment of the quality of the studies.

A full systematic review of the epidemiology of constipation appears not to have been carried out and is beyond the scope of the present study.

Chapter 2

Treatment of constipation

There are several methods of clinically managing constipation but the most commonly used are laxative agents. These fall into four broad classes.

1. ***Bulking agents*** (e.g. bran, ispaghula) increase the amount of fibre in the diet, increasing the weight and water-absorbent properties of the stool. Bulk-forming laxatives may not work immediately but appear to have few side-effects. There is a widespread clinical impression that they are less effective than the more rapidly-acting stimulant laxatives (Bateman & Smith, 1988).

2. ***Stimulant laxatives*** (e.g. senna, bisacodyl) increase intestinal motility by stimulation of colonic nerves and may cause abdominal cramping. Excessive use can result in diarrhoea (Gattuso & Kamm, 1993). Castor oil is a powerful stimulant laxative which has become obsolete in clinical use.

3. ***Faecal softeners*** such as liquid paraffin and seed oils soften the stool. Adverse effects include anal seepage of paraffin and subsequent irritation, and it is recommended that prolonged use be avoided. It has also been recommended that the use of these faecal softeners should be discouraged altogether (Gattuso & Kamm, 1994) on the grounds that there are equally effective, safer alternatives.

4. ***Osmotic agents*** (e.g. magnesium hydroxide, lactulose) also act by softening and increasing water absorption in the stool. In the UK, the most commonly used of these is lactulose, which may also have some stimulant effect. However, it may take up to 48 hours to act and bloating, flatulence, cramping, nausea and an unpleasant taste have all been reported (Sykes, 1994; Kot & Pettit-Young, 1992). Lactitol is a similar agent and may also work by improving stool characteristics through encouraging the fermentation of anaerobic bacteria.

Alternative and complementary treatments are also used by people in the self-treatment of constipation: boldo, for example, is an extract from the bark of a Chilean tree traditionally employed in folk medicine in treatment of gastro-intestinal disorders. The background search to this review also indicated that guar gum (a soluble dietary fibre), bread, bran, lentils, aloe vera, mineral water and fruit, such as prunes and rhubarb, have all been claimed to have a laxative effect. The first four of these may act by increasing dietary fibre. Aloe vera is an old folk remedy, widely advertised in health food stores as a 'natural purgative'. Like senna, it contains anthraquinone derivatives and may be categorised as a stimulant laxative. Fruit may work by increasing bulk and liquid in the diet, or by fermentation in the colon. Rhubarb also contains anthraquinone, giving it a stimulant effect.

A range of non-pharmacological treatments for constipation also exist, including abdominal massage, biofeedback, hypnosis, and yogic breathing; however, these are not considered further in this review.

Use of laxatives in the elderly

Use of laxatives, like constipation, becomes more frequent with age; laxatives are used by 20–30% of the population aged over 65 (Rouse *et al,* 1991). A random sample of older people (age range, 62–90 years) living in Edinburgh found that 39% of men and 50% of women reported using laxatives (Milne & Williamson, 1972). Laxatives were sometimes used even in the absence of constipation; although frequency of use diminished with increasing frequency of bowel movements, a small proportion of respondents who had daily bowel movements still used laxatives, perhaps signifying that laxatives are used in a preventive capacity. Campbell and colleagues (1993) also found that 19% of 778 respondents aged 70 years and over felt that they were moderately constipated, although they had a bowel motion at least every 2 days, and were correspondingly more likely than the rest

of the sample to take laxatives. Heaton and Cripps (1993), in their UK survey of 1892 adults, found that 3% of men and 5% of women aged 60–69 years reported use of laxatives once a week or more, and that 3% of those reporting laxative use denied ever being constipated.

Laxatives appear to be in very common use in the hospitalised elderly in Britain. Wood and colleagues (1995) have investigated the use of oral and rectal laxatives in 232 patients at three hospital sites in Leeds. Prescription charts were reviewed on a single day for all elderly patients to identify the number and type of preparations used. A total of 46% of patients were found to be taking oral laxatives. The majority were taking lactulose either singly or in combination and a minority (8%) were taking the bulk laxative, Fybogel®. There was no policy for assessment of constipation or choice of treatment, which resulted in a wide range of treatment practices across the hospital wards surveyed. In a subsequent 2-week prospective survey, only one case was found where the prescriber attempted to diagnose the cause of constipation and choose an appropriate laxative on that basis. On another ward, the need for laxatives was assessed by staff performing digital rectal examinations every third day. The authors conclude their report by raising the question of whether health professionals are themselves guilty of laxative abuse.

Attitudes to defecation

Some of the lack of association between frequency of constipation and laxative use may be partly explained by the fact that the sufferer defines constipation differently from the clinician. While clinicians emphasise frequency, the elderly tend to define constipation in terms of symptoms, in particular, straining (Whitehead *et al,* 1989). Moore-Gillon (1984) attempted to find out what patients actually mean by the term 'constipated' by surveying 287 hospital attenders. Less than half of this group defined it in terms of frequency, as opposed to straining or pain. Probert and colleagues (1995) also emphasised the lack of overlap between slow gut transit time (> 92 hours), the Rome criteria for constipation (based on straining, incomplete evacuation, consistency and frequency) and self-perceived constipation ('do you consider yourself to be constipated?').

There are therefore two dynamics influencing the greater use of laxatives in the elderly. First, based on evidence, older people are actually at greater risk of constipation as a consequence of ageing. Second, the greater use of laxatives may partly reflect a cohort effect, since beliefs in bowel regularity and the necessity of purging the body of dangerous wastes were common earlier this century. These beliefs probably represent the lingering effects of popular Victorian theories of 'intestinal autointoxication' (Chen & Chen, 1989). Autointoxication is still an important selling point for some non-prescription treatments for constipation available today *(Table 2)*.

TABLE 2 *Excerpts from advertising material for non-prescription laxatives*

"Aloegold® forms a lining in the colon that keeps the toxic waste from re-entering the body"
"Intestinal and colon hygiene is very important to our overall health. By limiting saturated fats and other more difficult to digest foods...you have a much better chance of avoiding the build up of toxins in the lower digestive tract"
"When the colon is eliminating regularly, less bacteria forms, and therefore less bacteria is absorbed into the system, or stays in the colon where any number of discomforts can occur" (advertisement for gum karaya)

The regular use of laxatives may, therefore, be partly due to the belief in the necessity of frequent regular defecation. In support of this, a UK postal survey of beliefs about bowel function in 171 patients aged 55 years and over found that 79% of respondents believed that a daily bowel movement was important, and 90% believed that regularity was necessary for good health (MacDonald & Freeling, 1986).

Serious side-effects of laxative use

It has been suggested that many laxatives came into use before rigorous drug studies were required; hence, there is little information on the side-effects of such preparations (Kamm, 1989). Excessive use of laxatives may exacerbate the problem of constipation by causing colonic damage (Read *et al,* 1995). Chronic use of laxatives has been claimed to lead to intractable constipation or 'cathartic colon', caused by loss of colonic motility, although there is no evidence from prospective studies to support this (Gattuso

& Kamm, 1993). Laxative abuse can precipitate general practitioner consultations for diarrhoea, resulting in unnecessary expenditure on tests to exclude other diagnoses, and 4% of new cases of diarrhoea at gastroenterology clinics have been found to be laxative-induced (Duncan *et al*, 1992). More seriously still, abuse of some laxatives has been associated with colorectal cancer. Two large retrospective studies have found significant relative risks for colorectal cancer associated with laxative abuse (Siegers *et al*, 1993; Nusko *et al*, 1993), although Sonnenberg and Müller's (1993) meta-analysis suggested that the relationship may be caused by the confounding effects of diet. No separate analyses were carried out to examine the risks associated with different types of laxative.

Costs of laxatives

Apparently, the majority of constipated elderly people would, in the first instance, treat themselves with laxatives for the condition (MacDonald & Freeling, 1986). Nevertheless, NHS expenditure on laxative preparations is considerable. Constipation has been estimated to contribute to 1% of general practitioner consultations in adults (Passmore, 1995). The net ingredient cost of prescription laxative items is approximately £43 million per year in England (*Department of Health Statistical Bulletin*, 1996/17) *(Figure 2)*. This places laxatives twelfth in the top 60 British National Formulary sections (BNF; 1997) in terms of cost, ahead of, for example, expenditure on anti-hypertensive medications, drugs used in diabetes, and contraceptives. The percentage increase in expenditure between 1994 and 1995 was 3% (compared with 0% for 1993–94). As the net cost per item for laxatives has only risen by 1%, the overall increase in expenditure partly reflects the steadily increasing total number of items being prescribed – from 10.2 million items in 1993, to 10.6 million in 1994, to 10.9 million items in 1995 (*Department of Health Statistical Bulletin*, 1995/15; 1996/17). However, it may also reflect increased prescribing of more expensive laxatives. (Note: the number of items prescribed does not directly reflect the number of patients treated, as some of these will be repeat prescriptions.)

The costs of 1 week of treatment with the four types of laxative are given in *Table 3*. This shows a wide range of costs for 1 week of treatment,

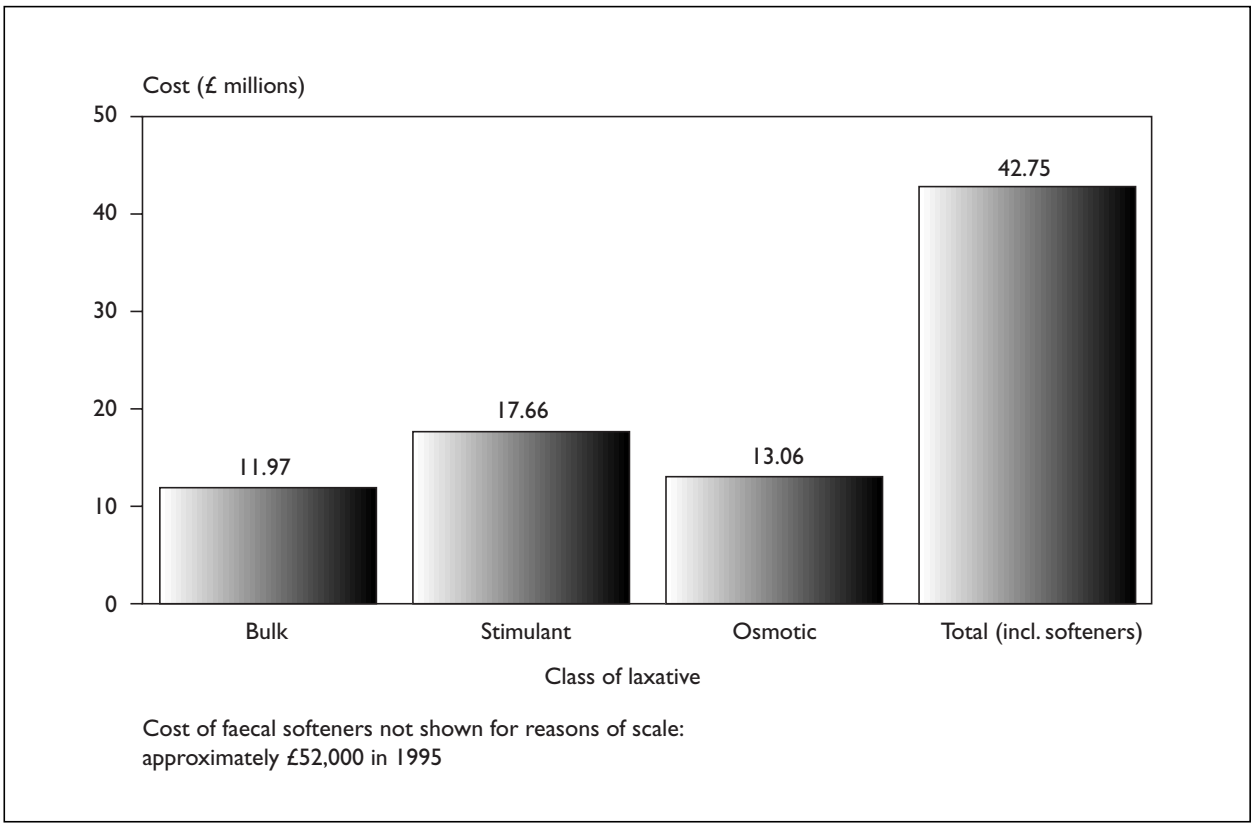

FIGURE 2 *Total costs of classes of prescribed laxatives in England, 1995 (Source:* Department of Health Statistical Bulletin, 1996/17)

TABLE 3 *Costs of 1 week's treatment with laxatives prescribable on the NHS (based on September 1997 BNF costs)*

