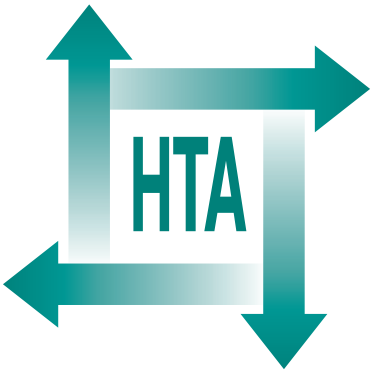
Health Technology Assessment 2006; Vol. 10: No. 19

Cognitive behavioural therapy in addition to antispasmodic therapy for irritable bowel syndrome in primary care: randomised controlled trial

TM Kennedy, T Chalder, P McCrone,
S Darnley, M Knapp, RH Jones and S Wessely

June 2006

Health Technology Assessment
NHS R&D HTA Programme



How to obtain copies of this and other HTA Programme reports.
An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (http://www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

– fax (with **credit card** or **official purchase order**)
– post (with **credit card** or **official purchase order** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you **either** to pay securely by credit card **or** to print out your order and then post or fax it.

Contact details are as follows:

HTA Despatch
c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can only be purchased for the current or forthcoming volume.

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *Direct Mail Works Ltd* and drawn on a bank with a UK address.

Paying by credit card
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

Paying by official purchase order
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

How do I get a copy of *HTA on CD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. *HTA on CD* is currently free of charge worldwide.

The website also provides information about the HTA Programme and lists the membership of the various committees.

Cognitive behavioural therapy in addition to antispasmodic therapy for irritable bowel syndrome in primary care: randomised controlled trial

TM Kennedy,[1] T Chalder,[2] P McCrone,[3] S Darnley,[1] M Knapp,[3] RH Jones[1*] and S Wessely[2]

[1] Department of General Practice and Primary Care, Guy's, King's and St Thomas' School of Medicine, King's College, London, UK
[2] Department of Psychological Medicine, Guy's, King's and St Thomas's School of Medicine, King's College, London, UK
[3] Centre for the Economics of Mental Health, Health Services Research Department, Institute of Psychiatry, King's College, London

* Corresponding author

Declared competing interests of authors: RH Jones has acted as a consultant to Solvay Heathcare, Boots, Novartis and Glaxo, all of whom have a therapeutic interest in IBS

Published June 2006

This report should be referenced as follows:

Kennedy TM, Chalder T, McCrone P, Darnley S, Knapp M, Jones RH, *et al*. Cognitive behavioural therapy in addition to antispasmodic therapy for irritable bowel syndrome in primary care: randomised controlled trial. *Health Technol Assess* 2006;**10**(19).

Health Technology Assessment is indexed and abstracted in *Index Medicus*/MEDLINE, *Excerpta Medica*/EMBASE and *Science Citation Index Expanded (SciSearch®)* and *Current Contents®*/Clinical Medicine.

NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA Programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, service-users groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including service users) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or conducting a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a short time period.

Criteria for inclusion in the HTA monograph series
Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 96/13/04. The contractual start date was in February 1999. The draft report began editorial review in May 2003 and was accepted for publication in November 2005. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.

Abstract

Cognitive behavioural therapy in addition to antispasmodic therapy for irritable bowel syndrome in primary care: randomised controlled trial

TM Kennedy,[1] T Chalder,[2] P McCrone,[3] S Darnley,[1] M Knapp,[3] RH Jones[1*] and S Wessely[2]

[1] Department of General Practice and Primary Care, Guy's, King's and St Thomas' School of Medicine, King's College, London, UK

[2] Department of Psychological Medicine, Guy's, King's and St Thomas's School of Medicine, King's College, London, UK

[3] Centre for the Economics of Mental Health, Health Services Research Department, Institute of Psychiatry, King's College, London

* Corresponding author

Objectives: To determine whether cognitive behavioural therapy (CBT) in addition to antispasmodic treatment offers a cost-effective benefit to primary care patients with irritable bowel syndrome (IBS) and to identify predictors of outcome.

Design: This was a randomised controlled trial in primary care of the addition of CBT to standard general practice management of IBS, using the antispasmodic agent mebeverine hydrochloride. The study set out to compare the addition of a standardised package of IBS-specific CBT to treatment with mebeverine hydrochloride.

Setting: Ten general practices, serving a population of around 45,000 patients, located principally in south London, with some patients resident in north London.

Participants: Patients identified as having IBS by their GPs, aged between 17 and 54 (mean 34) years and predominantly white; 82% were female and half had had IBS for more than 5 years.

Interventions: Practice nurses delivered CBT in a randomised trial of the addition of CBT to mebeverine in patients who had IBS of moderate or greater severity after 2 weeks of GP care and 4 weeks of mebeverine. The Symptom Severity Scale (SSS) was used to identify patients with moderate or severe IBS. Patients who continued to report moderate or severe IBS after 4 weeks of mebeverine at a dose of 270 mg three times a day were randomised to receive six sessions of CBT in addition to mebeverine (72 patients) or mebeverine alone (77 patients). These patients were followed at 3, 6 and 12 months after treatment. As part of the baseline evaluation, blood tests for antiendomysial and antigliadin antibodies were carried out on 141 patients to determine the prevalence of coeliac disease in this population.

Main outcome measures: The principal outcome measure was the SSS. Others included the Hospital Anxiety and Depression Scale, psychopathology, the Work and Social Adjustment Scale (WASA, disability), a modified version of the Illness Perception Questionnaire (illness perceptions), the Beliefs about Medicine Questionnaire (attitudes to medication), the Reported Adherence to Medication Scale (adherence to prescribed medication), the Client Service Receipt Inventory (economic analysis), the Cognitive Scale for Functional Bowel Disorders (illness cognitions) and the Behaviour Scale for IBS (IBS coping behaviour).

Results: The addition of CBT produced a significant benefit compared with the mebeverine-only group at 3 months after treatment on all outcome measures, except for the adherence to medication scales. The difference between the groups was 107.8 points on the SSS, 24.5 points on question 4 of the SSS and 6.3 points on the WASA, representing therapeutic gains of approximately 20%, 28% and 40%, respectively. However, there was also evidence that these improvements began to wane, so that at 6 and 12 months follow-up significant therapeutic benefit of the addition of CBT could only be detected on question 4 of the SSS and on the WASA. The behaviour scale for IBS detected significant, positive

changes in coping behaviours at up to 6 months after treatment. Three factors predicting a poor outcome were identified: male gender, believing that IBS had serious consequences and belief in an external aetiology, all of which were associated with greater than average disability at follow-up. The addition of CBT to mebeverine did not reduce overall treatment or social costs. The nested study on testing for coeliac disease provides cautious support for the inclusion of antiendomysial and antigliadin antibody testing in the investigation of patients thought to have IBS.

Conclusions: Specially trained practice nurses can provide effective CBT to primary care patients with a clinical diagnosis of IBS, which although effective does not reduce service or social costs. Using a variety of measures the beneficial therapeutic effects of the addition of CBT to antispasmodic therapy persist for up to 6 months. Future research might include studies of the long-term follow-up of IBS patients treated with CBT, cost–benefit analyses comparing CBT with other therapeutic approaches to IBS, and evaluating means of training both non-specialist health professionals and GPs to deliver CBT.

Contents

List of abbreviations

A&E	accident and emergency
BMQ	Beliefs about Medicine Questionnaire
BS-IBS	Behaviour Scale for Irritable Bowel Syndrome
CBT	cognitive behavioural therapy
CEAC	cost-effectiveness analysis curve
CI	confidence interval
CRP	C-reactive protein
CS-FBD	Cognitive Scale for Functional Bowel Disorders
CSRI	Client Services Receipt Inventory
ESR	erythrocyte sedimentation rate
FBC	full blood count
FU	follow-up
HAD	Hospital Anxiety and Depression Scale
IBS	irritable bowel syndrome
IPQ	Illness Perception Questionnaire
ITT	intention-to-treat
NA	not applicable
OR	odds ratio
RAM	Reported Adherence to Medication Scale
RCT	randomised controlled trial
SD	standard deviation
SPSS	Statistical Package for the Social Sciences
SSS	Symptom Severity Scale
WASA	Work and Social Adjustment Scale

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Background

Effective treatment of irritable bowel syndrome (IBS) in primary care continues to represent a challenge. Building on evidence of the efficacy of cognitive behavioural therapy (CBT) in functional bowel disorders in other settings, a randomised controlled trial was undertaken of CBT in primary care, delivered by specially trained nurses as an adjunct to standard treatment with the antispasmodic agent mebeverine hydrochloride.

Objective

The aim was to determine whether CBT in addition to antispasmodic treatment offers a cost-effective benefit to primary care patients with IBS and to identify predictors of outcome.

Methods

Practice nurses delivered CBT in a randomised trial of the addition of CBT to mebeverine in patients who had IBS of moderate or greater severity after 2 weeks of GP care and 4 weeks of mebeverine. The Symptom Severity Scale (SSS) was used to identify patients with moderate or severe IBS. Patients who continued to report moderate or severe IBS after 4 weeks of mebeverine at a dose of 270 mg three times a day were randomised to receive six sessions of CBT in addition to mebeverine (72 patients) or mebeverine alone (77 patients). These patients were followed at 3, 6 and 12 months after treatment.

The principal outcome measure was the SSS. Other measures were the fourth question on the SSS (measuring the 'global' impact of IBS), the Hospital Anxiety and Depression Scale, psychopathology, the Work and Social Adjustment Scale (WASA, disability), a modified version of the Illness Perception Questionnaire (illness perceptions), the Beliefs about Medicine Questionnaire (attitudes to medication), the Reported Adherence to Medication Scale (adherence to prescribed medication), the Client Service Receipt Inventory (economic analysis), the Cognitive Scale for Functional Bowel Disorders (illness cognitions) and the Behaviour Scale for IBS) (IBS coping behaviour).

As part of the baseline evaluation, blood tests for antiendomysial and antigliadin antibodies were carried out on 141 patients to determine the prevalence of coeliac disease in this population.

Results

The patients were aged between 17 and 54 (mean 34) years and were predominantly white; 82% were female and half had had IBS for more than 5 years.

The addition of CBT produced a significant benefit compared with the mebeverine-only group at 3 months after treatment on all outcome measures, except for the adherence to medication scales. The difference between the groups was 107.8 points on the SSS, 24.5 points on question 4 of the SSS and 6.3 points on the WASA, representing therapeutic gains of approximately 20%, 28% and 40%, respectively. However, there was also evidence that these improvements began to wane, so that at 6 and 12 months follow-up significant therapeutic benefit of the addition of CBT could only be detected on question 4 of the SSS and on the WASA. The behaviour scale for IBS detected significant, positive changes in coping behaviours at up to 6 months after treatment.

Three factors predicting a poor outcome were identified: male gender, believing that IBS had serious consequences and belief in an external aetiology, all of which were associated with greater than average disability at follow-up.

The addition of CBT to mebeverine did not reduce overall treatment or social costs.

The nested study on testing for coeliac disease provides cautious support for the inclusion of antiendomysial and antigliadin antibody testing in the investigation of patients thought to have IBS.

Conclusions

Specially trained practice nurses can provide effective CBT to primary care patients with a clinical diagnosis of IBS, which although effective does not reduce service or social costs. Using a variety of measures the beneficial therapeutic effects of the addition of CBT to antispasmodic therapy persist for up to 6 months.

Implications for healthcare

Non-specialist practice nurses can be trained to deliver CBT in primary care, and the CBT delivered in this way is likely to be beneficial, at least in the medium term, to patients with IBS whose symptoms have not responded to standard therapy.

Recommendations for research

Future research might include:

- studies of the long-term follow-up of IBS patients treated with CBT, perhaps testing the value of top-up sessions to sustain the therapeutic effect
- cost–benefit analyses comparing CBT with other therapeutic approaches to IBS
- evaluating means of training both non-specialist health professionals and GPs to deliver CBT.

Chapter 1
Background

Introduction

Irritable bowel syndrome (IBS) is a chronic non-inflammatory condition characterised by abdominal pain, altered bowel habit (diarrhoea, constipation) and abdominal bloating, but with no detectable pathological change (no identifiable structural or biochemical disorder). IBS is considered to have a psychophysiological basis and therapy is generally directed at symptom control and the reduction of disability. Although symptom-based criteria aid diagnosis they are rarely used in everyday clinical practice[1,2] (see *Boxes 1* and *2*).

IBS is not life-threatening, but is common, affecting 14–24% of women and 5–19% of men in the general population. There is a female predominance with a ratio of 1.4:1 The prevalence of IBS declines with age in women and peak prevalence is in the 20–30-year age group.[3–7] Although the prevalence of IBS remains constant over time there is considerable patient turnover; approximately 2% of men and 4% of women develop symptoms of IBS over 5 years, and 20–30% of patients with IBS lose their symptoms over 5 years.[8,9]

Only 25% of adults with IBS will consult their GP about their symptoms over a 12-month period,[6] yet this represents 4–5% of the adult UK population. As mentioned, there is considerable turnover of new patients in IBS and as long-term follow-up studies have not been conducted the lifetime consultation rate is unknown.

There is no diagnostic test for IBS. GPs are encouraged to identify IBS by its symptoms, to beware of alarm symptoms that may indicate more worrying pathology and to screen the patient with full blood count (FBC) and erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP); tests that should be normal in IBS.[10,11] Further investigations and gastrointestinal endoscopy are recommended if there is concern that the patient might have an alternative condition. Evidence-based guidance has been developed to assist GPs in diagnosing and managing IBS (see www.pcsg.org.uk and Appendix 1). Patients with IBS consult their GP more often over a 6-month period than do age- and gender-matched controls with organic illness.[12] Compared with non-consulting IBS patients, patients with IBS who consult a GP are likely to fear that their symptoms may indicate a dangerous condition, in particular cancer, and they also rate their abdominal pain at a greater severity than do non-consulters.[13]

The majority of IBS patients are managed in primary care and at least over a 12-month period their interaction with the NHS is principally contained within primary care. A minority of patients are referred to secondary care, but may account for up to 50% of the patients seen in gastroenterology outpatient clinics.[14] Patients with IBS may have many extraintestinal, in particular urinary, symptoms and they are frequently referred to urologists, gynaecologists and gastrointestinal surgeons.[15–20] There is an excess of hysterectomy, cholecystectomy and laparoscopy[19,21,22] among these patients and it may be that some of these procedures result from the diagnostic confusion engendered by IBS symptoms. In addition to the direct and indirect costs of IBS there is a significant opportunity cost to the NHS in terms of reduction in the availability of investigation and treatment for patients with other disorders such as inflammatory bowel disease, gastrointestinal cancer and gynaecological pathology.

In 1978 researchers at Bristol derived the Manning criteria from a retrospective analysis of symptoms reported by patients with abdominal pain attending a hospital gastroenterology department[2] (*Box 1*). The criteria were subsequently validated in a community setting. The Rome I (*Box 2*) and Rome II criteria are consensus criteria derived by an international group of gastroenterologists.[1] The Rome criteria have been promoted for use in epidemiological studies and as entry criteria for clinical trials. The Rome II criteria result in greater specificity for IBS but, it has been argued, reduced utility, as the criteria are so specific that they may only identify a minority of patients who would acquire a clinical diagnosis of IBS.

Most GPs do not recognise the Rome criteria, and even the Manning criteria, although useful,

Recurrent abdominal pain and two or more of the following:

- relief of pain with defecation
- more frequent stools at onset of the pain
- looser stools at onset of the pain
- visible abdominal distension
- passage of mucus per rectum
- sensation of incomplete evacuation

BOX 1 *Manning criteria*

Continuous or recurrent symptoms of:

- abdominal pain or discomfort that is:
  relieved with defecation
  and/or
  associated with a change in frequency of stool
  and/or
  associated with a change in consistency of stool

And

- two or more of the following for at least a quarter of occasions or days:
  altered stool frequency
  altered stool form
  passage of mucus
  bloating or a feeling of abdominal distension

BOX 2 *Rome I criteria*

probably do not adequately reflect the clinical use of the term IBS. The resultant diagnostic heterogeneity means that the patient case-mix that would be referred for CBT from clinical practice is likely to be more varied than that which would be recruited to a study where fulfilling either the Rome criteria or the Manning criteria was a necessary prerequisite. The clinical relevance to the NHS of a study that restricted recruitment to patients fulfilling the Rome or Manning criteria would be limited.

GPs are more likely to refer patients who do not acknowledge a psychological aspect to their illness and patients who they have been unable to reassure.[23] Although there are anecdotal reports that referral and investigation may alleviate the concerns of IBS patients there is no published literature to support referral on those grounds. Drawing parallels from chronic fatigue and non-cardiac chest pain (two other medically unexplained syndromes), it may be that such referral and investigation exacerbate problems for at least some patients with IBS.

There is a lack of agreement regarding the aetiology and physiology of IBS, but theories include abnormal gastrointestinal motor function,[24–26] enhanced visceral perception,[27–29] the influence of psychosocial factors such as a history of childhood abuse,[30] genetic predisposition[31–33] and a possible role for enteric mucosal inflammation[34] such as that precipitated by acute bacterial gastroenteritis.[35] To date, studies on the aetiology of IBS have been descriptive or retrospective and longitudinal studies are needed to clarify matters. In keeping with the above discussion the principal triggers to consultation are thought to be psychosocial.[36–38] It would be helpful to gain further information on the interplay among symptoms, cognitions and health behaviour.

Considering that a range of physiological, cognitive, behavioural and social mechanisms precipitates and perpetuates this disorder, it is not surprising that a variety of physical and psychological therapies has been proposed for IBS. In a recent review of available therapies no treatment had a particularly strong benefit over placebo or control.[39] Most of the published studies have been on selected populations; either those attending specialist gastroenterology outpatients or those fulfilling strict trial entry criteria, and this makes it difficult to extrapolate to the patients attending primary care, with their reported differences in psychopathology and symptom severity.

Several pharmaceutical companies are actively engaged in developing medications for IBS. The presently available therapies, although not very effective, are cheap and many are available without prescription. Any new prescription-only medications are likely to increase service costs in IBS. IBS is considered to be a chronic relapsing and remitting disorder and none of the preparations under current research claims to cure the condition. The costs of IBS to the NHS may well be set for a significant increase.

Antispasmodics and cognitive behavioural therapy

There is evidence from a somewhat controversial meta-analysis that some antispasmodics including mebeverine hydrochloride are effective in improving symptoms, as indicated by change in the global effect of IBS. Any effects on unhelpful cognitions and behaviour were not evaluated.[40,41]

Hospital-based studies have reported that IBS may benefit from individual and group cognitive behavioural therapy (CBT).[42–46] This approach to

treatment has not been investigated in primary care and there has been little assessment of the effect of such therapy on the cognitions and behaviour of IBS patients.

Usual care

If one accepts that the usual care provided by a medical practitioner can be helpful to many patients with IBS,[46] whether due to the effect of the doctor–patient interaction or to placebo, and if one also agrees that mebeverine hydrochloride and CBT are of some benefit, then there are two key questions: can these therapies be delivered effectively in primary care and how can the therapy be made available? Mebeverine hydrochloride is already in common use in UK general practice, but some patients who do not improve satisfactorily with GP care and mebeverine hydrochloride may benefit from the addition of CBT.

A cognitive behavioural model for understanding IBS

Although CBT for IBS has been studied in hospital populations the therapies have in the main not been well described. Several studies have shown that stress, for example life events,[47–49] and childhood abuse[50,51] are related to the development of IBS symptoms, thus contributing to vulnerability. There is also evidence that IBS symptoms are exacerbated during stress;[52,53] this is supported by a study showing abnormal gastrointestinal motility in subjects experiencing laboratory-induced stress.[53] It may be that fearful cognitive responses are evoked during stress. Catastrophic cognitions about the meaning of symptoms appear to be common among patients who have particular concerns about their IBS[54] and may result in unhelpful behaviours such as an increase in consulting behaviour. For example, van Dulmen and colleagues found that patients who continue to attribute their symptoms to a purely physical cause are more likely to continue to consult.[45] Unhelpful behaviour may also manifest in a number of other ways such as constantly altering dietary intake, symptom monitoring and a search for a satisfactory therapy. This is usually in order to bring about both control and a reduction in symptoms. Patients may become trapped in a vicious cycle of fear and avoidance. Physiological, cognitive and behavioural responses therefore appear to be interdependent and responsible for maintaining the disorder. Changing cognitions, behaviour or both may bring about improvement in symptoms.

Who should deliver the therapy?

Training courses for CBT in the UK impart generic CBT skills and are relatively intensive. Recruitment is principally restricted to specialist mental health workers and the resultant therapists work almost exclusively in hospital or community psychiatry teams and rarely in the primary care team.

A feature of the primary care nurse is her or his location within the primary care team, working closely with GPs and usually attached to a particular general practice that serves its local population. Primary care nurse training has evolved over the last couple of decades with specialist courses being offered by professional bodies such as the Royal College of Nursing. A feature of practice nursing is the modular nature of skill enhancement. Practice nurses are familiar with courses that equip them with particular skills such as family planning, clinical audit and the management of chronic diseases including asthma, diabetes mellitus and hypertension. If one wishes to increase the availability and accessibility of CBT for IBS then it may be appropriate to develop training courses that are shorter and focused on particular conditions and to broaden the recruitment base for therapists to include non-specialist nurses.

The research team have had prior experience with CBT for medically unexplained conditions through their work on CBT for chronic fatigue syndrome.[55] This study went one step further and provided IBS specific CBT training to experienced primary care nurses with general nursing training, the nurses did not have prior specialist training in psychiatry or gastroenterology. These nurses integrated themselves into the primary care teams in the study practices and provided therapy in the patients' local GP surgery. The service was offered as an addition to the primary care team.

Study case-mix: selection of patients with IBS

As mentioned, there is significant heterogeneity among patients diagnosed with IBS. Some patients diagnosed with IBS by their GP do not fulfil the formal research criteria proposed for the condition [see the paragraph on diagnostic uncertainty (p. 1)]. The GP's pragmatic diagnostic practices

reflect the everyday reality of IBS management in the NHS. Accordingly, it was important in this study to evaluate interventions in patients with a clinical diagnosis as identified by their GP.

CBT for IBS is likely to continue to be a scarce resource. It is probable that if the therapy were to be available in primary care it would be reserved for those patients in whom conventional therapy has failed. It is therefore necessary to identify these subjects for the purpose of this trial. At present it seems that the most useful therapy may be the explanation and advice that patients receive from their GP subsequent to limited investigation and assessment.[46] As mentioned above, there is some evidence to support the use of mebeverine hydrochloride and it is in current use in primary care in the UK. It is relatively inexpensive and it is considered to be a safe therapy. As mebeverine will continue to be a readily available and accepted therapy it would be helpful to determine whether CBT offers any additional benefit for patients who have troublesome IBS in spite of having received usual GP care and a trial of mebeverine hydrochloride. This study design is pragmatic and reflects the management strategy that would be likely to evolve in primary care in the NHS if CBT were to be available for the treatment of IBS.

Choice of study design

A strong placebo effect has been reported among patients with IBS.[56] In addition, the symptoms of IBS can change over time and some patients may become asymptomatic. To control for these factors patients were initially observed for 2 weeks while they received usual care from their GP. All subjects with persistent and significant symptoms were then offered mebeverine hydrochloride and those who had not improved after 4 weeks of therapy were randomised to continue with mebeverine hydrochloride alone or to receive CBT in addition. This study design allowed the researchers to control for any improvement resulting from usual GP care, placebo response and temporal changes in symptoms over the introductory 6 weeks. It follows the recommendations for trials in IBS, and in particular those for therapeutic trials in primary care.[57]

Economic analyses

There have been several cross-sectional surveys of the economic impact of IBS. These have concentrated on the direct and indirect costs. Caution is required when drawing parallels between costs in the USA and in the UK owing to the lack of a comparable denominator and the particular expense of healthcare in the USA. American studies have reported how costly IBS is both in terms of healthcare use and lost productivity, whereas assessments in the UK have been more cautious.[58–66] There has been surprisingly little assessment of the opportunity costs of IBS. In addition, although various new pharmaceutical preparations have been trialled there has been little published economic analysis of these treatments.[67]

CBT will require considerable initial investment in terms of therapist training and sessional treatment. The benefits of CBT may, however, be enduring. This study assessed the effect of CBT on reducing service use in primary and secondary care and on reducing lost productivity.

Predictors of outcome

Several studies have investigated factors that predict outcome in IBS. For example, Blanchard and colleagues reported that elevated scores for anxiety, either measured by the trait scale of Speilberger's State–Trait anxiety inventory,[68] or meeting the criteria for one or more psychiatric disorders as defined in the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition (DSM-III), predicted a poor outcome in IBS.[69]

Harvey and colleagues also reported that greater initial psychological disturbance was associated with poorer outcome in hypnotherapy[70] but, in contrast, Guthrie and colleagues showed that patients with features of anxiety or depression, who identified stress as a factor that exacerbated their abdominal pain and who had IBS of recent onset were most likely to benefit from psychotherapy.[42] They found major differences in physical and psychological status between chronic attendees and new referrals and reported that chronic attendees perceived their abdominal and non-colonic symptoms as being more severe and were more concerned about the possible serious effects of their IBS. Lembo and colleagues showed that patients with IBS of more than 5 years duration had greater psychological morbidity than those with IBS of less than 2 years' duration.[71] In another study the link between the perceived severity of IBS symptoms and psychological morbidity was reinforced when patients whose gastrointestinal symptoms improved also became less anxious and depressed.[72]

The patient's age has been identified as a factor by others and in a study of hypnotherapy, patients over 50 years of age did less well; however, it may be that in this study age actually reflects the duration of the IBS before therapy.[73] There is evidence for a greater therapeutic benefit when the doctor is shown to demonstrate a better understanding of the impact of IBS. Van Dulmen and colleagues showed that patients with IBS who do not improve after consulting a doctor had more somatic attributions and catastrophising cognitions as well as fewer internal causal attributions and expectations of self-efficacy.[46] In other patients anxiety, catastrophising cognitions and a fear of cancer reduced with successive consultations, and patients who improved were less likely to attribute their symptoms to somatic abnormalities. Van Dulmen and colleagues felt that medical consultations had a beneficial effect on dysfunctional cognitions and that beneficial changes that persisted to at least 6 months' follow-up were associated with an improvement in perceived symptoms. Patients improved more when they visited the same doctor throughout and when they were more satisfied with the consultation.[74] When doctors correctly perceived the patient's complaint-related cognitions, positive changes were more likely to occur and in particular patients were more likely to attribute their IBS to psychological factors.

Patients have reported being more satisfied if they are taken seriously and helped to manage their symptoms, although the manner in which this is done can be fraught, leaving many to feel that they are labelled as neurotic.[75] Patients consulting in primary care are more likely than non-consulters with IBS to fear that their symptoms are due to a serious condition such as cancer and also to perceive their symptoms as being more severe than non-consulters.[13] Patients referred to secondary care have greater symptom severity than those retained in primary care and also attribute their symptoms less to stress than do primary care patients.[76] This is in keeping with the findings of a prospective study conducted in UK primary care where referral to a specialist could be predicted by the patient's denial of a role of stress, undergoing multiple testing in primary care and reporting frequent bowel movements.[77] Many of the patients seen in general practice feared that they had cancer and the authors reported that multiple testing may have prolonged their anxiety, citing a paper that emphasises the double-edged nature of normal tests.[78]

Choice of outcome measures

An assessment of the benefit of a therapy in IBS should preferably include measures of clinical, psychological and economic outcomes. In addition, the study aimed to identify factors that predicted a better outcome in IBS. Measures were chosen for each of these outcomes while attempting to keep the number of measures to a minimum.

Follow-up

Because of the relapsing and remitting nature of IBS and the strong placebo effect reported in other studies of IBS therapy, the follow-up in this study extended to 1 year after therapy, making it almost unique in a trial of therapy in IBS.

Chapter 2
Methods

The research team

This study was a collaboration between three departments: the Department of General Practice and Primary Care, initially of the United Medical and Dental Schools of Guy's and St Thomas' Hospitals (UMDS) and latterly, after merger, of Guy's, King's and St Thomas' Medical School (GKT); the Department of Psychological Medicine, initially of King's Medical School and latterly of GKT; and the Centre for the Economics of Mental Health of the Institute of Psychiatry, London. Each department contributed its own expertise, in the epidemiology and management of IBS, the development of CBT for medically unexplained symptoms and the economic analyses of psychological therapies in primary care. At protocol stage the study benefited from the advice of the co-applicants, Dr PJ Whorwell, Specialist Gastroenterologist and Senior Lecturer at Manchester University, and Dr David Armstrong, Reader in Sociology as Applied to Medicine from the Department of General Practice and Primary Care, GKT. Dr Sophia Rabe-Hesketh, Senior Lecturer in Bio-Statistics at the Institute of Psychiatry, provided statistical assistance during data analysis.

A nurse tutor, skilled in CBT and with a background in psychiatric nursing (Mr Simon Darnley, SD) was recruited as a research associate. Four practice nurses were recruited to train as nurse therapists: Ms Rebecca Holt, Ms Tricia Lewis, Ms Sheila Morton and Ms Lyndsey Shephard. These were G-grade nurses who had a general nursing training and who had previously been employed as practice nurses. They were selected by formal interview after advertisement in the general press. A G-grade post is a relatively senior nursing grade and there was a large number of high-quality applicants for the posts. None of the practice nurses had undergone specialist mental health training, specialist training in gastroenterology or training either in the treatment of IBS or in delivering CBT. None of the nurses was known to the study team before recruitment. The training that the nurses received is detailed in the training manual (Appendix 2). In addition to CBT training, the nurses were taught about the clinical aspects of IBS and about the differential diagnosis of gastrointestinal symptoms.

Overview of the study

This was a randomised controlled trial (RCT) in primary care of the addition of CBT to standard GP management of IBS, using the antispasmodic agent mebeverine hydrochloride. The subjects were patients identified as having IBS by their GPs (see section 'Participants', p. 8), and the setting was urban and metropolitan general practice in London. Ten general practices were recruited, serving a population of around 45,000 patients, located principally in south London, with some patients resident in north London; these practices were approached because of existing research or teaching links with the Department of General Practice. All practices were provided with an information pack on the study and were offered a meeting with members of the research team, if required.

