Alimentary Pharmacology & Therapeutics

The cost-effectiveness of macrogol 3350 compared to lactulose in the treatment of adults suffering from chronic constipation in the UK

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Publication data
Submitted 10 September 2009
First decision 3 October 2009
Resubmitted 12 October 2009
Accepted 30 October 2009
Epub Accepted Article 3 November 2009

ABSTRACT

Background
It is unknown whether macrogol 3350 (Movicol) affords the UK's National Health Service (NHS) a cost-effective addition to the current range of laxatives.

Aim
To estimate the cost-effectiveness of macrogol 3350 compared with lactulose in the treatment of chronic constipation, from the perspective of the UK's NHS.

Methods
A decision model depicting the management of chronic constipation was constructed using clinical outcomes and resource use values derived from patients suffering from chronic constipation in The Health Independent Network (THIN) database. The model was used to estimate the cost-effectiveness of a GP prescribing macrogol 3350 instead of lactulose to treat adults ≥18 years of age suffering from chronic constipation.

Results
Sixty-eight percent of patients given macrogol 3350 were successfully treated within 6 months after starting treatment compared to 60% of patients given lactulose. Patients' health status at 6 months was estimated to be 0.458 and 0.454 quality-adjusted life years (QALYs) in the macrogol 3350 and lactulose groups respectively. The total 6-monthly NHS cost of initially treating patients with macrogol 3350 or lactulose was estimated to be £420 (US $688) and £419 (US $686) respectively. Hence, the cost per QALY gained with macrogol 3350 was estimated to be £250 (US $410).

Conclusion
Macrogol 3350 affords the NHS a cost-effective addition to the range of laxatives available for this potentially resource-intensive condition.

Aliment Pharmacol Ther **31**, 302–312

doi:10.1111/j.1365-2036.2009.04191.x

INTRODUCTION

Constipation is one of the most common conditions in Western countries and is generally defined by clinicians as fewer than three bowel movements per week.[1] The estimated prevalence ranges from 0.02 to 0.27 and increases with age, but it is not a physiological consequence of normal ageing.[2–4] Many age-related problems (e.g. decreased mobility, comorbid medical conditions, increased use of medications with a side-effect profile that includes constipation, and dietary changes) may contribute to the increased prevalence of constipation in older adults. In addition, it is more common in women than in men, with a ratio of 2:1.[2–4]

The management of chronic constipation can be difficult. Patients with chronic constipation can generally benefit from osmotic laxatives. They exert their effect within the colonic lumen by increasing the water-carrying capacity of the intestinal contents without having any systemic effect. However, they have been associated with electrolyte imbalance within the colonic lumen and may precipitate hypokalaemia, fluid and salt overload and diarrhoea.

Macrogol 3350 (Movicol; Norgine Ltd, Harefield, Middx, UK) and lactulose are both osmotic laxatives. Macrogol 3350 is polyethylene glycol, a non-absorbable, long linear polymer which is administered along with extra fluids, thereby increasing the water content and volume of the stools. Lactulose is a polysaccharide that can be metabolized by the bacteria in the lower intestine. This leads to acidification of the intestine causing a reduction in ammonia absorption which in turn draws water from the body resulting in an increase in the water content and volume of the stools. [5]

The Health Independent Network (THIN) database comprises the longitudinal medical records of 6.5 million members of the general public from across the UK.[6] Three hundred general practices from across the UK using the Vision practice management software contribute annonymized patients to the database. The patient data within these practices have been shown to be generalizable to the UK population[7] and patients' morbidity is listed using Read codes.

Using outcomes from clinical trials, we have previously demonstrated that macrogol 3350 is a cost-effective laxative compared with lactulose in the treatment of chronic constipation in the UK[8] and Belgium.[9] However, it is also important to know whether macrogol 3350 affords the UK's National Health Service (NHS) a cost-effective addition to the range of laxatives, based on actual clinical practice. Hence, the present study aimed to estimate the cost-effectiveness of macrogol 3350 compared with lactulose in the treatment of chronic constipation arising from any cause in the UK, using patient data extracted from the THIN database.