Laxative	Course of treatment	Cost per week
Bulk-forming laxatives		
Bran		
Trifyba®	1 sachet 2–3 times daily	£0.82–£1.23
Ispaghula husk		
Fybogel®	1 sachet twice daily	£0.99
Konsyl® sugar-free	1 sachet 1–3 times daily	£0.93–£2.79
Konsyl® Orange, Dex	1 sachet 1–3 times daily	£0.47–£1.40
Isogel® (granules)	2 tsp (5 ml) daily 1–2 times daily	£0.28–£0.56
Regulan® (powder)	1 sachet 1–3 times daily	£0.50–£1.49
Methylcellulose		
Celevac®	3–6 tablets twice daily	£1.01–£2.02
Sterculia		
Normacol®	1–2 sachets 1–2 times daily	£0.54–£2.18
Normacol® plus	1–2 sachets 1–2 times daily	£0.58–£2.32
Stimulant laxatives		
Bisacodyl	1–2 or 3–4 tablets per night	£0.07–£0.14 or £0.21–£0.28
Danthron		
Co-danthramer suspension	5–10 ml per night	£1.31–£2.63
Co-danthramer strong suspension	5 ml per night	£3.35
Co-danthrusate capsules	1–3 capsules per night	£1.50–£4.49
Docusate sodium		
Dioctyl® (capsules)	up to 500 mg daily	≤ £1.63
Senna		
Senna tablets	2–4 tablets at night	£0.21–£0.42
Manevac® (granules)	5–10 ml 1–2 times daily for 3 days	£0.40–£1.61
Sodium picosulphate		
Sodium picosulphate elixir	5–15 ml per night	£0.65–£1.94
Osmotic laxatives		
Lactitol		
Lactitol powder	20 g initially, then 1 g daily	£0.80
Lactulose solution	15 ml twice daily, reduced as necessary	£1.10
Macrogols (polyethylene glycols)		
Movicol®	Elderly: 1 sachet per day	£3.45
Liquid paraffin & magnesium hydroxide emulsion BP	5–20 ml p.r.n.	£0.10–£0.40* (based on one dose daily)
Magnesium hydroxide mixture BP	25–50 ml p.r.n.	£0.60–£1.19*

**MeReC (1994)*

p.r.n., as and when required

with the stimulant laxatives, bisacodyl and senna, being the cheapest and the stimulant laxatives, co-danthramer and co-danthrusate, being among the most expensive. Given the variations in cost of treatment, it has been suggested that it is appropriate to prescribe the cheaper laxatives (Sykes, 1994). For example, lactulose costs about £1.10 for 1 week's treatment compared with £0.42 for senna tablets, for example, and it has been recommended that its use be confined to patients who do not respond to other laxatives (Bateman & Smith, 1988).

The actual costs of prescribed laxatives by class have been calculated and are shown in *Table 4* for 1995–96. Osmotic laxatives are the most frequently prescribed group overall, with about 4.4 million items prescribed during 1995,

TABLE 4 *Total costs of selected prescribed laxatives and number of items prescribed in each class in England: January 1995 – March 1996 (from data supplied by Prescription Prescribing Authority)*

Class of laxative (BNF section)	**Cost (£)**				
	Jan–Mar 1995	**Apr–June 1995**	**July–Sept 1995**	**Oct–Dec 1995**	**Jan–Mar 1996**
Bulk (1.6.1)					
Bran	16,547	15,794	15,072	14,479	14,151
Ispaghula	2,644,076	2,649,419	2,698,889	2,680,534	2,674,785
Methylcellulose	56,391	54,035	54,425	52,785	53,385
Sterculia	260,462	256,339	254,221	250,805	247,377
Total cost of section 1.6.1 (number of items)	2,977,492 (724,344)	2,975,596 (734,386)	3,022,618 (733,114)	2,998,635 (684,493)	2,989,724 (682,470)
Stimulant (1.6.2)					
Co-danthramer	1,500,292	1,573,896	1,673,393	1,827,024	1,943,597
Co-danthrusate	1,590,642	1,636,120	1,717,699	1,823,249	1,808,406
Bisacodyl	102,953	94,024	97,501	94,972	96,531
Docusate sodium	106,314	109,603	114,716	119,481	123,180
Senna	682,209	685,280	704,122	714,564	732,131
Sodium picosulphate	124,284	124,271	125,836	123,832	127,128
Total cost of section 1.6.2 (number of items)	4,157,899 (864,546)	4,270,491 (874,291)	4,480,475 (902,327)	4,749,829 (915,813)	4,877,782 (926,862)
Faecal softeners (1.6.3)					
Arachis oil	5751	5486	5763	5445	5921
Paraffin	7726	6904	6600	6822	7092
Total cost of section 1.6.3 (number of items)	13,767 (6850)	12,593 (6649)	12,871 (6266)	12,429 (6366)	13,498 (6827)

The category totals differ slightly from the sum of the costs shown as expenditure on infrequently prescribed agents is omitted – e.g. £37 was spent on oxphenysatin in first quarter of 1995. Magnesium sulphate and magnesium citrate costs are £200–400 per quarter.

continued

TABLE 4 contd *Total costs of selected prescribed laxatives and number of items prescribed in each class in England: January 1995 – March 1996 (from data supplied by Prescription Prescribing Authority)*

Class of laxative (BNF section)	Cost (£)				
	Jan–Mar 1995	Apr–June 1995	July–Sept 1995	Oct–Dec 1995	Jan–Mar 1996
Osmotic (1.6.4)					
Lactitol	24,797	25,267	25,638	25,453	24,106
Lactulose	2,918,726	2,839,046	2,619,730	2,645,277	2,646,056
Magnesium hydroxide	37,364	39,823	46,336	49,630	51,875
Phosphates (rectal)	128,103	130,480	135,243	131,778	132,372
Sodium citrate (rectal)	298,070	301,119	312,734	313,237	308,710
Total cost of section 1.6.4 (number of items)	3,411,114 (1,093,185)	3,339,891 (1,083,652)	3,143,950 (1,097,054)	3,169,282 (1,108,585)	3,167,535 (1,112,167)

The category totals differ slightly from the sum of the costs shown as expenditure on infrequently prescribed agents is omitted – e.g. £37 was spent on oxphenysatin in first quarter of 1995. Magnesium sulphate and magnesium citrate costs are £200–400 per quarter.

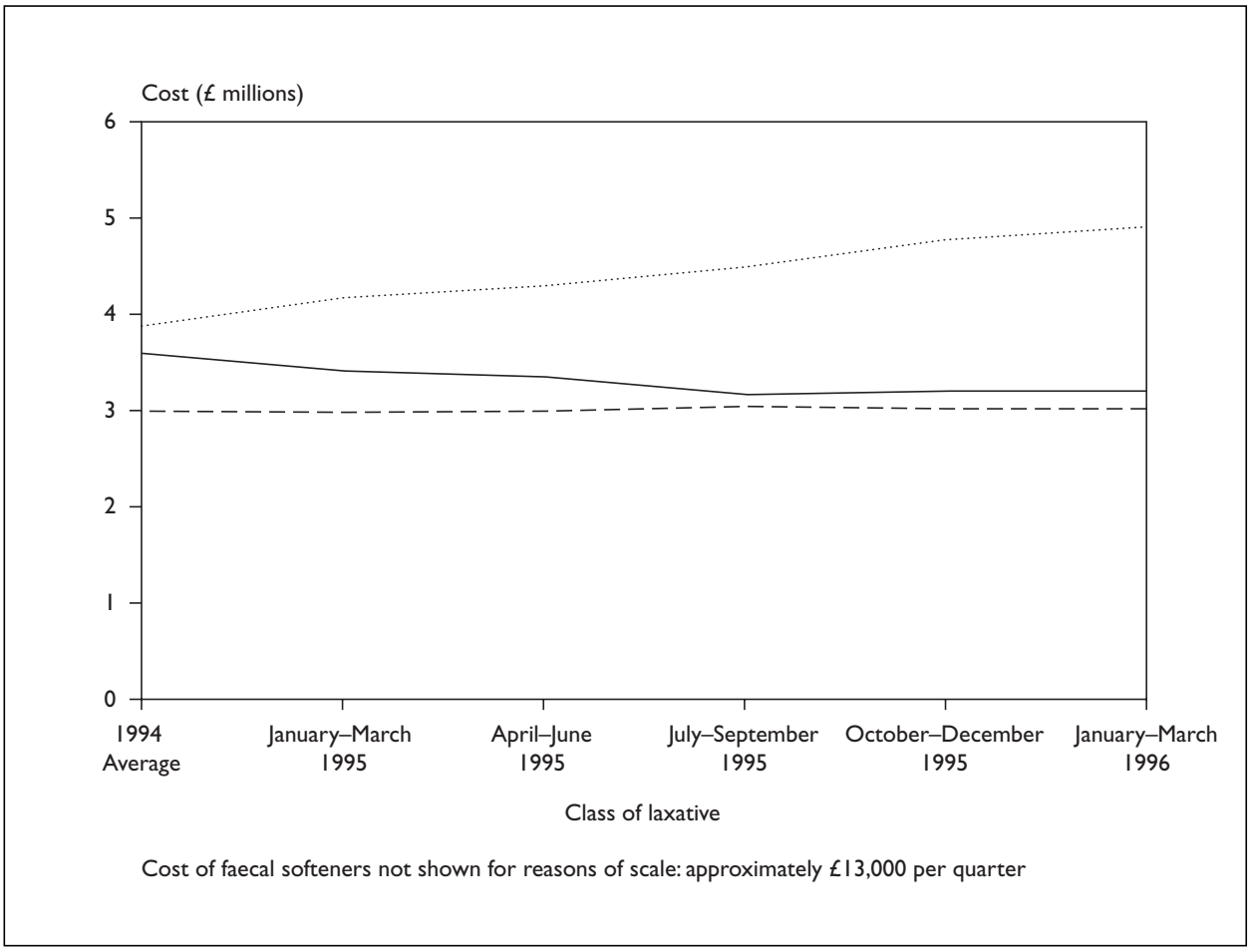

FIGURE 3 *Total costs of classes of prescribed laxatives in England: January 1995 – March 1996 (·····, stimulant; ——, osmotic; – – – –, bulk)*

followed closely by stimulant laxatives with about 3.5 million items prescribed during 1995. However, more is spent on stimulant laxatives, approximately £17.8 million, than on osmotic laxatives, £13 million. About 2.9 million non-bulk laxative items were prescribed during 1995 at a cost of approximately £12 million. Faecal softening agents are relatively rarely used.

Several trends are apparent over this period *(Figure 3)*. The prescribing of bulk laxatives appears to decline slightly while prescribing of stimulants appears to be increasing steadily. The volume of stimulant laxatives increased by 7% from 1995 to 1996, compared with a 1% decrease in the volume of all other classes of laxative. The overall cost of prescribing stimulant laxatives increased accordingly, and this increase appears to be caused by the increasing costs of prescribing two particular stimulant laxatives, co-danthramer and co-danthrusate *(Table 4)*. These, with Konsyl® sugar-free (a formulation of isphagula) and Movicol®, represent the most expensive treatments for constipation on a cost per week basis. In the case of co-danthramer, for example, expenditure increased by almost £0.5 million in 1 year, compared to an increase of £50,000 for senna.

The volume of prescribing of osmotic laxatives increased slightly and there was no clear change in the numbers of faecal softeners prescribed.

In this chapter it has been assumed that all of these prescriptions are for the treatment of constipation. The BNF (1997) states that "before prescribing laxatives it is important to be sure that the patient **is** constipated". However, it is possible that some of these prescriptions are for prevention rather than treatment of constipation.

Chapter 3
Methods

Research questions for the current review

The current systematic review was carried out in order to:

(i) compare the effectiveness of pharmacological and non-pharmacological interventions in the prevention and treatment of constipation in the elderly, including examination of the effectiveness of the different classes of laxatives (bulk, osmotic, faecal softeners and stimulants)
(ii) establish, where possible, the cost-effectiveness of pharmacological and non-pharmacological laxatives
(iii) identify, on the basis of the systematic review, those areas where further research should be undertaken.

The review was carried out using structured guidelines for systematic reviews (NHS Centre for Reviews and Dissemination, 1996). A range of sources were searched in order to identify trials of laxatives. Abstracts of experimental studies of the use of laxatives were retrieved and screened for inclusion by two reviewers. Data were extracted and are presented in tabular form. The sources, inclusion criteria and assessment of study validity are described below. In addition, a search was carried out to identify other systematic reviews and meta-analyses in this area. Retrieved review articles were quality-assessed to determine whether these could act as useful source documents for the review. A separate search concentrating specifically on cost-effectiveness data was also carried out with the aim of identifying any primary studies and reviews of economic evaluation.

Sources

A recently published systematic review of the treatment of constipation in adults carried out at the San Antonio Cochrane Center, USA, (Tramonte *et al,* 1997) was used as a main source of trials. The authors of this review had searched Medline (1966–95), *Biological Abstracts* (1990–95), Micromedex, bibliographies and textbooks, and had contacted laxative manufacturers and experts. For the current review of laxatives in elderly patients, a supplementary search of databases not previously searched was undertaken. Sources for this search were computerised Embase (1982–December 1996), Psychlit (1974–December 1996), Medline (to December 1996), the Cochrane Library database, the nursing database CINAHL (Citation Index for Nursing and Allied Health Literature), International Pharmaceutical Abstracts (1985–July 1996) and the alternative therapies database, AMED (see Appendix 2 for further details). The core search strategy for trials is presented in Appendix 2. All UK laxative manufacturers were also contacted in an attempt to locate other published and unpublished studies.