The study set out to compare the addition of a standardised package of IBS-specific CBT to treatment with mebeverine hydrochloride at a dose of 270 mg three times a day, chosen on the basis of a previous clinical trial,[79] and which is twice the dose normally recommended in the British National Formulary.[80] This was a pragmatic RCT, in which patients identified by GPs as having IBS, and whose symptoms persisted, were randomised to either continuation of mebeverine alone or the addition of CBT. Throughout the trial all patients were free to consult their GPs as usual, and no effort was made to interfere with normal primary care, apart from reminders to participating GPs to refer patients with a clinical diagnosis of IBS who they thought might be appropriately included in this study.

Objectives

Aims of the study

- To determine the clinical benefit of CBT over and above antispasmodic therapy for IBS in primary care

- to carry out a cost-effectiveness analysis of therapies for IBS in primary care
- to identify factors that predict response in IBS.

A priori hypotheses

The principal hypothesis was that:

- CBT will have additional benefits over mebeverine hydrochloride at 6 months' follow-up.

The subsidiary hypotheses were that:

- mebeverine will alleviate symptoms at discharge, but treatment gains will not be sustained to long-term follow-up
- poor outcome will be associated with an avoidant coping style as measured by the new IBS-specific scale
- symptom improvement will correlate with change in fearful cognitions and avoidant behaviour.

Participants

Stage 1: GPs who participated in this study were asked to refer eligible patients aged between 16 and 51 years who had been diagnosed as having active IBS by their GP, or by a hospital specialist. The patients were not rendered ineligible by the presence of any specific co-morbidity (see inclusion and exclusion criteria, Appendix 3), but were excluded if they were pregnant or breast-feeding, reported any alarm symptoms suggestive of significant inflammatory or neoplastic gastrointestinal disorder (such as unexplained weight loss or unexplained or uninvestigated rectal bleeding), had a past or present disease that would complicate evaluation of the study (including inflammatory bowel disease or a diagnosis of coeliac disease), had abdominal pain relieved by acid-inhibiting drugs (indicating the possibility of a co-existing peptic ulcer disease) or were, for linguistic or intellectual reasons, unable to fill in the self-completed questionnaires. Patients who had a personal history of colorectal cancer or a family history of the disease in a first or second degree relative were also excluded. If the GPs felt that there was no cause for concern in particular patients, they were accepted back into the trial.

Recruitment

The GPs were asked to inform the patients briefly about the purpose of the study and to provide them with an information sheet describing it. Desktop and computer-based reminders and a regular study newsletter were used to encourage recruitment.

Patients were seen by a study nurse in their practice, and completed a baseline assessment and screening for exclusion criteria. At this point the nurses took a blood sample for FBC and ESR, if there was not a record of these tests having been completed in the previous 12 months. Informed consent was obtained at this stage.

The laboratory results were then forwarded to the patient's GP, who was free to carry out further investigations and referral as appropriate, and if necessary to withdraw the patient from the study on the basis of these tests. It was hoped that this reflected normal clinical practice as far as possible, with clinical responsibility being retained by the patient's GP.

Stage 2: After 2 weeks all patients recruited at stage 1 were followed up by one of the study nurses. The 2 weeks between stage 1 and stage 2 replicated normal procedure, where the GP can follow up the blood test results, give advice to the patient and negotiate further management or investigation. Patients completed the same assessment instruments as at baseline and were offered mebeverine hydrochloride at a dose of 270 mg three times a day if they still fulfilled the criteria for IBS and reported moderate or greater severity of IBS on the irritable bowel Symptom Severity Scale (SSS). Study nurses made extensive use of mobile and landline telephones to confirm appointments and facilitate new appointments where necessary. Patients also had access to an answerphone facility where messages could be left out of office hours. Patients who failed to attend their appointment were telephoned and encouraged to attend. The study nurse provided subjects with a prescription for mebeverine signed by their GP. This mirrors current practice in primary care and similar arrangements are common for prescription of the oral contraceptive pill, asthma therapy and the management of other chronic diseases in nurse-led clinics.

Stage 3: Patients were followed up 4 weeks later (6 weeks after recruitment), when they were seen by the study nurse and completed the assessment instruments. If they still had IBS of moderate or greater severity on the SSS they were randomised to continue with their present therapy or to receive CBT in addition to mebeverine hydrochloride. This design allowed the researchers to control for any effect of the doctor–patient

interaction, the strong placebo effect noted in IBS and the spontaneous improvement in IBS that can occur over time.

Stage 4: Patients had an initial follow-up assessment at stage 4 (9 weeks after randomisation), at which time they were discharged from treatment and back to their own GPs. They were then followed up by postal questionnaire at 3, 6 and 12 months postdischarge.

An attempt was made to monitor all of the patients referred to the study, including those who only received advice and explanation from their GPs, those who received mebeverine but did not proceed to randomisation and those who were allocated to the trial therapies. Patients unable to attend the second, third or fourth appointment were contacted by telephone and were asked to complete the study instruments by post.

Interventions

The intervention in this study was the addition of a course of CBT consisting of six 50-minute sessions delivered by face-to-face contact with a trained nurse. The therapy was delivered as described in the CBT manual (see Appendix 2) and all sessions were audiotaped. SD reviewed all therapy sessions in the company of the nurse therapists. Treatment progress was reviewed at each session and goals were adjusted in collaboration with the nurse. These review sessions were used to refine the skills of the nurse therapists.

Both CBT and control groups continued to receive prescriptions for mebeverine hydrochloride from their GP at a dose of 270 mg three times a day. The study nurse arranged the medication at the appropriate assessment intervals. The care of the study patients remained with their GP, but the study nurse attempted to see all subjects for a follow-up assessment.

Outcome measures

Study nurses collected initial data on age, gender and social class from all subjects, who also completed baseline instruments assessing the clinical severity of their IBS (SSS),[81] their levels of psychopathology [Hospital Anxiety and Depression (HAD) Scale],[82] their perception of their illness [Illness Perception Questionnaire (IPQ)],[83] and their coping behaviour [Behaviour Scale for Irritable Bowel Syndrome (BS-IBS)], as well as their cognitions regarding IBS [Cognitive Scale for Functional Bowel Disease (CS-FBD)],[84] the disability resulting from IBS [Work and Social Adjustment Scale (WASA)][85] and the costs of their IBS [Client Service Receipt Inventory (CSRI)].[86] Concordance with medication was assessed by the RAM scale.[87] The patients' beliefs about medication in general and IBS medicines in particular were assessed using the BMQ.[87] Copies of unpublished scales are appended (Appendices 3–5). These measures were repeated at randomisation, at the completion of therapy and at 3-, 6- and 12-month subsequent time-points.

Patients were asked how long they had had IBS, and whether their IBS had begun with gastroenteritis, whether they had consulted for psychological problems in the previous 5 years, whether they had a family history of IBS and whether they used alternative or complementary treatment for IBS. They were asked to indicate their ethnic background.

The Symptom Severity Scale (SSS)

The SSS is an IBS-specific instrument that is sensitive to change over time. The SSS was used in preference to the Functional Bowel Disorder Severity Index as the SSS is more comprehensive and includes an assessment of the impact of IBS on general well-being. Symptom diaries were not used, as such instruments are difficult to maintain over a long follow-up period. The SSS is easy to complete and has satisfactory reliability in secondary care. The maximum score on the scale is 500 and patients may be considered to have mild IBS (75–174), moderate IBS (175–299) or severe IBS (300–500). Scores below 75 indicate normal bowel function.

The Hospital Anxiety and Depression Scale (HAD)

The HAD is a measure of psychopathology that avoids overlap with somatic distress. It is commonly used in IBS studies. Although initially developed for use in hospital populations it has also been used successfully in general practice.

It consists of seven depression items and seven anxiety items. All items are represented on a four-point scale and some items are reverse scored. Scores for each item range from 0 to 3 and the higher the score the more severe the disorder. The maximum score for each subscale is 21. Scales are also interpreted according to whether they would be likely to represent clinically significant anxiety

or depression as judged by psychiatric interview. Scores between 11 and 21 are likely to indicate definite anxiety and depression (i.e. cases), while scores between 8 and 10 are likely to be obtained by mildly disturbed patients (doubtful cases).

The Illness Perception Questionnaire (IPQ) adapted for IBS [IPQ (ibs)]

The IPQ was developed by Professor John Weinman, a colleague at the Department of Psychology, GKT. The authors' adapted version helped them to identify the coping beliefs of people with IBS; whether they are patients who do or do not benefit from GP advice, treatment with mebeverine hydrochloride or additional treatment with CBT. The instrument seemed well suited to assessing changes in perception of illness and symptoms.

It has five scales providing information on five components considered to underlie the cognitive representation of illness. These are: identity (the symptoms that the patient associates with the illness), cause (personal ideas about aetiology), timeline (the perceived duration of the illness), consequences (expected effects and outcome) and cure-control (how one controls or recovers from the illness).

For this study the SSS was used to assess symptoms and so the identity scale was not scored. The other IPQ scales were rated on a five-point scale ranging from strongly disagree (scored as 1) to strongly agree (scored as 5). After reverse-scoring appropriate items the scores for timeline, consequences and cure-control were obtained by summing the relevant scale items and dividing by the number of items constituting that component. For the cause scale the items that address external versus internal factors were identified and summed in a similar manner to that described above. The scores for each component therefore range from 1 to 5.

The results for the components can be interpreted as follows: a high score on the external cause component indicates greater agreement that IBS has an external cause, with similar interpretations available for score on the internal cause, component. A high score for the timeline component indicates greater agreement that IBS will last for a long time or may be permanent, and on the consequences component that the consequences of having IBS are more likely to be serious with significant impact on the patient's life, their economic well-being, how they view their health, how they view themselves and how they believe others view them.

The cure-control component is scored in an optimistic fashion, with a high score indicating agreement that the condition will respond to therapy, and is not due to chance or fate, and that the patient can do a lot to improve his or her illness. Again it is scored from 1 to 5.

The Client Services Receipt Inventory (CSRI)

The CSRI was developed by Professor Martin Knapp and enabled a detailed description to be completed of service use patterns, employment and household/family responsibilities, as well as an analysis of the cost-effectiveness of the various treatment strategies, including direct and indirect costs.

Data were collected on the current living accommodation and expenses of the patients, including income, employment and accommodation, followed by questions on the use of health care, social care and other services over a defined period. Unit costs for each of these services are applied to the resource-use data to obtain the total costs associated with each client's use of services. Patients were asked to provide details of services they had used during the previous 3 months (deemed to allow for relatively accurate recall and to be representative of service use). Services assessed were GP, practice nurse and other primary care services, inpatient care, outpatient care, osteopaths, chiropractors, physiotherapists, counsellors and acupuncturists/homoeopaths. Patients were asked for details of the hospital speciality attended and length of inpatient stay was recorded. For other services patients were asked for details of the number and average duration of contacts. The costs for outpatient attendances were the average for each speciality; these and other unit costs were obtained from an available source[88] (Appendix 6).

Production costs were calculated from details of employment status and time lost from work.

Work and Social Adjustment Scale (WASA)

This measure of handicap consists of five visual analogue scales covering ability to work, ability to manage the home, social and private leisure activities, and relationships. Respondents were asked how much their IBS symptoms affected each of these designated areas.

Patients scored the impact of IBS on their ability to carry out day-to-day tasks. These tasks were divided into work, home management, social leisure activities, private leisure activities, and family and relationships. Each component of the scale was assessed on a Likert scale ranging from 0 (not impacting at all) to 8 (impacting very severely). The total score ranged from 0 to 40.

Reported Adherence to Medication Scale (RAM)

Non-adherence is indicated by the tendency to forget to take medication and deliberately to adjust or alter the dose from that recommended. The scale comprises five adherence statements scored on five-point Likert scales, where 1 = always true and 5 = never true. The results are presented as the sum of the scale items divided by the number of questions in the scale, and range from 1 to 5. A higher score indicates greater reported adherence.

Behaviour Scale for Irritable Bowel Syndrome (BS-IBS)

This is a new questionnaire designed and validated by the researchers. It allows assessment of changes in specific coping behaviours used by patients with IBS. The scale has 29 items, each with a Likert scale from 1 (never) to 7 (always), indicating how persistently the particular behaviour is carried out. The total score, calculated by summing the responses to the 29 components, ranges from 29 to 203.

Cognitive Scale for Functional Bowel Disorders (CS-FBD)

This validated scale allows assessment of a patient's illness cognitions regarding their functional bowel disorder. It is scored using a Likert scale for each item ranging from 1 (strongly disagree) to 7 (strongly agree) with no reversed scoring. The composite score, derived by summing the values for the individual questions in the scale, ranges from 25 to 175. High scores on the scale indicate negative cognitions regarding IBS symptoms, consequences and self-worth.

Beliefs about Medicine Questionnaire (BMQ)

The BMQ comprises two sections: the BMQ specific, which assesses representations of medicines prescribed for personal use, and the BMQ general, which assesses beliefs about medicines in general. The BMQ specific comprises two five-item factors assessing beliefs about the necessity of particular medication (specific – necessity) and concerns about prescribed medication based on beliefs about the danger of dependence and long-term toxicity and the disruptive effect of medication (specific – concerns). The BMQ general comprises two four-item factors assessing beliefs that medicines are harmful, addictive poisons that should not be taken continuously (general – harm), and that medicines are overused by doctors (general – overuse). The questions are scored on five-point Likert scales ranging from 1 (strongly disagree) to 5 (strongly agree).

Additional information was collected on bowel and dietary habits, medication consumption, and the number of GP visits before and after treatment. Assessments were repeated at each follow-up, principally by postal questionnaires.

Interpretation

The IPQ has a number of subscales all based on five-point Likert scales ranging from 1 to 5. Scores greater than 2.5 indicate the patient's belief that IBS has an external or an internal cause, or that IBS will be an enduring condition and have serious consequences but will be curable and within the patient's control.

Scores greater than 2.5 for subscales on the BMQ have similar implications with regard to the patient's beliefs that medicines in general are overused or harmful and that the patient's medications for IBS are necessary or pose cause for concern.

The RAM Scale is rated from 1 to 5, with a higher score indicting greater reported adherence.

Screening for coeliac disease

Coeliac disease is an inherited gastrointestinal condition characterised by an intolerance of gliadin, a subfraction of the gluten protein present in wheat and some other grains. The present understanding of the epidemiology of coeliac disease has been transformed by the development of highly sensitive and specific serological tests. It is now known to be more common than has been previously recognised and that a spectrum of disorder exists. Some patients have classical symptoms of malabsorption, others report atypical symptoms secondary to iron-deficiency anaemia and osteoporosis, while a further asymptomatic group with latent coeliac disease is considered to have the potential to develop problematic coeliac disease. Patients with positive serology who subsequently undergo confirmatory jejunal biopsy

are advised to keep to a life-long gluten-free diet. One study has reported a high prevalence of positive serology in patients attending a specialist gastrointestinal clinic who fulfilled the Rome II criteria for IBS. This has prompted concern that coeliac disease may be misdiagnosed as IBS, not only in secondary care, but also in primary care, where standardised criteria are rarely used. Some authorities have recommended the routine use of serological testing in patients thought to have IBS. The researchers took advantage of this trial of CBT to determine the prevalence of positive serology for IBS among patients referred to the trial and to match their results with information on place of diagnosis (primary or secondary care) extracted from the GP notes. This was an additional study question and ethical approval was needed before proceeding. Some patients had already been recruited to the study before ethical approval was received. The results and implications of testing for coeliac disease are reported separately in Chapter 5.

Sample size calculation

A sample size calculation conducted before the study assumed that follow-up in the CBT plus mebeverine group would see a mean score on the SSS of 133 (mild IBS) (SD = 80), and a score of 180 (moderate IBS) (SD = 80) at follow-up in the mebeverine hydrochloride group. This indicated that 62 patients would be needed in each group to reject the null hypothesis, that there is no difference between the groups, with 90% power and 95% confidence. Using the pretrial assumptions for dropout and attrition rates, it was estimated that the study would need to recruit 240 patients with IBS to meet the requirements. In total, 235 patients were recruited; 72 patients were allocated to the mebeverine plus CBT arm and 77 to the mebeverine arm. Nine of the patients allocated to CBT and mebeverine declined to take part.

Randomisation

All eligible patients were randomised into two therapy groups using random numbers derived in blocks of four from random number tables. A statistician unconnected to the study generated the randomisation. He kept a copy of the randomisation codes and provided a further copy to a clerical member of the departmental staff who was not involved in the study and who was tasked to prevent access to the list from the study team to assure concealment. The study numbers are sufficiently large to expect homogeneity of the two groups. Written informed consent was obtained from each subject before randomisation and patients were allocated to therapy if they were eligible for therapy after completion of their third set of assessment instruments. The clerical staff member maintained a record of the allocations and planned allocations were checked against actual therapies received at the end of the study.

Statistical methods and data analysis

Data were entered onto a personal computer using the Statistical Package for the Social Sciences (SPSS). Missing items were dealt with by creating a prorated or imputed score when at least 75% of the items used to create a score were present (e.g. HAD and SSS). Simple data summaries were carried out in SPSS, as well as linear regression to identify variables that when assessed at baseline predict improved outcome on the WASA. The data were then transferred to Stata (version 8.2) for the analysis of the effect over time of randomised treatment on the outcome measures described above.

This study design led to the randomisation of patients into two groups after their third assessment. Eligible patients were allocated to continue on mebeverine hydrochloride alone or to receive CBT in addition to mebeverine hydrochloride. It is these two groups that were eligible for analysis on an intention-to-treat (ITT) basis.

There was, however, another group, comprised of those patients who were not allocated to therapy because either they did not attend the necessary visits or they did not gain a sufficient score on the IBS SSS in the run-up to randomisation. Some analysis of these patients has been included out of interest. Comparison of the results from these patients to the results from the therapy groups must be treated with caution as the patients were not part of the ITT analysis.

Many of the study instruments such as the HAD generated a summed score. If some of the constituent questions were incomplete a prorated value was imputed when 75% or more of the score's constituent data were available.

For each continuous variable, a fully saturated multiple regression model was used to assess the

treatment effect at every visit after randomisation (1.5, 3, 6 and 12 months). To adjust for chance differences between treatment groups and increase accuracy, the baseline value of the same variable (averaged across the first three visits) was added as a covariate.[89] To take account of the longitudinal design, with repeated measurements observed on the same subjects, regression using generalised estimating equations (GEE)[90] with robust standard errors based on the sandwich estimator for clustered data was used.[91] GEE is a population-averaged method, which in this context gives equal weight to each patient, rather than to each observation, thereby adjusting for missing data. In addition to handling the interdependence of observations on the same person, these standard errors are also sufficiently robust to model misspecifications such as departures from normality or non-constant residual variances. For subjects with missing data, all available data contributed to the analysis.

The SSS banding is an ordinal (ordered) scale. It was analysed using ordered logistic regression, again with robust standard errors for clustered data, with the same predictors.

In all cases, following model estimation, the average treatment effect was estimated by a suitable linear contrast, and a model-based test was carried out for any differences in treatment effect over time.

Graphs for each outcome show the means and confidence interval (CI) at all time-points, calculated by standard methods.

Economic analysis

An economic evaluation of the direct and indirect costs of managing IBS and a cost-effectiveness analysis of the two treatments were carried out using data collected from the CSRI. Effects on service-use patterns, employment and household/family responsibilities were also investigated. Costs were calculated as the best approximations of long-run marginal opportunity costs, and reflected the local realities of service provision. This study offered an opportunity to carry out a global economic assessment of the costs of IBS, as subjects with IBS progressed through the various staged treatment options.

Recruitment

Patients were recruited between July 1999 and October 2001. The IBS SSS had not previously been used in a primary-care population and it was difficult to predict how many referred patients would be suitable for randomisation if this instrument were to be used to screen for severity. Referral to the study exceeded predicted referral rates, but the attrition rate in response to 2 weeks of GP care followed by 4 weeks of mebeverine hydrochloride was greater than expected and so it took a little longer than predicted to reach the target number of patients for randomisation. The study nurses were recruited on a part-time basis, so allowing four nurses to be recruited and a greater number of practices to be covered for a longer period than would otherwise have been feasible within the allocated funds. The trial profile showing the disposition of patients at each stage is shown in *Figure 1*.

Research ethics approval

Ethical approval was obtained from the research ethics committees serving each of the three areas in which patients were recruited.

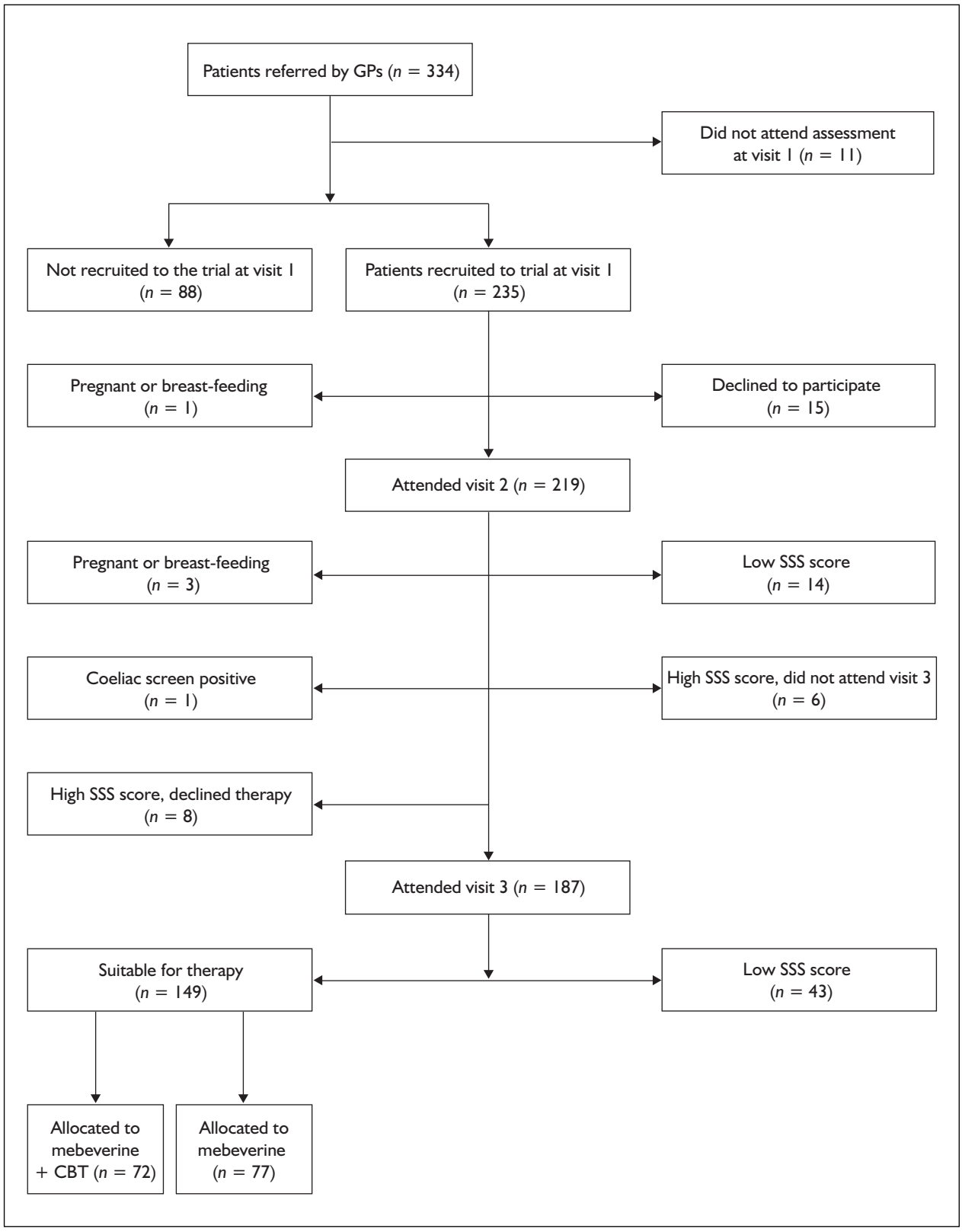


FIGURE 1 *Trial profile (continued in* Figure 2, *p. 20)*

Chapter 3
Results

Patient recruitment

Over a period of 27 months, 334 patients were referred to the study from ten general practices with a study population of 45,000 patients. One patient did not attend the assessment visit and of those attending 88 did not proceed to the second assessment. *Table 1* details the reasons why the 88 patients did not proceed. Some of the study practices were also recruiting to a trial of psychological therapy in chronic fatigue syndrome and one of the patients referred to this trial had already been recruited to that study. That patient was excluded from this study. Of the 31 patients declining recruitment at visit 1 there were 19 women and ten men. The most frequent reason given was difficulty in leaving work or family commitments to attend the CBT sessions.

A study nurse saw all patients in their local general practice surgery within 2 weeks of referral to the study. Each patient's GP was informed by letter as to the outcome of any consultation with the study nurse. There were eight protocol violations when patients who should have been excluded as exceeding the upper age limit were recruited to the study; five of these were allocated to the mebeverine plus CBT arm of the trial and three to the mebeverine-only arm. The oldest was 54, six were 51 and one was 52.

Baseline patient characteristics

The baseline demographics of the 235 patients who agreed to participate in the study are shown in *Table 2*. The mean age was 33.8 years (SD 8.6).

TABLE 1 *Patients not recruited to the trial after assessment at visit 1*

	Not recruited to the trial at visit 1
Reason	***n* (%)**
Declined to participate	31 (31.6)
Too old	46 (52.3)
Too young	1 (1.1)
Moving out of study area	3 (3.4)
Recruited to chronic fatigue trial	3 (3.4)
Awaiting *in vitro* fertilisation	1 (1.1)
Learning difficulty	1 (1.1)
Prior diagnosis of colitis	1 (1.1)
Breast-feeding	1 (1.1)

The majority of patients were women and most identified their ethnic origin as being white. Just over half the patients had been diagnosed with IBS for less than 5 years. A considerable proportion of patients had tried alternative or complementary therapy for their IBS. The severity of IBS was distributed across the four bands of the SSS, with 1.7% having normal IBS, 7.7% mild IBS, 38.3% moderate IBS and 52.3% severe IBS. A considerable proportion (43%) of patients had consulted a health professional regarding a psychological problem in the previous 5 years and the Rome I criteria for the diagnosis of IBS were fulfilled by 84.7% of patients.

A summary of historical data on the 235 patients recruited to the study is given in *Table 3*. This gives an overview of some clinical aspects of IBS and, notably, indicates that almost one-fifth of subjects believed that their IBS started with an episode of gastroenteritis. *Table 4* describes the demography of the study sample in greater depth

TABLE 2 *Demographic characteristics of patients entering the trial (n = 235)*

Age, (years)	
Mean (SD)	33.8 (8.6)
Range	17–54
Gender, *n* (%)	
Male	43 (18.3)
Female	192 (81.7)
Ethnicity, *n* (%)	
White British	153 (65.1)
Irish	6 (2.6)
Any other white origin	21 (8.9)
Black Caribbean	13 (5.5)
Black African	8 (3.4)
Any other black origin	1 (0.4)
White and black Caribbean	3 (13)
White and Asian	2 (9)
Any other mixed origin	3 (1.3)
Pakistani	1 (0.4)
Bangladeshi	2 (0.9)
Any other Asian origin	2 (0.9)
Any other origin	3 (1.3)
No ethnicity identified	17 (7.2)
Marital status, *n* (%)	
Single	84 (35.7)
Married/cohabiting	105 (44.7)
Widowed/separated/divorced	46 (14.6)

TABLE 3 *Relevant clinical data at recruitment*

Variable		*n* (%)
Duration of IBS before recruitment	3 months to 1 year	38 (16.2)
	1–5 years	84 (35.7)
	> 5 years	113 (48.1)
Family history of IBS	Yes	82 (34.9)
	No	153 (65.1)
Use of alternative therapies for IBS before recruitment	Yes	61 (26.0)
	No	174 (74.0)
Consulted a health professional for psychological problems in the 5 years before recruitment	Yes	102 (43.4)
	No	133 (56.6)
Considers IBS to have begun following an episode of gastroenteritis	Yes	39 (16.6)
	No	196 (83.4)
Expressed therapy preference before randomisation	CBT and mebeverine	94 (40.0)
	Mebeverine alone	24 (10.2)
	No preference expressed	43 (18.3)
	Missing data	74 (31.5)

and allows comparison between the two therapy groups with no significant differences between them.

Diagnosis of IBS

The GP records of 213 consecutive patients were reviewed. Of these, 149 (70%) had been diagnosed by their GP without referral to hospital gastroenterology departments and 64 (30%) had been referred to secondary care before diagnosis. Rome I criteria were fulfilled by 85.1% of patients diagnosed in primary care only and by 87.5% of patients who had also been seen by a specialist gastroenterologist (χ^2 test, $p > 0.6$).

Results of investigations

Blood samples for FBC were taken from 208 patients. Two patients had reduced haemoglobin (<11.5 g dl^{-1}). One had a prestudy diagnosis of an autoimmune disorder (not inflammatory bowel disease) and the other patient was a woman with a haemoglobin of 10.1 g dl^{-1} with no cause identified for her anaemia. Samples for ESR were taken from 207 patients, of which 12 had an elevated result. There were relevant prestudy diagnoses for some of these; one patient had respiratory tuberculosis, three patients had autoimmune disorders (not inflammatory bowel disease), three patients had undergone extensive gastrointestinal investigation with normal results, and five patients with elevated tests did not have a satisfactory explanation for their result in their prestudy GP notes. The patients' GPs were informed by letter regarding all test results. Results of testing for coeliac disease are provided in Chapter 5.

Quantitative data

Results were available at some stage on all 235 patients. Follow-up response rates are shown in *Table 5*. Some patients only completed the main outcome instruments in their questionnaire packs. Some patients were not taking any medication for IBS, and this is indicated under the table entry for the RAM. Patients were reminded to return their questionnaires by telephone, with further questionnaires being sent out as necessary. Telephone contact also facilitated the maintenance of accurate address details. Patients' mobile phone numbers were of particular use.