METHODS

Perspective

This study estimated the cost-effectiveness of using macrogol 3350 compared with lactulose to treat adults suffering from chronic constipation, from the perspective of the NHS in the UK.

Decision model

A decision model depicting the management of chronic constipation (Figure 1) was constructed using the software, TreeAge Pro 2007 (TreeAge Software Inc., Williamstown, MA, US). The model considers the decision by a GP to initially treat a patient aged ≥18 years with macrogol 3350 or lactulose. The model was populated with clinical outcomes and resource use derived from patients suffering from chronic constipation in the THIN Database[6] and spans a period of 6 months from the start of laxative treatment.

Subjects

The records of a sample of 1000 macrogol 3350-treated patients were randomly extracted from the THIN database. To be eligible for inclusion in the data set, patients had to be ≥18 years of age and have:

- A Read code for constipation.
- A history of constipation for two years or more before they received their first prescription for macrogol 3350, to ensure that they were genuinely suffering from chronic constipation.
- Received their first prescription for macrogol 3350 before 1 July 2007.
- At least 6 months' follow-up data following the start of macrogol 3350.
- Not been taking lactulose for at least 3 months prior to starting macrogol 3350.

The macrogol 3350-treated patients who met these admission criteria were matched with 1000 lactulose-treated patients according to age ± 5 years, gender and time between starting lactulose and the previous

