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Abstract

Cognitive–behaviour therapy for health anxiety in medical patients (CHAMP): a randomised controlled trial with outcomes to 5 years

Peter Tyrer,[1]* Paul Salkovskis,[2] Helen Tyrer,[1] Duolao Wang,[3] Michael J Crawford,[1] Simon Dupont,[4] Sylvia Cooper,[1] John Green,[4] David Murphy,[5] Georgina Smith,[4] Sharandeep Bhogal,[1] Shaeda Nourmand,[1] Valentina Lazarevic,[6] Gemma Loebenberg,[7] Rachel Evered,[7] Stephanie Kings,[6] Antoinette McNulty,[7] Yvonne Lisseman-Stones,[8] Sharon McAllister,[8] Kofi Kramo,[1] Jessica Nagar,[7] Steven Reid,[4] Rahil Sanatinia,[1] Katherine Whittamore,[6] Gemma Walker,[1] Aaron Philip,[1] Hilary Warwick,[1] Sarah Byford[9] and Barbara Barrett[9]

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Background: Health anxiety is an under-recognised but frequent cause of distress that is potentially treatable, but there are few studies in secondary care.

Objective: To determine the clinical effectiveness and cost-effectiveness of a modified form of cognitive–behaviour therapy (CBT) for health anxiety (CBT-HA) compared with standard care in medical outpatients.

Design: Randomised controlled trial.

Setting: Five general hospitals in London, Middlesex and Nottinghamshire.

Participants: A total of 444 patients aged 16–75 years seen in cardiology, endocrinology, gastroenterology, neurology and respiratory medicine clinics who scored ≥ 20 points on the Health Anxiety Inventory (HAI) and satisfied diagnostic requirements for hypochondriasis. Those with current psychiatric disorders were excluded, but those with concurrent medical illnesses were not.

Interventions: Cognitive–behaviour therapy for health anxiety – between 4 and 10 1-hour sessions of CBT-HA from a health professional or psychologist trained in the treatment. Standard care was normal practice in primary and secondary care.

Main outcome measures: Primary – researchers masked to allocation assessed patients at baseline, 3, 6, 12, 24 months and 5 years. The primary outcome was change in the HAI score between baseline and 12 months. Main secondary outcomes – costs of care in the two groups after 24 and 60 months, change in health anxiety (HAI), generalised anxiety and depression [Hospital Anxiety and Depression Scale (HADS)] scores, social functioning using the Social Functioning Questionnaire and quality of life using the EuroQol-5 Dimensions (EQ-5D), at 6, 12, 24 and 60 months, and deaths over 5 years.

Results: Of the 28,991 patients screened over 21 months, 5769 had HAI scores of ≥ 20 points. Improvement in HAI scores at 3 months was significantly greater in the CBT-HA group (mean number of sessions = 6) than in the standard care, and this was maintained over the 5-year period (overall $p < 0.0001$), with no loss of efficacy between 2 and 5 years. Differences in the generalised anxiety ($p = 0.0018$) and depression scores ($p = 0.0065$) on the HADS were similar in both groups over the 5-year period. Gastroenterology and cardiology patients showed the greatest CBT gains. The outcomes for nurses were superior to those of other therapists. Deaths ($n = 24$) were similar in both groups; those in standard care died earlier than those in CBT-HA. Patients with mild personality disturbance and higher dependence levels had the best outcome with CBT-HA. Total costs were similar in both groups over the 5-year period (£12,590.58 for CBT-HA; £13,334.94 for standard care). CBT-HA was not cost-effective in terms of quality-adjusted life-years, as measured using the EQ-5D, but was cost-effective in terms of HAI outcomes, and offset the cost of treatment.

Limitations: Many eligible patients were not randomised and the population treated may not be representative.

Conclusions: CBT-HA is a highly effective treatment for pathological health anxiety with lasting benefit over 5 years. It also improves generalised anxiety and depressive symptoms more than standard care. The presence of personality abnormality is not a bar to successful outcome. CBT-HA may also be cost-effective, but the high costs of concurrent medical illnesses obscure potential savings. This treatment deserves further research in medical settings.

Trial registration: Current Controlled Trials ISRCTN14565822.