Treatment allocation and baseline values

It can be seen from the study profile (*Figure 1*) that there was considerable attrition of the sample between referral and the third assessment, when treatment allocations were made. Of the 235 patients recruited at the first assessment with the study nurse, 219 attended the second appointment, at which time, if they were eligible, they were provided with a 4-week course of mebeverine hydrochloride. By the third assessment 187 patients were assessed and 149 were eligible for randomisation. At allocation 72 patients were offered CBT in addition to their mebeverine hydrochloride and 77 were allocated to continue on mebeverine hydrochloride alone.

TABLE 4 *Demographic profiles at baseline by ITT*

	ITT group		
	Mebeverine + CBT (*n* = 72)	**Mebeverine (*n* = 77)**	**Not allocated to therapy (*n* = 43)**
Age (years)			
Mean (SD)	33.8 (9.7)	33.6 (8.6)	34.3 (8.1)
Gender, *n* (%)			
Women	61 (84.7)	66 (85.7)	35 (81.4)
Men	11 (15.3)	11 (14.3)	8 (18.6)
Ethnicity, *n* (%)			
White British	51 (70.8)	48 (62.3)	32 (74.4)
Irish	3 (4.2)	1 (1.3)	
Other white origin	7 (9.7)	7 (9.1)	3 (7.0)
Black Caribbean	4 (5.6)	5 (6.5)	3 (7.0)
Black African	2 (2.8)	4 (5.2)	1 (2.3)
Other black origin			
Pakistani		1 (1.3)	
Bangladeshi	1 (1.4)	1 (1.3)	
Other Asian origin		2 (2.6)	
White and black Caribbean	1 (1.4)	2 (2.6)	
White and Asian	1 (1.4)		
Other mixed origin			2 (4.7)
Any other origin		2 (2.6)	1 (2.3)
Missing	2 (2.8)	4 (5.2)	1 (2.3)
IBS duration, *n* (%)			
3 months to 1 year	10 (13.9)	14 (18.2)	4 (9.3)
1–5 years	28 (38.9)	23 (28.9)	20 (46.5)
> 5 years	34 (47.2)	40 (51.9)	19 (44.2)
Family history of IBS, *n* (%)			
No	45 (62.5)	46 (59.7)	30 (69.8)
Yes	27 (37.5)	31 (40.3)	13 (30.2)
Alternative therapies, *n* (%)			
No	58 (80.6)	54 (70.1)	27 (62.8)
Yes	14 (19.4)	23 (29.9)	16 (37.2)
Psychological problems in previous 5 years, *n* (%)			
No	33 (45.8)	45 (58.4)	28 (65.1)
Yes	39 (54.2)	32 (41.6)	15 (34.9)
IBS began with gastroenteritis, *n* (%)			
No	59 (81.9)	62 (80.5)	37 (86.0)
Yes	13 (18.1)	15 (19.5)	6 (14.0)
Treatment preferences, *n* (%)			
No preference	22 (30.6)	19 (24.7)	1 (2.3)
CBT + mebeverine	42 (58.3)	42 (54.5)	7 (16.3)
Mebeverine	8 (11.1)	16 (20.8)	
Missing data	0	0	35 (81.4)
Rome positive at visit 1, *n* (%)			
No	11 (15.3)	8 (10.4)	9 (20.9)
Yes	61 (84.7)	69 (89.6)	34 (79.1)

In all, 155 patients were offered mebeverine at visit 2. In those who completed the study assessment pack at visit 3 but were not offered therapy, a low SSS score had been recorded by 39 at visit 3, and by 14 at visit 2, making them ineligible for allocation. *Table 6* summarises the quantitative data on patients recruited to the study, and patients represented in *Table 7* constitute the ITT group. Using *t*-tests no statistically significant differences were shown between the two therapy groups in any of the variables recorded at the third assessment.

TABLE 5 *Data availability*

Measure	Visit 1 *n* (%)			Visit 2 *n* (%)			Visit 3 *n* (%)			Visit 4 *n* (%)			Visit 5 *n* (%)			Visit 6 *n* (%)			Visit 7 *n* (%)		
	Meb	Meb + CBT	No therapy	Meb	Meb + CBT	No therapy	Meb	Meb + CBT	No therapy	Meb	Meb + CBT	No therapy	Meb	Meb + CBT	No therapy	Meb	Meb + CBT	No therapy	Meb	Meb + CBT	No therapy
SSS	77 (100)	72 (100)	43 (100)	77 (100)	72 (100)	43 (100)	777 (100)	72 (100)	43 (100)	71 (92.2)	58 (80.6)	35 (81.4)	49 (63.6)	52 (72.2)	31 (72.1)	58 (75.6)	53 (73.6)	29 (67.4)	58 (75.3)	52 (72.2)	27 (62.8)
HAD	76 (98.7)	72 (100)	43 (100)	76 (98.7)	72 (100)	42 (97.7)	75 (97.4)	70 (97.2)	43 (100)	70 (90.9)	57 (79.2)	35 (81.4)	52 (67.5)	53 (73.6)	31 (72.1)	56 (72.7)	52 (72.2)	28 (65.1)	57 (74.0)	53 (73.6)	29 (67.4)
WASA	77 (100)	72 (100)	43 (100)	75 (97.4)	72 (100)	43 (100)	74 (96.1)	69 (95.8)	43 (100)	70 (90.9)	55 (76.4)	35 (81.4)	50 (64.9)	52 (72.2)	31 (72.1)	58 (75.3)	54 (75.0)	29 (67.4)	58 (75.3)	51 (70.8)	27 (62.8)
CS-FBD	77 (100)	72 (100)	43 (100)	76 (98.7)	72 (100)	43 (100)	75 (97.4)	69 (95.8)	43 (100)	70 (90.9)	56 (77.8)	35 (81.4)	50 (64.9)	52 (72.2)	31 (72.1)	57 (74.0)	54 (75.0)	28 (65.1)	52 (67.5)	50 (69.4)	23 (53.5)
BS-IBS	73 (94.8)	68 (94.4)	40 (93.0)	NA	NA	NA	NA	NA	NA	70 (90.9)	57 (79.2)	34 (79.1)	50 (64.9)	52 (72.2)	31 (72.1)	57 (74.0)	54 (75.0)	28 (65.1)	53 (68.8)	50 (69.4)	24 (55.8)
IPQ(ibs)	77 (100)	72 (100)	43 (100)	76 (98.7)	72 (100)	43 (100)	75 (97.4)	69 (95.8)	43 (100)	70 (90.9)	56 (77.8)	35 (81.4)	50 (64.9)	52 (72.2)	31 (72.1)	58 (75.3)	53 (73.6)	28 (65.1)	53 (68.8)	50 (69.4)	24 (55.8)
BMQ	77 (100)	72 (100)	43 (100)	76 (98.7)	72 (100)	43 (100)	73 (94.8)	69 (95.8)	43 (100)	70 (90.9)	55 (76.4)	35 (81.4)	50 (64.9)	52 (72.2)	31 (72.1)	58 (75.3)	53 (73.6)	29 (67.4)	53 (68.8)	50 (69.4)	24 (55.8)
RAM	76 (98.7)	71 (98.6)	43 (100)	77 (100)	72 (100)	44 (100)	74 (97.4)	68 (94.4)	42 (97.7)	70 (90.9)	55 (76.4)	34 (79.1)	49 (62.3)	52 (70.8)	31 (72)	57 (79.2)	55 (76.4)	29 (67.4)	46 (59.7)	47 (65.3)	21 (48.8)
Not taking Meb	19 (23.4)	15 (18.1)	14 (23.6)	16 (20.7)	14 (19.4)	14 (32.6)	1 (1.3)	0	3 (7.0)	4 (5.2)	3 (4.2)	5 (11.6)	3 (4.0)	3 (4.2)	4 (9.3)	6 (7.8)	7 (9.7)	5 (11.6)	4 (5.2)	3 (4.2)	3 (7.0)

Meb, mebeverine hydrochloride; NA, not applicable.

TABLE 6 *Summary of data recorded at the first assessment for the 235 patients recruited to the study*

Assessment instrument	Mean (SD)
SSS total score	297.7 (94.8)
SSS question 4	66.0 (22.4)
WASA	14.3 (8.1)
CS-FBD	108.7 (30.3)
HAD total score	18.1 (7.2)
HAD anxiety score	11.0 (4.5)
HAD depression score	7.2 (3.8)
BS-IBS (at visit 1)	92.2 (24.5)
IPQ	
External cause	2.6 (0.5)
Internal cause	3.1 (1.1)
Timeline	3.2 (0.9)
Consequences	2.8 (0.8)
Cure control	3.0 (0.6)
BMQ general	
Medicines are overused	3.1 (0.8)
Medicines in general are harmful	2.5 (0.6)
BMQ specific	
My IBS medicines are necessary	2.9 (0.9)
I am concerned about taking my IBS medicines	2.9 (0.8)
RAM	3.6 (0.8)

TABLE 7 *Data recorded at the third assessment (just before randomisation) for those in the ITT group*

Assessment instrument	Mebeverine (*n* = 77) Mean (SD)	Mebeverine + CBT (*n* = 72) Mean (SD)	*p*
SSS total score	310.2 (84.4)	295.5 (75.7)	0.3
SSS question 4	63.6 (23.1)	60.5 (17.0)	0.4
WASA	15.1 (8.3)	15.3 (8.7)	0.9
CS-FBD	112.4 (27.6)	111.2 (25.4)	0.8
HAD total score	18.1 (7.4)	16.6 (6.4)	0.2
HAD anxiety score	11.0 (4.7)	9.9 (4.3)	0.1
HAD depression score	7.1 (3.3)	6.7 (3.0)	0.5
BS-IBS (at visit 1)	96.1 (24.3)	98.4 (21.3)	0.5
IPQ			
External cause	2.5 (0.5)	2.6 (0.6)	0.5
Internal cause	2.9 (1.0)	2.9 (1.2)	0.9
Timeline	3.6 (0.8)	3.6 (0.7)	0.8
Consequences	3.1 (0.7)	3.0 (0.6)	0.3
Cure-control	3.5 (0.5)	3.5 (0.4)	0.9
BMQ general			
Medicines are overused	2.9 (0.8)	3.1 (0.8)	0.1
Medicines in general are harmful	2.4 (0.6)	2.5 (0.6)	0.5
BMQ specific			
My IBS medicines are necessary	2.7 (0.8)	3.0 (0.9)	0.05
I am concerned about taking my IBS medicines	2.7 (0.8)	2.8 (0.7)	0.7
RAM	3.3 (1.0)	3.4 (1.0)	0.5

Delivery of CBT

Many of the 72 patients allocated to mebeverine plus CBT did not attend the full course of therapy. Some declined, some dropped out, and others moved out of the study area and were unable to travel to take part in the CBT sessions. The progress of patients though therapy is illustrated in *Figure 2* and detailed in *Tables 8* and *9*. The therapists reported on whether they felt the patient had adequately completed therapy and, if not, they recorded a reason for non-completion when possible. There were four nurse therapists and the number of patients for CBT per therapist ranged from 11 to 23.

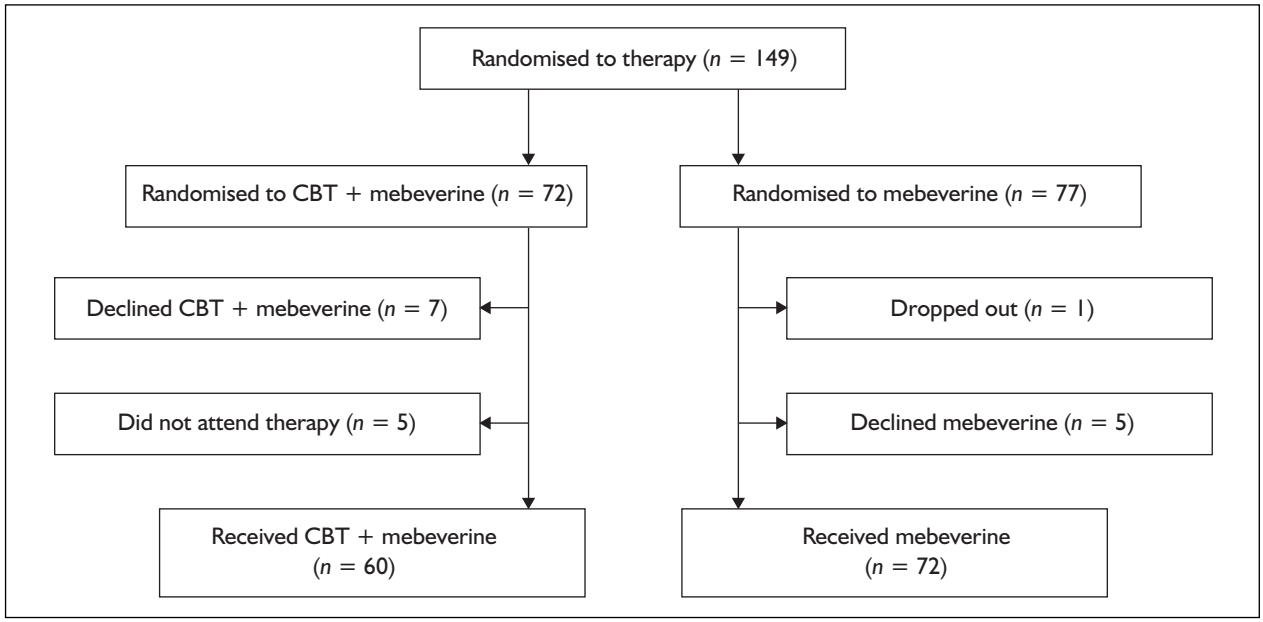


FIGURE 2 *Trial profile (continued from* Figure 1*)*

TABLE 8 *Therapists' assessment of time spent in CBT and whether therapy was completed*

Therapists' assessment	**CBT outcome *n* (%)**	
Completed treatment	44 (61.1)	
Declined therapy after initial session(s)	13 (18.1)	
Declined therapy after initial sessions owing to ill health	1 (1.4)	
Dropped out of therapy (uncontactable)	1 (1.4)	
Moved out of area and uncontactable	3 (4.2)	
Did not attend owing to work or home commitments	6 (8.4)	
Did not attend owing to ill-health	1 (1.4)	
Did not want therapy	1 (1.4)	
Declined therapy, no reason given	3 (4.2)	
	Mean time (minutes) (95% CI)	**Centiles**
Time spent in CBT	254.86 (217.2 to 290.49)	25% < 120 minutes 50% < 360 minutes 75% < 390 minutes

TABLE 9 *Number of CBT sessions attended by patients allocated to mebeverine plus CBT*

	Total no. of sessions attended *n* (%)							
	0	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Attendance	12 (16.7)	3 (4.2)	7 (9.7)	4 (5.6)	2 (2.8)	5 (6.9)	33 (45.8)	6 (8.3)

Completion of therapy

It was intended that patients would receive six CBT therapy sessions, each lasting for 50 minutes (total 300 minutes). Nurses were urged to keep to the planned number of appointments and to resist pressure for further sessions even if requested to provide these by the patient. However, six patients received seven sessions because they found the CBT helpful and pressed for a further session, and less than 50% of patients were considered by the therapist to have completed therapy, with 40.5% either declining therapy or dropping out for other reasons. Reflecting the age group that was recruited, the most common reason given for non-attendance was that the patient had been unable to take time from work or from home commitments such as childcare.

Outcome measures

Total score on the SSS

The mean SSS is plotted against time for the two treatment groups in *Figure 3*. The difference between treatment groups was significant at 1.5 and 3 months; and the treatment by time interaction was highly significant ($p < 0.0001$). The estimated treatment effects at each follow-up are given in *Table 10*.

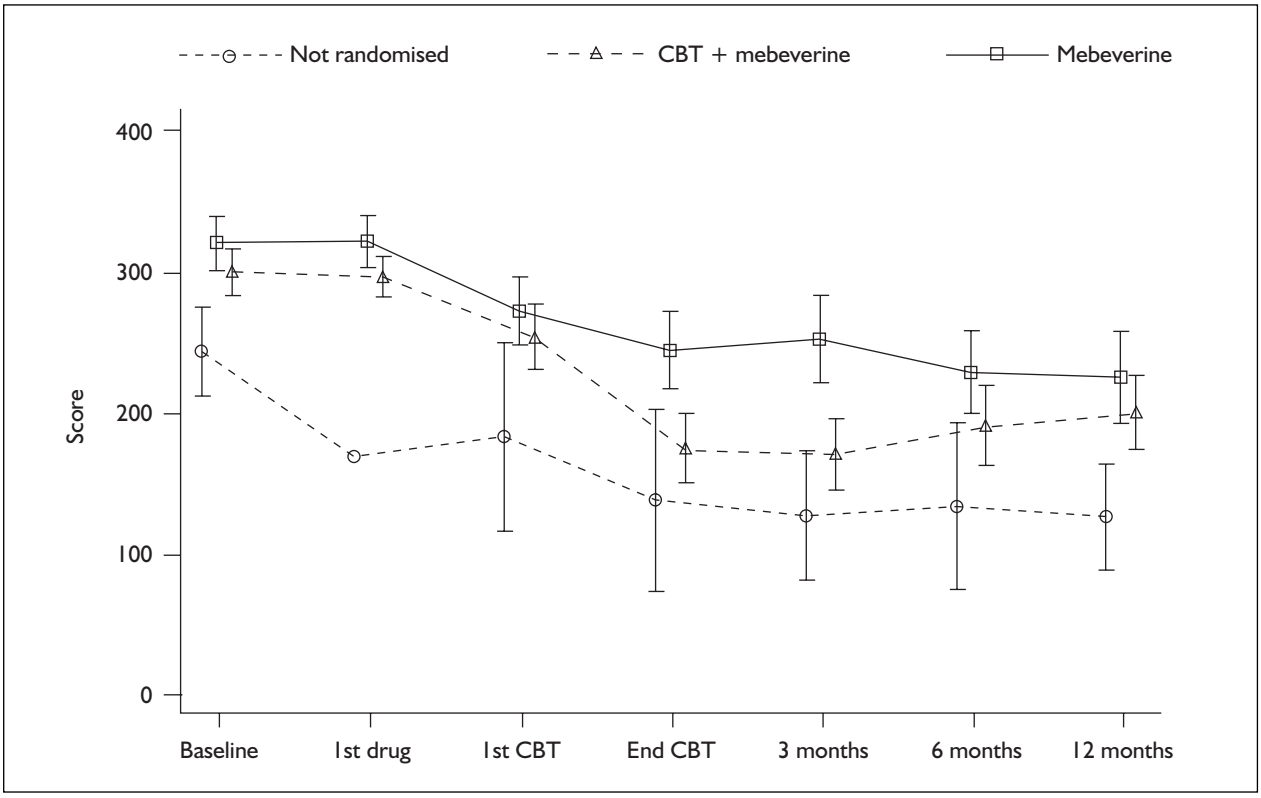


FIGURE 3 *Mean total scores on the SSS*

TABLE 10 *SSS total score: estimated treatment effects at follow-up*

Follow-up (months)	Difference in means CBT vs control	95% CI
1.5	–68	–104 to –32
3	–71	–109 to –32
6	–14	–51 to 23
12	3	–35 to 40
Mean	–37	–67 to –8

SSS question 4

The mean of question 4 of the SSS (How much is the IBS affecting your life in general?) is plotted against time for the two treatment groups in *Figure 4*. The difference between treatment groups was significant up to 6 months, and the treatment by time interaction was highly significant ($p = 0.001$). The estimated treatment effects at each follow-up are given in *Table 11*.

SSS banding

Ordered logistic regression was used to estimate odds ratios (ORs) relative to a change from baseline from one band of the SSS to the next, more severe band. Odds ratios are given in *Table 12* with 95% confidence intervals comparing CBT and control at each follow-up period.

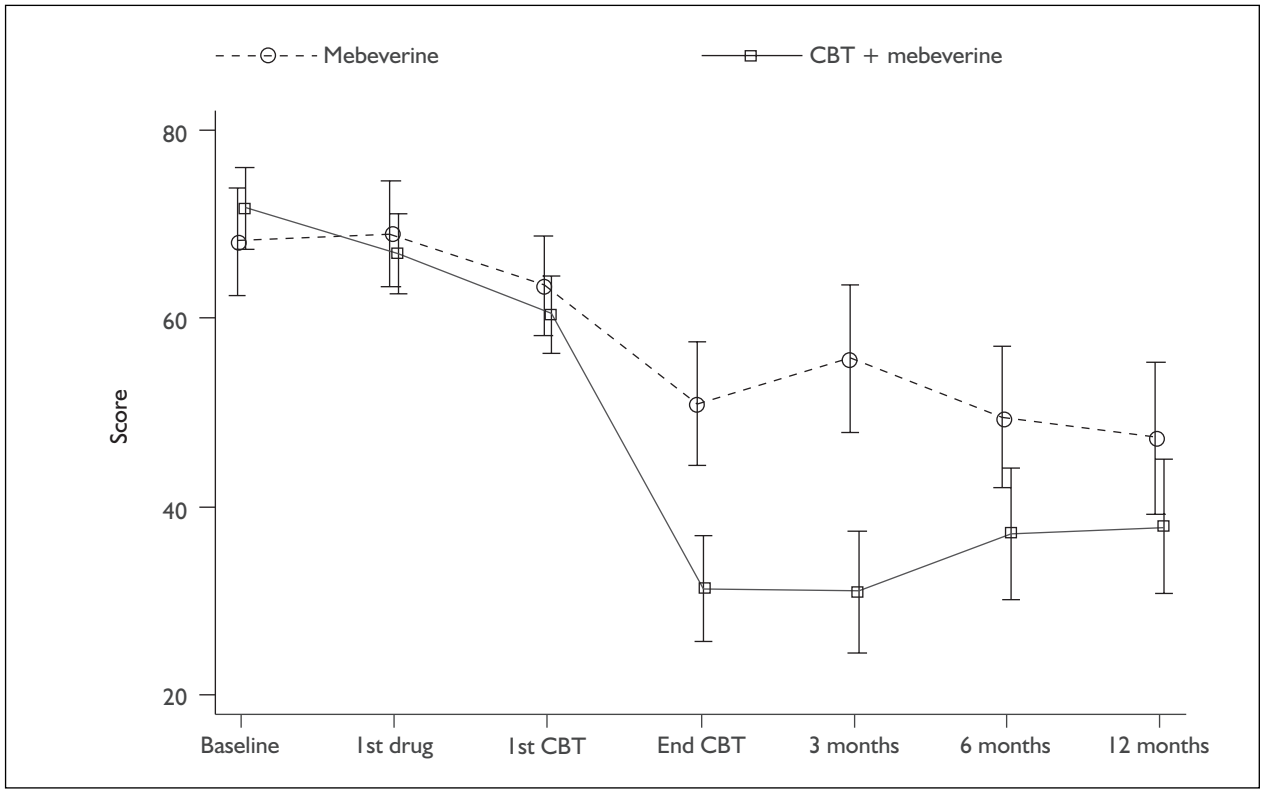


FIGURE 4 *Mean scores on question 4 of the SSS*

TABLE 11 *SSS question 4: estimated treatment effects at follow-up*

Follow-up (months)	Difference in means CBT vs control	95% CI
1.5	–18	–26 to –10
3	–21	–30 to –13
6	–11	–19 to –3
12	–7	–15 to 1
Mean	–14	–21 to –8

TABLE 12 *SSS banding*

Follow-up (months)	OR (CBT vs control)	95% CI
1.5	0.32	0.16 to 0.62
3	0.17	0.084 to 0.35
6	0.71	0.35 to 1.47
12	0.89	0.44 to 1.79
Mean	0.43	0.25 to 0.75

HAD (total score)

A graph of the mean HAD total score by time and treatment group is shown in *Figure 5*. There was no significant treatment by time interaction ($p = 0.12$). The CBT group mean was 2.0 points lower than the control group mean (95% CI –3.5 to –0.5), with no evidence that the treatment effect had declined by 12 months.

HAD (anxiety subscale)

A graph of the mean HAD anxiety score by time and treatment group is shown in *Figure 6*. There was no significant treatment by time interaction ($p = 0.39$). The CBT group mean was 1.4 points lower than the control group mean (95% CI –2.4 to –0.4), with no evidence that the treatment effect had declined by 12 months.

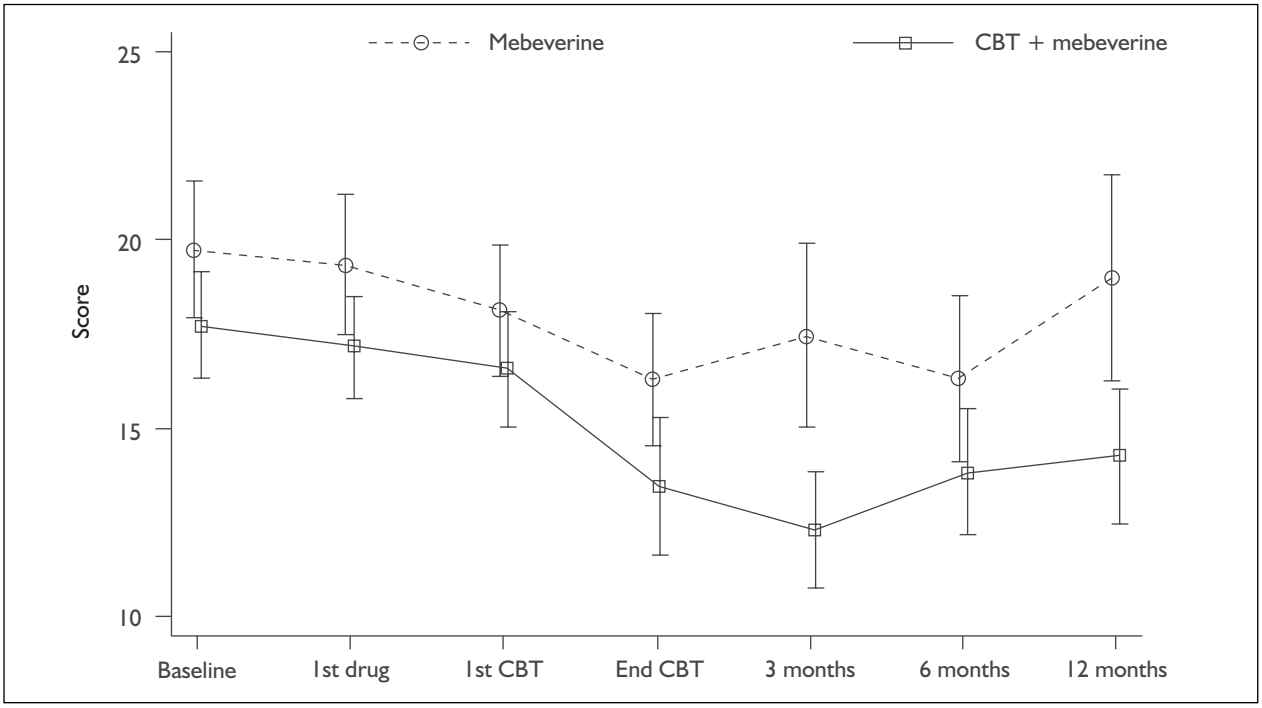


FIGURE 5 *Mean total scores on the HAD*

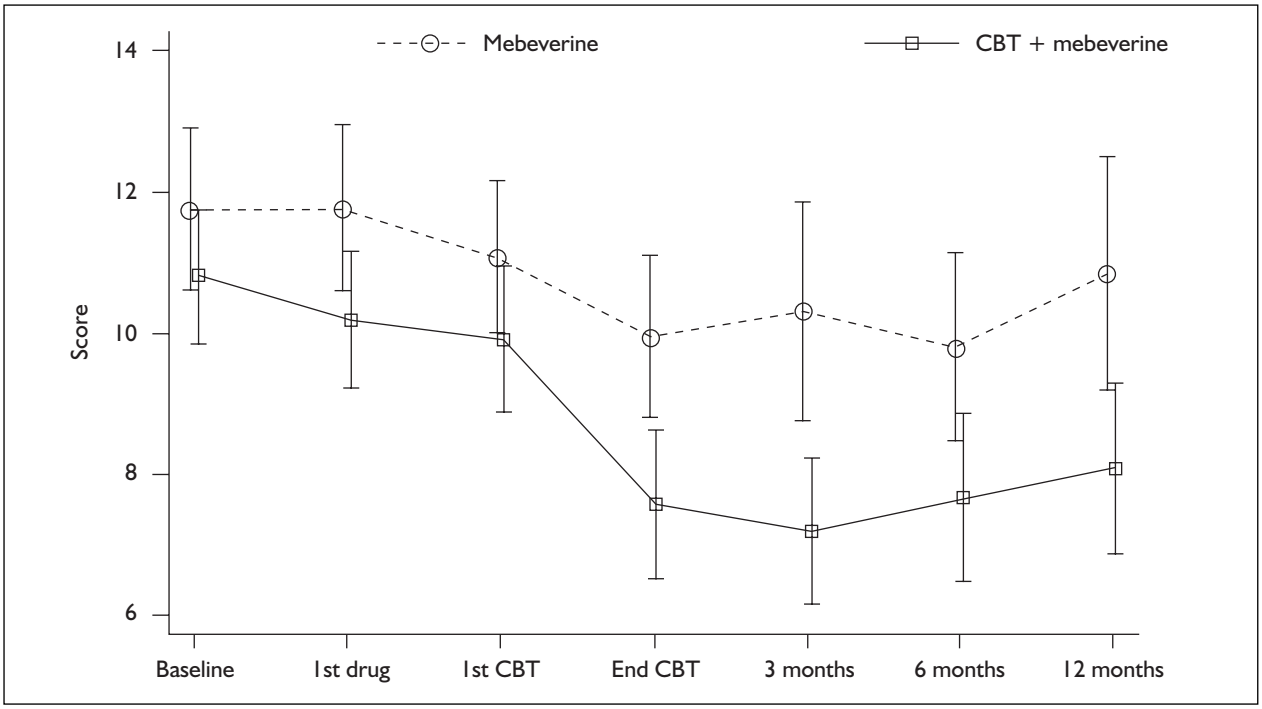


FIGURE 6 *Mean scores for anxiety on the HAD*

HAD (depression subscale)

A graph of the mean HAD depression score by time and treatment group is shown in *Figure 7*. There was no significant treatment by time interaction ($p = 0.09$). The CBT group mean was 0.7 points lower than the control group mean (95% CI –1.5 to 0.1), but this difference was not conventionally significant ($p = 0.08$).