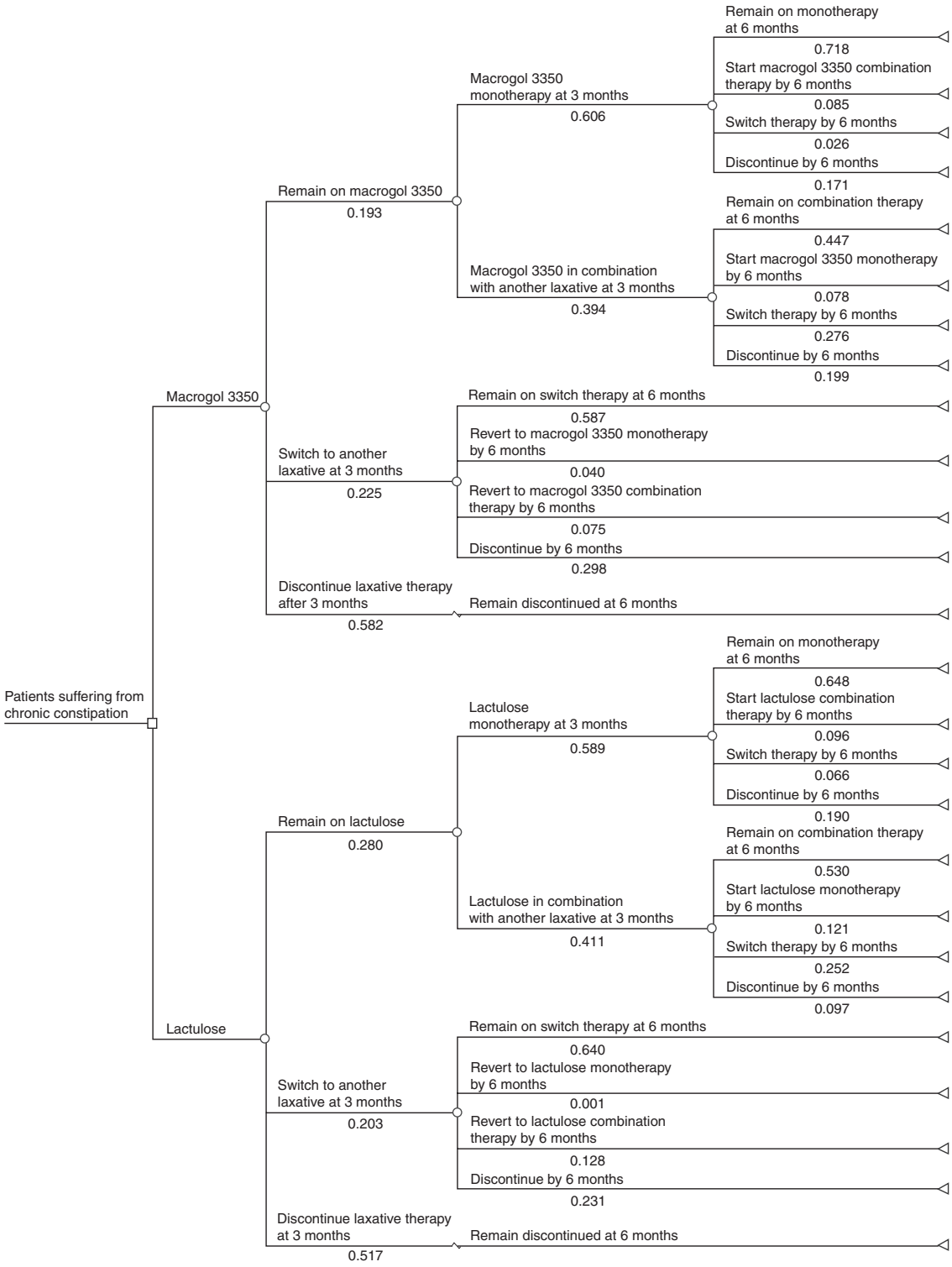

Figure 1. Decision tree modelling the management of chronic constipation with macrogol 3350 and lactulose. Numbers denote the probability of a patient following a particular path.

laxative. Additionally, these patients had to have started their first lactulose prescription within 6 months of patients' starting their first macrogol 3350 prescription, not received macrogol 3350 for at least 3 months prior to starting lactulose, a history of constipation for two years or more before they received their first prescription for lactulose and at least 6 months' follow-up data following the start of lactulose.

Patients' constipation-related resource use was extracted over a period of 6 months from the time of the first prescription for macrogol 3350 or lactulose and quantified for each treatment group.

Model inputs

Clinical. The time horizon for the analysis was limited to 6 months as patients are expected to be either successfully treated or not during this period. The model assumes that:

- Patients who discontinued their initial laxative within 1 month and received no further prescriptions for laxatives were successfully treated.
- Patients who remained on their initial laxative either as monotherapy or in combination with another laxative for the whole 6 months were well controlled.
- Patients who switched from their initial laxative were unsuccessfully managed with their initial laxative, possibly because of side-effects, lack of efficacy or non-compliance. Thus, the impact of these outcomes has been assessed via the switch to an alternative laxative.

The probabilities of patients remaining on their initial laxative, or switching or discontinuing are shown in Figure 1.

Healthcare resource use. Healthcare resource use associated with managing chronic constipation with each laxative was quantified over a period of 6 months from the start of treatment. The 6 monthly number of clinician visits, hospital admissions, accident and emergency attendances, laboratory tests, diagnostic procedures and laxative prescriptions were obtained from the records of the patients in the THIN data set.

Patients' utilities

Patients' health-related quality of life was not collected in the THIN database. Hence, published utilities for chronic constipation we previously obtained from members of the general public across the UK using standard gamble methodology[10] were assigned to the respective states in the model, enabling patients' health status in terms of the number of quality-adjusted life years (QALYs) at 6 months following the start of treatment to be estimated.

Model outputs

Two primary outcome measures were used. One measure was the percentage of successfully treated patients at 6 months following the start of laxative treatment. The other measure was the number of QALYs at 6 months following the start of laxative treatment.

Unit resource costs at 2007/08 prices,[11, 12] and laxative costs obtained from the Drug Tariff[13] or the British National Formulary[14] were applied to the resource utilization estimates within the decision model to perform cost-effectiveness analyses over a 6-month period and sensitivity analyses.

Cost-effectiveness analyses. The cost-effectiveness of macrogol 3350 relative to lactulose was calculated as the difference between the costs of the two treatment strategies over 6 months divided by the difference in effectiveness between the two treatment strategies at 6 months. When the measure of effectiveness was the percentage of successfully treated patients, the cost-effectiveness of macrogol 3350 relative to lactulose was defined as the cost for each additional patient successfully treated with macrogol 3350. When the measure of effectiveness was the number of QALYs, the cost-effectiveness of macrogol 3350 relative to lactulose was defined as the cost per QALY gained.