In addition, a database of trials that were excluded from the review by Tramonte and colleagues (1997) was obtained. This database was reviewed by two reviewers to determine whether any trials were eligible for inclusion in this review of laxatives in the elderly.

Cost-effectiveness information was searched for in Current Contents/Clinical Medicine, Medline and the NHS Economic Evaluation Database. The search covered reviews of economic evaluations, cost-effectiveness studies (including cost-minimisation and cost–consequences analyses), cost–benefit analyses and costing studies.

Inclusion/exclusion criteria

The review included RCTs of laxatives in the treatment or prevention of constipation in the elderly in any language. A trial was eligible for inclusion if all participants were aged 55 years or older and being treated for chronic constipation.

Treatment of constipation as a side-effect of therapy and laxative treatments of the side-effects of constipation (e.g. faecal impaction) were eligible for inclusion.

Treatments included were bulk-forming, stimulant, osmotic and faecal-softening laxatives. Trials which included symptoms, quality of life

and side-effects of laxatives as endpoints were included, as were trials examining the use of laxatives in the prevention of severe side-effects of constipation. Non-English language studies were translated and included if they met the inclusion criteria.

Studies of constipation in spinal cord injury and parkinsonism were excluded. Trials of enemas (e.g. soapsuds, Fleet®) and of bowel cleansing programmes in preparation for surgery or colonoscopy were excluded.

Study validity, data extraction and synthesis

If a trial met the inclusion criteria and had been included in the review by Tramonte and colleagues (1997), the appropriate clinical data were included. The data had been extracted independently by two reviewers. Data from any supplementary trials identified were extracted by one reviewer using the same data extraction form as the Cochrane reviewers. Authors were contacted for additional information if necessary and, when possible, *p* values and other statistics not presented in original papers were calculated. Quality of primary studies was summarised using the same scale used in the Cochrane review. This involved methodological assessment using a 6-point scale covering reporting of inclusion and exclusion criteria, randomisation method, standardised assessment of adverse effects, double-blind design, description of withdrawals, and statistical analysis (Hedges & Olkin, 1985). Studies were grouped according to class of laxative, if appropriate, and the data summarised using meta-analysis.

Chapter 4
Results

Search results – previous systematic reviews

Four previous systematic reviews were identified in which the effective management of constipation was examined. These were identified using a search strategy for identifying systematic reviews developed by the NHS Centre for Reviews and Dissemination (CRD) information staff and are described below.

1. Müller-Lissner's (1988) meta-analysis of the effects of wheat bran incorporated 20 comparative studies (non-RCTs); bran supplementation was found to increase stool weight and decrease gastrointestinal transit time in both healthy and constipated adults. Although stool weight increased in constipated patients receiving bran, the stool weight still remained below that of control patients. This suggested that low dietary fibre intake may not be the only factor influencing constipation. This review was not confined to RCTs, and improvements in symptoms and frequency were not a focus of the review.

2. The review by Kot and Pettit-Young (1992) was confined to an examination of the relative effectiveness of lactulose in various age groups, including the elderly. However, it does not appear to be a full systematic review (no details of search, or inclusion or exclusion criteria are given). In elderly patients, the data suggested a clinical improvement with lactulose compared with placebo; however, in comparisons with other laxative preparations (poloxalkol-dihydroxyanthroquinolone, sorbitol), lactulose appeared to be similarly effective, although deficiencies in the included studies are noted. Generally, in clinical trials in adults, lactulose appeared to be more effective than placebo, although in some trials that improvement was not considered by the authors to be of clinical importance.

3. Camilleri and colleagues (1994) reviewed the management of intractable constipation. The inclusion and exclusion criteria of this study are unclear, and the conclusions appear to be based on feedback from a symposium rather than on the results of clinical studies.

4. Tramonte and colleagues (1997) examined the effectiveness of laxative and fibre therapies in improving symptoms and bowel movement frequency in adults with chronic constipation. The review did not focus specifically on the elderly. It included only those RCTs which studied patients with a minimum duration of constipation of 2 weeks, evaluated treatment for at least 1 week, and assessed clinical outcomes such as bowel movement frequency, stool consistency and symptoms. The literature was found to be very limited. A total of 36 trials were identified for inclusion involving 1815 individuals, of whom 70% were women, in a variety of settings, including clinics, hospitals and nursing homes. The results of this review are summarised below.

   - ***Frequency*** The average weighted mean increase in frequency of bowel movement per week associated with treatment with bulking agents or fibre was 1.4 bowel movements per week, while the increase associated with treatment with other laxative agents was 1.5 bowel movements per week. No significant differences were found between fibre and non-bulk laxatives in terms of frequency of bowel movement.

   - ***Pain and consistency*** Of ten trials comparing a single agent, eight showed an improvement in symptoms with treatment, with a non-significant improvement in two other trials. Most trials which evaluated fibre or bulk laxatives found an improvement in abdominal pain with treatment, although no comparisons were significant. Of four trials that examined abdominal pain with non-bulk laxatives, one showed an increase associated with lactulose treatment and another showed a decrease with cisapride treatment. Consistency of the stool was improved with laxatives compared with placebo.

- ***Adverse effects and quality of life*** Few studies used standardised techniques to assess this outcome, although most studies that assessed symptoms did not report an increase in pain with fibre or non-bulk laxatives. Only two trials examined improvements in general well-being, neither of which showed any difference between fibre and laxatives.

The authors concluded that in trials comparing laxative agents to a placebo in adults the increase in frequency of bowel movement was similar for bulking and non-bulking laxatives (about 1.4 bowel movements per week). Fibre and bulk laxatives were found to decrease pain and to improve stool consistency compared with placebo, while most non-bulk laxative data were inconclusive. There were insufficient data to determine whether fibre or non-bulking laxatives were superior, or whether one class of laxative was superior to any other.

No systematic review was identified which examined the effectiveness of laxatives specifically in the elderly. While the review by Tramonte and colleagues (1997) was being undertaken, CRD staff contacted this review group and then undertook a series of supplementary searches in order to identify trials of laxatives in the elderly.

Studies of the prevention of constipation

Most of the studies of the prevention of constipation have been observational studies. Typically these involve a population (e.g. a hospital ward) where there is a high incidence of constipation and frequent use of laxatives. The patients usually receive some preventive dietary measure, and changes in bowel movement patterns and the need for laxatives or enemas are recorded. Such studies do not provide good evidence for the effectiveness of an intervention as it is often difficult to be certain that any changes seen in patients are, in fact, due to the intervention. Two RCTs were found which examined prevention in older adults, although both studies included some younger patients. However, these are discussed here as they are the only RCTs identified in the search. Neither trial was double-blinded. Both examined the effectiveness of dietary fibre supplementation.

- Schmelzer (1990) randomised orthopaedic patients (mean age 65 years; range 42–81) to receive either wheat bran baked into muffins and cookies or similar foods made with white flour (the control group). The trial was of low power (16 patients in total). Bran did not appear to prevent constipation, although those patients receiving it did have more bowel movements and required fewer laxatives than the control group.

- Kochen and colleagues (1985) randomly assigned 200 hospitalised patients (mean age 62 years; standard deviation (SD) 18) to receive either a dietary supplement of 40 g bran daily or no dietary supplement. A quarter of the patients in the bran group refused to take their bran from the very beginning, one-third stopped bran consumption during the study, and only 42% of the patients continued on bran until discharge or death. Neither the incidence of constipation nor the laxative requirement was significantly different between treatment and control group, and it was concluded that the administration of bran as a prophylactic laxative was ineffective in patients hospitalised for a relatively short time (mean length of stay was 16.2 days).

In another RCT of prevention (Broader *et al,* 1974), no difference was found in the incidence of constipation in a comparison of sterculia (bulking agent) with placebo. However, no patient ages are given. The RCT of prevention by Goodman and colleagues (1976) has not been included because, although the patients are described as elderly, their mean age was only 56 years.

Non-RCTs of prevention of constipation

Given the lack of RCTs examining prevention of constipation it may be useful to summarise the non-randomised studies which were identified, bearing in mind the biases inherent in observational studies. One crossover study examined the role of stool softeners in preventing constipation in elderly (age range 65–90 years) nursing-home patients and found them ineffective (Castle *et al,* 1991). Most studies of prevention, however, have experimented with methods of increasing fibre and fruit intake in the elderly through alterations in diet: for example, by addition of oats, fruit juice and other mixtures. Marked

effectiveness and high acceptability and compliance have been claimed for some of these simple treatments.

- Pattee and West (1988) supplemented the diets of 24 nursing-home residents with a dietary fibre product consisting of 75% powdered cellulose (equivalent to 6–12 mg of dietary fibre) over a 99-day period. Frequency of bowel movement and laxative interventions were monitored during the study, and the rate of intervention was compared with that in the month preceding the supplementation programme. The majority of residents either experienced significant reductions in the rate of laxative intervention or maintained an acceptable frequency of bowel movement. The incidence of intervention with laxatives was reduced from 72% of the observation days pre-study to 3–7% during the study. The powdered cellulose fibre supplement was found to be convenient and palatable, with only two residents withdrawing from the trial.

- Hagberg and colleagues (1987) supplemented the diets of 21 elderly nursing-home patients (mean age 89 years) with bran. Fluid intake was also increased. Bowel movement frequency was improved with no adverse effects.

- Groth (1988) compared the effect of wheat bran in preventing constipation in 22 orthopaedic patients (mean age 69 years). Bran supplementation increased frequency of bowel movements and stool consistency.

- Odes (1993) studied the effects of a high dietary fibre breakfast cereal containing oats, wheat and soya bean and found it improved frequency of bowel movement and stool consistency, and use of laxatives was reduced.

These and other observational studies report that the addition of bulking agents such as fibre to the diet of elderly patients is an effective means of preventing constipation (Hull *et al,* 1980; Meier *et al,* 1990; Pringle *et al,* 1984; Richards-Hall *et al,* 1995; Rodrigues-Fisher *et al,* 1993).

Observational studies of the effect of fruit mixtures have also been described. One comparative study of the traditional Chinese treatment, mulberry, found marked improvements in both bowel movement frequency and consistency (Minghan & Zhu, 1989). Beverley and Travis (1992) described the use of a "natural laxative mixture" in 35 geriatric patients. The mixture, which comprised prunes, currants, figs, dates and prune concentrate, was shown to be very effective. Frequency of bowel movement and stool consistency improved and laxative costs were reduced.

In a non-randomised comparative study, Gibson and colleagues (1995) added a mixture of Kellogg's All Bran®, apple sauce and prune juice (2 tablespoons per day) to the diet of 45 patients on a geriatric ward and found that treated patients were significantly less likely than controls to require enemas or laxatives, with no differences in side-effects. A laxative jam of dates and prunes has also been reported to be effective in preventing constipation in the hospitalised elderly by Durand and colleagues (1991), and a laxative pudding has been claimed to be effective in a small study among the homebound elderly (Neal, 1995). Behm (1985) also reported that the addition of a 'special recipe' of bran, apple sauce and prune juice to the diets of a sample of nursing-home patients with physical and mental disabilities resulted in improved stool consistency and reduced laxative use.

Stewart and colleagues (1997) reported the use of dietary strategy for preventing constipation in a sample of UK psychogeriatric patients aged 68–102 years. This involved increased amounts of cereals, fruit and vegetables, and soups and other fluids. This added £0.20 per head to the daily ward food bill but laxative use became negligible. However, there is no quantitative data in the study and few other details.

There is also one study in which a community intervention aimed at reducing laxative sales and promoting consumption of wholemeal/wholemeal bread by the elderly is reported (Egger *et al,* 1991). Small retirement communities in New South Wales, Australia, were targeted using the theme, *Bread: It's a Great Way to Go.* There was a 49% decrease in laxative sales and a 58% increase in sales of wholemeal/wholegrain bread in the group at which the community organisation strategy, involving the media and social marketing, was aimed.

Fluid intake

The role of fluid in the diet is also worth mentioning in this context. It has been suggested that fluid intake may play an important role in influencing development of constipation

(Richards-Hall *et al,* 1995; Maestri-Banks & Burns, 1996), and increasing fluid intake has been recommended as a method of preventing constipation (Klauser & Müller-Lissner, 1993; Marshall, 1990). However, there appear to have been few studies which have demonstrated the effects of low fluid intake on constipation while controlling adequately for other factors. A background search on Medline (1966–96) was carried out for this review but no trials were found in which constipated adults had been treated by increasing hydration. Several observational studies have studied increased fluid intake but this has typically been an adjuvant to some other dietary manipulation, such dietary fibre supplementation (Hope & Down, 1986; Maddi, 1979).