WASA

The mean WASA measurements for the two treatment groups are shown in *Table 13* and *Figure 8*. There was a significant time by treatment interaction ($p = 0.03$), with a decline in efficacy after 3 months.

BS-IBS

There was a significant treatment by time interaction ($p = 0.01$). The difference in-group means decreased on average by 3.6 points per month (95% CI from 0.9 to 6.2) (*Figure 9*). The estimated mean differences between the groups at each follow-up are given in *Table 14*.

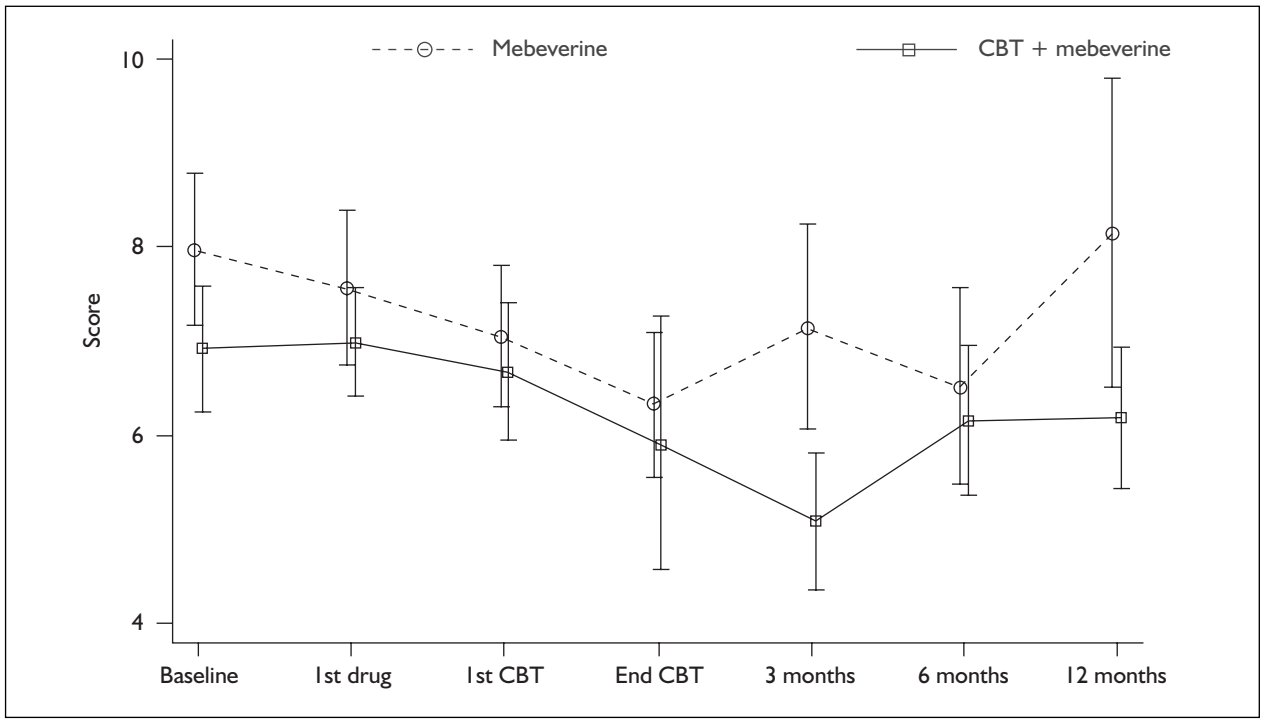


FIGURE 7 *Mean scores for depression on the HAD*

TABLE 13 *WASA: mean differences*

Follow-up (months)	Difference in means CBT–control	95% CI
1.5	–4.1	–6.4 to –1.8
3	–5.0	–7.5 to –2.6
6	–1.7	–4.1 to 0.7
12	–2.8	–5.2 to –0.4
Mean	–3.4	–5.3 to –1.5

TABLE 14 *BS-IBS: mean differences*

Follow-up (months)	Difference in means CBT–control	95% CI
1.5	–32.0	–43.7 to –0.3
3	–26.6	–35.4 to –7.9
6	–16.0	–23.4 to –8.6
12	5.4	–14.6 to 25.3

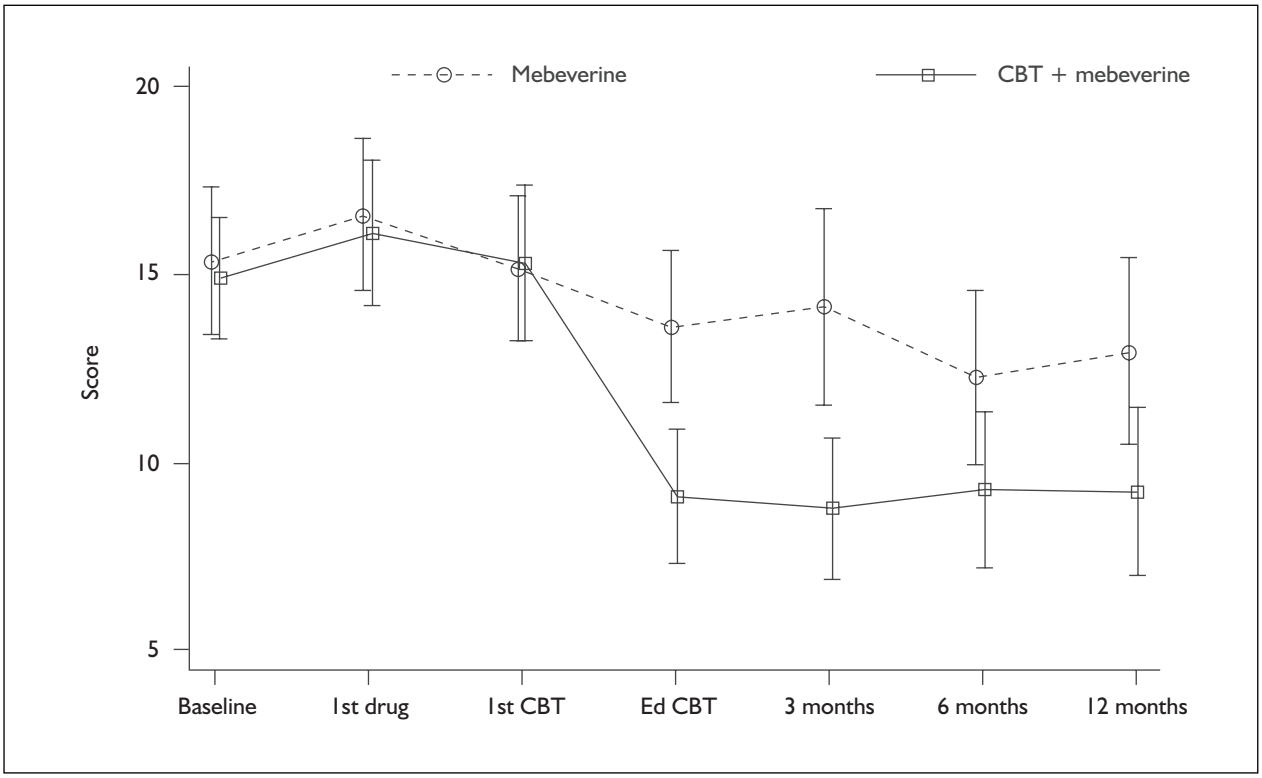


FIGURE 8 *Mean total scores on the WASA*

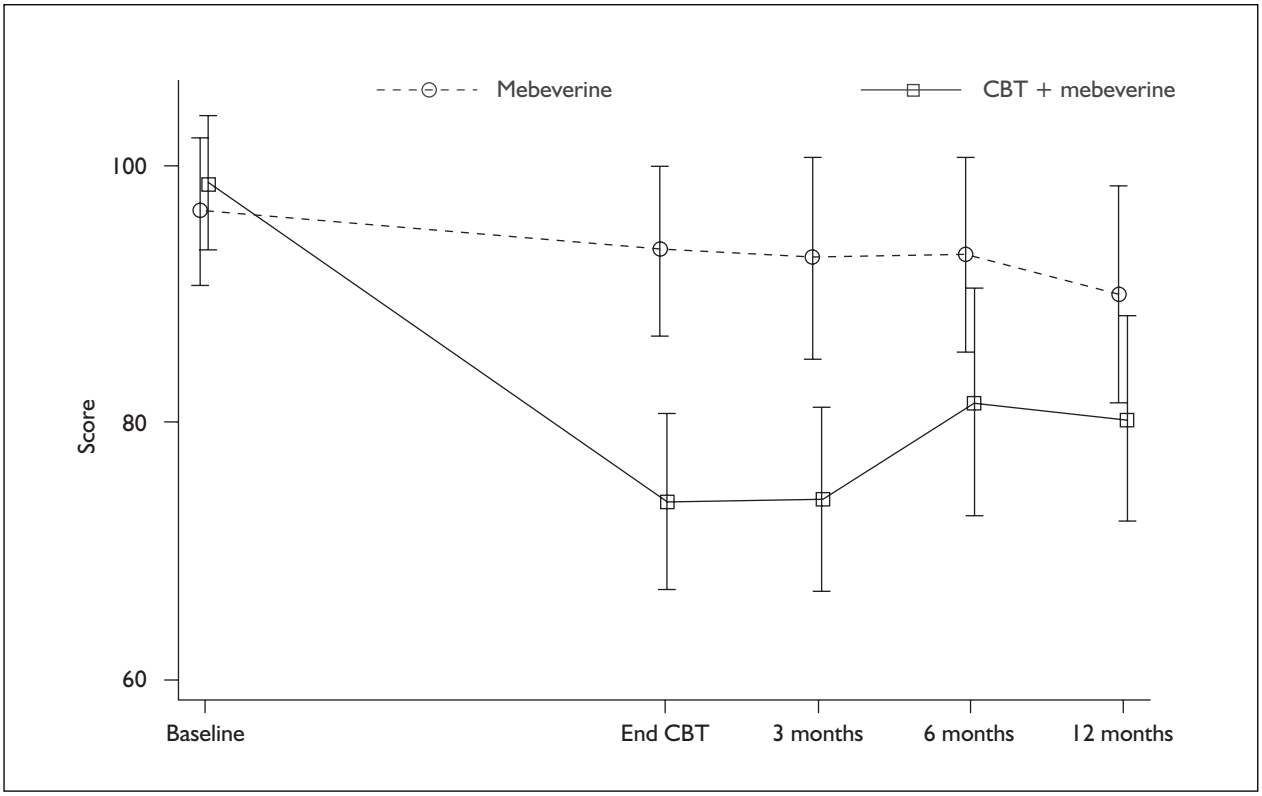


FIGURE 9 *Mean scores on the BS-IBS*

TABLE 15 *CS-FBD: mean differences*

Follow-up (months)	Difference in means CBT–control	95% CI
1.5	–16	–25 to –7
3	–21	–31 to –12
6	– 6	–15 to 4
12	– 8	–17 to 2
Mean	–13	–20 to –5

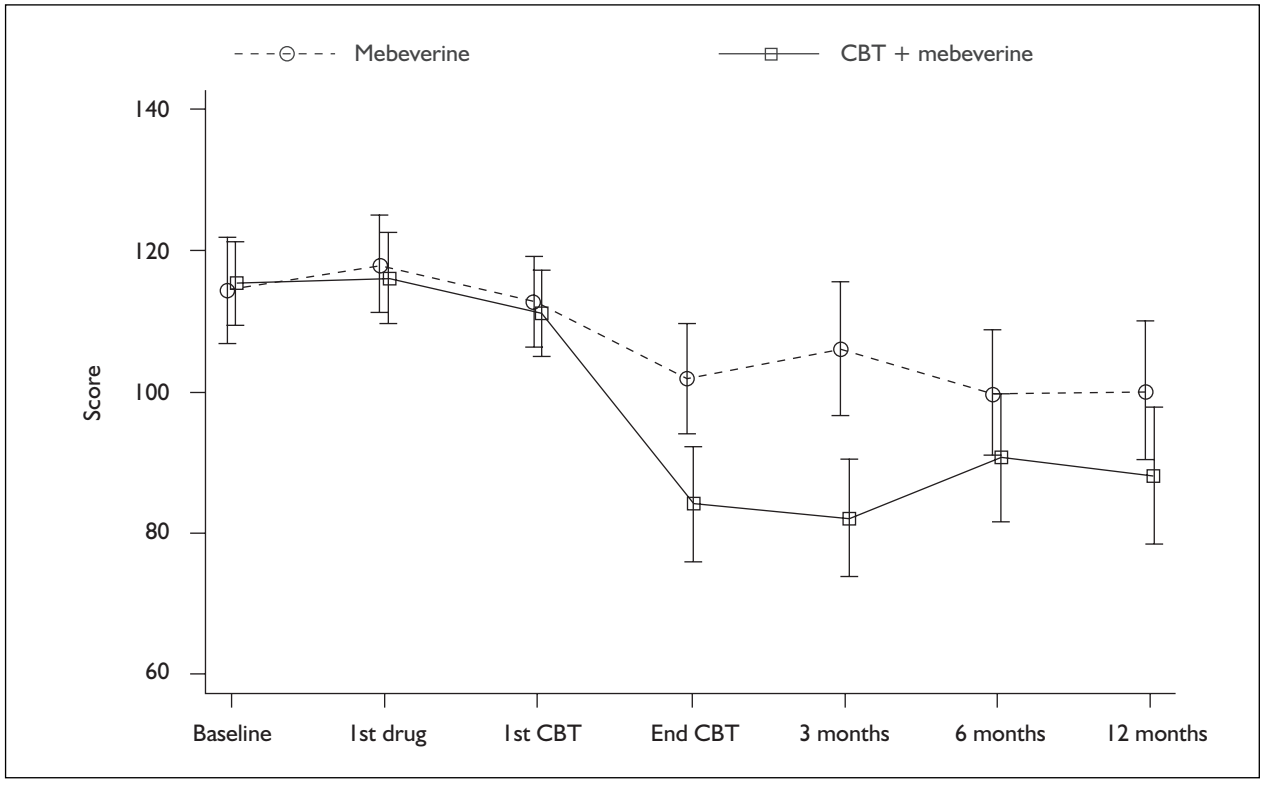


FIGURE 10 *Mean scores on the CS-FBS*

CS-FBD

There was a significant treatment by time interaction ($p = 0.001$) with a decrease in treatment effect after 3 months (*Table 15* and *Figure 10*).

RAM

A graph of the mean HAD anxiety score by time and treatment group is shown in *Figure 11*. There was no significant treatment by time interaction ($p = 0.93$). The CBT group mean was similar to the control group mean (difference –0.1 points, 95% CI –0.1 to 0.3), with no evidence of any treatment effect or any consistent change over time

Predictors of outcome

Data collected at the first visit (baseline) were used in a linear regression to identify variables that predict outcome in IBS. In the trial of therapy a significant improvement had been shown in the disability experienced by patients as recorded by the scores on the WASA. It was decided to use change on the WASA at 3, 6 and 12 months' follow-up to investigate the predictors of outcome. The mean of the scores at 3, 6 and 12 months was calculated and this new variable was used as the dependent variable in the linear regression.

The linear regression was carried out on data from the ITT group (allocated to mebeverine or mebeverine and hydrochloride at visit 3). Each variable mentioned in *Table 16* was tested separately in a linear regression to identify those variables likely to be of greatest importance, those with $p < 0.05$. Next, the variables identified as most relevant were each entered into a linear

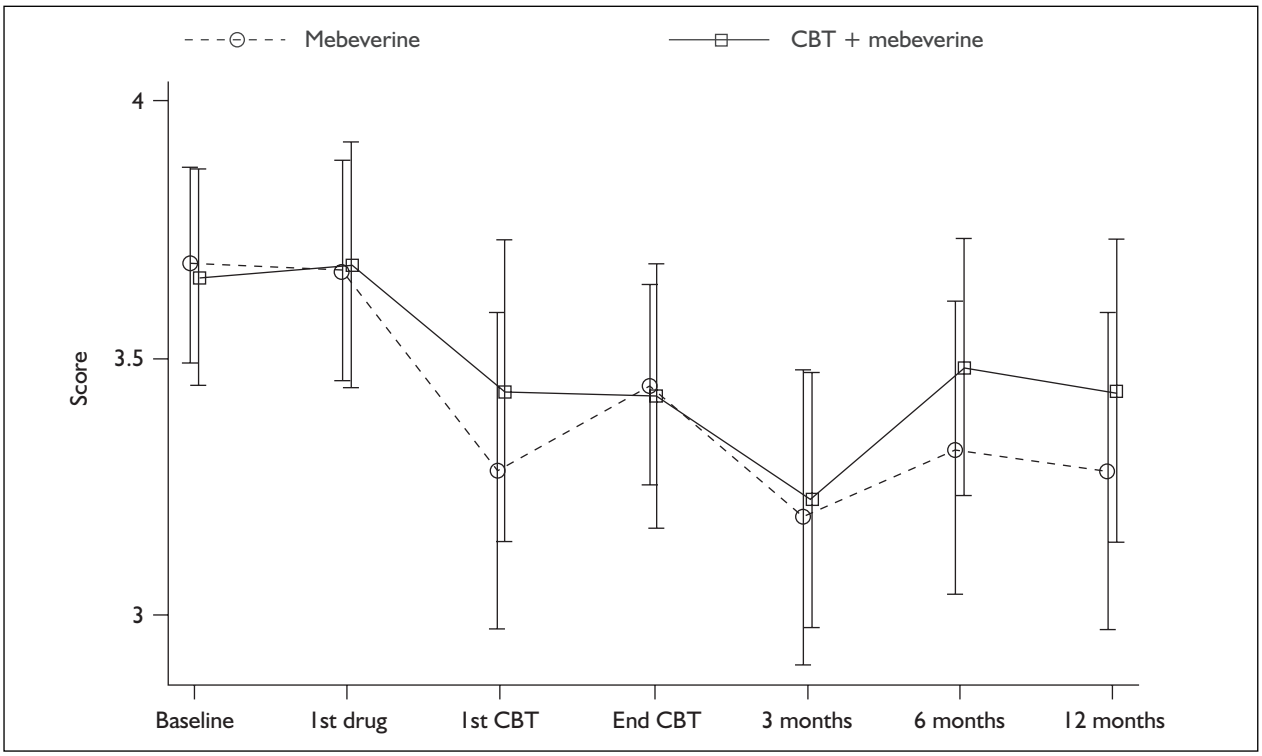


FIGURE 11 *Mean scores on the RAM*

TABLE 16 *Linear regression with the mean (of values at 3, 6 and 12 months) outcome on the WASA as the dependent variable*

	Unadjusted		Main predictors	
Variables	**β coefficient (95% CI)**	***p***	**β coefficient (95% CI)**	***p***
Gender	5.77 (2.11 to 9.42)	0.002	3.49 (0.46 to 6.52)	0.025
IPQ consequences	4.22 (2.68 to 5.77)	0.001	–0.15 (–2.02 to 1.73)	0.877
IPQ external	3.58 (1.03 to 6.13)	0.006	2.03 (–0.16 to 4.21)	0.069
Therapy allocation	–3.27 (–5.88 to –0.65)	0.015	–2.86 (–4.98 to –0.74)	0.009
HAD depression	1.09 (0.74 to 1.45)	0.001	0.33 (–0.09 to 0.75)	0.119
HAD anxiety	0.79 (0.53 to 1.04)	0.001	0.13 (–0.17 to 0.43)	0.380
HAD total score	0.59 (0.41 to 0.73)	0.001	Excluded from regression	
WASA	0.53 (0.38 to 0.68)	0.001	0.23 (0.05 to 0.42)	0.014
BS-IBS	0.16 (0.11 to 0.21)	0.001	0.14 (0.08 to 0.20)	0.001
Q4 on SSS	0.13 (0.08 to 0.19)	0.001	0.04 (–0.03 to 0.10)	0.263
CS-FBD	0.09 (0.05 to 0.14)	0.001	–0.06 (–0.118 to –0.004)	0.035
SSS	0.03 (0.012 to 0.045)	0.001	0.009 (–0.01 to 0.03)	0.282
Rome positive at recruitment	–2.32 (–6.16 to 1.55)	0.238		
Saw GP for psychological problems in prior 5 years	1.70 (–0.97 to 4.36)	0.210		
BAM general harmful	1.04 (–1.51 to 3.59)	0.423		
IBS duration	0.91 (–0.95 to 2.77)	0.334		
BAM specific necessity	–0.87 (–2.59 to 0.85)	0.318		
IPQ timeline	0.84 (–0.60 to 2.28)	0.251		
BAM specific concerns	0.72 (–1.34 to 2.78)	0.490		
Adherence to medication	0.61 (–1.40 to 2.63)	0.548		
IPQ cure-control	–0.45 (–3.01 to 2.10)	0.727		
IPQ internal	0.45 (–0.78 to 1.67)	0.473		
BAM general overuse	–0.42 (–2.32 to 1.48)	0.663		
Age	0.12 (–0.03 to 0.27)	0.103		
Patient preference before therapy allocation	0.01 (–0.001 to 0.02)	0.088		

regression while controlling for the other variables that had shown a significant effect.

Finally, the relationship between each variable and the dependent variable was investigated while controlling for first the patient's gender and then both gender and therapy allocation (*Table 17*). When these latter two variables were controlled for, the influence of the patient's baseline perceptions regarding the aetiology and consequences of their IBS became evident.

TABLE 17 *Linear regression continued from* Table 16

	Controlled for gender		Controlled for gender and therapy	
Variables	**β coefficient (95% CI)**	***p***	**β coefficient (95% CI)**	***p***
Gender				
IPQ consequences	4.00 (2.48 to 5.51)	0.001	3.82 (2.32 to 5.31)	0.01
IPQ external	3.59 (1.13 to 6.05)	0.005	3.63 (1.24 to 6.03)	0.003
Therapy allocation	–3.41 (–5.93 to –0.89)	0.008		
HAD depression	1.38 (0.68 to 1.39)	0.001	0.98 (0.62 to 1.33)	0.001
HAD anxiety	0.74 (0.48 to 0.99)	0.001	0.69 (0.44 to 0.95)	0.001
HAD total score	0.54 (0.38 to 0.70)	0.001	0.51 (0.35 to 0.67)	0.001
WASA	0.50 (0.35 to 0.65)	0.001	0.49 (0.35 to 0.64)	0.001
BS-IBS	0.16 (0.11 to 0.21)	0.001	0.16 (0.12 to 0.21)	0.001
Q4 on SSS	0.12 (0.06 to 0.18)	0.001	0.12 (0.06 to 0.18)	0.001
CS-FBD	0.09 (0.05 to 0.13)	0.001	0.09 (0.05 to 0.13)	0.001
SSS	0.03 (0.01 to 0.04)	0.001	0.03 (0.01 to 0.04)	0.002
Rome positive at recruitment	–1.46 (–5.24 to 2.33)	0.447	–1.7 (–5.42 to 1.97)	0.358
Saw GP for psychological problems in prior 5 years	1.51 (–1.08 to 4.09)	0.251	1.89 (–0.65 to 4.42)	0.143
BAM general harmful	1.23 (–1.24 to 3.70)	0.325	1.58 (–0.83 to 4.00)	0.197
IBS duration	0.95 (–0.85 to 2.74)	0.299	0.98 (–0.77 to 2.74)	0.270
BAM specific necessity	–0.48 (–2.13 to 1.18)	0.569	–0.3 (–1.95 to 1.38)	0.738
IPQ timeline	0.71 (–0.69 to 2.11)	0.316	0.62 (–0.75 to 1.99)	0.372
BAM specific concerns	1.35 (–0.63 to 3.32)	0.178	1.38 (–0.58 to 3.34)	0.165
Adherence to medication	0.79 (–1.13 to 2.71)	0.418	0.68 (–1.22 to 2.59)	0.478
IPQ cure-control	–0.57 (–3.04 to 1.90)	0.650	–0.5 (–2.89 to 1.95)	0.702
IPQ internal	0.37 (–0.82 to 1.55)	0.542	0.38 (–0.78 to 1.53)	0.523
BAM general overuse	–0.17 (–2.01 to 1.68)	0.858	0.31 (–1.53 to 2.15)	0.740
Age	0.11 (–0.03 to 0.26)	0.117	0.11 (–0.03 to 0.25)	0.111
Patient preference before therapy allocation	– 0.002 (–2.11 to 2.1)	0.998	–0.2 (–2.30 to 1.82)	0.818

Chapter 4
Economic analysis

Analysis methods

The economic analysis included an evaluation of the direct and indirect costs of managing IBS as well as a cost-effectiveness analysis of the two treatments. The principal data collection instrument for this was a version of the CSRI that was adapted for use in IBS.

The effects on service-use patterns, employment and household/family responsibilities were analysed and costs were calculated as the best approximations of long-run marginal opportunity costs.

Hypotheses

There were three hypotheses:

- Mebeverine plus CBT would result in significantly lower service costs than mebeverine alone at 3-, 6- and 12-month follow-ups.
- Mebeverine plus CBT would result in significantly lower total costs (including lost production) than mebeverine alone at 3-, 6- and 12-month follow-ups.
- Mebeverine plus CBT would be more cost-effective than mebeverine alone.

Method

There had been no a priori power calculation for the economic analysis. All economic analysis was conducted on an ITT basis and as such is aimed at the two groups allocated to therapy.

Intervention cost

The cost of CBT was measured by multiplying the number of sessions received by the unit cost of CBT. The therapy was delivered by practice nurses who had a unit cost of £31 per hour of patient contact[88] (Appendix 6). This figure includes qualifications, capital costs and overheads. The nurse therapists attended a 12-day initiation course and the estimated cost of this was £3000 per nurse (including nurse time and trainer time). Nurses received weekly supervision while delivering therapy, at an estimated cost of £51 per hour (nurse time and supervisor time). These costs were divided by the number of CBT sessions delivered by each nurse as part of the study.

Mebeverine hydrochloride was not costed as patients in both arms of the trial received the drug and it was therefore cost-neutral.

Other services

The CSRI[86] was used to record service use in the 3 months before the baseline interview and the 3-, 6- and 12-month follow-up interviews. Patients were asked for details of the number of contacts with specific services and, where relevant, for the average contact duration. Unit costs were obtained from a recognised source[88] and attached to the service-use data.

Analyses

The proportion of patients in both groups using specific services was tested using Fisher's exact test. Cost differences for individual services were not tested for statistical significance in order to avoid problems of multiple testing and to focus on differences in the two summary measures: total service costs and total social costs (i.e. including lost employment).

Mean costs were tested using regression analysis with the randomisation group as the independent variable. Cost data are often positively skewed and this may limit the applicability of linear regression. The regression model was bootstrapped so that more accurate *p*-values and 90% confidence intervals could be obtained in the presence of potentially skewed data distributions that are common in economic evaluations. Bootstrapping methods make no assumptions about the distribution of the statistics of interest.[92]

Confidence intervals of 90% were chosen. This is common practice in economic analyses as it is assumed that researchers are less risk averse about making inaccurate inferences with economic data

TABLE 18 *Number (%) of patients using services and with lost employment before baseline and at follow-up interviews*

Service	Baseline			3-month FU			6-month FU			12-month FU		
	Drug (*n* = 69)	**Drug + CBT (*n* = 67)**	***p***	**Drug (*n* = 47)**	**Drug + CBT (*n* = 50)**	***p***	**Drug (*n* = 38)**	**Drug + CBT (*n* = 40)**	***p***	**Drug (*n* = 51)**	**Drug + CBT (*n* = 49)**	***p***
Inpatient care	3 (4)	2 (3)	1.000	2 (4)	2 (4)	1.000	1 (3)	1 (3)	1.000	4 (8)	5 (10)	1.000
Outpatient care (gastroenterology)	8 (12)	2 (3)	0.097	5 (10)	2 (4)	0.436	4 (11)	2 (5)	0.425	5 (10)	4 (8)	1.000
A&E	7 (10)	7 (11)	1.000	3 (6)	3 (6)	1.000	1 (3)	0 (0)	0.487	4 (8)	0 (0)	0.117
Outpatient care (other)	17 (25)	13 (20)	0.539	7 (14)	5 (10)	0.759	5 (13)	10 (25)	0.253	8 (16)	10 (20)	0.795
GP	58 (84)	54 (82)	0.820	28 (57)	22 (45)	0.312	16 (42)	14 (35)	0.642	28 (57)	23 (47)	0.419
Practice nurse	22 (32)	18 (27)	0.577	4 (8)	8 (16)	0.356	3 (8)	3 (8)	1.000	8 (16)	10 (20)	0.795
District nurse	2 (3)	0 (0)	0.497	0 (0)	0 (0)	NA	0 (0)	0 (0)	NA	0 (0)	1 (2)	1.000
Social worker	0 (0)	2 (3)	0.237	0 (0)	0 (0)	NA	0 (0)	0 (0)	NA	1 (2)	0 (0)	1.000
Dietitian	4 (6)	3 (5)	1.000	2 (4)	0 (0)	0.495	1 (3)	1 (3)	1.000	1 (2)	0 (0)	1.000
Occupational therapist	1 (1)	1 (2)	1.000	2 (4)	1(2)	1.000	0 (0)	0 (0)	NA	0 (0)	2 (4)	0.495
Home care worker	0 (0)	0 (0)	NA	0 (0)	0 (0)	NA	0 (0)	0 (0)	NA	0 (0)	0 (0)	NA
Mental health professional	4 (6)	0 (0)	0.120	9 (18)	3 (6)	0.121	2 (5)	0 (0)	0.234	6 (12)	3 (6)	0.487
Other services	7 (10)	3 (5)	0.326	5 (10)	3 (6)	0.715	3 (8)	1 (3)	0.352	7 (14)	2 (4)	0.159
Lost employment	36 (52)	34 (52)	1.000	22 (45)	26 (53)	0.545	18 (47)	21 (53)	0.651	20 (41)	24 (49)	0.543

FU, follow-up; A&E, accident and emergency.