Sensitivity analyses

Probabilistic sensitivity analyses were undertaken using Monte Carlo simulations (10 000 iterations of the model) by simultaneously varying the probabilities, unit costs, resource use values and utilities within the model. The probabilities and utilities were varied randomly according to a beta distribution by assuming a 5% standard distribution around the mean. Unit resource costs and resource use values were varied randomly according to a gamma distribution by assuming a 10% standard distribution around the mean. Additionally, deterministic sensitivity analyses were performed to identify how the incremental cost-

effectiveness of one treatment relative to another would change by varying different parameters in the model.

Ethical approval

Ethical approval to perform this study was obtained from the London Multi-Centre Research Ethics Committee, Harrow, Middlesex.

RESULTS

Patient characteristics

The patients' mean age was 65.6 (95% CI: 64.4; 66.8) years in the macrogol 3350 group and 65.6 (95% CI: 64.4; 66.7) years in the lactulose group. Thirty-three percent of patients in both groups were men. Patients were well matched according to their comorbidities (Table 1) and time between their last laxative prescription and starting the study drug. However, more macrogol 3350-treated patients had received a prior laxative than lactulose-treated patients (89% vs. 76%; $P < 0.001$) (Supporting information Tables S1 and S2).

Expected outcomes

Significantly more patients ($P < 0.0001$) treated with macrogol 3350 (68% (95% CI: 65%; 71%)) were successfully treated within 6 months compared with lactulose-treated patients (60% (95% CI: 58%: 63%)) (Table 2). Patients' health status was estimated to be 0.458 (95% CI: 0.429; 0.486) and 0.454 (95% CI: 0.427; 0.482) QALYs at 6 months in the macrogol 3350 and lactulose groups respectively. Hence, treatment with macrogol 3350 instead of lactulose is expected to increase the probability of being successfully treated by 13% at 6 months, but yield only a 1% improvement in health gain.

Expected healthcare resource use and costs

Patients taking macrogol 3350 used a mean 1.5 (95% CI: 1.4; 1.6) sachets per day and lactulose-treated patients used a mean 20.8 mL per day (95% CI: 19.9; 21.7). The percentage of patients receiving different adjunctive laxatives and patients' switching patterns after stopping macrogol 3350 or lactulose are summarized in Table 3.

Table 1. Percent of patients with co-morbidities

Co-morbidity	Percentage of patients in the THIN data set with co-morbidity who started treatment with: Macrogol 3350 (%)	Lactulose (%)
Arthritis	25	43
Ischaemic heart disease	21	23
Cancer	15	15
GI non-inflammatory disease	14	29
Depression	13	5
Diabetes mellitus	12	8
None	11	7
Diverticular disease	10	12
Inflammatory bowel disease	10	16
Haemorrhoid	10	17
Musculoskeletal disorder	10	5
Bone disease	9	8
Asthma	7	16
Cerebrovascular disease	7	6
Renal disease	7	7
Chronic wound	7	15
Hypothyroidism	6	6
Hernia	6	21
Prostate disorder	4	8
Chronic obstructive pulmonary disease	3	4
Psychosis	3	2
Gynaecological disorder	3	3
Anal fissure	3	3
Epilepsy	3	2
Parkinson's disease	3	1
Multiple sclerosis	2	1
Fracture (vertebral)	2	1
Skin disease	2	3
Lipoma	2	9
Eating disorder	2	5
Mental and physical disability	2	2
Vascular disease	2	4
Cardiovascular disorder	2	1
Dementia	2	2
Anaemia	1	5
Hyperthyroidism	1	0
Ear, nose and throat disorder	1	1
Liver disease	1	1
Neurological disorder	1	1
Coeliac disease	1	1
Hydrocephalus	0	2

Table 2. Outcomes at 3 and 6 months

	Percent of patients initially treated with			
	Macrogol 3350 at		Lactulose at	
Outcome	3 months	6 months	3 months	6 months
Well controlled on monotherapy	12	10	16	12
Well controlled on combination therapy	8	6	12	10
Unsuccessfully treated	23	16	20	18
Successfully treated*	58	68	52	60

* The difference between the two treatments at 3 months and 6 months was significantly different; $P < 0.0001$.