Summary

Observational studies which have increased dietary fruit and fibre intake have emphasised their effectiveness in preventing constipation. However, RCTs are likely to be less biased than non-randomised observational studies which tend generally to produce inflated estimates of the effects of treatment. For example, in the current context the few RCTs which have been carried out to examine the effectiveness of fibre in prevention of constipation have not supported the results of observational studies, although larger studies with a higher degree of compliance with treatment may be required. RCTs of the effects of fruit mixtures appear not to have been carried out. Specific recommendations for research in this area appear at the end of this report.

RCTs of the effectiveness of laxatives in treating constipation in the elderly

The supplementary search across additional databases found 13 RCTs of laxative treatment of constipation. Twelve studies did not include elderly patients and were therefore excluded from the current review. Five reports were from Germany, three were English, three were Italian, and one Swedish. Details of these studies have been passed to the Cochrane review group to be assessed for inclusion in the next update of the systematic review of laxatives in adults. One unpublished RCT in elderly patients was identified but did not meet the inclusion criteria. The results of these trials are described in Appendix 4.

Two RCTs of the use of laxatives to treat constipation in the elderly were found which had not been identified in the review by Tramonte and colleagues (1997). Data were abstracted from these studies (Marchesi, 1982; Doffoel *et al,* 1990) and analysed together with data from the nine trials in the elderly already identified (using data abstracted by Tramonte and colleagues).

RCTs comparing single laxative agents with placebo

Characteristics of trials

Ten trials were therefore identified in which single agents were compared with placebo in the treatment of constipation in the elderly, in a total of 367 patients *(Table 5).* The mean age of the patients in these trials was estimated to be 74 years. Two of the ten trials which were identified presented no information on the sex of the participants; in the other eight trials, just over half of the patients included were women (54%).

In the majority of these studies (n = 7) elderly patients were examined in an institutional setting, such as nursing homes or hospitals. One study reported results for out-patients who were living in the community (Cheskin *et al,* 1995) and one study did not report a setting (Wesselius-de-Casparis, 1968). One study involved adults with diverticular disease with constipation as their initial complaint but who were otherwise healthy (Ewerth *et al,* 1980). Four trials examined the effectiveness of bulk laxatives, three examined osmotic laxatives, two examined stimulant laxatives, and one trial examined the effectiveness of a faecal softener.

Effect of laxatives on frequency

In trials comparing single active treatments with placebo, seven were identified which presented data on frequency of bowel movements. Data on bowel movement frequency was estimated from a graph in one study (Vanderdonckt *et al,* 1990).

The trials identified are shown in *Figure 4* (a summary of the characteristics and outcomes of the trials is also given in *Table 5*). The figure shows the increase in bowel movements per week associated with treatment in each trial identified. When adequate information has been provided by authors, confidence intervals are plotted. When not enough information was presented in the paper, the authors were contacted. However, several trials (for example, Cheskin *et al,* 1995;

TABLE 5 *Summary of RCTs of prevention and treatment of constipation in the elderly*

Study (country)	Class of laxative	Study population, sample size	Trial description, follow-up	Results: bowel movements per week, and other outcomes	Comments (methodological score)
Prevention of constipation					
Schmelzer, 1990 (USA)	Bulk	Orthopaedic patients n = 16 Mean age 65 years	**Treatment:** 20 g/day wheat bran added to meals **Control:** Similar foods with white flour 1 week	No significant difference in number of bowel movements (p = 0.09) or in incidence of constipation (p = 0.12). Amount of bran consumed negatively correlated with number of laxatives required (p = 0.04)	No blinding, low power due to small sample, and little statistical information available (**3**)
Kochen *et al,* 1985 (Germany)	Bulk	Hospitalised general medical patients n = 200 Mean age 63.3 years	**Treatment:** 40 g/day unrefined bran added to diet **Control:** No further treatment Median 5 days	Incidence of constipation: 55% vs. 46% (p = 0.20, NS). % of days on laxatives: 8.7 vs. 7.4 (p > 0.05, NS)	Short length of follow-up, little statistical information (**3**)
Treatment of constipation – RCTs comparing laxative with placebo or normal diet					
Cheskin *et al,* 1995 (USA)	Bulk	10 community-living patients Mean age > 66 years	**Treatment:** Psyllium, 6 g four times daily **Control:** Placebo 4 weeks	9.1 vs. 5.6 (p = 0.1). Fibre did not improve stool consistency: consistency scores 2.7 vs. 3.0 (NS)	Drop-outs = 30% (**4**)
Ewerth *et al,* 1980 (Sweden)	Bulk	Patients with constipation and diverticuli n = 10 Mean age 68 years	**Treatment:** Psyllium, 6 g twice daily **Control:** Placebo 8 weeks	6.9 vs. 7.1 (p > 0.05, NS). Number of symptoms and abdominal pain less in treated group. Consistency improved with treatment (p = 0.02)	Stated to be double-blinded Drop-outs = 10% (**3**)
Finlay, 1988 (UK)	Bulk	Nursing-home patients n = 12 Mean age 80 years	**Treatment:** Bran, 1.5 g four times daily **Control:** Normal diet 6 weeks	No difference in number of days on which defecation occurred or need for laxatives (p = 0.7). Consistency improved, but no data	Drop-outs = 33% (**3**)

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Boldo = Chilean bark extract (folk remedy)
DCS, dioctyl calcium sulphosuccinate; DSS, dioctyl sodium sulphosuccinate; NS, not significant

continued

TABLE 5 contd *Summary of RCTs of prevention and treatment of constipation in the elderly*

Study (country)	Class of laxative	Study population, sample size	Trial description, follow-up	Results: bowel movements per week, and other outcomes	Comments (methodological score)
continued ***Treatment of constipation – RCTs comparing laxative with placebo or normal diet***					
Rajala *et al,* 1988 (Finland)	Bulk	Hospitalised patients n = 51 Mean age 78 years	**Treatment:** Yoghurt + bran, 150 ml twice daily **Control:** Yoghurt 2 weeks	5.8 vs. 4.5 (p = 0.3). Abdominal pain and overall symptoms improved in treated group. Also less need for laxatives	Double-blind (described) Drop-outs = 33% (**4**)
Marchesi, 1982 (Italy)	Stimulant	Hospitalised patients n = 28 Mean age 71 years	**Treatment:** Cascara, 2400 mg, + boldo, 500 mg, four times daily **Control:** Placebo 3 weeks	6.0 vs. 3.4 (p < 0.05). Consistency improved in treated group	Drop-outs not stated (**3**)
Stern, 1966 (USA)	Stimulant	Nursing-home patients n = 25 Mean age > 71 years	**Treatment:** Prucara, 2 tablets twice daily **Control:** Placebo 3 weeks	Overall improvement in consistency, control over frequency in 88% of treated group vs. 0% of controls. Few side-effects	Double-blind (described) Drop-outs not stated (**3**)
Hyland & Foran, 1968 (UK)	Softener	Hospitalised patients n = 40 Mean age > 60 years	**Treatment:** DSS, 100 mg three times daily **Control:** Placebo 4 weeks	3.3 vs. 2.5 (p = 0.06). Overall symptom improvement significantly greater with treatment (p < 0.05)	Double-blind (described) Drop-outs = 60% (**4**)
Sanders, 1978 (USA)	Osmotic	Nursing-home patients n = 45 Mean age 85 years	**Treatment:** Lactulose, 30 ml four times daily **Control:** Placebo 12 weeks	4.9 vs. 3.6 (p = 0.1). Reduction in five symptoms significantly greater with lactulose (p = 0.04)	Drop-outs = 22% (**3**)
Vanderdonckt *et al,* 1990 (Belgium)	Osmotic	Nursing-home patients n = 43 Mean age 84 years	**Treatment:** Lactitol, 20 g four times daily **Control:** Placebo 4 weeks	Number of bowel movements increased with treatment (p < 0.001). Consistency improved with treatment (p < 0.001). Less abdominal pain (NS) and less need for laxatives (p < 0.05)	Stated to be double-blind Drop-outs = 2% (**6**)

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continued

TABLE 5 contd *Summary of RCTs of prevention and treatment of constipation in the elderly*

Study (country)	Class of laxative	Study population, sample size	Trial description, follow-up	Results: bowel movements per week, and other outcomes	Comments (methodological score)
continued ***Treatment of constipation – RCTs directly comparing laxatives***					
Wesselius-de-Casparis *et al,* 1968 (The Netherlands)	Osmotic	Not stated n = 103 Mean age > 60 years	**Treatment:** Lactulose, 15 ml four times daily **Control:** Placebo	Significantly less need for laxatives in treatment group ($p < 0.001$)	Double-blind (described) Drop-outs not stated (**3**)
Treatment of constipation – RCTs directly comparing laxatives					
Chokhavatia *et al,* 1988 (USA)	Bulk vs. bulk	Out-patients n = 42 Age range 55–81 years	**Treatment 1:** Calcium polycarbophil, 2 g, four times daily **Treatment 2:** Psyllium, 9.5 g, four times daily 3 weeks	8.3 vs. 9.1 ($p = 0.3$). No difference in stool consistency ($p < 0.05$)	Drop-outs = 7% (**3**)
Pers & Pers, 1983 (Sweden)	Bulk + stimulant vs. bulk + stimulant	Hospital patients n = 20 Mean age 83 years	**Treatment 1:** Agiolax®, 1 sachet four times daily **Treatment 2:** Lunelax®, 1 sachet four times daily 2 weeks	3.3 vs. 3.9 ($p < 0.05$). No difference in number of enemas required during treatment	Drop-outs = 5% (**3**)
Kinnunen *et al,* 1993 (Finland)	Osmotic vs. bulk + stimulant	Nursing-home patients n = 30 Mean age 82 years	**Treatment 1:** Lactulose, 30 ml, four times daily **Treatment 2:** Agiolax®, 20 ml, four times daily 5 weeks	2.2 vs. 4.5 ($p < 0.001$). Greater need for laxatives during lactulose treatment; loose stools more common with Agiolax ($p < 0.05$)	Drop-outs = 20% (**4**)
Passmore *et al,* 1993a; b (UK)	Osmotic vs. bulk + stimulant	Nursing-home patients n = 77 Mean age 83 years	**Treatment 1:** Lactulose, 15 ml, twice daily **Treatment 2:** Agiolax®, 10 ml, four times daily 5 weeks	4.2 vs. 5.6 ($p = 0.006$). Consistency better with Agiolax ($p < 0.005$), no difference in adverse effects.	Double-blind Drop-outs = 20% (**7**)
Marchesi, 1982 (Italy) (1)	Stimulant vs. stimulant	Hospital patients n = 14 Mean age 75 years	**Treatment 1:** Cascara, 2400 mg, + boldo, 500 mg, four times daily **Treatment 2:** Cascara, 2400 mg, + boldo, 500 mg, four times daily + inositolo, 1750 mg + vitamin B_{12}, 350 µg (3 weeks)	5.4 vs. 6.0 ($p = 0.6$)	Drop-outs = 0% (**3**)

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continued

TABLE 5 contd *Summary of RCTs of prevention and treatment of constipation in the elderly*

Study (country)	Class of laxative	Study population, sample size	Trial description, follow-up	Results: bowel movements per week, and other outcomes	Comments (methodological score)
continued ***Treatment of constipation – RCTs directly comparing laxatives***					
Marchesi, 1982 (Italy) (2)	Stimulant vs. stimulant	Hospital patients n = 14 Mean age 75 years	**Treatment 1:** Cascara, 2400 mg, + boldo, 500 mg, four times daily **Treatment 2:** Cascara, 120 mg, + boldo, 12 mg, four times daily + inositolo, 250 mg + vitamin B_{12}, 50 µg (3 weeks)	5.2 vs. 6.0 ($p = 0.6$)	Drop-outs = 0% (**3**)
Williamson *et al,* 1975 (UK)	Stimulant + softener vs. stimulant	Nursing-home patients n = 40 Mean age 76 years	**Treatment 1:** Dorbanex®, 10 ml four times daily **Treatment 2:** Sodium picosulphate, 20 ml four times daily (Laxoberal®) 2 weeks	6.7 vs. 6.0 ($p < 0.05$). More soft or loose bowel movements and less need for enemas or suppositories with Laxoberal	Drop-outs = 5% (**2**)
Fain *et al,* 1978 (USA) (1)	Stimulant vs. softener	Nursing-home patients n = 29 Mean age 82 years	**Treatment 1:** DSS (Colace®), four times daily **Treatment 2:** DCS (Surfak®) 3 weeks	1.95 vs. 2.8 ($p = 0.2$). No group difference in consistency. Surfak group less likely to need enema/ suppositories ($p = 0.02$)	Drop-outs = 2% (**3**)
Fain *et al,* 1978 (USA) (2)	Stimulant vs. softener	Nursing-home patients n = 29 Mean age 82 years	**Treatment 1:** DSS (Colace®), four times daily **Treatment 2:** DCS (Surfak®) 3 weeks	2.29 vs. 2.8 ($p = 0.6$). No difference in consistency. Little difference between Colace, four times daily, and Colace, twice daily	Drop-outs = 2% (**3**)
Kinnunen & Salokannel, 1987 (Finland)	Osmotic vs. bulk	Nursing-home patients n = 64 Mean age 81 years	**Treatment 1:** Magnesium hydroxide, 20 ml four times daily **Treatment 2:** Laxamucil®, 9 gm four times daily 8 weeks	3.3 vs. 2.6 ($p = 0.04$). Greater improvement in consistency with magnesium hydroxide ($p < 0.001$) and less need for laxatives ($p < 0.01$)	Drop-outs = 5% (**3**)