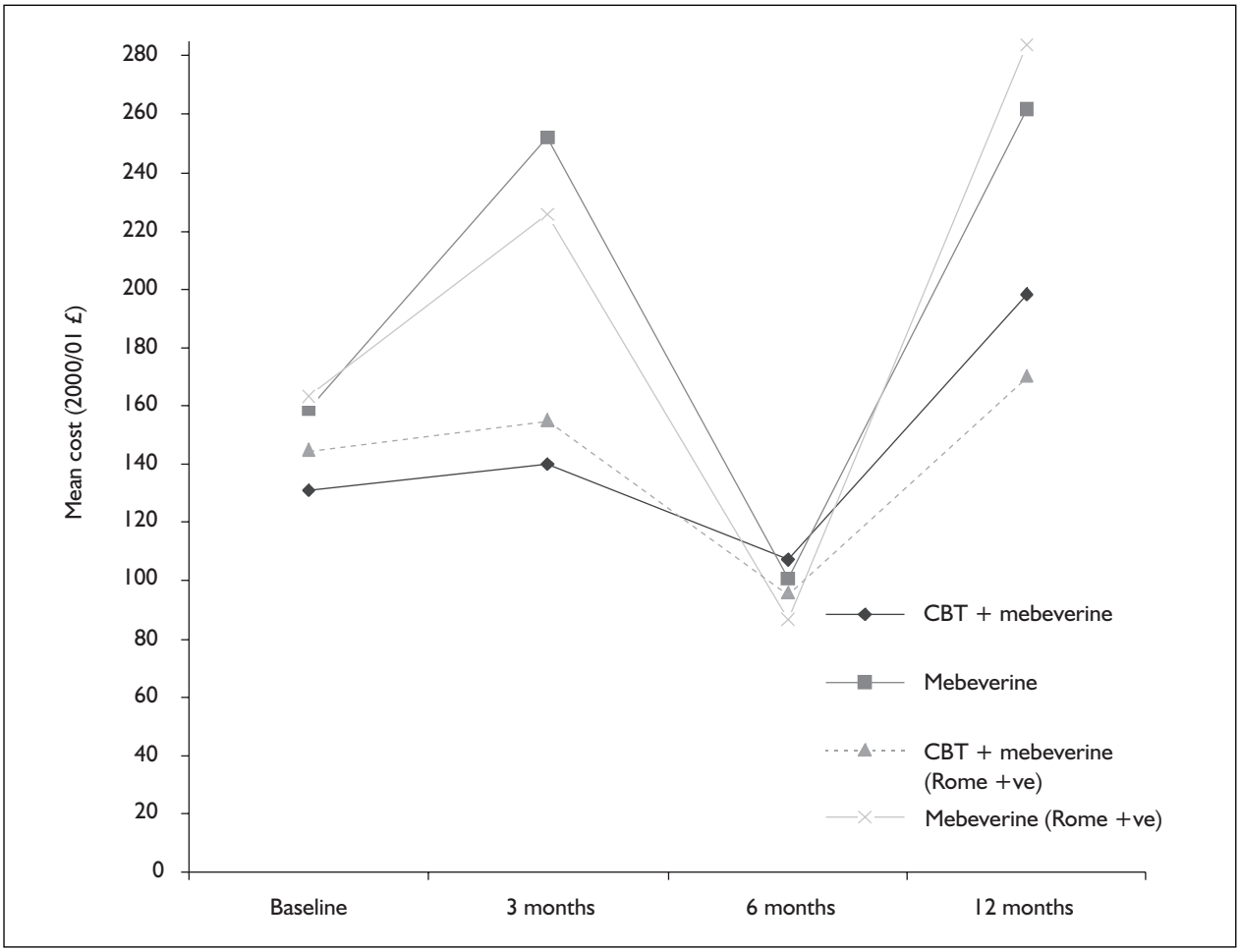


FIGURE 12 *Change in mean service costs between baseline and 12-month follow-up*

than they are with clinical data. Discounting was not conducted, as data collection did not progress beyond 12 months' follow-up.

Patients recruited to this trial had a clinical diagnosis of IBS and a sizeable minority of these were Rome I negative at recruitment. A separate analysis was conducted to determine whether restricting therapy to such patients would be more cost-effective than treating those with a clinical diagnosis.

Results

The number of CBT sessions delivered and the cost per session were as follows:

- therapist 0: 69 sessions, £79 per session
- therapist 1: 33 sessions, £131 per session
- therapist 2: 88 sessions, £69 per session
- therapist 3: 112 sessions, £61 per session.

The mean number of CBT sessions completed in the group randomised to therapy was 4.1 (SD 2.5), with a mean cost of £308 (SD £202).

Table 18 shows the use of services and the occurrence of lost employment during the 3 months before the baseline interview and the follow-up interviews. There were no statistically significant differences for any services or for lost employment at any period, with the exception of gastroenterology outpatient visits at baseline. Therefore, there was no evidence that CBT resulted in a change in the proportion of patients using specific services and it had demonstrable impact on the proportion with lost employment.

Table 19 gives details of service costs and lost employment. Again, the two groups were similar and the total service and social costs did not differ significantly, as can be seen from the *p*-values and 90% confidence intervals. *Tables 18* and *19* also

TABLE 19 *Mean (SD) service and lost employment costs before baseline and at follow-up interviews*

Service	Baseline		3-month FU		6-month FU		12-month FU	
	Drug (*n* = 69)	**Drug + CBT (*n* = 67)**	**Drug (*n* = 47)**	**Drug + CBT (*n* = 50)**	**Drug (*n* = 38)**	**Drug +CBT (*n* = 40)**	**Drug (*n* = 51)**	**Drug + CBT (*n* = 49)**
Inpatient care	25 (126)	26 (181)	35 (171)	44 (278)	13 (79)	30 (191)	74 (258)	89 (359)
Outpatient care (gastroenterology)	10 (29)	2 (13)	16 (56)	5 (24)	10 (31)	8 (34)	9 (30)	8 (28)
A&E	9 (30)	8 (26)	14 (72)	4 (15)	2 (10)	0 (0)	5 (17)	0 (0)
Outpatient care (other)	36 (87)	25 (68)	18 (48)	14 (44)	13 (35)	39 (132)	31(78)	26 (78)
GP	52 (49)	56 (78)	54 (98)	24 (37)	34 (72)	27 (66)	50 (79)	44 (117)
Practice nurse	3 (7)	2 (4)	2 (8)	3 (9)	1 (4)	1 (4)	4 (14)	2 (5)
District nurse	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)
Social worker	0 (0)	5 (30)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)
Dietician	2 (8)	2 (16)	1 (5)	0 (0)	1 (5)	1 (5)	1 (7)	0 (0)
Occupational therapist	1 (5)	0.4 (3)	7 (47)	4 (26)	0 (0)	0 (0)	0 (0)	2 (9)
Home care worker	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mental health professional	5 (20)	0 (0)	6 (181)	37 (174)	22 (94)	0 (0)	73 (231)	25 (113)
Other services	17 (63)	4 (17)	42 (217)	6 (26)	7 (30)	1 (6)	14 (48)	2 (9)
Total service cost	159 (187)[1]	131 (266)[1]	252 (398)[2]	140 (355)[2]	101 (178)[3]	107 (277)[3]	262 (421)[4]	198 (401)[4]
Total service costs (Rome +ve)	163 (192)[1a]	145 (291)[1a]	226 (337)[2a]	155 (381)[2a]	87 (148)[3a]	96 (258)[3a]	284 (441)[4a]	170 (287)[4a]
Lost employment	203 (396)	280 (447)	194 (416)	172 (327)	248 (523)	113 (200)	138 (250)	237 (546)
Total social cost	362 (432)[5]	411 (529)[5]	446 (689)[6]	313 (578)[6]	349 (590)[7]	220 (319)[7]	400 (458)[8]	435 (731)[8]
Total social costs (Rome +ve)	382 (450)[5a]	410 (513)[5a]	440 (700)[6a]	350 (617)[6a]	359 (624)[7a]	221 (307)[7a]	431 (477)[8a]	371 (629)[8a]

All figures are in 2000/01pounds sterling.
Significance of total cost differences (90% CI)
[1] $p = 0.594$ (–83 to 55), [1a] $p = 0.768$ (–82 to 79), [2] $p = 0.173$ (–231 to 24), [2a] $p = 0.439$ (–189 to 79), [3] $p = 0.850$ (–68 to 123), [3a] $p = 0.788$ (–60 to 136), [4] $p = 0.487$ (–201 to 83), [4a] $p = 0.139$ (–263 to 13), [5] $p = 0.564$ (–83 to 194), [5a] $p = 0.721$ (–120 to 173), [6] $p = 0.309$ (–350 to 76), [6a] $p = 0.534$ (–336 to 147), [7] $p = 0.187$ (–352 to 28), [7a] $p = 0.200$ (–405 to 38), [8] $p = 0.738$ (–149 to 280), [8a] $p = 0.657$ (–248 to 178).

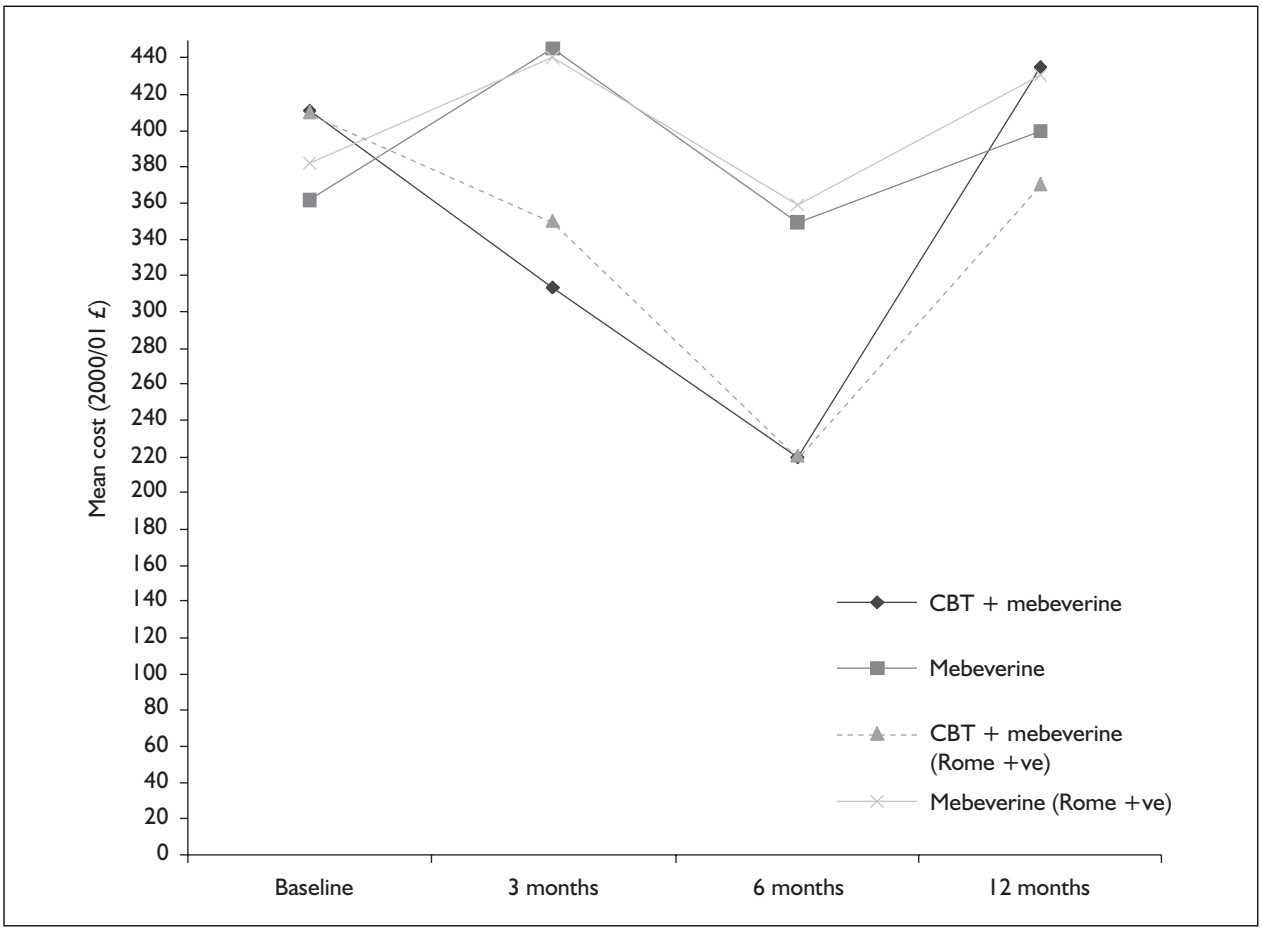


FIGURE 13 *Change in mean social costs (including lost employment) between baseline and 12-month follow-up*

give the number of patients who completed the CSRI questionnaire.

Figure 12 illustrates the changes in mean service costs over time and *Figure 13* changes in mean social costs. *Tables 20* summarises the use of services and *Table 21* the service and social social costs incurred by those patients who were not eligible for allocation to therapy by the third assessment. These tables also report the response rate for completed CSRIs in this group. Inpatient costs were considerable at 12 months, partly owing to the influence of one patient admitted to an orthopaedic ward for a prolonged stay. The graphs in *Figures 14* and *15* compare the costs incurred during the follow-up period between these patients and the two groups allocated to therapy.

Cost-effectiveness acceptability curves

An alternative way to compare the costs of the addition of CBT to the costs of mebeverine alone is to construct cost-effectiveness acceptability curves (CEACs).[93] These curves allow one to view the probability that CBT plus mebeverine hydrochloride is more cost-effective than mebeverine hydrochloride alone at various cost estimates for CBT.

As the longevity of any effect of CBT is uncertain, CEACs were created to 6 months post-therapy (*Figure 16*) and to 12 months post-therapy (*Figure 17*). As illustrated by the 6-month curves, the probability is less than 30% that the addition of CBT is more cost-effective than mebeverine alone when a 1-unit improvement on the WASA is costed at £100. The probability that there will be a 10-unit gain in the SSS at 6 months for an investment of £100 is less than 20%, and the probability for a 1-unit gain in the HAD at 6 months is less than 1%.

The CEACs at 12 months show that for a 10-unit gain in the SSS the probability that CBT will be more cost-effective is less than 25%; it is less than 20% for a 1-unit gain in the WASA and 40% for a 1-unit gain in the HAD.

TABLE 20 *Number (%) of non-eligible patients using specific services in the 3 months before baseline and at follow-up interviews*

Service	Baseline (*n* = 43)	3-month FU (*n* = 31)	6-month FU (*n* = 23)	12-month FU (*n* = 34)
Inpatient care	1 (2)	0 (0)	1 (4)	5 (15)
Outpatient care (gastroenterology)	1 (2)	0 (0)	0 (0)	4 (12)
A&E	4 (7)	0 (0)	3 (13)	3 (9)
Outpatient care (other)	17 (28)	6 (19)	6 (26)	8 (24)
GP	45 (75)	14 (45)	6 (26)	18 (53)
Practice nurse	14 (23)	4 (13)	2 (9)	9 (26)
District nurse	0 (0)	0 (0)	0 (0)	1 (3)
Social worker	1 (2)	0 (0)	0 (0)	0 (0)
Dietitian	2 (3)	1 (3)	1 (4)	1 (3)
Occupational therapist	0 (0)	0 (0)	0 (0)	1 (3)
Home care worker	0 (0)	0 (0)	0 (0)	0 (0)
Mental health professional	3 (5)	1 (3)	1 (4)	2 (6)
Other services	6 (10)	2 (6)	1 (4)	3 (9)
Lost employment	24 (40)	13 (42)	8 (35)	19 (56)

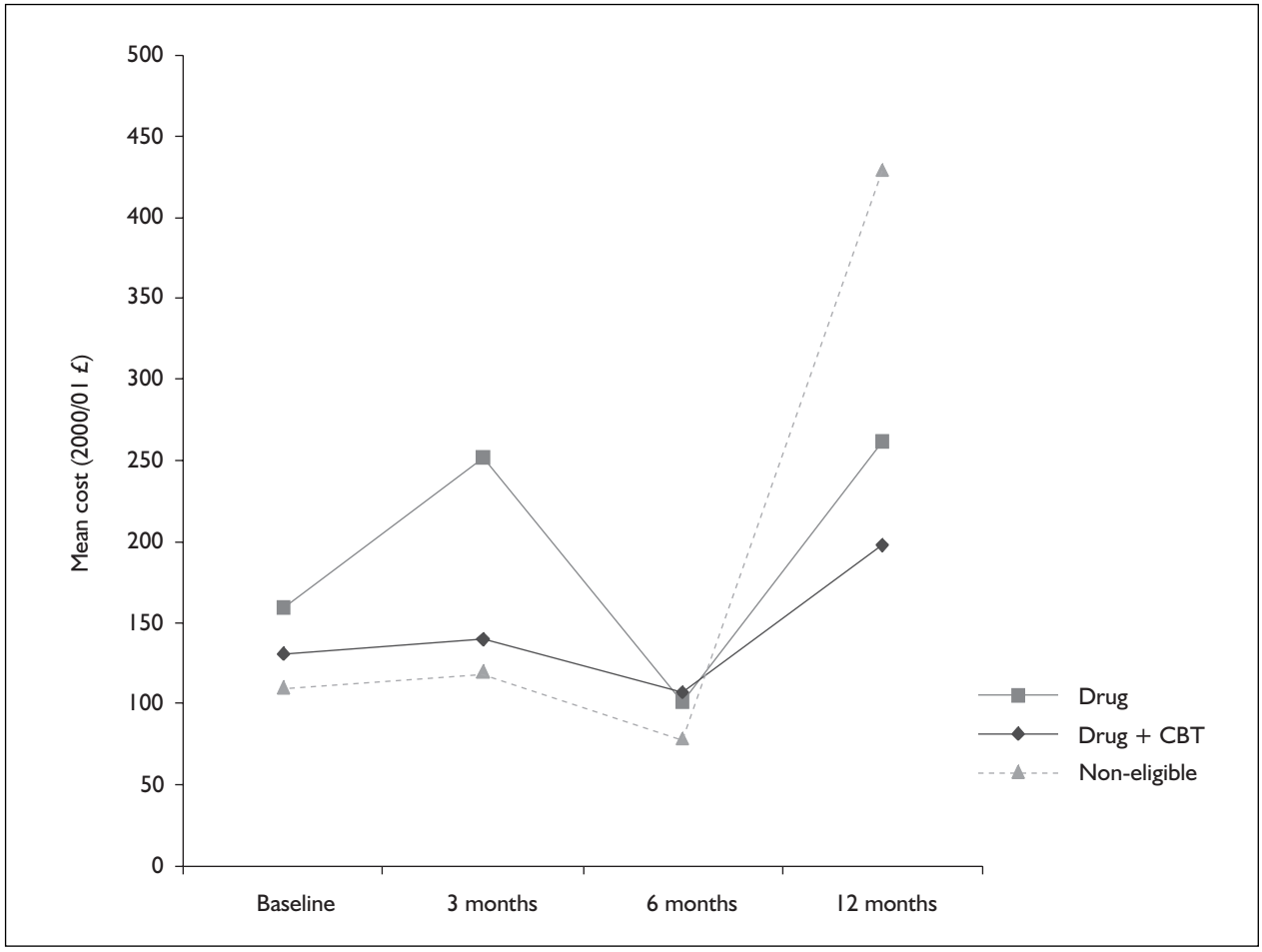


FIGURE 14 *Change in mean service costs between baseline and 12-month follow-up*

TABLE 21 *Mean (SD) cost of non-eligible patients using specific services in the 3 months before baseline and at follow-up interviews*

Service	Baseline (*n* = 43)	3-month FU (*n* = 31)	6-month FU (*n* = 23)	12-month FU (*n* = 34)
Inpatient care	4 (31)	0 (0)	32 (151)	299 (1254)
Outpatient care (gastroenterology)	1 (10)	0 (0)	0 (0)	11 (33)
A&E	4 (15)	0 (0)	11 (30)	7 (25)
Outpatient care (other)	28 (54)	33 (87)	14 (26)	36 (77)
GP	43 (50)	23 (41)	11 (25)	28 (34)
Practice nurse	5 (15)	2 (7)	1 (5)	3 (7)
District nurse	0 (0)	0 (0)	0 (0)	2 (13)
Social worker	0.5 (3.7)	0 (0)	0 (0)	0 (0)
Dietitian	1 (5)	1 (3)	3 (13)	1 (8)
Occupational therapist	0 (0)	0 (0)	0 (0)	2 (14)
Home care worker	0 (0)	0 (0)	0 (0)	0 (0)
Mental health professional	18 (103)	12 (69)	7 (33)	31 (128)
Other services	6 (29)	50 (269)	1 (4)	7 (32)
Total service costs	110 (138)	120 (291)	79 (190)	429 (1429)
Lost employment	178 (422)	52 (82)	163 (420)	398 (842)
Total social costs	288 (459)	172 (302)	242 (499)	827 (2038)

All figures are in 2000/01 pounds sterling.

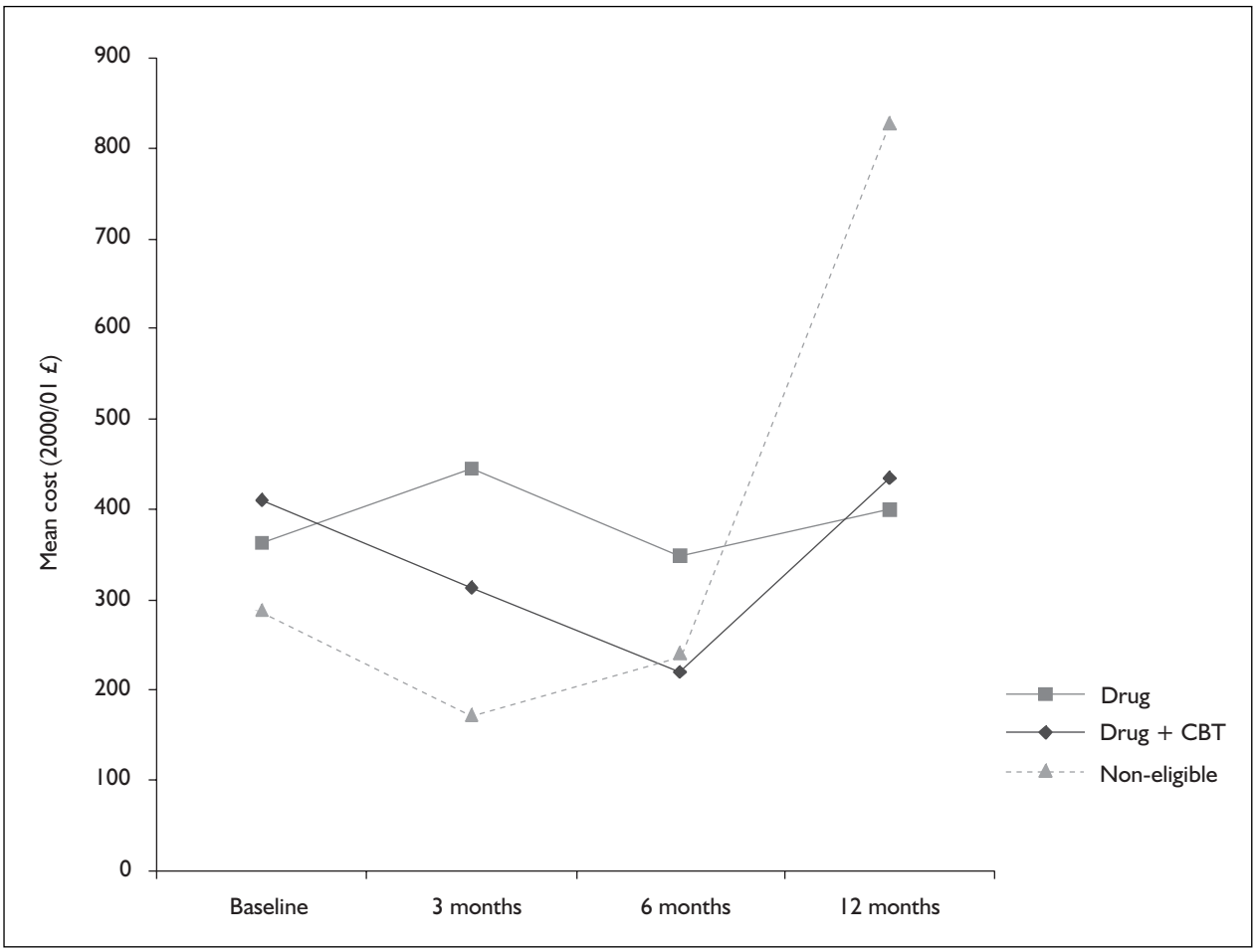


FIGURE 15 *Change in mean social costs (including lost employment) between baseline and 12-month follow-up*

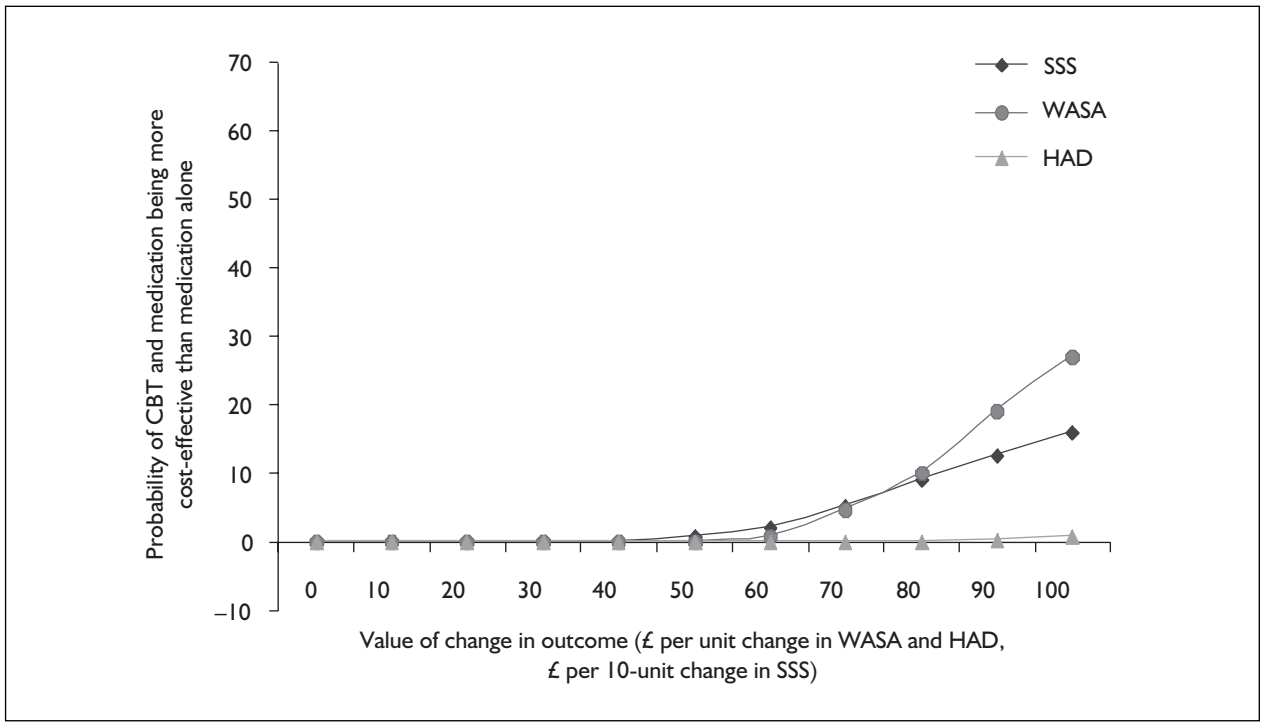


FIGURE 16 *CEACs at 6 months*

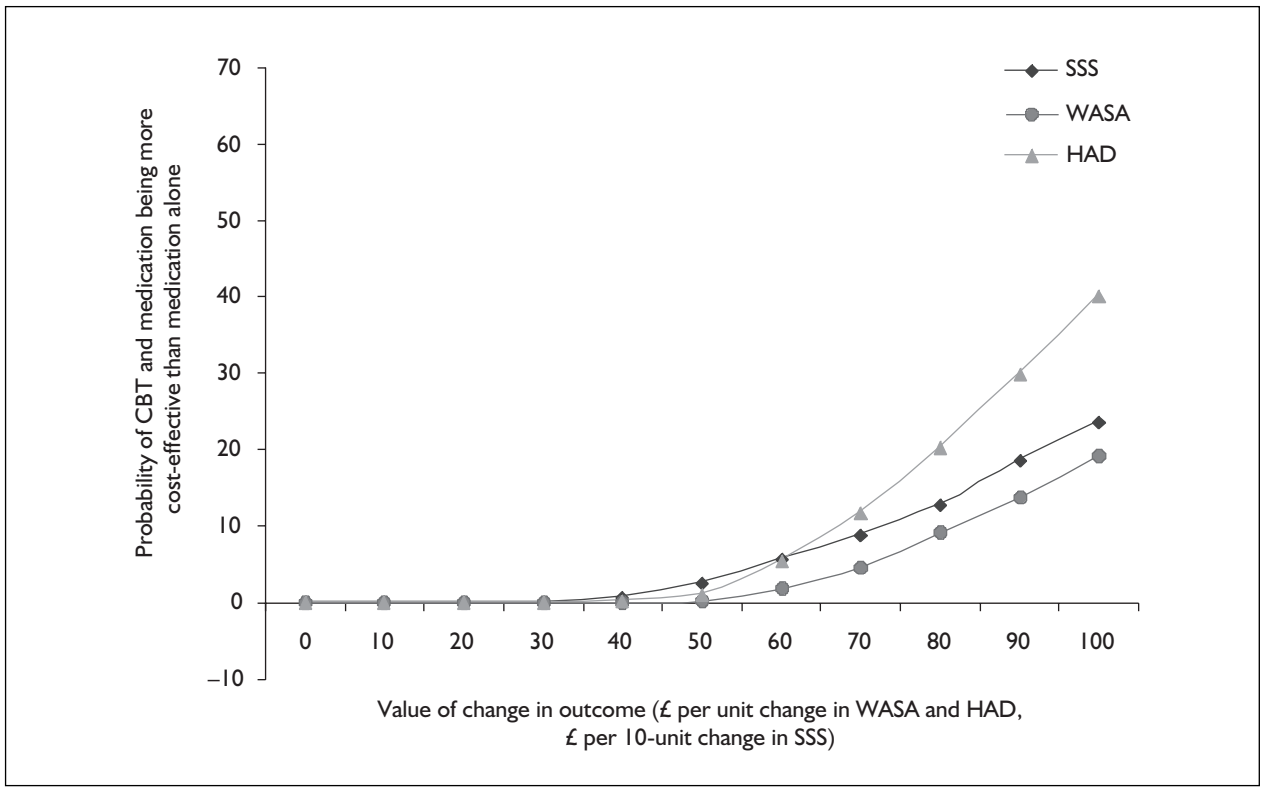


FIGURE 17 *CEACs at 12 months*

Chapter 5

Testing for coeliac disease

Introduction

Coeliac disease is a chronic condition that affects the small bowel of genetically predisposed children and adults. It is characterised, in adults, by chronic diarrhoea, weight loss, anaemia, abdominal distension, lassitude and general malaise and, in children, by failure to thrive, weight loss, short stature, vomiting and diarrhoea, recurrent abdominal pain, muscle wasting, irritability and unhappiness. All patients with coeliac disease may develop iron-deficiency anaemia, dermatitis herpetiformis, peripheral neuropathy, folic acid deficiency, reduced bone density and unexplained infertility.