Table 3. Distribution of adjunctive laxative use and switching patterns

	Percent of patients in the THIN data set who used laxatives:			
	As adjunctive therapy following treatment with:		After switching from:	
Laxative	Macrogol 3350	Lactulose	Macrogol 3350	Lactulose
Bulk-forming	17	33	21	32
Bulk-forming/ stimulant	4	3	5	5
Faecal softener/ stimulant	12	7	11	11
Osmotic	18	7	26	18
Stimulant	50	50	37	34

Macrogol 3350-treated patients had 4.86 (95% CI: 2.81; 6.88) GP visits over the 6 months and lactulose-treated patients had 5.03 (95% CI: 3.11; 6.97) visits. In addition, compared with macrogol-3350 treated patients, lactulose-treated patients were 1.3 times more likely to attend accident and emergency (3% vs. 4% chance) or be admitted into hospital (3% vs. 4% chance) or have a hospital out-patient visit (22% vs. 29% chance). Conversely, macrogol 3350-treated patients were 1.5 times more likely to have a GP domiciliary visit than lactulose-treated patients (24% vs. 16% chance) (Table 4).

According to the model, the total NHS cost over 6 months of initially treating patients with macrogol 3350 was estimated to be £420 (95% CI: £307; £531) [US $688 (95% CI: $503; $870)]. This compared with £419 (95% CI: £314; £523) [US $686 (95% CI: $514; $857)] for those initially treated with lactulose. GP visits emerged as the primary cost driver in both treatment groups, accounting for up to 63% of the expected costs. In contrast, laxative prescriptions accounted for 3–5% of the expected costs (Table 5).

Cost-effectiveness analyses

According to the decision model, initial use of macrogol 3350 instead of lactulose is expected to lead to a 13% improvement in successful treatment (from 0.60 to 0.68) and a 1% improvement in health gain (from 0.454 to 0.458 QALYs) over 6 months at no additional cost. If it was assumed that there was an incremental cost of £1 (US $1.6) over 6 months with macrogol 3350, then the cost per QALY gained with macrogol 3350 would be £250 (US $410). Probabilistic sensitivity analyses highlighted the distribution in the cost per QALY gained (Supporting Information: Figure S1), from which it was estimated that macrogol 3350 has a 0.78, 0.85 and 0.89 probability of being cost-effective for a threshold of £20 000 (US $32 760), £30 000 (US $49 147) and £40 000 (US $65 530) per QALY respectively (Supporting Information: Figure S2).

Table 4. Levels of healthcare resource use over 6 months

	Amount of resource use per patient over 6 months following initial treatment with:	
Resource	Macrogol 3350	Lactulose
Accident and emergency attendances	0.03	0.04
GP domiciliary visits	0.24	0.16
GP visits in the clinic	4.86	5.03
Practice nurse visits	0.01	0.01
Dietician visits	0.10	0.12
Hospital outpatient visits	0.22	0.29
Hospital admissions	0.03	0.04
Laboratory tests	1.45	1.62
Diagnostic procedures	0.22	0.22

Table 5. Distribution of healthcare resource costs at 2007/2008 prices

Resource	Expected NHS costs at 6 months following initial treatment with: Macrogol 3350 (%)	Lactulose (%)
Accident and emergency attendances	£2.33 (1)	£2.98 (1)
Diagnostic procedures	£39.17 (9)	£41.48 (10)
Dietician visits	£0.54 (<1)	£0.89 (<1)
GP domiciliary visits	£14.13 (3)	£9.28 (2)
GP visits in the clinic	£252.81 (60)	£262.80 (63)
GP telephone consultations	£13.66 (3)	£10.83 (3)
Hospital admissions	£34.39 (8)	£42.26 (10)
Laboratory tests	£4.50 (1)	£5.00 (1)
Lactulose	£0.86 (<1)	£7.21 (2)
Macrogol 3350	£17.33 (4)	£1.88 (<1)
Nurse visits	£1.61 (<1)	£1.74 (<1)
Other laxatives	£5.00 (1)	£4.97 (1)
Outpatient visits	£33.72 (8)	£28.09 (7)
Total	£420.06 (100)	£419.41 (100)

The percentage of the total expected cost attributable to each resource is in parentheses. (£1.00 corresponds to US $1.64).