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List of abbreviations

ADSUS	Adult Service Use Schedule
CBT	cognitive–behaviour therapy
CBT-HA	cognitive–behaviour therapy for health anxiety
CEAC	cost-effectiveness acceptability curve
CHAMP	cognitive–behaviour therapy for health anxiety in medical patients
CHASSIS	Confederation of Health Anxiety Sufferers Supporting Increased Services
CI	confidence interval
CONSORT	Consolidated Standards of Reporting Trials
DPQ	Dependent Personality Questionnaire
DSM-IV	*Diagnostic and Statistical Manual of Mental Disorders*-Fourth Edition
EQ-5D	EuroQol-5 Dimensions
GP	general practitioner
HADS	Hospital Anxiety and Depression Scale
HADS-A	Hospital Anxiety and Depression Scale (anxiety section)
HADS-D	Hospital Anxiety and Depression Scale (depression section)
HAI	Health Anxiety Inventory
IAPT	Improving Access to Psychological Therapies
ICD-10	*International Statistical Classification of Diseases*, Tenth Edition
ICD-11	*International Statistical Classification of Diseases*, Eleventh Edition
ICER	incremental cost-effectiveness ratio
MCD	meaningful clinical difference
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
openCDMS	Open Clinical Data Management System
PAS-Q	Quick Personality Assessment Schedule
QALY	quality-adjusted life-year
SD	standard deviation
SFQ	Social Functioning Questionnaire
SOCS	Short Obsessive–Compulsive disorder Screener
VAS	visual analogue scale

Plain English summary

Many people worry excessively about their health and suffer greatly as a consequence. They are frequent attenders in primary care and in medical clinics and secondary care. This study tested whether or not a modified form of cognitive–behaviour therapy for health anxiety (CBT-HA) given by supervised and trained therapists, most of whom were initially naive, was more effective than standard care in patients attending five types of medical clinic in five hospitals in England. We followed up these patients for 5 years.

We found that CBT-HA at an average of six sessions was much more effective than standard care in improving health anxiety and also led to greater improvement in anxiety and depressive symptoms. This greater improvement was found over the whole 5-year period. Those attending cardiology clinics had the most benefit. Costs were similar in both groups, mainly because many who took part had other medical illnesses as well as health anxiety. Nurses as therapists were at least as good as psychologists and other health professionals in giving the treatment.

We recommend that further work is needed in research to identify and treat the growing problem of health anxiety in hospitals.

Scientific summary

Background

Health anxiety is a special form of anxiety-related worry over illness. It has only recently been recognised as a separate condition that is closely linked, but not identical, to the former diagnosis of hypochondriasis. Most people with significant health anxiety have hypochondriasis but a proportion of those with hypochondriasis are not significantly anxious. One of the reasons for separating health anxiety from other forms of hypochondriasis is that it may be amenable to psychological interventions for anxiety, particularly cognitive–behaviour therapy (CBT).

People with health anxiety constantly fear that they have an undiagnosed medical illness and monitor and check their bodies frequently in response to this. They respond to their fears by consulting doctors, other health professionals and even relatives frequently, both for reassurance and for tests to exclude the feared disease. This group of patients attends primary care and secondary care clinics frequently. Previous trials have demonstrated the benefits of cognitive–behaviour therapy in patients in primary care and the pilot trial in secondary care also showed similar benefits, together with cost savings.

A large trial was therefore planned to see patients with excessive health anxiety attending secondary care clinics in general hospitals and to randomise them to a modified form of CBT specially adapted for health anxiety (CBT-HA) or standard care in the clinic. This was a pragmatic trial designed to replicate conditions in ordinary practice and so the therapists chosen to administer the treatment were not particularly skilled, but we hoped to train them to a sufficient standard to give the therapy effectively. We also wanted to examine the influence of personality status and obsessional symptomatology on outcomes.

As evidence of cost-effectiveness in the initial pilot trial was delayed, we planned to look at cost-effectiveness after 2 years but clinical effectiveness after 1 year. Follow-up was planned over a 5-year period.

Objectives

To determine the clinical effectiveness and cost-effectiveness of CBT-HA compared with standard care in the treatment of pathological health anxiety.

To examine the influence of concurrent personality pathology and obsessional symptoms on outcome in both treatment groups.