Coeliac disease is relatively common, and is thought to affect between 1:100 and 1:300 people in most parts of the world,[94] although many patients with the disease have minimal or atypical symptoms.

The diagnosis of coeliac disease is difficult to make clinically, because it mimics other conditions,[95] particularly IBS. There may be latent periods and it seems that clinicians have a relatively low index of suspicion for making the diagnosis by appropriate serological testing.

The cause of coeliac disease is an enteropathy precipitated by the ingestion of gluten-containing foods, such as are commonly found in wheat, rye, barley and oats. The immunological response to gluten causes damage to the small intestinal mucosa, impairing absorption of key nutrients. As well as the conditions described above, most of which are related to malabsorption, patients with coeliac disease are more likely to develop gastrointestinal malignancies.

The condition can be treated, and effectively cured, by the exclusion of gluten from the diet, and can be diagnosed by the use of highly sensitive and specific serological tests, which generally need to be followed up with a confirmatory jejunal biopsy.

Because IBS and coeliac disease can present in such similar ways, and because the diagnosis of the latter can be precise and lead to effective treatment, the question has arisen of whether testing for coeliac disease should form an integral part of the work-up of patients with IBS (and has also raised interest in research questions about the relative frequency of coeliac disease in patients with a definite diagnosis of IBS).

The researchers took advantage of the trial of CBT in IBS to determine the prevalence of positive serology for IBS among patients referred to the trial, in an attempt to provide information that may shed light on this controversy.

Methods

The GP records of 17 patients diagnosed with IBS in primary care noted that they had undergone antiendomysial and antigliadin antibody testing before referral to the study. A further seven patients diagnosed with IBS following referral to secondary care had a prestudy record in their GP notes of these tests having been done in secondary care. This equates to prestudy testing for coeliac disease in 11.4% of patients diagnosed in primary care and 10.9% of patients seen in secondary care. One patient had a record of a negative jejunal biopsy in secondary care followed some years later by a negative antiendomysial and antigliadin antibody test in primary care.

Antiendomysial and antigliadin blood tests were performed on 141 patients who had no prestudy record of these tests. A further three patients declined to have the test. Of the patients who were tested, 96 (68.1%) had been diagnosed with IBS in primary care and 45 patients (31.9%) had also been seen in secondary care.

Of the 141 patients tested for coeliac disease during the study, 136 patients identified their ethnic origin: 93 were white British, three were Irish, 13 were of other white origin, three were of white and black Caribbean origin, one was of white and Asian origin, one was Pakistani, two were Bangladeshi and one was of other Asian origin. A further ten were black Caribbean, five were of black African origin, one was of another black origin and two patients said that their origin did not fit any of the above groups.

The diagnosis of coeliac disease was regarded as being confirmed when both antiendomysial and antigliadin antibody tests were positive.

Results

Of the 141 patients tested for coeliac disease during the study, 19 (13.5%) had been diagnosed for 3 months to 1 year, 48 (34.0) for between 1 and 5 years, and 71 (50.4) for more than 5 years. One patient tested positive for these two tests, giving a prevalence of positive serology for coeliac disease of 0.7% (95% CI 0.66 to 0.74) in primary care patients with a clinical diagnosis of IBS. The patient who tested positive was a 43-year-old white British woman who had a 1–5 year history of IBS. On questioning, she recalled being told that she had coeliac disease following childhood investigations, but thought that she had 'outgrown it'.

If patients whose IBS was diagnosed only after referral to a specialist gastroenterologist are excluded from this analysis, so that the population denominator consists of patients whose diagnosis of IBS was made by their GP alone, the prevalence rises to 1.4% (95% CI 0.84 to 1.24%).

Discussion

The prevalence of positive serology for coeliac disease in this study was less than that recorded in a study of patients with Rome II positive IBS attending a gastroenterology outpatients clinic,[95] and also lower than the 3.3% reported by Sanders and colleagues in their cross-sectional study in primary care.[96] It is thought that the prevalence of coeliac disease is higher in the Irish population than in most other countries, because of a greater genetic susceptibility among Irish individuals. For example, a sample of 1823 Irish adults showed that 1:152 had positive serology for coeliac disease, equivalent to a prevalence of 0.7% (95% CI 0.68 to 0.72%), but Sanders and colleagues' recent survey of 1200 volunteers from five general practices in South Yorkshire, UK, reported a prevalence of 1% (95% CI 0.4 to 1.3%). In this study the prevalence of positive serology in a subsample of 123 primary-care IBS patients was found to be 3.3% (95% CI 2.7 to 3.9%).[96] These figures are comparable to the study by Mein and Ladabaum,[97] who found a prevalence of coeliac disease in irritable bowel syndrome of 3%, and concluded that testing for coeliac disease in patients with suspected IBS is likely to be cost-effective. In another recent study, Spiegel and colleagues[98] found that testing for coeliac disease was likely to be cost-effective at a prevalence above 1%.

These results suggest that the prevalence of coeliac disease in a primary-care IBS population is unlikely to be significantly different from that in the general population, but given the relative ease of undertaking the investigation and the considerable benefits accruing to patients found to have gluten sensitivity, taken with Spiegel's recommendation on cost-effectiveness, it seems appropriate to suggest that, at least at some point in their work-up, testing for coeliac disease is considered in patients with a differential diagnosis of IBS in primary care.

Chapter 6
Discussion

Main findings

This study is the first reported RCT on the efficacy of CBT in primary care for IBS. It has shown that the addition of CBT to mebeverine hydrochloride, in the context of usual GP care, is beneficial in patients who have IBS of moderate or greater severity, with the effect of therapy persisting for up to 6 months, but waning at 12 months' follow-up. The study has shown that the addition of CBT produces benefit in terms of the clinical severity of IBS, and the impact of IBS on patients' lives, adverse illness cognitions and coping behaviours. Significantly, CBT also reduces the disability caused by IBS and the level of psychopathology reported by patients.

As important secondary findings, this study has demonstrated that practice nurses, without prior specialisation in gastroenterology or in psychology, can effectively acquire skills in IBS-specific CBT, and deliver IBS-specific CBT in a general practice surgery under the supervision of a CBT tutor.

In this study, a belief in an external ideology for IBS symptoms and the likely serious significance and consequences of these symptoms, along with male gender, predict a worse outcome and a poor response to treatment in IBS.

The economic analysis indicates that the additional costs of providing CBT for patients with IBS in general practice are not offset by the additional service and social costs incurred by these patients over the 12-month study period.

Strengths of the study

This study had a number of design features that are likely to make its findings generalisable to the large population of patients in primary care with IBS of moderate or greater severity and who have not responded to the usual primary-care package of explanation, reassurance, dietary advice and antispasmodic therapy. The inclusion criteria used in this study were not unduly restrictive, so that patients diagnosed by their GPs as having IBS were included, rather than using the Rome II criteria, which can lead to the selection of a patient population that is not representative of those seen and treated in primary care.

The addition of CBT to mebeverine as the comparator intervention is, similarly, pragmatic and representative of typical clinical practice, again supporting the likely generalisability of the study's findings to the care of IBS in primary care. The authors recognise that the availability of CBT is limited, but because this study has shown that effective IBS-specific CBT can be delivered by trained general nurses, they believe that this choice of intervention was a realistic one, with potential wide applicability.

The study was appropriately powered and sufficient patients were recruited to meet the sample size requirements, assuring statistically meaningful comparisons for the primary and secondary outcome measures selected. The choice of the SSS as the primary outcome measure, and the use of a range of other scales as ancillary measures, plus the economic analysis based on the CSRI, are further strengths of the study, enabling a range of physical, psychological, behavioural and economic outcomes to be reported. This comprehensive package of measures enables the significance of the study findings to be better understood and to be seen in the context of the multifactorial aetiology of IBS.

The nested analysis of testing for coeliac disease in this population has provided further useful information both about the prevalence of the condition in IBS and about the appropriateness, or otherwise, of routine coeliac disease testing in patients being investigated for IBS.

Weaknesses of the study

The overall study design might be criticised for the lack of a placebo arm, in which an 'attention control' intervention of some kind was added to mebeverine, and compared with the CBT plus mebeverine arm. The advantage of attempting to do this would be to determine, in an explanatory rather than a pragmatic sense, whether the intrinsic components of the nurse-delivered CBT package were, indeed, the effective ingredient in

the intervention, or whether the contact, explanation, reassurance and support value of the CBT sessions were, in a general sense, responsible for their therapeutic benefits. The researchers decided against this design for two main reasons. First, attention control placebo interventions in trials of psychological therapies are difficult to implement in a credible way and, second, the additional information obtained in this essentially pragmatic primary-care trial was not thought to be worth the considerably increased costs that would necessarily be incurred in mounting a larger study. However, the authors acknowledge that while the CBT was very carefully designed and tailored for the treatment of patients with IBS, it is possible that non-specific components of the contact between patients and the study nurses were at least in part responsible for the beneficial effects of the CBT sessions.

A second weakness of the study was the failure to assure complete blinding of the nurse therapists to the proposed treatment allocation of patients interviewed at the time of recruitment. Although measures were put in place to ensure that therapists were, indeed, blind to treatment allocation status (by the use of sealed envelopes containing the randomly generated treatment codes), it transpired that on a number of occasions the treatment allocation status of patients was known to the nurses at this time. It is possible that awareness of treatment allocation would have influenced the interaction between nurses and patients, although the direction of this influence is difficult to predict and it could, arguably, work in any direction. For example, it is possible that awareness of treatment allocation status could lead to either an overestimate or underestimate of symptom severity.

Third, it could be argued that an intervention has been designed and tested which, despite the above comments about the practicability of training general nurses to deliver CBT, is unlikely to be readily available in primary care in the UK. It is certainly true that the management of gastrointestinal disorders in general has not emerged as a priority in the Quality Outcomes Framework, which forms the basis of the new NHS contract for GPs; however, the government's policy initiative to develop GPs and other practitioners with special clinical interests would support the idea of providing additional expertise, through appropriately trained nurses, in primary care. Nurse practitioners with special clinical interests are already working in fields such as drug and alcohol misuse and mental health, and the principle of training primary care nurses to deliver CBT (which could also find a therapeutic role in conditions such as chronic fatigue syndrome, other medically unexplained conditions and mental health problems) would be consistent with these policy developments.

Finally, this study reported on an economic analysis, which indicates that the provision of CBT in addition to usual treatment is associated with excess service costs, and attempted to demonstrate the potential costs and benefits to payers by the use of CEACs. Potential limitations of this approach, and the use of the CSRI, include the use of resource data derived from patient recall (rather than by direct access to clinical notes), possible underpowering of the health economic analysis and the absence of sensitivity analyses covering a wide range of costing options. However, the data presented in this report provide the basis for further cost-effectiveness and cost–benefit research in this important area.

The therapeutic context: applicability

Where do these results fit into current therapeutic approaches to IBS, and how likely are they to add to the quality of care provided to patients with IBS in primary care?

Previous therapeutic trials in IBS have, as previously described, rarely included patients selected from primary-care populations, have not measured effects on illness cognitions (and have frequently only measured symptomatic outcomes), have rarely incorporated economic analyses and have often been characterised by short follow-up periods.[99–101] Indeed, most research into IBS has been driven by pharmaceutical developments, and in recent years new agents, based on 5-hydroxytryptamine (5-HT_3 and 5-HT_4) receptor mechanisms, thought to be involved in the aetiology of IBS, have been tested in a series of trials, generally of 3 months' duration.[102,103]

The management of IBS begins with a careful description of symptoms and the identification of those symptoms most troublesome to individual patients. In recent years clinicians have been encouraged to allocate patients with IBS into one of three symptomatic subtypes: constipation-predominant IBS (IBS-C), diarrhoea-predominant IBS (IBS-D) and IBS with alternating constipation and diarrhoea (IBS-A). It has argued that in doing so more appropriate therapeutic agents are likely

to be selected and it is certainly true that subtype classification has led to the development of novel pharmacological agents effective within a relative narrow range of IBS symptoms.

Simple therapies in IBS can be readily tailored to patients' most troublesome symptoms, so that the addition of fibre or another bulking agent, with plenty of fluids, is appropriate for patients with constipation-predominant symptoms and, conversely, antidiarrhoeal agents such as loperamide are appropriate for patients who are troubled by diarrhoea. Meta-analyses of the effects of smooth muscle relaxants and antispasmodic agents and of low-dose antidepressants show a consistent, but rather moderate, benefit for all of these.[40] The newer therapeutic agents have shown some therapeutic promise, but enthusiasm for them has been tempered by problems with side-effects. One agent, alosetron, was shown to be effective in women with diarrhoea-predominant IBS,[103] but was withdrawn from general prescription because of the development of ischaemic colitis and the deaths of elderly patients taking the drug. A related agent, cilansetron, has failed to obtain regulatory approval because of similar concerns about safety, coupled with a lack of convincing evidence of efficacy. Tegaserod, a new agent intended for constipation-predominant IBS, has a modest therapeutic benefit,[100] but can also cause side-effects, including diarrhoea, and has not yet obtained regulatory approval for use in a number of European countries.

Psychological therapies, in contrast, are not restricted to any one IBS subtype, and, if effective, offer considerable advantages over newer and more expensive therapeutic agents intended for use in a particular subgroup of IBS patients.[104] Patients in the present study were not restricted to any IBS subgroup, and in addition no adverse effects, either physical or therapeutic, were identified in either the mebeverine or mebeverine plus CBT group. Well-designed and effectively delivered psychological interventions clearly have a significant potential role in the management of IBS in primary care, not least because of their safety and freedom from the side-effects and other problems associated with pharmacological therapies.

Recommendations for future research

This study provides useful evidence of a short- to medium-term benefit for the addition of CBT, delivered by specially trained nurses, to patients with IBS in primary care. The questions that now need to be answered are: first, whether it is possible to sustain the therapeutic benefits of CBT in some way; second, to determine whether the current or any future package of CBT provides a more cost-effective approach to selected patients than the newer, and more expensive, drugs being developed for IBS; and third, whether it is possible to select patients most likely to benefit from particular therapeutic approaches. Although a small number of predictors of poor outcomes was identified in this study, the results did not enable the building of a patient profile likely to be associated with notable benefit from CBT.

The authors' recommendations for future research, therefore, are as follows:

- Studies are needed on the long-term follow-up of IBS patients treated with CBT, perhaps testing the value of top-up sessions at 3-6 months or 3–6-monthly intervals, to sustain the therapeutic effect.
- Cost–benefit analyses comparing CBT with other therapeutic approaches to IBS are needed. Although the package of CBT delivered in this trial entails additional service costs, it may well be that, for treatment-resistant patients who need to go on to IBS-specific drugs, CBT will prove a more cost-effective therapy.
- Studies could be conducted to evaluate means of training both non-specialist health professionals and GPs to deliver CBT. This may be of particular importance in the context of practice-based commissioning in the NHS, and it would be interesting to speculate, for example, on ways in which a cluster of practices might pool resources to provide a CBT service for patients with IBS and perhaps other conditions for which this approach to treatment is effective.
- There is limited research evidence to suggest that short-form CBT (for the treatment of depression in one study) can be incorporated into the general practice consultation.[105] CBT-based approaches to explanation and patient education could readily form part of the standard general practice conversation with IBS patients, and training in this aspect of clinical and communication skills may empower interested GPs to provide more effective management and support for their IBS patients.

Acknowledgements

Contribution of authors

Tom Kennedy (General Practitioner) was the principal investigator, prepared the original design and was involved with the conduct of the trial, data analysis and the final writing up of the report. Trudie Chalder (Professor of Psychological Medicine) contributed to the original idea, advised on CBT and was involved in the contribution to analysis and the final writing up of the report. Paul McCrone (Senior Lecturer in Health Economics) contributed to the design of the health economics study and undertook health economics analysis for the report. Simon Darnley (Research Associate and Study Co-ordinator) contributed to the development of the study, recruitment, training nurses in CBT and management of the study. Martin Knapp (Director, Centre for the Economics of Mental Health) contributed to the design of the trial and health economic analysis. Roger Jones (Wolfson Professor of General Practice) devised the original idea for design of the trial, and was involved with the conduct of the trial, data analysis and the final writing up of the report. Simon Wessely (Professor of Epidemiology and Liaison Psychiatry) devised the original idea for design of the trial, and was involved with the conduct of the trial, data analysis and the final writing up of the report.

References

1. Thompson WG, Creed F, Drossman DA, Heaton KW, Mazzacca G. Functional bowel disease and functional abdominal pain. *Gastroenterology International* 1992;**2**:75–91.
2. Manning AP, Thompson WG, Heaton KW, Morris AF. Towards a positive diagnosis of the irritable bowel. *BMJ* 1978;**ii**:653–4.
3. Boyce PM, Koloski NA, Talley NJ. Irritable bowel syndrome according to varying diagnostic criteria: are the new Rome II criteria unnecessarily restrictive for research and practice? *Am J Gastroenterol* 2000;**95**:3176–83.
4. Kay L, Jorgensen T, Jensen KH. The prevalence of irritable bowel syndrome in a random population: prevalence, incidence, natural history and risk factors. *J Intern Med* 1994;**236**:23–30.
5. Saito YA, Schoenfeld P, Locke GR III. The epidemiology of irritable bowel syndrome in North America: a systematic review. *Am J Gastroenterol* 2002;**97**:1910–15.
6. Jones R, Lydeard S. Irritable bowel syndrome in the general population. *BMJ* 1992;**304**:87–90.
7. Kennedy TM, Jones RH, Hungin AS, O'Flanagan H, Kelly P. Irritable bowel syndrome, gastro-oesophageal reflux and bronchial hyper-responsiveness in the general population. *Gut* 1998;**43**:770–4.
8. Talley NJ, Weaver AL, Zinsmeister AR, Melton LJ III. Onset and disappearance of gastrointestinal symptoms and functional gastrointestinal disorders. *Am J Epidemiol* 1992;**136**:165–77.
9. Agreus L, Svardsudd K, Nyren O, Tibblin G. Irritable bowel syndrome and dyspepsia in the general population: overlap and lack of stability over time. *Gastroenterology* 1995;**109**:671–80.
10. Jones R. Irritable bowel syndrome. *Practitioner* 1991;**235**:811–14.
11. Holmes KM, Salter RH. Irritable bowel syndrome – a safe diagnosis. *BMJ* 1982;**285**:1533–4.
12. Hahn B, Watson M, Yan S, Gunput D, Heuijerjans J. Irritable bowel syndrome symptom patterns: frequency, duration, and severity. *Dig Dis Sci* 1998;**43**:2715–18.
13. Kettel J, Jones R, Lydeard S. Reasons for consultation in irritable bowel syndrome; symptoms and patient characteristics. *Br J Gen Pract* 1992;**42**:459–61.
14. Harvey RF, Salih SY, Read AE. Organic and functional disorders in 2000 gastroenterology outpatients. *Lancet* 1983;**i**:632–4.
15. Whorwell PJ, McCallum M, Creed FH, Roberts TC. Non-colonic features of the irritable bowel syndrome. *Gut* 1986;**27**:37–40.
16. Prior A, Wilson K, Whorwell PJ, Faragher EB. Irritable bowel syndrome in the gynecological clinic. Survey of 798 new referrals. *Dig Dis Sci* 1989;**34**:1820–4.
17. Francis CY, Duffy JN, Whorwell PJ, Morris J. High prevalence of irritable syndrome in patients attending urological outpatient departments. *Dig Dis Sci* 1997;**42**:404–7.
18. Whorwell PJ, Lupton EW, Erduran D, Wilson K. Bladder smooth muscle dysfunction in patients with irritable bowel syndrome. *Gut* 1986; **27**:1014–17.
19. Longstreth GF, Preskill DB, Youkeles L. Irritable bowel syndrome in women having diagnostic laparoscopy or hysterectomy. Relation to gynaecological features and outcomes. *Dig Dis Sci* 1990;**35**:1286–90.
20. Fielding JF. A year in outpatients with the irritable bowel syndrome. *Ir J Med Sci* 1977;**146**:162–5.
21. Kennedy TM, Jones RH. Epidemiology of cholecystectomy and irritable bowel syndrome in a UK population. *Br J Surg* 2000;**87**:1658–63.
22. Kennedy TM, Jones RH. The epidemiology of hysterectomy and irritable bowel syndrome in a UK population. *Int J Clin Pract* 2000;**54**:647–50.
23. Thompson WG, Heaton KW, Smyth GT, Smyth C. Irritable bowel syndrome in general practice: prevalence, characteristics and referral. *Gut* 2000;**46**:78–82.
24. Prior A, Maxton DG, Whorwell PJ. Anorectal manometry in irritable bowel syndrome: differences between diarrhea and constipation predominant subjects. *Gut* 1990;**31**:458–62.
25. Gorard DA, Libby GW, Farthing MJ. Ambulatory small intestinal motility in diarrhea predominant irritable bowel syndrome. *Gut* 1994;**35**:203–10.
26. Kellow JE, Philips SF. Altered small bowel motility in irritable bowel syndrome is correlated with symptoms. *Gastroenterology* 1987;**92**:1885–93.
27. Mayer EA, Geebhart GF. Basic and clinical aspects of visceral hyperalgesia. *Gastroenterology* 1994;**107**:271–93.

28. Mertz H, Morgan V, Tanner G, Pickens D, Price R, Shyr Y, *et al*. Regional cerebral activation in irritable bowel syndrome and control subjects with painful and non-painful rectal distention. *Gastroenterology* 2000;**118**:842–8.

29. Mertz H, Naliboff B, Munakata J, Niazzi N, Mayer EA. Altered rectal perception is a biological marker of patients with irritable bowel syndrome. *Gastroenterology* 1995;**109**:40–52.

30. Delvaux M, Denis P, Allemand H. Sexual abuse is more frequently reported by IBS patients than by patients with organic digestive diseases or controls: results from a multicentre inquiry. *Eur J Gastroenterol Hepatol* 1997;**9**:345–52.

31. Locke GR III, Zinsmeister AR, Talley NJ, Fett SL, Melton LJ III. Familial associations in adults with functional gastrointestinal disorders. *Mayo Clin Proc* 2000;**75**:907–12.

32. Levy RL, Jones KR, Whitehead WE, Feld SI, Talley NJ, Corel YA. Irritable bowel syndrome in twins; heredity and social learning both contribute to etiology. *Gastroenterology* 2001;**121**: 799–804.

33. Morris-Yates A, Talley NJ, Boyce PM, Nandurkar S, Andrews G. Evidence of a genetic contribution to functional bowel disorder. *Am J Gastroenterol* 1998;**93**:1311–17.

34. Collins SM. Is the irritable gut an inflamed gut? *Scand J Gastroenterol* 1992;**27**(Suppl 192):102–5.

35. Gwee KA, Leong YL, Graham C, McKendrick MW, Collins SM, Walters SJ, *et al*. The role of psychological and biological factors in postinfective gut dysfunction. *Gut* 1999;**44**:400–6.

36. Drossman DA, McKee DC, Sandler RS, Mitchell CM, Cramer EM, Lowman BC, *et al*. Psychosocial factors in the irritable bowel syndrome. *Gastroenterology* 1988;**95**:701–8.

37. Heaton KW, O'Donnell LJD, Braddon FEM, Mountford RA, Hughes AOE, Cripps PJ. Symptoms of irritable bowel syndrome in a British urban community; consulters and non-consulters. *Gastroenterology* 1992;**102**:1962–7.

38. Whitehead WE, Bosmajian L, Zonderman AB, Costa PT Jr, Schuster MM. Symptoms of psychological distress associated with irritable bowel syndrome. Comparison of community and medical clinic samples. *Gastroenterology* 1988;**95**:709–14.

39. Kennedy TM, Rubin GP, Jones RH. *Irritable bowel syndrome*. Review of therapies. Clinical Evidence series. London: BMA Publishing Group; 2005.

40. Poynard T, Regimbeau C, Benhamou Y. Meta-analysis of smooth muscle relaxants in the treatment of irritable bowel syndrome. *Aliment Pharmacolacol Ther* 2001;**15**:355–61.

41. Poynard T, Naveau S, Mory B, Chaput JC. Meta-analysis of smooth muscle relaxants in the treatment of irritable bowel syndrome. *Aliment Pharmacol Ther* 1994;**8**:499–510.

42. Guthrie E, Creed F, Dawson D, Tomenson B. A controlled trial of psychological treatment for the irritable bowel syndrome. *Gastroenterology* 1991;**100**:450–7.

43. Payne A, Blanchard EB. A controlled comparison of cognitive therapy and self help support groups in the treatment of irritable bowel syndrome. *Journal Consulting and Clinical Psychiatry* 1995;**63**:779–86.

44. Blanchard EB, Schwarz SP, Suls JM, Gerardi MA, Scharff LS, Greene B, *et al*. Two controlled evaluations of multi-component psychological treatment of irritable bowel syndrome. *Behav Res Ther* 1992;**30**:172–89.

45. van Dulmen AM, Fennis JSM, Bleijenberg G. Cognitive behavioural group therapy for irritable bowel syndrome and long term follow up. *Psychosom Med* 1996;**58**:508–14.

46. van Dulmen AM, Fennis JF, Mokkink HG, van der Velden HG, Bleijenberg G. Persisting improvements in complaint-related cognitions initiated during medical consultations in functional abdominal complaints. *Psychol Med* 1997;**27**:725–9.

47. Creed F, Craig T, Farmer R. Functional abdominal pain, psychiatric illness and life events. *Gut* 1988;**29**:235–42.

48. Craig TK, Brown GW. Goal frustrating aspects of life event stress in the aetiology of gastro-intestinal disorder. *J Psychosom Res* 1984;**28**:411–21.

49. Drossman DA, Leserman J, Nachman G, Li ZM, Gluck H, Toomey TC, Mitchell CM. Sexual or physical abuse in women with functional or organic gastrointestinal disorder. *Ann Int Med* 1990;**113**: 828–33.

50. Talley NJ, Fett SL, Zinsmeister AR, Melton LJ III. Gastrointestinal tract symptoms and self reported abuse: a population based study. *Gastroenterology* 1994;**107**:1040–9.

51. Chaudhary NA, Truelove SC. The irritable colon. A study of the clinical features predisposing causes and prognosis in 130 cases. *QJM* 1962;**31**:307–22.

52. Whitehead W. Assessing the effects of stress on physical symptoms. *Health Psychol* 1994;**13**:99–102.

53. Welgan P, Pour HM, Beeler M. Effect of anger on colon motor and myoelectric activity in the irritable bowel syndrome. *Gastroenterology* 1990;**94**:1150–6.

54. Gomborone J, Dewsnap P, Libby G, Farthing M. Abnormal illness attitudes in patients with irritable bowel syndrome. *J Psychosom Res* 1995;**39**:227–30.

55. Deale A, Chalder T, Marks I, Wessely S. A randomised controlled trial of cognitive behaviour versus relaxation therapy for chronic fatigue syndrome. *Am J Psychiatry* 1997;**154**:408–14.

56. Klein KB. Controlled treatment trials in the irritable bowel syndrome: a critique. *Gastroenterology* 1988;**95**:232–41.

57. Whorwell P, Coremans G, Dapoigny M, Jones R, Muller-Lissner S, Muris J, *et al*. Conference report: undertaking therapeutic trials in irritable bowel syndrome in the primary care setting. *European Journal of General Practice* 1997;**3**:149–51.

58. Talley NJ, Gabriel SE, Harmsen WS, Zinsmeister AR, Evans RW. Medical costs in community subjects with irritable bowel syndrome. *Gastroenterology* 1995;**109**:1736–41.

59. Donker GA, Foets M, Spreeuwenberg P. Patients with irritable bowel syndrome: health status and use of health care services. *Br J Gen Pract* 1999;**49**:787–92.

60. Wells NEJ, Hahn BA, Whorwell PJ. Clinical economics review: irritable bowel syndrome. *Aliment Pharmacol Ther* 1997;**11**:1019–30.

61. Shih Ya-Chen T, Barghout VE, Sandler RS, Jhingran P, Sasane M, Cook S, *et al*. Resource utilisation associated with irritable bowel syndrome in the United States 1987–1997. *Dig Dis Sci* 2002;**47**:1705–15.

62. Levy RL, Von Korff M, Whitehead WE, Stang P, Saunders K, Jhingran P, *et al*. Costs of care for irritable bowel syndrome patients in a health maintenance organisation. *Am J Gastroenterol* 2001;**96**:3122–9.

63. Gralnek IM, Hays RD, Kilbourne A, Naliboff B, Mayer EA. The impact of irritable bowel syndrome on health related quality of life. *Gastroenterology* 2000;**119**:654–60.

64. Hahn BA, Kirchdorfer LJ, Fullerton S, Mayer E. Patient-perceived severity of irritable bowel syndrome in relation to symptoms, health resource utilization and quality of life. *Aliment Pharmacl Ther* 1997;**11**:553–9.

65. Hahn BA, Yan S, Strassels S. Impact of irritable bowel syndrome on quality of life and resource use in the United States and United Kingdom. *Digestion* 1999;**60**:77–81.

66. Gralnek IM, Hays RD, Kilbourne A, Naliboff B, Mayer EA. Health care utilization and economic issues in irritable bowel syndrome. *Eur J Surg* 1998;**164**(Suppl 583):73–6.