Sensitivity analyses

Deterministic analyses (Table 6) found the relative cost-effectiveness of macrogol 3350 to be marginally sensitive to the probability of remaining on the initial laxative, or switching to adjunctive therapy or discontinuing treatment at 3 months or utility values. However, plausible changes in these values do not affect the results. The relative cost-effectiveness of macrogol 3350 is less sensitive to changes in any other model input including resource use.

DISCUSSION

Chronic constipation is common among adults and management of this condition is a critical part of the care for older patients.[15] Individual symptoms are often severe and bothersome, and many patients are dissatisfied with traditional treatment options, primarily because of lack of efficacy.[16] Notwithstanding this, 40% of men and 55% of women aged 60 years and above in the UK are using laxatives.[17] Moreover, 14.4 million prescriptions for laxatives were written in primary care in England in 2007.[18] Nevertheless, there have been relatively few studies in recent years assessing the health economic impact of constipation to both health services and society in the UK.[19] Patients with constipation generally have an impaired quality of life compared with the general population, although studies in older patients are limited.[15] However, the health-related quality of life of constipated people is influenced by social and demographic factors.[20] Hence, strategies for prevention and minimization of constipation have the potential to improve substantially the quality of life of sufferers.[15] Against this background, the health economic impact of macrogol 3350 was compared with that of lactulose in the treatment of chronic constipation. Lactulose was chosen as the comparator as it is the principal alternative treatment for chronic constipation in the UK and the most likely laxative to be displaced by macrogol 3350.

The results have been truncated at 6 months and exclude the costs and consequences of patients experiencing a second episode of constipation. Hence, this study represents an assessment of macrogol 3350 and lactulose use among adults with chronic constipation in clinical practice in the UK over a 6-month period. A period of 6 months was selected as it was considered to be of sufficient length in which to assess whether patients were successfully treated. It could be argued that this is an arbitrary period. However, the same period of follow-up has been applied to both groups ensuring an equitable estimation of the costs and outcomes for both treatments.

Clinical trials have shown that macrogol 3350 is more efficacious than lactulose in treating adults with chronic constipation.[21] Notwithstanding this, it was decided to estimate the effectiveness of using macrogol 3350 and lactulose using 'real world' data obtained from the THIN database. The advantage of using the THIN database is that the economic impact of macrogol 3350 and lactulose in this study is based on actual clinical practice rather than trial protocol-driven resource use. However, this naturalistic approach does have its limitations. Resource use was not collected prospectively and patients were not randomized to treatment, although patients in each treatment group were matched. However, significantly more macrogol 3350-treated patients had received a prior laxative than lactulose-treated patients. This reflects the prescribing pattern one would expect to see in general practice with a well established laxative like lactulose being used more often as a first-line treatment and a

Table 6. Sensitivity analyses. (£1.00 corresponds to US $1.64)