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continued

TABLE 5 contd *Summary of RCTs of prevention and treatment of constipation in the elderly*

Study (country)	Class of laxative	Study population, sample size	Trial description, follow-up	Results: bowel movements per week, and other outcomes	Comments (methodological score)
continued ***Treatment of constipation – RCTs directly comparing laxatives***					
Doffoel *et al*, 1990 (France)	Osmotic vs. osmotic	Nursing-home patients n = 60 Mean age 79 years	**Treatment 1:** Lactitol, 15 g/day **Treatment 2:** Lactulose, 15 ml/day (665 g/l) increased as necessary 2 weeks	5.5 vs. 4.9 (p = 0.0001). Stools more often of normal consistency with lactulose (NS)	Drop-outs = 3% (**4**)
Lederle *et al*, 1990 (USA)	Osmotic vs. osmotic	Nursing-home patients n = 31 Mean age 72 years	**Treatment 1:** Lactulose, 30 ml **Treatment 2:** Sorbitol, 30 ml 4 weeks	7.0 vs. 6.7 ($p < 0.05$). No significant group differences in overall symptoms or need for other laxatives	Double-blind (described) Drop-outs = 3% (**6**)

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Boldo = Chilean bark extract (folk remedy)
DCS, dioctyl calcium sulphosuccinate; DSS, dioctyl sodium sulphosuccinate; NS, not significant

Ewerth *et al*, 1980; Vanderdonckt *et al*, 1990) do not present enough information (SDs or standard errors) to allow calculation of confidence intervals and, for these cases, the point estimate is plotted, together with an indication of significance.

It can be seen from *Figure 4* that two trials reported a significant increase in bowel movements per week compared with placebo. Marchesi (1982) found a stimulant laxative containing cascara to produce a mean increase of 2.6 bowel movements per week, and Vanderdonckt and colleagues (1990) found an increase with an osmotic laxative (lactitol) of 1.9 bowel movements per week.

Non-significant benefits of fibre are shown in two trials (Cheskin *et al*, 1995; Rajala *et al*, 1988); however, the fibre mixture used as a laxative in the trial by Rajala and colleagues was sweetened with lactitol, which has an osmotic laxative effect and, hence, any benefit may not be due solely to the fibre. Two trials found statistically non-significant trends in favour of a faecal softener (Hyland & Foran, 1968) and an osmotic laxative (Sanders, 1978). It can also be seen from *Table 5* that all the trials identified involved very small patient numbers and it is therefore possible that those trials in which non-significant results were found lacked enough power to detect any significant differences.

One other trial (Finlay, 1988) assessed bowel movement frequency, but not actual numbers of bowel movements. In this study, supplementary bran was found to have no statistically significant effect on the number of days on which bowel movements occurred.

Other outcomes: consistency, pain, laxative use

Stool consistency was measured in six trials of single agents. The methods used to assess consistency varied between trials. Passmore and colleagues (1993a; b), for example, used a 6-point scale ranging from 0 ('no bowel movement') to 5 ('loose'), while Kinnunen and colleagues (1993) used a 3-point scale ('hard', 'normal', or 'watery'). Quantitative data on consistency was not therefore pooled. The

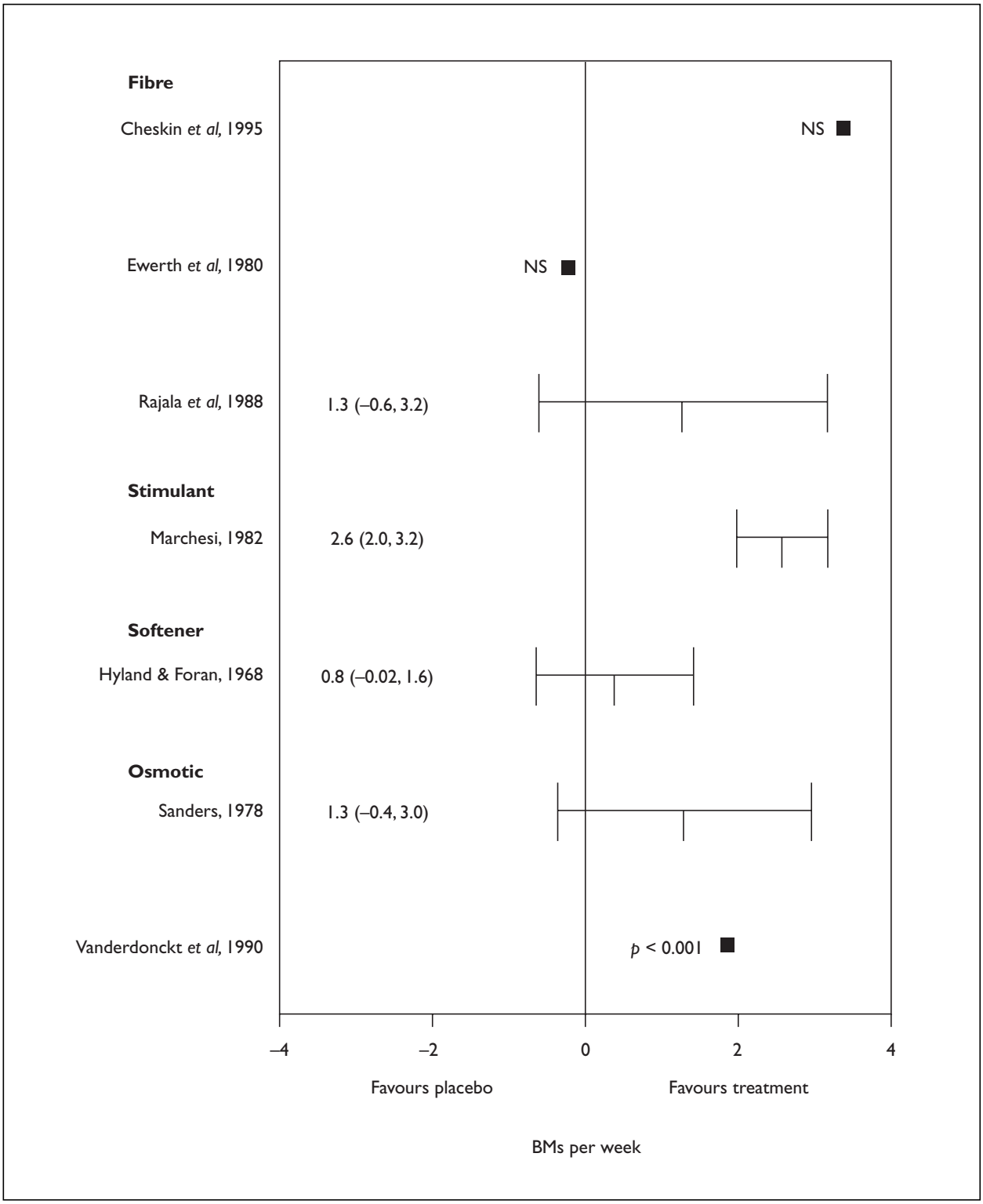

FIGURE 4 *Effectiveness of laxatives (in bowel movements per week, with 95% CIs) in placebo-controlled trials (NS, not significant)*

results of comparisons of this outcome are, however, presented in *Table 5*. Two trials reported a significant improvement in consistency, one as a result of treatment with fibre and the other as a result of treatment with the osmotic laxative, lactitol. Although all the other trials which examined this outcome report non-significant differences, stool consistency was improved in most of them with treatment. Again, these trials may have lacked the statistical power to detect any significant differences that may have existed.

Reduction in abdominal pain was also not assessed in a similar manner across the trials which reported this outcome. Pain outcomes included the number of symptoms (Ewerth *et al,* 1980), severity scores (Sanders, 1978), weekly incidence of pain in number of days (Rajala *et al,* 1988), and the number of patients reporting pain (Vanderdonckt *et al,* 1990). Although no trial found significant differences, non-significant benefit with treatment was reported in four of the trials. This was as a result of treatment with fibre in two of these trials (Ewerth *et al,* 1980; Rajala *et al,* 1988) and with osmotic laxatives in the other two (Sanders, 1978; Vanderdonckt *et al,* 1990). As before, the lack of power to detect differences in this outcome associated with treatment must be noted; not only are the trials small but the number of patients reporting pain is smaller still.

Four trials also reported information on overall symptom improvement. In two of these, statistically significant improvements in overall symptoms were reported following treatment with a faecal softener and with an osmotic laxative (Hyland & Foran, 1968; Sanders, 1978). Significant symptom improvement with psyllium was reported in one trial (Ewerth *et al,* 1980) and, in another, a non-significant improvement with bran was reported (Rajala *et al,* 1988).

The use of breakthrough laxatives was assessed in five trials. This typically refers to the need to use a suppository or enema if the patient has not had a bowel movement. For example, in one trial any participant who did not have a bowel movement for 4 days was given a 10 mg Dulco-Lax® suppository. All five trials all reported a reduction in use of laxatives but this difference only achieved significance in one trial comparing lactulose to placebo in a double-blind trial (Wesselius-de-Casparis *et al,* 1968).

Summary

There is some evidence that laxatives can improve frequency, consistency, and symptoms in constipated elderly people. However, most of the placebo-controlled trials have examined hospitalised elderly or nursing-home patients rather than older people living in the community. Moreover, methodological problems with most of these trials prevent clear conclusions being drawn regarding the effectiveness of different classes of laxative.

A significant increase in bowel movement frequency was shown with an osmotic laxative (lactulose, 30 ml four times daily) and with a stimulant formulation (containing cascara and boldo). However, most trials showed non-significant trends in favour of treatment, and small sample sizes limited the power of the trials to detect real differences where they may exist. (Although authors were contacted to obtain additional data for pooling, either they could not supply information or did not reply to requests, perhaps because most of the trials are quite old.) Similarly, many trials report non-significant improvements in consistency and pain.

Quality of trials and effect size

This hypothesis of a relationship between low methodological quality and underestimation of effectiveness was explored by plotting the change in number of bowel movements per week with treatment against the quality score of each of the trials of single agents in the elderly *(Figure 5).* Each point represents one trial and a quality score was derived as described earlier (see chapter 3). There is an apparent tendency towards a larger effect size in better quality trials; however, the number of studies is low and the overall association is not statistically significant when studies are weighted by sample size ($F_{2,6} = 0.37$; $p > 0.1$). A similar association can be seen when the results of the trials in adults from the Cochrane review are plotted against their quality scores (see Appendix 3). Again, however, when the individual studies are weighted for sample size there is no statistically significant association between quality and effect size. It is possible that the apparent relationship is caused by the better quality studies examining the more effective treatments.

Comparisons between laxative agents

A total of ten trials compared one laxative agent with another in elderly patients *(Table 5).* The quality scores ranged from 2 to 6, out of a possible maximum of 8 points. Only two trials were double-blinded and drop-outs ranged from 0% to 20%. The highest quality score achieved (by two trials) was 6.

The mean age of participants in these trials is estimated at 77 years. Only one of these trials (Chokhatavia *et al,* 1988) examined patients in an outpatient setting. Seven trials were carried out in nursing homes and two in hospitals. Stimulant laxatives were most commonly examined: six trials examined a stimulant either alone or in combination with another laxative. Osmotic laxatives were examined in five trials and bulk laxatives, alone or in combination, in five trials.