67. Jhingran P, Decker C, Watson M, Northcutt A, Ricci JF. Alosetron reduces time lost from work in women with diarrhoea-predominant irritable bowel syndrome: Data from phase III placebo-controlled clinical trials. *Clin Drug Invest* 2001;**21**:843–52.

68. Blanchard EB, Scharff L, Payne A, Schwarz SP, Sub JM, Malamood H. Prediction of outcome from cognitive-behavioural treatment of irritable bowel syndrome. *Behav Res Ther* 1992;**30**:647–50.

69. Blanchard EB, Schwarz SP, Neff DF. Two year follow up of behavioural treatment of irritable bowel syndrome. *Behavior Therapy* 1988;**19**:67–73.

70. Harvey RF, Hinton RA, Gunary RM, Barry RE. Individual and group hypnotherapy in treatment of refractory irritable bowel syndrome. *Lancet* 1989;**1**(8635):424–5.

71. Lembo T, Fullerton S, Diehl D, Raeen H, Munakata J, Naliboff B, Mayer EA. Symptom duration in patients with irritable bowel syndrome. *Am J Gastroenterol* 1996;**91**:898–905.

72. Blanchard EB, Radnitz C, Schwarz SP, Neff DF, Gerardi MA. Psychological changes associated with self-regulatory treatments of irritable bowel syndrome. *Biofeedback and Self Regulation* 1987;**12**:31–8.

73. Whorwell PJ, Prior A, Colgan SM. Hypnotherapy in severe irritable bowel syndrome. Further experience. *Gut* 1987;**28**:423–5.

74. van Dulmen AM, Ferris JFM, Mokkink HGA, van der Valden HGM, Bleijenberg G. Doctor-dependent changes in complaint related cognitions and anxiety during medical consultations in functional abdominal complaints. *Psychol Med* 1995;**25**:1011–18.

75. Dixon-Woods M, Critchley S. Medical and lay views of irritable bowel syndrome. *Fam Pract* 2000; **17**:108–113.

76. van der Horst HE, van Dulman AM, Schelleris FG, van Eijk JThM, Fennis JFM, Bleijenberg G. Do patients with irritable bowel syndrome in primary care differ from outpatients with irritable bowel syndrome? *Gut* 1997;**41**:669–74.

77. Thompson WG, Heaton KW, Smyth GT, Smyth C. Irritable bowel syndrome in general practice: prevalence characteristics and referral. *Gut* 2000;**46**:78–82.

78. McDonald IG, Daly J, Jelinek VM, Panetta F, Gutman JM. Opening Pandora's box: the unpredictability of reassurance by a normal test result. *BMJ* 1996;**313**:329–32.

79. van Outryve M, Mayeur S, Meeus MA, Rosillon D, Hendrickx B, Ceuppens M. A double blind crossover comparison study of the safety and efficacy of mebeverine with mebeverine sustained release in the treatment of irritable bowel syndrome. *J Clini Pharmacol Ther* 1995;**20**:277–82.

80. *British National Formulary*. London: British Medical Association and the Royal Pharmaceutical Society of Great Britain; 2003.

81. Francis CY, Morris J, Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. *Aliment Pharmacol Ther* 1997;**11**:395–402.

82. Zigmond AS, Snaith RP. The Hospital Anxiety Depression scale. *Acta Psychiatr Scand* 1993; **67**:361–70.

83. Weinman J, Petrie KJ, Moss-Morris R, Horne R. The Illness Perception Questionnaire: a new method for assessing cognitive representation of illness. *Psychology and Health* 1996;**11**:431–55.

84. Toner BB, Stuckless N, Ali A, Downie F, Emmott S, Akman D. The development of a cognitive scale for functional bowel disorders. *Psychosom Med* 1998;**60**:492–7.

85. Marks I. *Behavioural psychotherapy: Maudsley pocket book of clinical management*. Bristol: Wright; 1986.

86. Beecham J, Knapp M. Costing psychiatric interventions. In Thormicroft G, editor. *Measuring mental health needs*. 2nd ed. London: Gaskell; 2001. pp. 200–4.

87. Horne R, Weinman J, Hankins M. The beliefs about medicine questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health* 1999;**14**:1–24.

88. Netten A, Rees T, Harrison G. *Unit costs of Health and social care*. Canterbury: PSSRU; 2001.

89. Frison L, Pocock S. Repeated measures in clinical trials: analysis using mean summary statistics and its implication for design. *Stat Med* 1992; **11**:1685–704.

90. Lian K-Y, Zeiger SL. Longitudinal analysis using generalised linear models. *Biometrika* 1986; **73**;13–22.

91. Binder DA. On the variances of asymptotically normal estimators from complex surveys. *International Statistical Review* 1983;**51**:279–92.

92. Mooney CZ, Duval RD. *Bootstrapping: a non-parametric approach to statistical inference*. Newbury Park, CA: Sage; 1993.

93. Löthgren M, Zethraeus N. Definition, interpretation and calculation of cost-effectiveness acceptability curves. *Health Econ* 2000;**9**:623–30.

94. Hin H, Bird G, Fisher P, Mahy N, Jerwell D. Coeliac disease in primary care: case finding study. *BMJ* 1999;**318**:164–7.

95. Saunders DS, Carter MC, Harlstone DP, Pearce A, Milford Ward A, McAlindon ME, *et al.* Association of adult coeliac disease with irritable bowel syndrome: a case-control study in patients fulfilling Rome II criteria referred to secondary care. *Lancet* 2001;**358**:1504–8.

96. Sanders DS, Patel D, Stephenson TJ, Ward AM, McCloskey EV, Hadjivassiliou M, *et al.* A primary care cross-sectional study of undiagnosed adult coeliac disease. *Eur J Gastroenterol Hepatol* 2003;**14**(4):407–13.

97. Mein SM, Ladabaum U. Serological testing for coeliac disease in patients with symptoms of irritable bowel syndrome: a cost-effectiveness analysis. *Aliment Pharmacol Ther* 2004;**19**:1199–210.

98. Spiegel BMR, DeRosa VP, Gralnek JM, Wang V, Dulai GS, *et al.* Testing for coeliac sprue in irritable bowel syndrome with predominant diarrhoea: a cost-effectiveness analysis. *Gastroenterology* 2004;**126**:1721–32.

99. Akehurst R, Kaltenthaler E. Treatment of irritable bowel syndrome: a review of randomised controlled trials. *Gut* 2001;**48**:272–82.

100. Jackson JL, O'Malley PG, Tomkins G, Balden E, Santoro J, Kroenke K. Treatment of functional gastrointestinal disorders with antidepressant medications: a meta-analysis. *Am J Med* 2000;**108**:65–72.

101. Talley NJ, Owen BK, Boyce P, Paterson K. Psychological treatments for irritable bowel syndrome: a critique of controlled treatment trials. *Am J Gastroenterol* 1996;**91**:277–83.

102. Muller-Lissner SA, Fumagalli I, Bardhan KD, Pace F, Pecher E, Nault B, Ruegg P. Tegaserod, a 5-HT(4) receptor partial agonist, relieves symptoms in irritable bowel syndrome patients with abdominal pain, bloating and constipation. *Aliment Pharmacol Ther* 2001;**15**:1655–66.

103. Jones RH, Holtmann G, Rodrigo L, Ehsanullah RS, Crompton PM, Jacques LA, *et al*. Alosetron relieves pain and improves bowel function compared with mebeverine in female nonconstipated irritable bowel syndrome patients. *Aliment Pharmacol Ther* 1999;**13**:1419–27.

104. Raine R, Haines A, Sensky T, Hutchings A, Larkin K, Black N. Systematic review of mental health interventions for patients with common somatic symptoms: can research evidence from secondary care be extrapolated to primary care? *BMJ* 2002;**325**:1082.

105. Scott CS, Scott J, Tacchi MJ, Jones RH. Abbreviated cognitive therapy for depression: a pilot study in primary care. *Behavioral and Cognitive Psychotherapy* 1994;**22**:57–64.

Appendix 1

Primary Care Society for Gastroenterology. Irritable bowel syndrome: guidelines for general practice

The strength of evidence for these recommendations ranges from **A** (randomised controlled trials), **B** (other controlled or quasi-experimental studies), **C** (descriptive studies) to **D** (expert opinion or clinical experience of respected authorities).

Overview

Irritable bowel syndrome (IBS) is a common, non-life threatening condition affecting 1.5–2 times as many women as men. It is a chronic disorder that fluctuates in intensity and is characterised by visceral hypersensitivity. It is costly to the NHS and has a significant impact on quality of life affecting 17% of the UK population; three quarters of these rely on self-care.

Clinical features

IBS is characterised by the presence of abdominal pain associated with altered bowel habit in the absence of an identifiable structural or biochemical disorder. There are four key symptoms: pain, constipation, diarrhoea, and abdominal bloating. The Rome II criteria are a set of diagnostic criteria formulated by experts. They are highly specific for IBS and are valuable for clinical trials but in clinical practice many doctors are less restrictive in reaching a diagnosis.

Rome II: criteria
Abdominal discomfort or pain for 12 consecutive weeks in the preceding 12 months that has two of three features:

- Relieved by defecation
- Onset associated with a change in stool frequency
- Onset associated with a change in form (appearance) of stool

The following cumulatively support the diagnosis of IBS:

- Abnormal stool frequency
- Abnormal stool form
- Abnormal stool passage
- Passage of mucus
- Bloating or feeling of abdominal distension

In a significant minority of patients, IBS is precipitated by an episode of bacterial gastroenteritis (**C**).

Associated non-colonic problems include upper gastrointestinal symptoms, functional urinary and gynaecological problems, back pain, lethargy and, less commonly, migraine, asthma and depression (**C**).

A patient-centred approach should be adopted as IBS symptoms are non-specific and patients often worry that they have a life-threatening illness (**C**).

Unnecessary investigations, referrals to non-gastrointestinal specialities and excess rates of surgery are reported for patients with IBS (**C**).

Making a safe diagnosis

- Patients over the age of 45 years with new onset symptoms and patients of any age with alarm features or a strong family history of gastrointestinal cancer should be referred for specialist assessment in order to exclude serious disease, particularly colorectal cancer (**C**). (Guidelines for the early detection of colorectal cancer in primary care: www.pscg.org.uk)

Alarm features
- Rectal bleeding in the absence of an obvious anal cause
- Weight loss
- Anaemia
- Abdominal mass

An abdominal examination, including rectal examination when appropriate, should be performed (**D**).

Full blood count, erythrocyte sedimentation rate and C reactive protein may help identify alternative or more serious disease (**C**).

The possibility of enteric infection, in particular giardiasis, should be considered, as should Crohn's disease, coeliac disease or pancreatic disease (**D**).

	Pain	Constipation	Diarrhoea	Bloating	Global improvement	NNT
Alverine	**Ib****					
Hyoscine	**Ib**					9
Ispaghula husk		**Ib**			**Ib**	4
Loperamide			**Ib**		**Ib**	15
Mebeverine	**Ia**				**Ia**	
Peppermint*						
Low dose tricyclic antidepressants	**Ib**				**Ib**	**3**

NNT: The number needed to treat in order to achieve any positive change in Global improvement.
(Evidence grading **Ia**, meta-analysis of randomised controlled trials; **Ib**, at least one RCT.)
* Conflicting evidence of benefit. ** Study conducted in primary care.

Lactose intolerance, bile salt malabsorption and dietary intolerance are contributing factors in a minority of patients with IBS and may be sought when the patient's history is suggestive or management proves problematic (**C**).

Initial management

- Patients report greater satisfaction if they have had an adequate explanation and time to address their concerns regarding serious pathology (**C**).

Specific therapies

Lifestyle advice

- A high fibre diet and supplementation with bran are of conflicting benefit (**A**). Patients with constipation predominant and mixed type IBS are most likely to benefit.
- Dietary manipulation is controversial and of unproven benefit but some patients report that their symptoms are strongly related to specific foodstuffs (**C**).

Drug therapies

- Drug therapy should be targeted at the patient's most troublesome symptoms.

The table above summarises the evidence for therapies in IBS. The quality of therapeutic trials in IBS is variable, large placebo effects occur and most trials have been conducted on secondary care populations.

Non-pharmacological therapy

Hypnosis, cognitive behavioural therapy, biofeedback and psychotherapy have evidence of benefit (**B**). Patients on Chinese herbal medicine showed a global improvement in one study (**Ib**). These reports were all based on hospital outpatients.

Self-help

The IBS Network (www.ibsnetwork.org.uk), telephone 0114 2611531 offers advice, support and information on managing IBS.

Reviewing the diagnosis

The diagnosis of IBS rarely alters over time. Nevertheless, be prepared to reconsider the diagnosis if the clinical picture changes.

Key points

The underlying abnormality in IBS is visceral hypersensitivity of uncertain cause. IBS is a chronic disorder that fluctuates in severity. Emotions and stress play an important role in the course of the disorder. IBS does not predispose to colorectal cancer or inflammatory bowel disease.

This guideline was developed by Greg Rubin, Yenal Dundar, Tom Kennedy and Roger Jones for the Primary Care Society for Gastroenterology. It will be reviewed in September 2003.

Department of Primary Health Care, Institute of Health Sciences, Old Road, Headington, Oxford OX3 7LF
Tel. 01865 226757
www.pcsg.org.uk

Appendix 2

Irritable bowel syndrome specific cognitive behavioural therapy: a manual for primary care

Introduction

This manual outlines the psychological treatment approach developed as part of a large randomised controlled trial of cognitive behavioural psychotherapy and antispasmodic therapy versus antispasmodic therapy alone for irritable bowel syndrome. General nurses in primary care were trained to deliver the cognitive behavioural therapy.

Irritable bowel syndrome (IBS)

Irritable bowel syndrome is the most common functional disorder and depending on the criteria used to make a diagnosis affects approximately 15–20% of the general UK population. The condition is non-life-threatening and is twice as common in women as in men.

IBS is characterised by the presence of abdominal pain and altered bowel habit with characteristic symptoms summarised in the box below. These symptoms, known as the Manning criteria, aid the diagnosis of IBS and the more of the symptoms that are present the more likely that the diagnosis is IBS. Other researchers have refined the diagnosis of IBS and although there is no diagnostic test for IBS there are a few factors that aid diagnosis.

In primary care most patients who consult regarding symptoms of IBS are in their late twenties or early thirties and will often have had symptoms for several years prior to consulting. Weight loss, nocturnal pain and gastrointestinal blood loss are not features of IBS and should alert one to the possibility of more serious pathology. One should consider referral for further investigation including lower gastrointestinal endoscopy if patients present with new gastrointestinal symptoms or a change in pre-existing ones after the age of 45 years. Patients at a younger age should be referred if there is a history of colorectal cancer in a first degree relative. At any age one should consider the possibility of inflammatory bowel disease (IBD), a more dangerous condition than IBS and one that may share its symptom profile. Performing a full blood count and a C-reactive protein (CRP) or erythrocyte sedimentation rate (three blood tests) helps in the detection of IBD and anaemia and abnormal results should prompt referral. There is uncertainty regarding the need to screen for coeliac disease, a condition characterised by an intolerance of gliadin, a protein found in wheat and certain other grains. The availability of a serological screening test does facilitate testing if this is considered appropriate.

The symptoms of IBS can be distressing, inconvenient and often disruptive. Although it seems the majority of patients with IBS do not consult about it, for some patients the condition is troubling and reduces their quality of life and their productivity. It is a remitting relapsing condition and there is no cure. The one-time association between IBS and psychiatric disorder is now considered to be due to consultation and referral bias. Although patients with IBS who are referred to secondary care do report a considerable degree of psychopathology this is tempered by the finding that patients with IBS in the general population who do not consult have normal psychological profiles. It is now thought that the reported gradation in psychopathology from non-consulters to consulters is a feature of consulting behaviour rather than of IBS. Similar findings have been shown for other medically unexplained conditions such as non-cardiac chest pain and chronic fatigue syndrome. Those patients with IBS who do consult report greater

Manning criteria to aid diagnosis of IBS
Recurrent abdominal pain and two or more of the following:

- Relief of pain with defecation
- More frequent stools at the onset of pain
- Looser stools at the onset of pain
- Visible abdominal distension
- Passage of mucus per rectum
- Sensation of incomplete evacuation

IBS is identified in patients with recurrent abdominal pain and two or more of the Meaning criteria.

severity of abdominal pain than do non-consulters and they also report a fear that their symptoms may be due to more serious conditions such as gastrointestinal cancer or heart disease.

Many patients report that their symptoms are worse when they are stressed, but as the pathophysiology of IBS is imperfectly understood it is uncertain as to how this is mediated. A commonly held theory is that IBS may be at least partly due to hypersensitivity of the enteric nervous system; that is the plexi of nerves that line the bowel may be overly sensitive and may respond to a level of stimulus that would not normally produce a response. The gut may then also be over-responsive and demonstrate excessive or aberrant motility.

Understanding where cognitive behavioural therapy (CBT) fits in

Key point: CBT is not a cure for IBS.

CBT is not a panacea and it is to be expected that patients with IBS will continue to experience symptoms after completing their CBT. Neither is CBT as presented here in conflict with therapy the patient may already be taking. We would expect patients to experience symptoms associated with irritable bowel syndrome after the treatment has been completed. CBT focuses on the behaviours, thoughts and feelings surrounding IBS. The aim is to improve the way people cope with day-to-day life. By improving these aspects it is hoped that the patient's perception of the physical symptoms of IBS will also improve.

The cognitive behavioural treatment rationale: the three systems model

Key point: Thoughts, behaviour and feelings maintain and intensify symptoms.

The way a patient thinks, acts and feels can intensify and maintain the symptoms of IBS. When a patient experiences pain, bloating, constipation or diarrhoea the way he/she then thinks about the symptoms will affect their levels of anxiety.

For example a patient may think, 'oh no. I've got that pain again. I've had it for a while now, that must mean that there is more to this than just IBS, the doctor must be wrong. I have something more serious'. Such thoughts may increase levels of anxiety and result in a perception of more severe symptoms culminating in associated behaviours such as an increase in consultation with a general practitioner and a request for referral to a specialist. We know for example that patients who continue to attribute their symptoms to a purely physical cause are more likely to consult than those who do not. The patient may then go on to develop other behaviours such as altering diet, symptom monitoring, straining and avoiding social situations in an attempt to gain control over and reduce the symptoms or to avoid the consequences of the symptoms that may result from embarrassment. Patients may become trapped in a vicious circle of fear and avoidance; these three systems, the physiological, cognitive and behavioural responses, appear to be interdependent and responsible for maintaining the disorder. Changing cognitions, behaviour or both is likely to bring about improvement in symptoms.

We can see how a person's thoughts, feelings and behaviours will affect how they respond to the symptoms. This in turn will affect many aspects of their daily life.

If patients experience a particularly nasty bout of symptoms they might focus on the symptoms much more (becoming hypersensitive to them) which in turn may then increase the impact and frequency of the IBS symptoms. This is referred to as symptom focusing.

The patient should understand that this does not mean that IBS is all in the mind. Rather, even though IBS may have physical causes that we do not fully understand, a CBT approach assumes

Case example
Kate has an important meeting with her boss in the morning that causes her some anxiety (feelings and thoughts).

She knows that these sorts of situations often cause her IBS to flare up, and cause more diarrhoea and bloating than usual.

She is further concerned that her diarrhoea will cause her to leave the meeting early (thought).

She decides to call in sick from work with diarrhoea (behaviour).

She then feels guilty and depressed about the effect of her IBS on her life (feelings and thoughts).

Kate thinks that maybe she should give up her job if she can't manage to go to meetings (behaviour and thoughts).

that what a person does, thinks and feels will aggravate and maintain many of the IBS symptoms. A CBT approach assumes that IBS is likely to be influenced by and to influence a patient's lifestyle, level of anxiety and the way he/she views the world. Therefore if possible during the assessment ascertain which thoughts and behaviours are aggravating or maintaining IBS symptoms.

The cognitive behavioural treatment rationale: engagement

Key point: Fit the CBT model to the patient's own experience of IBS.

Once the patient can understand the CBT model and how it fits with their own experience of IBS then the therapist should explain how further sessions will aim to lessen the impact of IBS and in turn reduce the symptoms.

The therapist should explain to the patient that treatment is collaborative, i.e. the therapist and patient will work together to identify possible maintaining factors. They can then test out different ways of coping with IBS. This style of therapy is often referred to as 'collaborative empiricism'. Thoughts and behaviours that may be maintaining aspects of the IBS are identified and alternative behaviours are suggested and tested.

The therapist should demonstrate a positive regard for the patient and their problems. The therapist should try to avoid using medical jargon and where possible use the patient's language. The therapist needs to have a good working knowledge of IBS and the problems associated with it.

Case example
Jane and her therapist identified the following possible maintaining behaviour. Jane avoided walking with her boyfriend for fear of being caught short without a public toilet and being incontinent. She had never been incontinent in the past. This restricted her life and affected her relationship with her boyfriend. She agreed to test out her fear and risk walking with her boyfriend without knowing where the toilet was. She subsequently found that even though she did have some urge to go to the toilet, she was able to control this until reaching a convenient place. By the end of treatment she was able to go into any situation without knowledge of where toilets were located and no longer avoided walking with her boyfriend.

Treatment does not focus on cause and onset. The patient is likely to still have IBS at the end of treatment and they will still have bouts of symptoms. The aim of treatment is to help the patient manage these symptoms in a way that will have minimal effect on their individual lifestyle.

Treatment outline

Each patient is offered six sessions of CBT lasting 50 minutes each. The following is an outline of the content of each session and the techniques that one might use.

All sessions should include

1. consent for tape recording the session in order to facilitate review with a CBT tutor
2. collaborative agenda setting.

Session 1 will focus on a cognitive behavioural assessment and defining problems and goals of treatment.

Sessions 2–6 will include the following:
1. feedback from previous session
2. homework review
3. homework discussion
4. goal setting
5. recap of key issues.

The treatment sessions will also include the following components as necessary:

1. information giving about the problems associated with IBS
2. continuing to identify maintaining factors in IBS
3. introducing IBS specific behavioural and cognitive strategies
4. checking understanding and acceptance of the treatment rationale
5. using questionnaires as a therapeutic tool to monitor progress
6. encouraging the use of diaries.

Specific session by session outline

Session 1

Assessment, engagement and problems and targets

Aims:

1. to build a therapeutic relationship
2. to obtain a detailed problem analysis

3. to agree a specific problem statement
4. to agree on a minimum of two specific treatment goals
5. to ensure the rationale of treatment is understood and agreed and the patient is willing to engage for six sessions using this approach.

A CBT assessment for IBS will involve the therapist gathering details about the patient's IBS, including reviewing the patient's symptoms in detail, explaining how the therapy may be able to help and agreeing on goals that the patient would like to achieve by the end of treatment.

The CBT assessment broadly focuses on five areas based on the identification of; the main problem associated with IBS, maintaining behaviours, maintaining cognitions, precipitating factors and discussion of the impact of IBS on the patient's life.

Main symptom identification
Useful questions in this area include: Can you tell me about your main symptoms in your own words? How does your IBS affect you physically? The following areas are enquired about: pain, diarrhoea, constipation, changing bowel pattern, tenesmus (non-productive straining at stool), bloating, mucus and flatulence.

Other useful questions in this area include: What about problems during the day/night? How long does it last? What do you usually do when you get the pain? Is there anything that makes it better/worse? Do any particular foods make it better/worse? How does stress/anxiety affect your symptoms? Does IBS affect your sex life? Does IBS affect your menstrual cycle? What else triggers the symptoms?

Identifying maintaining behaviours
Useful questions in this area include: How does IBS affect what you do? Is there anything you avoid because of the problem? Do you avoid certain places or particular food? Is there anything you currently do more than you ideally would like to, for example spending too much time on the toilet or needing to be aware of where the nearest toilet is? Are there particular things that you do when you go to the toilet that trouble you, for example straining, excessive wiping, checking for abnormalities? How many times do you go to the toilet and not pass anything?

Identifying maintaining cognitions
Useful questions in this area include: What thoughts/images do you have about IBS? What specific worries do you have with regard to IBS? What do you believe is the worst thing that could happen to you because of IBS? Determine how strongly the belief is held and determine whether the belief makes the patient feel emotionally anxious, angry, frustrated or low.

Identifying precipitating factors
Useful questions in this area include: When did this problem start? What was happening at that time? Was there a specific incident? Did you get stomach ache as a child? How did your family react? Did anyone in your close family have similar symptoms? Do they now? Is there any pattern to when your IBS is worse? Is there any pattern to when it is better?

Detailing the impact of IBS on a patient's life
Useful questions include: What impact does IBS have on your life or on the lives of others around you? Why have you come for treatment now?

An example of the rationale
Pain or discomfort in the abdomen, diarrhoea, flatulence and constipation occurs to most of us at some stage.

If you experience a particularly nasty bout of symptoms this can make you vulnerable to experiencing these symptoms more and more.

IBS is not a typical physical disease, it is a problem affecting the way the digestive system functions.

It cannot kill you and is unlikely to get much worse.

It normally comes and goes.

For some people IBS will go away completely and for others it will never totally get better.

Once you can accept the natural progress of IBS you can learn to control it.

This will make it much easier to live with and may even stop it for good.

It is thought that IBS is aggravated by stress.

This does not mean that IBS is all in the mind; far from it, IBS may have physical causes, but what you do, think and feel aggravates and maintains many of these physical causes.

IBS is likely to be connected to your lifestyle, to your level of anxiety and to the way you view the world and your IBS symptoms.

By looking at and modifying what you feel, think and do you will reduce the impact of IBS and lead a less restricted life.

It is OK to have IBS. It is nothing to be ashamed or apologetic about.

There are lots of things you can do to reduce the effect it has on you.

Explaining the treatment rationale

Once a clear understanding of the above areas is obtained the therapist will be able to explain the treatment rationale to the patient using examples from the patient's own history. Any explanation should be jargon free. Time should be spent making sure that the patient fully understands the rationale as this is an essential component of the therapy.

Once the rationale has been understood the goals of therapy should be reviewed. These are used as a basis from which to agree end of treatment targets which the patient and therapist rate at the beginning, middle and end of treatment. These targets are rated on a 0–8 scale, 0 indicating the patient is able to reach this target now without difficulty and 8 indicating that the target is unachievable at present. Define and rate a minimum of two long-term targets. Sample pieces of behaviour can be taken from different areas of the patient's life. This may be work, social, home management or personal.

It is important that these target statements contain specific, realistic and measurable samples of coping behaviour that the patient wishes to alter.

Example: end of treatment targets
- To use the gym for 1 hour 3 times weekly
- To be able to attend unplanned meetings for their duration without going to the toilet beforehand
- To use the toilet only when I have an urge to
- To eat three meals a day at regular intervals

Sometimes it is difficult to agree on long-term problems and targets in the first session. The therapist may suggest that the patient make a list of the goals of therapy before the next session.

First week's goal

From the long-term targets, an initial first goal may be agreed with the patient. This should be a small specific behaviour that the patient can identify as being a positive step in improving behaviour associated with their IBS, e.g. to spend a maximum of 15 minutes on the toilet each time I go this week.

This goal should have an approximately 85% chance of being successfully achieved within the following week. Therapist and patient will check for any possible problems or obstacles that may arise in the completion of this goal and will deal with these or adjust the goal accordingly.

Monitoring symptoms and behaviour

The patients are asked to use a diary for one week only in which to monitor symptom severity and the situations in which symptoms occur. Patients are asked to record the situations in which the symptoms arise and their thoughts and behaviours associated with these symptoms.

The aim of this diary is to gather information about the day-to-day effects of symptoms and behaviour and to provide information on which to construct targets during future therapy sessions.

Therapists should warn patients that focusing on symptoms for the first week may cause the symptoms to get worse. This may be used as an example of how focusing causes symptoms to increase.

Session 2

After an agenda has been agreed, the patient feeds back on the initial session.

If an initial target was set at session 1, this should be reviewed and problems associated with it discussed. Agreement should be reached as to the value of this target, how it relates to the CBT model and how it may be developed further.

The symptom-monitoring diary completed during the previous week is reviewed, looking for themes and trends in behaviour and cognitions.

A common example is that the patient fears that symptoms of IBS may mean they have cancer or a more serious illness. They may check their stools for blood or 'abnormalities'. They may worry that if they do not produce the 'ideal stool' then something must be seriously wrong.

Another patient may fear that the symptoms are uncontrollable and may worry about passing wind in public and the resulting embarrassment.

The therapist and patient will then identify, prioritise and agree upon targets for the following week. If possible these should be behavioural targets either facing previously avoided behaviour or reducing excess precautions or safety behaviour.

Example of second week's targets
- Not to read every time I use the toilet
- To use the toilet only when I have a definite urge to pass a stool
- To visit the cinema once a week (or another activity) without using the toilet for 1 hour before
- To eat two slices of toast for breakfast every weekday
- Not to check my stool for abnormalities this week
- Not to carry my IBS medication when going outside this week

The specific weekly targets chosen will vary according to each individual's needs and circumstances. The patient is encouraged to take a lead in choosing target behaviours from the first week's diary. His/her commitment is sought to undertake these targets even when symptomatic and not to abandon them when symptoms develop but to continue to practise according to an agreed, preset timetable. Patients are encouraged to telephone their therapist if they have any difficulties in between sessions. Homework diaries are given, with an explanation of how to complete them. Homework diaries record the particular targets and the patient's success on reaching these with records of each event associated with the target.

Session 3

The patient's reactions to the previous session, and homework are explored.

The homework and self-monitoring diaries are reviewed, new homework targets are set and any setbacks or difficulties are problem solved.

Sessions 3–6 are conducted in a similar manner, reinforcing the links between thoughts, feelings and behaviour, with specific strategies for specific symptoms.

These sessions involve:

1. reviewing the homework and self-monitoring diaries
2. eliciting the patient's reaction
3. rechecking the patient's acceptance and understanding of the treatment model
4. identifying specific difficulties in achieving the patient's targets
5. adopting a collaborative, problem-solving approach to any difficulties
6. setting new targets
7. predicting problems and generating potential solutions
8. emphasising the importance of maintaining a consistent programme.

Sessions 4 and 5

These sessions will also include education and discussion about how to challenge negative thoughts. An example of a negative thought would be regularity is next to godliness – if you empty your bowels regularly then you're in good health. My bowels are not regular so I must be unhealthy.