Scenario	Base case value	Effect
Probability of remaining on macrogol 3350 at 3 months ranges from 0.15 to 0.23.	0.19	The cost per QALY gained increases as the probability increases rising to £4400 at a probability of 0.23.
Probability of remaining on macrogol 3350 monotherapy at 3 months ranges from 0.49 to 0.73.	0.61	The cost per QALY gained increases as the probability decreases, rising to £1200 at a probability of 0.49.
Probability of switching from macrogol 3350 at 3 months ranges from 0.18 to 0.27.	0.23	The cost per QALY gained increases as the probability increases rising to £4500 at a probability of 0.27. Below a probability of 0.20, macrogol 3350 becomes the dominant treatment.
Probability of discontinuing macrogol 3350 at 3 months ranges from 0.46 to 0.70.	0.58	The cost per QALY gained decreases as the probability increases. Above a probability of 0.59, macrogol 3350 becomes the dominant treatment.
Probability of remaining on macrogol 3350 monotherapy at 6 months ranges from 0.57 to 0.86.	0.72	Changing the probability has negligible effect on the cost per QALY gained although macrogol 3350 becomes the dominant treatment below a probability of 0.63.
Probability of remaining on macrogol 3350 combination therapy at 6 months ranges from 0.36 to 0.54.	0.45	Changing the probability has negligible effect on the cost per QALY gained.
Probability of switching from macrogol 3350 at 6 months ranges from 0.47 to 0.70.	0.59	The cost per QALY gained increases as the probability increases rising to £2500 at a probability of 0.70. Below a probability of 0.55, macrogol 3350 becomes the dominant treatment.
Probability of remaining on lactulose at 3 months ranges from 0.22 to 0.34.	0.28	The cost per QALY gained increases as the probability decreases rising to £8500 at a probability of 0.22. Above a probability of 0.30, macrogol 3350 becomes the dominant treatment.
Probability of remaining on lactulose monotherapy at 3 months ranges from 0.47 to 0.71.	0.59	The cost per QALY gained increases as the probability increases rising to £3000 at a probability of 0.71.
Probability of switching from lactulose at 3 months ranges from 0.16 to 0.24.	0.20	The cost per QALY gained increases as the probability decreases rising to £4000 at a probability of 0.16. Above a probability of 0.21, macrogol 3350 becomes the dominant treatment.
Probability of discontinuing lactulose at 3 months ranges from 0.41 to 0.62.	0.52	The cost per QALY gained increases as the probability increases rising to £16 600 at a probability of 0.62. Below a probability of 0.51, macrogol 3350 becomes the dominant treatment.
Probability of remaining on lactulose monotherapy at 6 months ranges from 0.51 to 0.77.	0.64	The cost per QALY gained increases as the probability decreases rising to £2000 at a probability of 0.51. Above a probability of 0.70, macrogol 3350 becomes the dominant treatment.
Probability of remaining on lactulose combination therapy at 6 months ranges from 0.42 to 0.64.	0.53	Changing the probability has negligible effect on the cost per QALY gained.
Probability of switching from lactulose at 6 months ranges from 0.51 to 0.77.	0.64	The cost per QALY gained increases as the probability decreases rising to £2500 at a probability of 0.51. Above a probability of 0.68, macrogol 3350 becomes the dominant treatment.
Monthly utility value for constipation ranges from 0.03 to 0.09.	0.06	The cost per QALY gained ranges from £200 to £1300.
Monthly utility value for being well controlled on medication ranges from 0.04 to 0.10.	0.07	The cost per QALY gained ranges from £140 to £14 000.
Number of GP surgery visits ranges from 50% below to 100% above the base case value.	100%	Relative cost-effectiveness of macrogol 3350 remains unchanged.
Number of GP domiciliary visits ranges from 50% below to 100% above the base case value.	100%	Relative cost-effectiveness of macrogol 3350 remains unchanged.

newer laxative like macrogol 3350 being reserved more often for second-line use. This might bias this study's findings against macrogol 3350 as the severity of constipation may not be the same in both groups, with more hard-to-treat patients in the macrogol 3350 group. Consequently, the benefits of macrogol 3350 may have been underestimated in this study.

The published utilities assigned to the model[10] were previously obtained using standard gamble methodology.[22] The standard gamble approach to obtaining utility values requires subjects to choose between the certainty of an intermediate health state, and the uncertainty of a treatment with two possible outcomes, where one of the outcomes is more attractive than the certain outcome, and the other is less attractive (e.g. death).[22, 23] The inclusion of uncertainty makes standard gamble more consistent with standard economic utility theory than some other methods. Using this approach, utilities were derived from 308 subjects from the general public across the UK who were not all suffering from constipation at the time of the interviews.[10] However, the utility scores of subjects who were experiencing the symptoms of constipation at the time of the interviews were not significantly different from those of respondents who were not.[10] In addition, there were no significant differences between the utility scores of male and female subjects.[10] Consequently, it was assumed that the utility scores would reflect the utilities of the patients in the THIN data set suffering from constipation, who themselves were a random sample of subjects from the general public. The impact of changing these values on the relative cost-effectiveness of macrogol 3350 was assessed with sensitivity analyses.