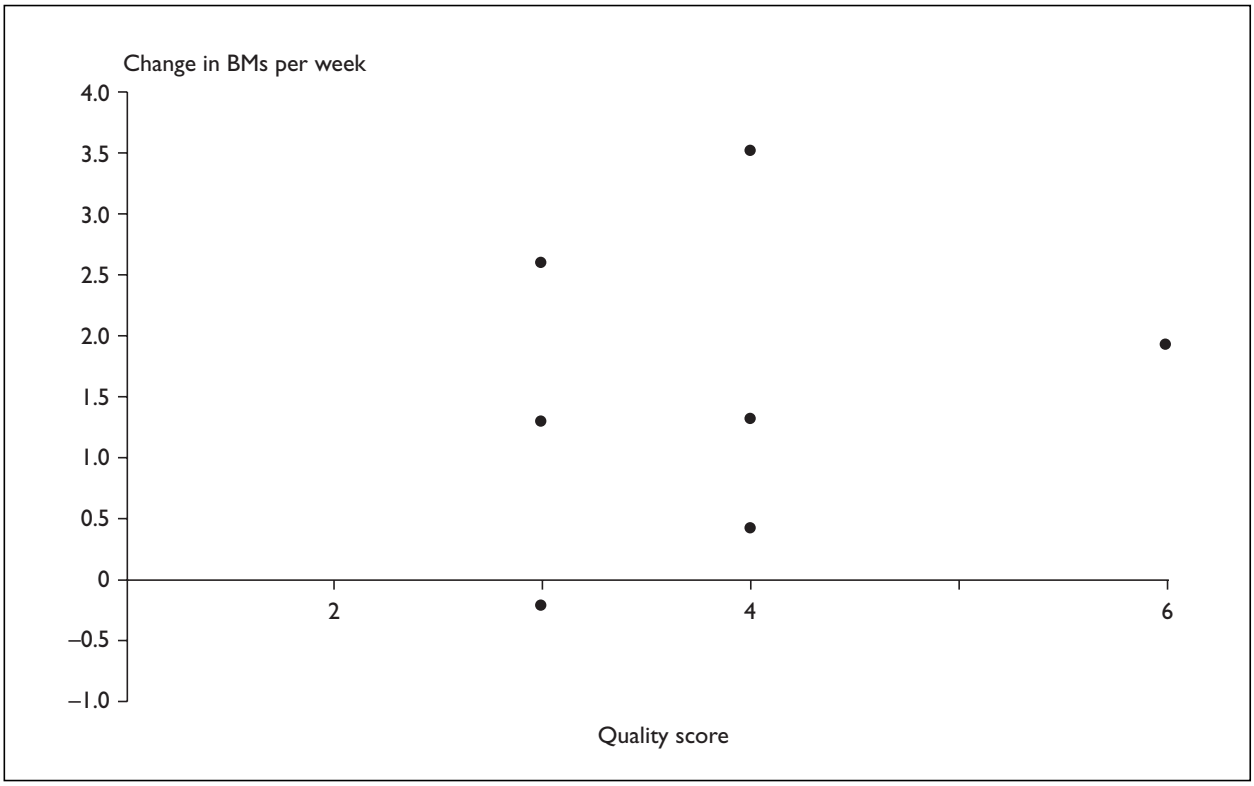

FIGURE 5 *Effect size by quality score (trials in the elderly only)*

The actual agents used are heterogeneous so it is difficult to make generalisations from this small set of trials.

Bulk laxatives

One trial (Chokhavatia *et al,* 1988) compared two bulk laxatives and found that bowel movement frequency was greater with psyllium than with calcium polycarbophil, although there was no significant difference in consistency. Patients preferred the latter laxative as flatulence was less common. One trial (Pers & Pers, 1983), in which two bulk plus stimulant combinations were compared, found that Lunelax® was more effective than Agiolax®, although the difference was non-significant and there was little examination of other outcomes. No differences in side-effects were reported but the study is small and may lack power.

A bulk plus stimulant combination (Agiolax) was found to be more effective in terms of frequency than an osmotic laxative, lactulose, in two trials (Kinnunen *et al,* 1993; Passmore *et al,* 1993a; b). Both trials also showed Agiolax to be associated with greater consistency, although only one trial showed a significant difference. Pooling of the frequency data from both these trials indicates an increase in bowel movement frequency of the order of about two per week with Agiolax treatment compared with lactulose *(Figure 6).* No treatment differences in adverse effects were found but, given the small sample sizes, the studies may have lacked the power to detect any such differences.

Osmotic laxatives

The osmotic laxative, magnesium hydroxide, was found to be more effective than a combination of osmotic laxative plus fibre (Laxamucil®) in terms of both frequency and consistency of stools (Kinnunen & Salokannel, 1987). In addition, a comparison of two osmotic laxatives, lactulose and sorbitol (Lederle *et al,* 1990), suggested that sorbitol may be equal in effectiveness to lactulose and may therefore be a cheaper alternative. One study found a small significant increase in frequency with lactitol compared with lactulose (Doffoel *et al,* 1990), although stool consistency appeared to improve more with lactulose treatment.

Stimulants

Marchesi (1982) compared three herbal mixtures of cascara, vitamin B and boldo in varying amounts and showed that the addition of a herbal mixture and vitamin B_{12} to cascara and boldo increased bowel movement frequency.

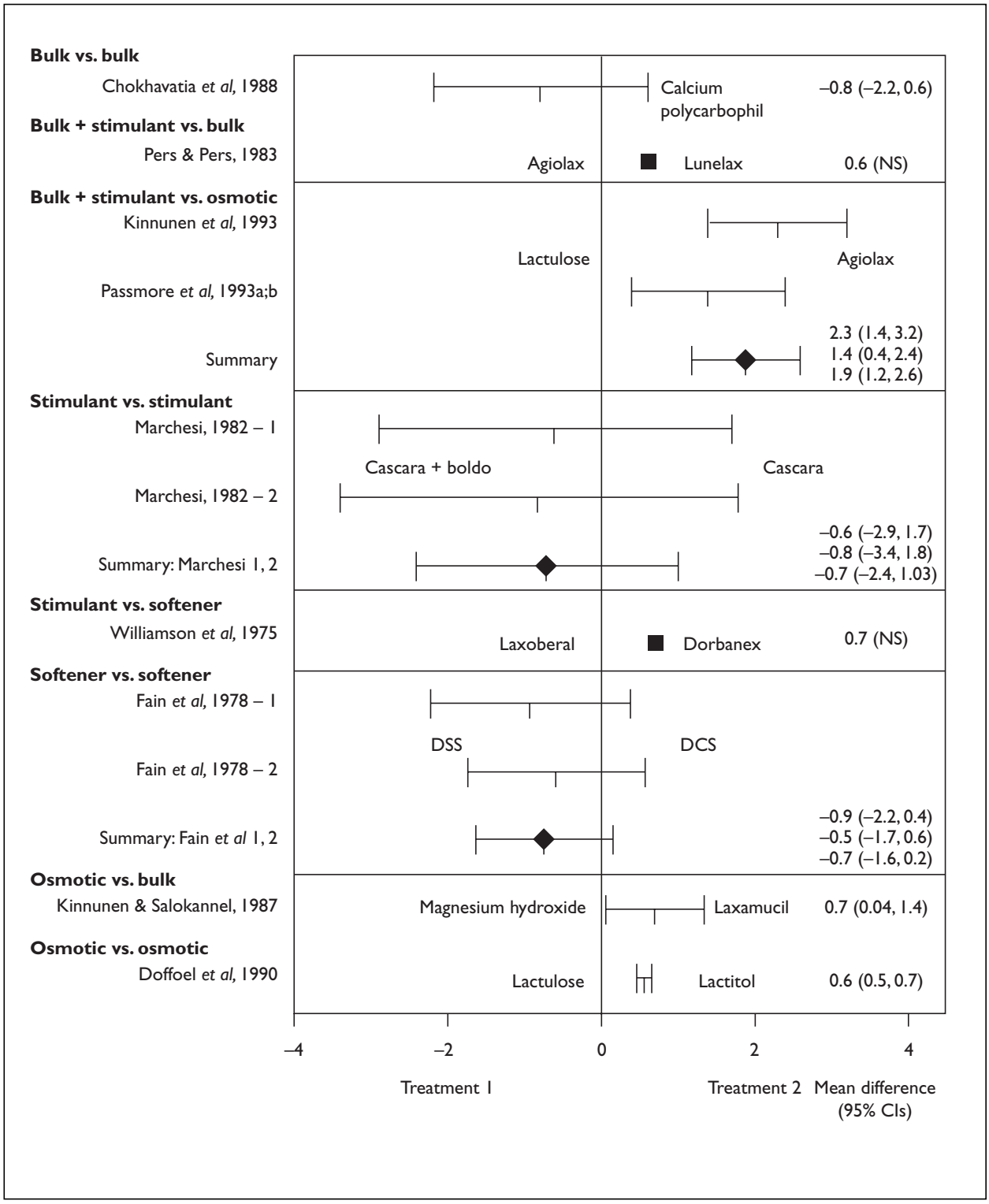

FIGURE 6 *Effectiveness of laxatives (in mean number of bowel movements per week) in trials reporting direct comparisons between treatments (NS, not significant)*

Faecal softeners

The categorisation of one of the treatments, dioctyl sodium sulphosuccinate, in the trial by Fain and colleagues (1978) requires qualification. Both the authors of this study and the Cochrane review authors class this agent as a faecal softener. However, it is classified as a stimulant in the BNF, with a comment that it may act as a stimulant and a softening agent. Dioctyl sodium sulphosuccinate is, however, primarily a detergent and wetting agent, and may more appropriately be categorised as a

faecal softener. No significant differences in bowel movement frequency or stool consistency were found between this preparation and dioctyl calcium sulphosuccinate.

The use of breakthrough laxatives was assessed in six trials. Only one trial (Kinnunen & Salokannel, 1987) found a significant difference between treatments; the osmotic laxative magnesium hydroxide was found to be associated with greater breakthrough laxative use.

Summary

There are few direct comparisons of laxative that allow their relative effectiveness to be judged. However, there is some evidence that a combination of bulk plus stimulant (Agiolax) is more effective in the elderly in improving consistency and bowel movement frequency than an osmotic laxative alone (lactulose). One of the trials reporting this finding had a high methodological score, with details of randomisation and standardised assessment of outcomes, adverse effects and double-blinding (Passmore *et al,* 1993a; b).

The single trial in this group which examined older people living in the community found no difference between two types of bulk laxative (psyllium and calcium polycarbophil) in terms of either frequency of bowel movement or stool consistency.

The only other trial in this group employing double-blinding found no difference between lactulose and sorbitol in terms of symptoms. A small statistically (but probably not clinically) significant difference was found in terms of frequency. Similarly, while other comparative trials in this group have reported statistically significant differences in terms of frequency, the absolute differences have been small.

Cost of laxatives

Passmore (1995) has reviewed economic evaluations of pharmacotherapy for chronic constipation. There have been very few such evaluations of laxative treatment of constipation. Aside from the costs of laxatives, general practitioner consultations for constipation were estimated to cost a minimum of £4.5 million year, based on 450,000 constipation-related consultations. The data were derived from 1981–82 general practice morbidity statistics (McCormick *et al,* 1995). Two UK studies have examined the cost-effectiveness of laxative treatment. Passmore and colleagues (1993a; b) in their RCT calculated the daily bowel frequency associated with treatment with a senna–fibre combination or with lactulose. The cost per stool was then calculated for both treatments, giving a cost of £0.397 per stool for lactulose and £0.103 per stool for senna–fibre. Overall, it was concluded that the senna–fibre combination was significantly more effective in the elderly than lactulose, and cost less.

In another RCT, Lederle and colleagues (1990) compared two osmotic agents, lactulose and sorbitol, and found them to be equally effective and similar in terms of adverse effects in the treatment of elderly patients. The authors concluded that sorbitol can be recommended as a cost-effective alternative to lactulose in adults, on the grounds that it is much cheaper but equally effective.

Other studies refer to costs of laxatives in passing but do not examine the cost-effectiveness of treatments in any detail. For example, Rouse and colleagues (1991) pointed out that the cost of one day's treatment with lactulose is almost twice that of one day's treatment with ispaghula, with similar efficacy in adults. Egger and colleagues (1991) reported that a campaign to increase bread consumption in an elderly community resulted in a corresponding decrease in laxative sales. Laxative sales decreased by 60% while wholemeal/wholegrain loaf sales rose by about 60%. The authors concluded that this represented a cost-effective approach to increasing fibre intake and improving gastrointestinal problems in the elderly. However, no cost-effectiveness data are reported.

Lederle (1995) briefly reviewed cost-containment strategies and noted that cost-containment primarily rests on reduction in the use of unnecessary laxatives by promoting increased fibre intake in the elderly. However, there is no formal assessment of the cost-effectiveness of this recommendation.

Prevention and treatment of faecal impaction

No RCTs were found which examined the role of laxatives specifically in preventing faecal impaction in the elderly. However, two RCTs of laxative treatment for constipation in the elderly also reported the incidence of impactions. The trial by Sanders (1978) involved an elderly group of nursing-home patients and found a significant difference in the incidence of impaction between patients whose constipation was treated with lactulose and those receiving a placebo (six impactions with lactulose

versus 66 with placebo, $p < 0.015$). Fain and colleagues (1978) analysed the incidence of impactions removed during an RCT of treatment of constipation with either dioctyl sodium sulphosuccinate or dioctyl calcium sulphosuccinate, both faecal softeners, but numbers treated were too small to permit statistical analysis.