Design

The design was a single-blind randomised controlled trial with assessments by research assistants masked to allocation of treatment.

Setting

The trial took place in five types of medical clinic in five general hospitals in England.

Participants

A total of 444 patients aged 16–75 years who had a score of ≥ 20 on the Health Anxiety Inventory (HAI) and satisfied the diagnostic criteria for *Diagnostic and Statistical Manual of Mental Disorders*-Fourth Edition (DSM-IV) hypochondriasis, and who were regarded as suitable for treatment by their consultants, took part in the trial. We identified potentially eligible participants by screening with the HAI.

Randomisation

Each patient was randomised to CBT-HA or standard care by a computerised system (Open Clinical Data Management System, Centre for Health Informatics, University of Manchester, Manchester, UK) using block randomisation with no stratification in randomised blocks of four and six.

Masking of assessments

A total of 17 research assistants were involved in recruiting and assessing patients over the 5-year period of the study. Patients were asked not to disclose the nature of their treatment to the research assistants and, if this was accidentally disclosed, a different research assistant was chosen to be involved in further assessments.

Interventions

Cognitive–behaviour therapy for health anxiety

Trainee psychologists, other interested health professionals in the clinics and nurses were chosen to administer CBT-HA. They were trained initially at two all-day workshops, and subsequently supervised by a practitioner trained in CBT-HA in administering between 4 and 10 sessions of treatment over a 2- to 4-month period. Each practitioner also received a written handout giving the essentials of the treatment. Recording 50% of interviews and assessing these independently at different centres allowed us to subsequently check the fidelity of treatment. As far as possible, treatment was given in or close to the clinic concerned. The possibility of a booster session after completing treatment was also allowed.

Standard care

Patients allocated to standard care continued to receive care in both primary and secondary care services as normal. The general practitioners and consultants were informed that they had qualified for excessive health anxiety at baseline.

Measures

Baseline information

The following assessments were carried out at baseline:

- HAI (initial screen)
- DSM-IV hypochondriasis diagnosis (initial assessment before randomisation)
- Hospital Anxiety and Depression Scale [(HADS) including generalised anxiety and depression components]
- Social Functioning Questionnaire (SFQ) – an eight-item self-rating scale
- personality assessment using the Quick Personality Assessment Schedule in an interview of 30 minutes, followed by conversion to the new *International Statistical Classification of Diseases*, Eleventh Edition personality severity levels in 2011

- the Short Obsessive–Compulsive disorder Screener (SOCS) (a set of seven questions that identify the likely presence of obsessive–compulsive disorder)
- the Dependent Personality Questionnaire (DPQ), an assessment of dependent personality traits (this was included as both dependent personality and obsessional symptoms associated with another condition may handicap response or complicate treatment)
- the EuroQol-5 Dimensions (EQ-5D) scale to measure quality of life
- the Adult Service Use Schedule (ADSUS) to record interventions and service usage at interview
- hospital data recording inpatient, outpatient and accident and emergency attendances, and investigations over the 5-year period.

Primary clinical outcome

The primary clinical outcome was set originally as the difference between baseline score and 1-year score on the HAI in the two treatment groups. After 5 years this was no longer relevant, so the primary outcome at this point was the difference between baseline score and 5-year score in the HAI.

Secondary clinical outcomes

The secondary clinical outcomes were changes between scores in the two groups in (1) the HAI at 3, 6, 24 and 60 months and overall; (2) the HADS at 6, 12, 24 and 60 months and overall; (3) the EQ-5D at 6, 12, 24 and 60 months and overall; and (4) the SFQ at 6, 12, 24 and 60 months and overall.

Economic outcomes

The economic evaluation took a health and social care perspective. The impact of the addition of productivity losses was examined in a sensitivity analysis.

Sample size

We calculated sample sizes for both the primary outcome measure (change in HAI score at 1 year) and the first secondary outcome measure, cost, choosing the larger of the two for the study.

Based on the pilot study in a genitourinary medicine clinic we assumed that the true difference in the change of HAI score between CBT and control at 2 years was 5.00 points (higher than a meaningful clinical difference) and that the standard deviation (SD) for the change of HAI score at 2 years was 7.58 points. Taking into account a 20% dropout by 24 months, the sample size was therefore estimated to be 152 patients.