The findings from this study show that treatment with macrogol 3350 instead of lactulose is expected to increase the relative chance of being successfully treated by 13% at 6 months ($P < 0.0001$). However, this yields only a 1% improvement in health gain. The expected QALY difference at 6 months is 0.004, resulting in a QALY gain costing £250 (US $410), if one assumes an incremental cost of £1 (US $1.6). The measure of 'successful treatment' suggests health improvements for both laxatives. However, the small QALY difference may indicate that the sample who participated in our original standard gamble study[10] did not value the symptoms of constipation sufficiently highly to warrant gambling with treatments that may shorten their life expectancy. Notwithstanding this, we were unable to find any other published cost-utility studies in constipation.

By way of comparison, the findings from this analysis based on the THIN data set were found to be concordant with those from our earlier study in which we estimated the cost-effectiveness of using macrogol 3350 compared with lactulose in the treatment of idiopathic constipation at 3 months.[8] The decision model in the earlier study was based on the outcomes from a clinical trial and resource use estimates which were derived from clinician interviews. Based on the trial, the earlier model showed that 53% of patients treated with macrogol 3350 would be successfully treated compared to 24% of lactulose-treated patients at 3 months.[8] However, the findings from this study (Table 5), based on actual clinical practice, show that 58% and 52% of patients treated with macrogol 3350 and lactulose respectively would be successfully treated at 3 months ($P < 0.0001$). The 3-monthly cost of using macrogol 3350 and lactulose was uprated to £116 (US $190) and £131 (US $215) per patient respectively at 2007/2008 prices, which is not inconsistent with the findings of this later study, which showed cost-neutrality at 6 months. In addition, we found GP visits to be the primary cost driver.

This study has several other limitations. Discontinuing laxative treatment may not necessarily be an indication of successful treatment. However, patients in the THIN data set had been suffering from constipation for at least 2 years. Hence, it seems reasonable to assume that if they stopped taking a laxative within a month of starting treatment, they were no longer suffering from the symptoms of this condition. The model used resource estimates for the 'average patient' and did not take into account such factors as age, gender, co-morbidities, suitability of patients for different treatments and other disease-related factors. Nevertheless, sensitivity analyses demonstrated that changes in resource use had minimal effect on the relative cost-effectiveness of macrogol 3350. In addition, 12% and 8% of patients in the macrogol 3350 and lactulose groups respectively were diabetic. Nevertheless, the costs of managing these patients were no different from the costs of managing the non-diabetic patients. The THIN database may have under-recorded use of some healthcare resources outside the GP's surgery, such as home visits made by GPs and nurses, hospital outpatient visits and attendance at accident and emergency units. The impact of this was addressed in the sensitivity analyses; changes in these values had minimal impact on the findings. The analysis excluded hospital-based prescribing, but this should have

minimal impact on the results as most prescribing was undertaken by GPs in the community.

Notwithstanding these limitations, this evaluation provides an estimate of the costs and consequences of using macrogol 3350 instead of lactulose in the treatment of adults suffering from chronic constipation in the UK. Switching patients from lactulose to macrogol 3350 would result in an improvement in the proportion of patients successfully treated and would be cost neutral. The National Institute for Health and Clinical Excellence (NICE) considers that a treatment that has a cost-effectiveness of <£20 000 (US $32 760) per QALY potentially affords an effective use of NHS resources.[24] Hence, macrogol 3350 affords the NHS a cost-effective addition to the range of laxatives available for this potentially resource-intensive condition.

ACKNOWLEDGEMENTS

Declaration of personal interests: None. *Declaration of funding interests:* This study was sponsored financially by Norgine Pharmaceuticals Ltd, Harefield, Middlesex, UK, manufacturers of macrogol 3350. However, the authors have no other conflicts of interest that are directly relevant to the content of this manuscript. In particular, Norgine had no input into the study design. Neither did they review the results or have any input into writing this manuscript.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article:

Figure S1. Scatterplot of the incremental cost-utility of macrogol 3350 compared to lactulose (n = 10 000 iterations of the model).

Figure S2. Acceptability curve.

Table S1. Time between last laxative prescription and starting study drug.

Table S2. Distribution of laxative use in the 3 months before starting the study drug.

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