One RCT examined the treatment of faecal impaction in 45 elderly patients (age range 70–91 years) (Puxty & Fox, 1986). These were randomised to receive either Golytely® (a polyethylene glycol/sodium sulphate preparation used to prepare patients for colonoscopy) plus lactulose, 30 ml twice daily, or lactulose, 30 ml twice daily. Both groups also received daily enemas. By the end of the 2 weeks of the trial, 87% of patients given Golytely had been successfully cleared of faecal impaction compared with 41% of those treated with lactulose and enemas alone. Two patients (9%) receiving Golytely had not been able to tolerate the full therapy (2 litres of fluid per day). The study is at the lower end of the scale in terms of methodological quality as there is no description of inclusion/exclusion criteria, no blinding, no standardised assessment of adverse effects and no appropriate statistical analysis of results.

Most studies of treatment of this complication of constipation involve management by enema or colonic irrigation, or behavioural treatments (e.g. 'prompted voiding'). No RCTs of these treatments were found and, indeed, most studies of faecal impaction appear to be case reports or case series, rather than studies of actual treatment.

There are, therefore, too little data to determine whether laxatives represent effective methods of preventing or treating faecal impaction. It has been suggested that the use of laxatives specifically to treat this complication of constipation may be inappropriate: the oral use of laxatives in treatment of faecal impaction has also been reported to be hazardous and may result in colonic perforation (Romero *et al,* 1996). Prevention of faecal impaction may be best managed by effective treatment of constipation (Kinnunen *et al,* 1993).

Chapter 5

Summary and research recommendations

Effective laxative treatments for constipation

Significant improvements in bowel movement frequency have been observed with a stimulant laxative containing cascara and, also, with an osmotic laxative. Non-significant effects of laxatives on frequency have been reported in four other placebo-controlled RCTs. Since the largest of these trials had only 51 participants, the trials may simply have lacked the statistical power to detect an effect. Information on other outcomes, such as improvements in symptoms and stool consistency, are not reported for all trials. However, improvements in both stool consistency and symptoms have been reported in placebo-controlled trials of psyllium, lactulose and lactitol treatment.

There is a commonly held clinical impression that fibre is less effective than other types of laxative in improving bowel movement frequency. However, to examine this question in detail, direct comparisons between fibre and other laxative classes and types within the same trial would be required. Very few of such direct comparisons appear to have been carried out in controlled trials. Eight trials compared laxative agents, and the two higher quality trials suggested that Agiolax may be more effective than lactulose.

These findings are in accord with the systematic review of the treatment of constipation in adults by Tramonte and colleagues (1997), in which it was concluded that laxatives and fibre consistently increased bowel movement frequency compared with placebo, with the increase being of the order of 1.5 bowel movements per week. Direct comparisons were found to be inconclusive because of the small number of studies found and methodological flaws. There was no direct evidence that fibre was more or less effective than any other laxative in adults.

The results of the trials in elderly people can also be summarised separately for two specific groups.

- ***Ambulant elderly people***
  The majority of trials have been conducted among a limited sample of elderly people. Most participants were recruited either in nursing homes or in hospitals, and only two trials included elderly patients treated as out-patients. In one of these, in which the bulk laxative psyllium was compared with placebo, a larger weekly increase in bowel movement frequency was found than in any other placebo-controlled trial, although the numbers of participants in the trial were small and the difference was not statistically significant. The other trial among elderly out-patients compared two bulk laxatives, psyllium and calcium polycarbophil. Psyllium was more effective in improving bowel movement frequency and stool consistency, although the latter was a non-significant trend. These results suggest that fibre may be effective in the ambulant elderly.

- ***Elderly people in hospitals and nursing homes***
  The trials in hospital and nursing-home patients suggest that stimulant and osmotic laxatives may be more effective in these patients than bulk agents in increasing bowel movement frequency. However, this result is based on a few studies and the results regarding improvement in symptoms and stool consistency are inconclusive.

The major criticism of the trials identified in this area is that they lack power and are, therefore, unlikely to detect effects of treatment. They are certainly too small to adequately assess effects of treatment on uncommon outcomes, such as impaction, and adverse effects.

A further potential problem lies in the assumption that the patients in the trials are a homogeneous group. There are many causes of constipation, some of which may be of particular relevance to the nursing home or hospital populations which feature in most of the trials, such as dietary, psychiatric and environmental causes (Moriarty

& Irving, 1992). However, the trials do not present separate analyses for either different clinical subgroups of patients or different subcategories of constipation (e.g. stratified according to the different aetiologies). This is, perhaps, because of the small sample sizes in most of the studies. Future larger trials may permit more detailed subgroup analyses to be carried out if appropriate and this would then permit different treatments to be targeted at the appropriate patient group.

Treatment of faecal impaction

There is little literature on the treatment of faecal impaction by laxatives. This may be because treatment is primarily by enema and/or manual disimpaction. One RCT has found that impaction can be treated and prevented with oral laxatives. However, it has also been suggested that the effective prevention of faecal impaction is more likely to depend on the effective prevention and treatment of constipation (Romero *et al,* 1996; Alessi & Henderson, 1988). Three RCTs of prevention of constipation were found, two using fibre and one using a stimulant laxative. None of these trials found laxatives to be effective. Prevention of constipation by improvements in the diet of elderly people has, however, been demonstrated in several observational studies.

Costs and cost-effectiveness of laxatives

The relative cost-effectiveness of different laxative classes will depend on the results of comparisons between different laxative preparations and this information is, by and large, not available. However, it has been found that lactulose is less cost-effective than either sorbitol or a combination of senna plus fibre. Based on the cost data presented earlier (see *Table 3),* the cheapest treatment is represented by stimulant laxatives, such as bisacodyl (£0.28 per week) and senna (£0.42 per week), or the bulk laxatives, Isogel® granules (£0.56 per week) and Fybogel (£0.99 per week). The most expensive treatments in common use are the group of danthron stimulant laxatives, such as co-danthrusate capsules (up to £4.08 per week) and co-danthramer suspension (up to £2.39 per week).

Stimulant laxatives are the second most commonly prescribed class of laxative and are prescribed more often than bulking laxatives. Also, the overall volume of stimulant laxatives prescribed is increasing faster than all other types of laxative, and the overall cost to the NHS of prescribing stimulant laxatives is correspondingly increasing. This increase appears to be caused mainly by the increasing number of prescriptions for the stimulant danthron laxatives, co-danthramer and co-danthrusate. The indications for these two laxatives are limited but include "constipation in geriatric practice" (BNF, 1997). However, this review has found little evidence to suggest major differences in effectiveness between the different laxatives. No trials were found, for example, which showed that danthron is more or less effective than any other stimulant agent (or any other class of laxative) in older people.

Conclusions and recommendations for future research

There have been so few comparative studies, and the trials have been so small, that it is difficult to determine what constitutes effective treatment of constipation in the elderly. The majority of trials have been carried out in hospitals and nursing homes, so there has been no adequate assessment of the effectiveness of laxatives in elderly people living in the community, who are likely to be younger and more mobile. There have been few direct comparisons between different classes of laxatives and between different types of laxative within classes (inter- and intra-class comparisons), apart from a few studies comparing different formulations of osmotic laxatives.

More generally, there is little guidance on what constitute effective **management** of constipation. Constipated elderly people are a diverse group of patients and laxatives may not be the appropriate treatment for all of them. An increase in dietary fibre may predispose immobile elderly to faecal impaction and the effectiveness of different types of laxative may be influenced by, for example, stool consistency and the presence of neuropathy (Barrett, 1992). However, laxatives are perhaps widely used in the absence of proven simpler or more cost-effective treatments. It is also possible that some of the laxatives currently prescribed are not actually needed; a proportion of older people take laxatives when not constipated and, for mobile older people, improvements in overall diet may be sufficient to prevent and treat the condition. Reduced calorie intake resulting in constipation may be an inevitable aspect of ageing and, in many older people, supplementary bulking agents may be considered a reasonable use of resources. Although observational studies suggest that

dietary interventions may be helpful, good quality RCTs are lacking.

If more were known about the effectiveness and cost-effectiveness of different treatments, constipation could be managed in a step-by-step approach. For example, a first approach (after exclusion of co-morbidity) could involve overall improvements in diet. If this failed, the next step would involve dietary supplementation, for example, with simple fruit–fibre treatments (if these are shown to be effective). If this failed, patients could be then prescribed the most cost-effective laxative treatment, and so on.

Research recommendations

The strategy proposed above allows several specific recommendations for research to be made.

1. ***Research into the effectiveness of overall dietary change (including increased fluid intake) in the treatment of constipation in the elderly***
   Observational studies which have increased overall consumption of dietary fruit and fibre have emphasised the effectiveness of this approach in preventing constipation, although the few RCTs which have been carried out have not supported these results. However, many of these trials have been small (with 15–30 patients typically) and compliance has been a problem. These treatments have been claimed to be effective both in elderly people living at home and among those in hospitals. An RCT with sufficient power to detect an effect of treatment, with assessment of compliance, would be required to determine whether or not constipation can be treated and prevented without recourse to pharmacological laxatives.

2. ***Trials of other bulk-forming and fibre-containing food supplements***
   There have been several observational studies in which the researchers have experimented with methods of increasing fibre and fruit intake in the elderly, using specific dietary supplements (for example, the addition of oats, fruit juice and other 'special mixtures' to diets). However, it has been suggested that bulking agents in elderly people may increase the risk of faecal incontinence (Barrett, 1992). Given the marked effectiveness, high acceptability and compliance claimed for some of these simple treatments, more formal evaluations (including assessment of adverse effects) may be appropriate.

Further studies of existing treatments are required, as follows.

3. ***Intra-class comparisons of bulk laxatives***
   There are wide variations in the cost of 1 week of treatment. NHS expenditure on ispaghula is more than ten times that of bran, yet there is little evidence to show that ispaghula is any more effective. There is also a requirement for comparisons of the different formulations of ispaghula (e.g. Fybogel, Isogel, Konsyl).

4. ***Inter-class comparisons of stimulant laxatives***
   Use of the stimulant laxatives, co-danthramer and co-danthrusate, is increasing. These laxatives are much more expensive than other laxatives in the same class, without any evidence that they differ in effectiveness. There is, therefore, no evidence that they should be prescribed in preference to cheaper laxatives. Trials should compare the effectiveness of co-danthramer and co-danthrusate with bisacodyl, with senna, and with bulk laxatives.

5. ***Additional areas for research***
   Other areas where comparisons are lacking are shown in *Table 6*. In particular, osmotic laxatives and stimulant laxatives appear to be the most widely used laxative agents. No trials were found that compared their effectiveness in the elderly.

Methodological recommendations

Most of the published studies have not been of high quality, and represent weak evidence for the effectiveness of various classes of laxative. It is important that any new trials should be methodologically sound. In particular, it is recommended that there should be sound randomisation in trials, and double-blinding where possible. Trials should be of sufficient power to detect differences in effects where they exist. A total sample size of about 93 patients would be required to detect a mean difference between treatments (or between treatment and placebo) of 1.5 bowel movements per week.[1] Measures of frequency and consistency should also be included. Not all published trials have assessed adverse effects in a consistent

[1] Assumptions: 90% power to detect a difference; SD in each group = 2.0, based on the mean of the SDs in the published trials; a difference of 1.5 bowel movements per week is based on *Figure 6;* significance level = 5%; the final figure also allows for a 20% drop-out rate.

TABLE 6 *Trials comparing laxatives in elderly patients*

	Bulk	**Stimulant**	**Faecal softener**	**Osmotic**	**Other**
Bulk	Calcium polycarbophil vs. psyllium				
Stimulant		Cascara + boldo vs. cascara + boldo			
Faecal softener		DSS vs. DCS			
Osmotic					Magnesium hydroxide vs. Laxamucil Lactulose vs. Agiolax (two trials)
Other		Dorbanex vs. Laxoberal			
Placebo	Bran (two trials) Psyllium (two trials)	Prucara Cascara (two trials)	DSS	Lactulose (two trials) Lactitol	

DSS, dioctyl sodium sulphosuccinate
DCS, dioctyl calcium sulphosuccinate

manner. As well as efficacy, studies should also measure tolerability of treatments; information on adverse effects (pain, nausea, bloating and flatulence) should therefore be collected prospectively in a standardised fashion. This research should be undertaken soon because of the potential cost-savings to the NHS.

Conclusion

Despite their frequent use and cost to the NHS, information on the effectiveness of laxatives in the elderly is extremely limited. The pharmaceutical industry has produced few new laxative products in recent years; hence, there has been no incentive to evaluate older remedies. Moreover, simple treatments, such as bran, fruit and high fibre diets, are not likely to receive the same degree of promotion and research as more expensive pharmaceutical products. The 'Cinderella' nature of the condition, and the patients it most affects, may also be relevant. This review has outlined those few areas where effective treatments have been found and highlighted the many areas of ignorance. Until the relevant comparative trials are carried out, it is impossible to determine which treatments are most effective, or most cost-effective. The clear implication of this is that there is no evidence to support the current trend toward prescribing the most expensive laxatives.