The negative thought diaries are reviewed and contents are discussed. The therapist will highlight the link between thoughts and symptoms and how negative thoughts increase the severity and frequency of symptoms. Illness attributions, self-esteem, performance and expectations will also be examined. If the patient has had difficulty identifying negative thoughts, this should be explored in more detail.

Methods of evaluating and looking at alternative thoughts are discussed: the therapist and patient can discuss the evidence for and against the negative thought, they can consider an alternative view, examine the advantages and disadvantages of a negative thinking style and look at logical thinking errors.

It is important that alternative thoughts are elicited from patients in a collaborative manner so that they learn to re-evaluate their thinking themselves. Instruction is given on the use of dysfunctional thought diaries, including recording alternative more helpful thoughts.

Session 6

This session will also include preparation for discharge and relapse prevention techniques. From session 4 there will have been an increasing delegation of responsibility for therapy. The patient is now expected to continue the behavioural and cognitive skills they have learned without requiring prompting from the therapist.

The aims of this final session are:

1. to anticipate setbacks and write a relapse plan preparing the patient for potential difficulties and setbacks in the future
2. to ensure that progress continues after active treatment is completed
3. to develop the patient's confidence and ability to deal appropriately with setbacks without relapsing. The patient is advised that this ability will wax and wane
4. to ensure that the patient's lifestyle and long-term plans are realistic and will facilitate the maintenance of therapy gains.

The idea that symptoms will continue to arise from time to time should be reinforced, as should the concept that the patient will be able to deal with them effectively. Patients are encouraged to write a list of what they have learnt/found most useful in treatment and to plan mini-programmes to deal with potential setbacks. This 'cue card' can be used as a reminder and prompt when problems arise in the future.

The patient and therapist should anticipate future problems and develop appropriate coping strategies. These can also be highlighted on the cue card. Session 6 should occur no longer than 9 weeks after the start of treatment. After this time all patients will be reassessed for improvements.

The kitbag approach

As specific issues arise the therapist will identify the specific technique that may be appropriate from a 'therapeutic kitbag'. The kitbag is a collection of techniques that have been derived from the cognitive behavioural model to address specific issues that often arise with patients with IBS. These will be used throughout treatment. The identification of the appropriate technique and the specific technique to use will rely on good communication between patient and therapist.

The kitbag can be divided into five sections.

1. Educational advice

Education and advice may be given to inform any misconceptions concerning bowel function.

Some of the common misconceptions are listed below:

Frequency and consistency of stool motion

Examples of misconceptions
'I should pass a stool every day'
'Stools must be a certain shape and form'

The hunt for the perfect stool: some patients will examine each stool that they pass, wanting to achieve a perfect stool that will never be achieved.

Therapists may discuss what affects the frequency and consistency of stools, the role of diet, stress, anxiety and worry or change of environment.

The nature of the digestive system

Example of misconceptions
'It is dirty/dangerous to be unable to get rid of all of my stool'

Therapists should have a working knowledge of the digestive system and how food passes through the body. For example, patients can be informed that the bowel is never completely empty.

The role of diet

Example of misconceptions
'By avoiding certain food I will avoid/control my symptoms'

'By avoiding eating at certain times I will avoid/control certain symptoms'

Some misconceptions will also contain statements that need a more cognitive intervention, e.g. 'should' statements. This approach is outlined below.

Misinterpretation of IBS symptoms

Some of the symptoms of IBS are often misinterpreted.

Example of symptom misinterpretation
Tricia often experiences a feeling of incomplete evacuation (a very common symptom in IBS). When experiencing this symptom she believes she must pass a stool because if she does not she believes she will suffer harm or damage. This leads to excessive straining or even occasional manual evacuation in the attempt to reduce this feeling.

During the session these thoughts and their resulting behaviour were discussed. It was explained that the feeling of incomplete evacuation is a symptom of IBS and does not mean that the Tricia must pass a stool. Once Tricia understood this, she was advised just to experience the symptom and not to react in the previous manner.

She was able to learn to distinguish between this feeling of incomplete evacuation and the actual feeling that she needed to pass a stool.

2. Behavioural techniques

Reintroducing avoided foods

Rationale: Often people with IBS may link specific foods and drinks to their symptoms. These are often very idiosyncratic and associations are frequently made after only one bad experience, e.g. I got the runs after drinking Ribena, and so I avoid it totally now. This can cause moderate to severe limitations on a person's life. Whilst in treatment it is an ideal opportunity to re-test these associations in a systematic way. The therapist can explain to patients that after re-testing previously avoided foods in a systematic manner they will be in a better position to make a decision about their exclusion of these from their diet.

Technique:

- Ask patients to make a list of avoided foods.
- Ask them to decide which food would be a good starting point to try and face. These may be foods that they would like/should be able to

eat/they think are good for them to eat. It may be that the avoidance of these foods is causing disruption to the patient's life.
- Agree and set targets for foods to try in the following 2 weeks specifying the frequency and amount of food to be eaten.
- Predict and prepare solutions for problems that may occur.

Improving toileting behaviour

Rationale: The act of going to the toilet often involves many microbehaviours that may help maintain IBS symptoms. As with food avoidance these behaviours need to be assessed and reduced.

Examples of microtoileting behaviour
- Excessive wiping, checking or time spent on toilet
- Manual evacuation

Straining: this is probably the most important behaviour to assess and reduce. Patients often strain because they feel they will be unable to pass a stool without doing so. Patients may strain for long periods of time and still only manage to pass small stools if any at all. The patient and therapist assess the length of time spent straining and the severity of the 'push' and agree on how this will be reduced. The aim should be to have completely stopped straining by the end of treatment.

3. Cognitive techniques

The role of negative automatic thoughts in maintaining IBS is discussed, the relationship of these thoughts to feelings and behaviour is explored, and there may be misconceptions about bowel habit. It is emphasised that negative automatic thoughts can initially be hard to identify. They are explained as distortions of reality that can influence the perception, response to and maintenance of symptoms, and that can lower mood.

Self-monitoring diaries

Self-monitoring diaries for thoughts are introduced, and their use is explained, reinforcing the feeling/thoughts/behaviour link. Patients are asked to record examples of situations in which they experience an unpleasant emotion or mood change, and to write down as exactly as possible what is going through their mind at the time.

Patients should be prepared for the possibility that recording negative thoughts may, by heightening awareness, temporarily increase feelings of depression or an increase in symptom sensitivity. Patients should be advised, if this occurs, to limit the time spent focusing on distressing thoughts.

Once these diaries have been completed the therapist and patient will use them to identify common themes and thinking errors and then to discuss suitable alternatives that may be used.

Testing out predictions

Examples of predictions patients make
- 'Others will notice the smell'
- 'I will have an accident if I wait more than one minute'

There are many ways to challenge thoughts. Therapists should use the ways they feel appropriate for the patient and situation. A number of ways that we have found helpful to challenge people's thoughts are suggested below.

The cake technique

Example of cognitive misconception
- 'My doctor has missed something that will cause me irrevocable harm'

The cake technique asks patients to list all possible alternatives and then to allocate percentage chances of each occurring as part of a cake (made up of 100%). As more and more possible alternatives are suggested and allocated a 'piece of the cake' the total percentage will usually be over 100% (sometimes many times more). This is a visual technique that allows patients to see how easy it is to overestimate the chances of a serious illness or that the GP has made a mistake.

The for and against technique

Example of belief
'I have a serious illness like bowel cancer'

Once the belief is identified, patients are asked to list statements that support the statement. They are then asked to rate their strength of belief for each statement. Next they list statements that disprove the belief, as well as rating the strength of belief in each. They are then asked to reassess their original statements.

4. Symptom management techniques

Reducing symptom focusing

Rationale: Bloating and abdominal pain are common symptoms of IBS. By attending to the abdominal area people are more likely to have an

increased sensitivity to any abdominal change. Once you focus on abdominal symptoms one is likely to experience more abdominal pain and bloating and to notice them with increasing frequency. By using a range of techniques we can reduce symptom focusing and thus reduce pain and bloating.

Techniques: Patients are asked to watch out for when they make predictions about the onset of bloating and pain.

Example of symptom focusing
'I have just eaten a cheese roll, that's going to give me hell!'

The therapist may respond by explaining:
'Once we have these types of thoughts we are more likely to focus on the abdominal area. This will make us more sensitive to any changes that may have occurred anyway. Once we have felt a change we are more likely to think in ways that support our previous assertion, for example: "Oh no, I can feel it starting, its getting worse, I can't control this". These thoughts increase our focusing on the area and are more likely to exacerbate our perceptions of the severity of the symptoms.'

Patients need to be aware that when they are focusing, they must not ignore the pain, but carry on with it. The therapist will teach them to be aware of their thoughts the moment they first become aware of the symptoms and to address any unhelpful thoughts.

The getting a second head technique

When patients experience lots of negative thoughts about their symptoms, e.g. 'I'm not coping with it at all', it can be helpful to put a distance between themselves and the thought. This is what the second head technique is designed to do. It allows the patient to identify negative thoughts and makes it easier for them to come up with alternatives.

Explain to patients that when they get these negative thoughts they can imagine themselves stepping out of their head and looking at their thoughts and symptoms from another perspective. Explain that it is the difference between 'I am not coping with it all' and 'I am having thoughts about not coping with my IBS'.

The first approach, 'I am not coping with it all', will naturally make a person feel worse. It does not allow one to do anything about the way that they feel. It is a dead-end statement.

The second approach, 'I am having thoughts about not coping with my IBS', allows one room to manoeuvre and to challenge the negative thoughts.

See your thoughts, don't **be** your thoughts.

Accepting IBS

Accepting IBS is a key stage in the reduction of symptoms. Once a patient can accept that they have IBS and not anything more serious and that they are likely to have this for some time then they will experience a reduction in anxiety and therefore fewer symptoms. Learning to accept IBS is an ongoing process and therapists and patients need to be aware that the process will continue long after therapy.

Example of what a therapist may say about accepting IBS
This sounds easy to say but it is very important in the reduction of symptoms. What do you say to yourself when you get symptoms of IBS? If you think 'Oh my god, I've started to feel bloated, it's bound to get worse and then ruin my night out' this is more likely to lead to increased worry, stress and focusing on the bloating. The way we think about our IBS will affect our symptoms. Recognise when this is happening and challenge those thoughts, for example 'OK, I have bloating, but I have had it this bad before, I will still go out and make the most of my night out. I will not let the IBS rule me. By still going out I will be in control'.

5. Mixed techniques

Special diets and food intake

Special diets have been shown to be of little benefit in IBS. It was thought, for example, that a high-fibre diet was beneficial, but recent studies have shown that this is not necessarily so. It is important that the patient does not become too obsessed with diet, otherwise their eating habits can be governed by fear that the discomfort or pain may return.

It is important to stabilise the patient's diet during treatment. This will allow the therapist and the patient to evaluate any changes made as a result of the therapy and not anything else. A constant regular diet may also help reduce some of the IBS symptoms.

Healthy bowel routine

The following is a list of basic guidelines to facilitate a healthy bowel routine

1. Keep regular mealtimes.
2. Drink sufficient liquid each day.

3. Maintain a regular programme of physical exercise and activity. We suggest three sessions a week each lasting a minimum of 30 minutes.
4. Avoid delaying the urge to have a bowel movement.
5. Avoid straining.

Specific stress management techniques

The main aim of these is to reduce autonomic activity.

Stress is caused by an imbalance in daily demands and a person's perceived coping abilities. Patients experience stress when they feel unable to cope with the demands made of them at work or at home. This is considered to be a two-way process. If a patient's perceived coping abilities outweigh the demands placed on them (for example a graduate who takes a job that does not allow them to use their expertise) then they will also experience stress.

There are a number of effective strategies that may help reduce stress levels:

1. saying 'no' to requests that will result in excessive demands
2. prioritising
3. timekeeping
4. looking after yourself, for example by taking breaks
5. asking for help/further training
6. giving yourself regular treats
7. not being hard on yourself.

Appendix 3

Baseline data collection instruments

IBS STUDY	Gen practice	Pat initials	Pat No.
	Visit No.1	Date of visit	

PATIENT DETAIL Patient's Name:

Date of Birth: Male/female Contact Address:

Contact Telephone:

ROME CRITERIA

At least 3 months of continuous or recurrent symptoms of abdominal pain or discomfort of at least moderate severity that is:

	No	Yes
(a) Relieved with defecation; and/or	( )	( )
(b) Associated with a change in frequency of stool; and/or	( )	( )
(c) Associated with a change in consistency of stool;	( )	( )

and:

Two or more of the following at least on one-quarter of occasions or days:

(a) Altered stool frequency (more than three bowel movements each day or fewer than three bowel movements each week);	( )	( )
(b) Altered stool form (lumpy/hard or loose/watery stool);	( )	( )
(c) Altered stool passage (straining, urgency, or feeling of incomplete evacuation);	( )	( )
(d) Passage of mucus; and/or	( )	( )
(e) Bloating or feeling of abdominal distension.	( )	( )

INCLUSION CRITERIA

	No	Yes
Aged 17–50 inclusive	( )	( )
Signed consent	( )	( )

IBS STUDY Gen practice Pat initials Pat No.

Visit No.1 Date of visit

EXCLUSION CRITERIA	No	Yes
Any alarm symptoms	( )	( )
Any unexplained weight loss	( )	( )
Any uninvestigated rectal bleeding	( )	( )
Past or present disease likely to complicate evaluation of the study	( )	( )
Abdominal pain relieved by acid-inhibiting drug	( )	( )
Pregnancy or lactation	( )	( )
Inability to complete the questionnaire	( )	( )
Family history of bowel cancer in a first or second degree relative, i.e. grandparents, parents, siblings, children.	( )	( )

Conclusion Fulfils all inclusion and none of the exclusion criteria — No ( ) Yes ( )

If yes to the last question proceed with the study

CURRENT MEDICATION (for any indication)

Drug Name Dose Frequency

Medication used during the past 12 months

Has any of the following medication been used during the past 12 months?

Benzodiazepines	( )	Bulk laxatives	( )
Antidepressants	( )	Acid suppression (zantac, tagamet, pantoprazole, losec, zoton)	( )
Barbiturates	( )	Gaviscon/antacids	( )
Psychotropics	( )	Antispasmodics (loperamide, buscopan, mebeverine hcl)	( )
Analgesics	( )	Antidiarrhoeal agents	( )
Prokinetics (cisapride, metoclopramide)	( )	Alternative medicines, e.g. herbal compounds	( )

Appendix 4

Cognitive scale for functional bowel disorders

Please indicate how much you agree or disagree with each statement

1——2——3——4——5——6——7
Strongly Disagree — Neither Agree or Disagree — Strongly Agree

	1	2	3	4	5	6	7
I don't get to the toilet in time							
I'm always unwell with the bowel problem							
My symptoms are too much to handle							
I can't function normally when sick with bowel problems							
My bowel symptoms are agony							
I do my absolute best at everything							
I am frustrated by my bowel symptoms							
My pain will never go away							
I feel very down about my bowel symptoms							
I worry about breaking wind in public							
I worry about not finding a toilet when I need one							
My bowel problems interfere with feeling good about myself							
I worry about my bowel symptoms when out							
I can't concentrate due to pain							
It's embarrassing to keep going to the toilet							
I'm concerned I won't last through events							
Being late upsets me							
I hate making a fool of myself							
I do not take advantage of opportunities due to bowel problems							
My symptoms make me feel out of control							
I have bowel symptoms in restaurants							
With frequent toilet visits others think something is wrong							
I worry about losing control of my bowels in public							
I feel guilty if I nurture myself							
I must get home when I have my symptoms							

Appendix 5

Behaviour scale for irritable bowel syndrome

Please consider each question and mark the choice that best applies to you with an 'X' in the appropriate box

	1	2	3	4	5	6	7
I eat specific foods to help me open my bowels more							
I eat specific foods to help me open my bowels less							
I strain when opening my bowels							
After opening my bowels I check for blood							
After opening my bowels I check my stool for abnormalities							
I spend more time on the toilet than ideally I would like							
I often go to the toilet to open my bowels and then do not pass anything							
I often go to the toilet to pass water and find I open my bowels							
I avoid exercise when I have stomach pains							
I avoid certain foods when I have bowel problems							
I smoke more to help me open my bowels							
I use sanitary pads/incontinence pads in case I have an accident							
I wear baggy clothing when my stomach feels bloated or distended							
I avoid going out in case I have problems with my IBS							
I avoid making plans in case I have problems with my IBS							
I carry other items (e.g.: wet wipes, sanitary towels, spare underwear) in case my IBS flares up.							
I take medication (e.g.: before going out) just in case my IBS flares up							
I carry medication with me in case my IBS flares up							
I avoid sex in case my IBS flares up (and causes embarrassment)							
When I go out I make sure I know where the nearest toilet is							
I ask for reassurance about my IBS							
I avoid certain work situations (e.g. meetings) because of my IBS							
I avoid certain social situations (e.g. restaurants) because of my IBS							
I avoid certain foods (e.g. dairy products, spicy foods) because of my IBS							
After I open my bowels I wipe more than I would like							
When I have diarrhoea I do things to ease it (e.g. take prescribed medication, take alternative medication)							
I am constantly aware of my stomach							
I avoid staying away from home overnight in case my IBS flares up							

Appendix 6

Unit service costs

TABLE 22 *Unit costs (2000/01 £) per hour unless otherwise stated*

Service	Cost (£)
GP (attendance)	17
Nurse	31
Inpatient (day)	242
Outpatient (attendance):	
Generic	74
General surgery	62
Dermatology	57
Gastroenterology	76
Neurology	109
Cardiology	75
Mental health	128
Oncology	107
Infectious diseases	248
Nephrology	91
Haematology	64
A&E	61
Other medical physician	148
Osteopath/chiropractor	20/18[a]
Physiotherapist	41
Counsellor	28
Acupuncturist	32/24[a]
Nutritionist	32
Reflexologist	20/19[a]
Social worker	82
Informal care	11

[a] The initial figure refers to the average price of an initial contact and the second figure refers to subsequent contacts.

Health Technology Assessment Programme

Prioritisation Strategy Group

Members

HTA Commissioning Board

Members

Current and past membership details of all HTA 'committees' are available from the HTA website (www.hta.ac.uk)

Diagnostic Technologies & Screening Panel

Members

Chair,
Dr Ron Zimmern, Director of the Public Health Genetics Unit, Strangeways Research Laboratories, Cambridge

Ms Norma Armston, Lay Member, Bolton

Professor Max Bachmann Professor of Health Care Interfaces, Department of Health Policy and Practice, University of East Anglia

Professor Rudy Bilous Professor of Clinical Medicine & Consultant Physician, The Academic Centre, South Tees Hospitals NHS Trust

Dr Paul Cockcroft, Consultant Medical Microbiologist and Clinical Director of Pathology, Department of Clinical Microbiology, St Mary's Hospital, Portsmouth

Professor Adrian K Dixon, Professor of Radiology, University Department of Radiology, University of Cambridge Clinical School

Dr David Elliman, Consultant Paediatrician/ Hon. Senior Lecturer, Population Health Unit, Great Ormond St. Hospital, London

Professor Glyn Elwyn, Primary Medical Care Research Group, Swansea Clinical School, University of Wales Swansea

Mr Tam Fry, Honorary Chairman, Child Growth Foundation, London

Dr Jennifer J Kurinczuk, Consultant Clinical Epidemiologist, National Perinatal Epidemiology Unit, Oxford

Dr Susanne M Ludgate, Medical Director, Medicines & Healthcare Products Regulatory Agency, London

Professor William Rosenberg, Professor of Hepatology, Liver Research Group, University of Southampton

Dr Susan Schonfield, Consultant in Public Health, Specialised Services Commissioning North West London, Hillingdon Primary Care Trust

Dr Phil Shackley, Senior Lecturer in Health Economics, School of Population and Health Sciences, University of Newcastle upon Tyne

Dr Margaret Somerville, PMS Public Health Lead, Peninsula Medical School, University of Plymouth

Dr Graham Taylor, Scientific Director & Senior Lecturer, Regional DNA Laboratory, The Leeds Teaching Hospitals

Professor Lindsay Wilson Turnbull, Scientific Director, Centre for MR Investigations & YCR Professor of Radiology, University of Hull

Professor Martin J Whittle, Associate Dean for Education, Head of Department of Obstetrics and Gynaecology, University of Birmingham

Dr Dennis Wright, Consultant Biochemist & Clinical Director, Pathology & The Kennedy Galton Centre, Northwick Park & St Mark's Hospitals, Harrow

Pharmaceuticals Panel

Members

Chair,
Dr John Reynolds, Chair Division A, The John Radcliffe Hospital, Oxford Radcliffe Hospitals NHS Trust

Professor Tony Avery, Head of Division of Primary Care, School of Community Health Services, Division of General Practice, University of Nottingham

Ms Anne Baileff, Consultant Nurse in First Contact Care, Southampton City Primary Care Trust, University of Southampton

Professor Stirling Bryan, Professor of Health Economics, Health Services Management Centre, University of Birmingham

Mr Peter Cardy, Chief Executive, Macmillan Cancer Relief, London

Professor Imti Choonara, Professor in Child Health, Academic Division of Child Health, University of Nottingham

Dr Robin Ferner, Consultant Physician and Director, West Midlands Centre for Adverse Drug Reactions, City Hospital NHS Trust, Birmingham

Dr Karen A Fitzgerald, Consultant in Pharmaceutical Public Health, National Public Health Service for Wales, Cardiff

Mrs Sharon Hart, Head of DTB Publications, *Drug & Therapeutics Bulletin*, London

Dr Christine Hine, Consultant in Public Health Medicine, South Gloucestershire Primary Care Trust

Professor Stan Kaye, Cancer Research UK Professor of Medical Oncology, Section of Medicine, The Royal Marsden Hospital, Sutton

Ms Barbara Meredith, Lay Member, Epsom

Dr Andrew Prentice, Senior Lecturer and Consultant Obstetrician & Gynaecologist, Department of Obstetrics & Gynaecology, University of Cambridge

Dr Frances Rotblat, CPMP Delegate, Medicines & Healthcare Products Regulatory Agency, London

Professor Jan Scott, Professor of Psychological Treatments, Institute of Psychiatry, University of London

Mrs Katrina Simister, Assistant Director New Medicines, National Prescribing Centre, Liverpool

Dr Richard Tiner, Medical Director, Medical Department, Association of the British Pharmaceutical Industry, London

Dr Helen Williams, Consultant Microbiologist, Norfolk & Norwich University Hospital NHS Trust

Therapeutic Procedures Panel

Members

Chair,
Professor Bruce Campbell,
Consultant Vascular and General Surgeon, Department of Surgery, Royal Devon & Exeter Hospital

Dr Aileen Clarke,
Reader in Health Services Research, Public Health & Policy Research Unit, Barts & the London School of Medicine & Dentistry, London

Dr Matthew Cooke, Reader in A&E/Department of Health Advisor in A&E, Warwick Emergency Care and Rehabilitation, University of Warwick

Dr Carl E Counsell, Clinical Senior Lecturer in Neurology, Department of Medicine and Therapeutics, University of Aberdeen

Ms Amelia Curwen, Executive Director of Policy, Services and Research, Asthma UK, London

Professor Gene Feder, Professor of Primary Care R&D, Department of General Practice and Primary Care, Barts & the London, Queen Mary's School of Medicine and Dentistry, London

Professor Paul Gregg, Professor of Orthopaedic Surgical Science, Department of General Practice and Primary Care, South Tees Hospital NHS Trust, Middlesbrough

Ms Bec Hanley, Co-Director, TwoCan Associates, Hurstpierpoint

Ms Maryann L Hardy, Lecturer, Division of Radiography, University of Bradford

Professor Alan Horwich, Director of Clinical R&D, Academic Department of Radiology, The Institute of Cancer Research, London

Dr Simon de Lusignan, Senior Lecturer, Primary Care Informatics, Department of Community Health Sciences, St George's Hospital Medical School, London

Professor Neil McIntosh, Edward Clark Professor of Child Life & Health, Department of Child Life & Health, University of Edinburgh

Professor James Neilson, Professor of Obstetrics and Gynaecology, Department of Obstetrics and Gynaecology, University of Liverpool

Dr John C Pounsford, Consultant Physician, Directorate of Medical Services, North Bristol NHS Trust

Karen Roberts, Nurse Consultant, Queen Elizabeth Hospital, Gateshead

Dr Vimal Sharma, Consultant Psychiatrist/Hon. Senior Lecturer, Mental Health Resource Centre, Cheshire and Wirral Partnership NHS Trust, Wallasey

Dr L David Smith, Consultant Cardiologist, Royal Devon & Exeter Hospital

Professor Norman Waugh, Professor of Public Health, Department of Public Health, University of Aberdeen

Expert Advisory Network

Members

Professor Douglas Altman, Director of CSM & Cancer Research UK Med Stat Gp, Centre for Statistics in Medicine, University of Oxford, Institute of Health Sciences, Headington, Oxford

Professor John Bond, Director, Centre for Health Services Research, University of Newcastle upon Tyne, School of Population & Health Sciences, Newcastle upon Tyne

Mr Shaun Brogan, Chief Executive, Ridgeway Primary Care Group, Aylesbury

Mrs Stella Burnside OBE, Chief Executive, Office of the Chief Executive. Trust Headquarters, Altnagelvin Hospitals Health & Social Services Trust, Altnagelvin Area Hospital, Londonderry

Ms Tracy Bury, Project Manager, World Confederation for Physical Therapy, London

Professor Iain T Cameron, Professor of Obstetrics and Gynaecology and Head of the School of Medicine, University of Southampton

Dr Christine Clark, Medical Writer & Consultant Pharmacist, Rossendale

Professor Collette Clifford, Professor of Nursing & Head of Research, School of Health Sciences, University of Birmingham, Edgbaston, Birmingham

Professor Barry Cookson, Director, Laboratory of Healthcare Associated Infection, Health Protection Agency, London

Professor Howard Cuckle, Professor of Reproductive Epidemiology, Department of Paediatrics, Obstetrics & Gynaecology, University of Leeds

Dr Katherine Darton, Information Unit, MIND – The Mental Health Charity, London

Professor Carol Dezateux, Professor of Paediatric Epidemiology, London

Mr John Dunning, Consultant Cardiothoracic Surgeon, Cardiothoracic Surgical Unit, Papworth Hospital NHS Trust, Cambridge

Mr Jonothan Earnshaw, Consultant Vascular Surgeon, Gloucestershire Royal Hospital, Gloucester

Professor Martin Eccles, Professor of Clinical Effectiveness, Centre for Health Services Research, University of Newcastle upon Tyne

Professor Pam Enderby, Professor of Community Rehabilitation, Institute of General Practice and Primary Care, University of Sheffield

Mr Leonard R Fenwick, Chief Executive, Newcastle upon Tyne Hospitals NHS Trust

Professor David Field, Professor of Neonatal Medicine, Child Health, The Leicester Royal Infirmary NHS Trust

Mrs Gillian Fletcher, Antenatal Teacher & Tutor and President, National Childbirth Trust, Henfield

Professor Jayne Franklyn, Professor of Medicine, Department of Medicine, University of Birmingham, Queen Elizabeth Hospital, Edgbaston, Birmingham

Ms Grace Gibbs, Deputy Chief Executive, Director for Nursing, Midwifery & Clinical Support Services, West Middlesex University Hospital, Isleworth

Dr Neville Goodman, Consultant Anaesthetist, Southmead Hospital, Bristol

Professor Alastair Gray, Professor of Health Economics, Department of Public Health, University of Oxford

Professor Robert E Hawkins, CRC Professor and Director of Medical Oncology, Christie CRC Research Centre, Christie Hospital NHS Trust, Manchester

Professor Allen Hutchinson, Director of Public Health & Deputy Dean of ScHARR, Department of Public Health, University of Sheffield

Dr Duncan Keeley, General Practitioner (Dr Burch & Ptnrs), The Health Centre, Thame

Dr Donna Lamping, Research Degrees Programme Director & Reader in Psychology, Health Services Research Unit, London School of Hygiene and Tropical Medicine, London

Mr George Levvy, Chief Executive, Motor Neurone Disease Association, Northampton

Professor James Lindesay, Professor of Psychiatry for the Elderly, University of Leicester, Leicester General Hospital

Professor Julian Little, Professor of Human Genome Epidemiology, Department of Epidemiology & Community Medicine, University of Ottawa

Professor Rajan Madhok, Medical Director & Director of Public Health, Directorate of Clinical Strategy & Public Health, North & East Yorkshire & Northern Lincolnshire Health Authority, York

Professor David Mant, Professor of General Practice, Department of Primary Care, University of Oxford

Professor Alexander Markham, Director, Molecular Medicine Unit, St James's University Hospital, Leeds

Dr Chris McCall, General Practitioner, The Hadleigh Practice, Castle Mullen

Professor Alistair McGuire, Professor of Health Economics, London School of Economics

Dr Peter Moore, Freelance Science Writer, Ashtead

Dr Sue Moss, Associate Director, Cancer Screening Evaluation Unit, Institute of Cancer Research, Sutton

Mrs Julietta Patnick, Director, NHS Cancer Screening Programmes, Sheffield

Professor Tim Peters, Professor of Primary Care Health Services Research, Academic Unit of Primary Health Care, University of Bristol

Professor Chris Price, Visiting Chair – Oxford, Clinical Research, Bayer Diagnostics Europe, Cirencester

Professor Peter Sandercock, Professor of Medical Neurology, Department of Clinical Neurosciences, University of Edinburgh

Dr Eamonn Sheridan, Consultant in Clinical Genetics, Genetics Department, St James's University Hospital, Leeds

Dr Ken Stein, Senior Clinical Lecturer in Public Health, Director, Peninsula Technology Assessment Group, University of Exeter

Professor Sarah Stewart-Brown, Professor of Public Health, University of Warwick, Division of Health in the Community Warwick Medical School, LWMS, Coventry

Professor Ala Szczepura, Professor of Health Service Research, Centre for Health Services Studies, University of Warwick

Dr Ross Taylor, Senior Lecturer, Department of General Practice and Primary Care, University of Aberdeen

Mrs Joan Webster, Consumer member, HTA – Expert Advisory Network

Feedback

The HTA Programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (http://www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 23 8059 5639 Email: hta@hta.ac.uk
http://www.hta.ac.uk

ISSN 1366-5278