The existing research is equivocal on the subject of prevention of constipation; again, further trials are required. Many laxatives came into use before rigorous drug studies were seen to be necessary and so there is also little information on the side-effects of such preparations (Kamm, 1989).

It is perhaps ironic that some of the oldest drugs in common use should be among the least investigated, and this must be due in part to the prosaic nature of the condition they are used to treat. As a result of this relative lack of research interest, a significant amount of work of good methodological quality is required in this area. While this would finally answer questions about the relative effectiveness of different treatments, it would also permit a cost-effective management strategy for constipation to be defined. Until that research is available, it is unclear what exactly constitutes the 'best-buy for constipation' in older people and, moreover, there is currently no evidence to suggest that this is represented by the danthron laxatives.

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Appendix 1

Search strategies

Constipation/laxative studies

MeSH subject headings

Constipation
Defecation
Diarrhoea
Faecal incontinence
Faeces, impacted*

Textword terms/synonyms

Bowel function$
Bowel habit$
Bowel pattern$
Bowel movement$
Bowel symptom$
Colon$ adj transit
Evacuation
Faecal adj incontinence
Impaction
Impacted adj f?eces
Intestinal adj motility
Irritable adj bowel adj syndrome
Stool$
Stool$ with (hard or impacted)
Strain$
Void$

Laxatives

MeSH subject headings

Cathartics [= agar, bisacodyl, cascara, emodin, castor oil, dioctyl sulfosuccinates, karaya gum, lactulose, magnesium hydroxide, magnesium oxide, methyl-cellulose, mineral oil (= liquid paraffin), oxyphenisatin acetate, psyllium, senna, tragacanth].
Dietary fiber
Enema
Fruit
Glycerin
Magnesium compounds
Phenolphthaleins
Phosphates
Polyethylene glycols
Sorbitol

Plus BNF laxative terms and brand names.

Textword terms/synonyms

A. Names of drugs (to be adapted from San Antonio search strategy).

B. Synonyms/related words (preliminary list):
bulk
casanthranol
cellulose
glucitol
glycerol
laxative$
purgative$
fe?cal adj softener$
liquid adj paraffin
roughage
stool adj softener$
suppositories

C. Names of particular foods (preliminary list), including:
bran
fruit adj juice$
prune$
rhubarb

Age group

MeSH subject headings

Adolescent
Adult
Aged
Aged 80 and over
Frail elderly

Textword terms/synonyms

Elderly
Geriatric$
Older

Human

MeSH subject headings

Exclude HUMAN not (HUMAN and ANIMAL)

Pre-defined search strategy for reviews/RCTs

(i) Search performed: 1 and 2 and 3 and 4 and 5. This result was NOT be limited to English language publications only.
Exclude PREGNANCY.

(ii) Fluid therapy in constipation
Explode CONSTIPATION/all subheadings
This was combined with the following terms to pick up all studies (including reviews) referring to fluid therapy:
FLUID
FLUIDS
HYDRATION
REHYDRATION
FLUID or FLUIDS or HYDRATION or REHYDRATION
FLUID-THERAPY

This strategy produced 54 hits. A total of 18 papers examined the role of fluid in constipation. Of these, 11 were reviews mentioning the importance of fluid intake. One was a survey, one a case-control study of risk factors for constipation. The remaining five studies were non-comparative studies of fluid therapy, in all of which fluid intake was altered in addition to dietary changes (e.g. by adding fibre).

(iii) Exercise therapy in constipation
The term constipation and its sub-headings were combined with either EXERCISE or EXERCISE-THERAPY or MOBILITY. This produce eight hits, none of which were studies of the use of exercise therapy in constipation.

Appendix 2

Additional databases searched

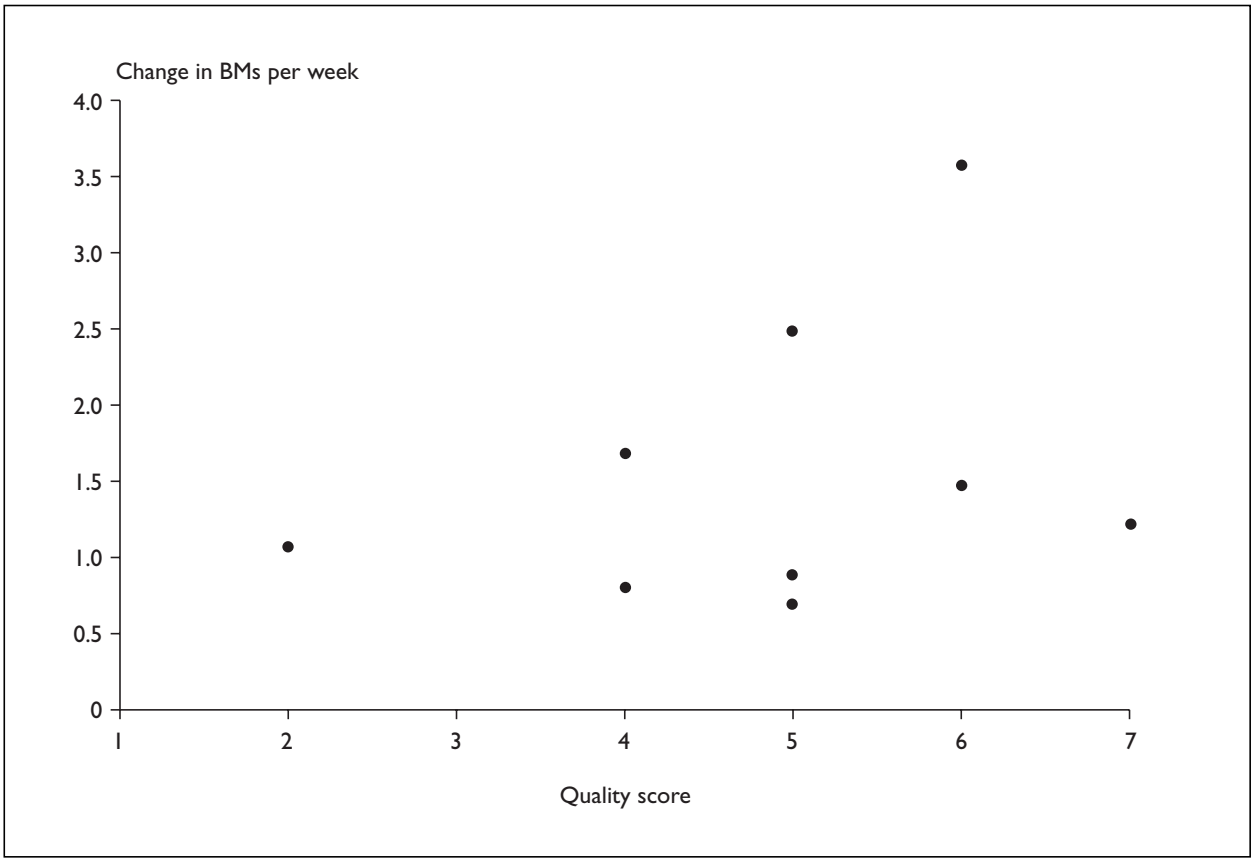
The following additional databases were searched.

Allied & Alternative Medicine (AMED)
Psychological Abstracts (Psychlit)
Cochrane library
Cumulative Index to Nursing & Allied Health Literature (CINAHL)
DHSS Data
Embase
IDIS drug file
Ageline
International Pharmaceutical Abstracts
Science Citation Index via BIDS

A Medline search was also undertaken to update the review by Tramonte and colleagues (1997). In addition, all trials excluded from the Cochrane review were examined for inclusion.

Appendix 3

Effect size by quality score for adult trials identified by Cochrane review (excluding trials in the elderly)



This graph of effect sizes (in bowel movements per week) from the trials of laxatives in adults shows an apparently higher effect size in higher quality trials. The implication is that poorer quality trials may underestimate the effects of treatment (but see page 27).

Appendix 4

Excluded studies

Those additional RCTs of laxative treatment of constipation that were identified by supplementary search but excluded from this review on age grounds are listed here. These reviews have been passed to the Cochrane review team in San Antonio, USA, who carried out the 1997 laxative review (Tramonte *et al*, 1997).

Trials evaluating single agents

Ashraf and colleagues (1995) – Bulk versus placebo

A total of 22 ambulatory constipated participants (aged 40–75 years) received fibre (psyllium) or placebo. Stool frequency increased by approximately 0.9 stools per week with treatment but not with placebo. Stool weight significantly increased with treatment but not with placebo. Stool consistency and pain also increased significantly with treatment but not with placebo.

Quality score: **5.**

Sculati and Giampiccoli (1984) – Bulk versus placebo

The 40 participants, aged 21–73 years, received Fibraform® (Testa Triticum Tricum, a bulking agent made from wheat bran) or placebo. After 30 days of follow-up, 85% of controls were severely or moderately constipated compared with 26% of the treatment group ($p < 0.001$). Consistency and pain were also significantly improved ($p < 0.05$).

Quality score: **4**.

Matek and colleagues (1982) – Bulk versus placebo

In this RCT a bulking agent based on psyllium was compared with placebo in patients aged 18–67 years. Stool weight was significantly increased and transit time significantly decreased after 1 week of treatment. (No quality assessment score has been awarded, as the paper has not been fully translated.)

Cantal and colleagues (1977) – Stimulant versus placebo

A group of 100 hospitalised patients, aged between 21 years and 61+ years, who were considered to be constipated if they had no bowel movement for 2 days, received either a stimulant (sodium sulisatin) or placebo. No data on bowel movement frequency is presented but a 'good' result was obtained with 72% of the treatment group compared with 14% of those receiving placebo ($p < 0.1$). However, the patients were not chronically constipated.

Quality score: **4**.

Möllenbrink and Bruckschen (1992) – Other versus placebo

The effect of treatment of constipation with *E. coli* bacteria was examined in 134 young patients (mean age = 19 years) in this double-blind RCT. Although the study is of crossover design, interim results are presented for the end of the first phase of treatment. Treated patients had 1.5 stools per week more than those on placebo at crossover. No side-effects of the treatment are reported. (No quality assessment score has been awarded as the paper has not been fully translated.)

Trials comparing two agents

Reichard and colleagues (1990) – Bulk versus bulk

A total of 68 patients aged over 25 years participated in this RCT comparing Testa Triticum Tricum (a bulking agent made from wheat bran) with ispaghula. Frequency increased in both groups of patients with no significant difference between treatments. There was no difference between treatments in terms of straining, number of painful defecations, flatulence, bloating or acceptability of treatment. (No quality assessment score has been awarded as the paper has not been fully translated.)

Hammer and Ravelli (1992) – Osmotic versus osmotic

The 61 patients participating in this study received lactitol or lactulose (no ages of patients are given). Treatments were equally effective in terms of frequency (approximately one bowel movement per day) and adverse effects, although tolerance was greater with lactitol. (No quality assessment score has been awarded as the paper has not been fully translated.)

Heitland and Mauersberger (1988) – Osmotic versus osmotic

A total of 60 chronically constipated patients (approximate age range 37–68 years) received either Lactitol or lactulose over the 2-week study period during which bowel movement frequency was monitored. The treatments were equally effective in improving frequency, with patients receiving either treatment producing a bowel movement on approximately three-quarters of study days, and consistency of stools was similar for both treatments. Both treatments were well tolerated. (No quality assessment score has been awarded as the paper has not been fully translated.)

Bobbio and colleagues (1995) – Osmotic versus osmotic plus fibre

In a double-blind RCT, 40 patients aged between 48 years and 84 years were treated with either lactulose or lactulose plus glucomannan (soluble fibre) for 4 weeks. At the end of the treatment period, the frequency of stools per week was slightly higher with lactulose alone (6.55 versus 5.75). The combination therapy was associated with significantly lower incidence of flatulence, meteorism and diarrhoea. (No quality assessment score has been awarded as the paper has not been fully translated.)

Bruckschen and Horosiewicz (1994) – Osmotic versus other

In this open trial, *E. coli* ('microbiological treatment') was compared with lactulose in the treatment of 108 adults aged > 18 years over a 14-week period. Frequency was significantly higher with the microbiological therapy than with lactulose (6.3 versus 5.5 stools per week). Consistency and ease of defecation was also superior with *E. coli* treatment. Adverse events were significantly higher with lactulose therapy. (No quality assessment score has been awarded as the paper has not been fully translated.)

Baldarassi and colleagues (1980) – Other versus other

In this single-blinded RCT, three herbal preparations containing varying quantities of potentially-laxative agents such as boldo, rhubarb, bile acids and phenolphthalein were compared. Frequency, consistency and tolerance were assessed and the authors concluded that the three mixtures differ markedly in effectiveness. (No quality assessment score has been awarded as the paper has not been fully translated.)

Unpublished data

One unpublished RCT was supplied by a drug manufacturer. In this, Codalax® was compared with lactulose in patients aged over 60 years. This study was not included as the patients included did not appear to be chronically constipated.

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