There remains no agreed approach to calculate the sample size required for an economic evaluation, particularly in areas such as health anxiety, in which the willingness to pay for improvements in outcomes is unknown. Based on the pilot study, we considered that the CBT intervention would be cost-effective if it improved HAI score and was no more costly than the control treatment. The sample size calculation for the economic evaluation was therefore based on the total costs over 24 months being equivalent.

With a sample size of 186 per group, the study had 80% power to reject the null hypothesis that the costs of the CBT and control are not equivalent (when the difference in mean costs is ≈£150) in favour of the alternative hypothesis that the means of the two groups are equivalent, assuming that the expected difference in means is 0 and the common SD is 580 (from pilot study data). With 466 patients, or fewer if the dropout rate is less, the study was therefore adequately powered to both detect the assumed difference in the primary outcome and assess the equivalence in the secondary economic outcome between CBT-HA and standard care groups.

Statistical measures and outcomes

The primary end point was analysed using a mixed model with time, treatment and time × treatment interaction as fixed effects, baseline measurement as covariate and patient as random effect. The treatment differences at each time point together with the 95% confidence interval were derived from the

mixed model. Missing data were treated as missing at random in the mixed-model analysis. To assess the sensitivity of the result to missing values, the last observation carried forward strategy was used to compute the missing HAI at the follow-up visits. Other assessments were analysed in a similar way. In addition, covariate-adjusted analysis was performed on the primary outcome analysis by a mixed model, controlling for three pre-specified potential predictors for the primary end point (clinic type, site and age).

All statistical analyses used the intention-to-treat principle using the statistical package SAS, version 9.3 (SAS Institute Inc., Cary, NC, USA). Deaths were reported separately for each group. The Consolidated Standards of Reporting Trials (CONSORT) procedure was used for reporting flow through the trial.

The primary economic evaluation included only those for whom complete data at baseline and at the 12-, 24- and 60-month follow-ups were available.

For each piece of service use information collected with the ADSUS, a unit cost was applied and the total costs calculated. The total cost per participant was calculated by summing all costs. All unit costs were for the financial year 2008–9. Costs beyond the first year were discounted at a rate of 3.5%.

Results

A total of 28,991 patients were screened during the 21 months of recruitment, and 20% of these ($n = 5769$) had HAI scores of ≥ 20 points. Many of the positive scorers for health anxiety declined to take part or were excluded for others reasons. A total of 445 patients were randomised, but one had been randomised twice, on both occasions to standard care, and only the first of these randomisations was included. A mean of six sessions of treatment was given to patients allocated to CBT-HA.

The primary outcome (HAI-score difference between groups at 1 year) was 2.97 points fewer in the CBT-HA group than in standard care ($p < 0.0001$). Significant differences in HAI score in favour of CBT-HA over standard care began at 3 months and were maintained on all occasions over the 5-year period (overall $p < 0.0001$), with no loss of efficacy between 2 and 5 years. Generalised anxiety ($p = 0.0018$) and depression scores ($p = 0.0065$) on the HADS also showed significantly greater improvement over the 5-year period. Differences between groups were maximal after 6 months. Patients treated in gastroenterology and cardiology clinics showed the greatest gains for CBT, with those for cardiology being maximal after 5 years ($p = 0.0012$). Secondary analyses showed therapist differences in outcome, with treatment given by nurses being superior to standard care, with an overall change of 5.5 points in HAI score ($p < 0.0001$). Deaths were similar in both groups, but those allocated to standard care died earlier than those allocated to CBT-HA, suggesting that CBT-HA did not lead to diagnostic overshadowing and failure to identify serious life-threatening disease.

Patients with mild personality disorder and personality difficulty had a markedly better outcome with CBT-HA than those with no personality dysfunction or moderate personality disorder. Similar findings were found with dependent personality measured by the DPQ. Those with high scores on the SOCS scale (≥ 6 points) at 5 years showed non-significant improvement with CBT-HA (score difference of 1.31 points) compared with those with low SOCS scores (score difference of 2.73 points; $p = 0.004$), suggesting that those with concurrent obsessional symptoms do not retain gains with treatment.

Total costs were similar in both groups over the 5-year period, but there was no evidence that CBT-HA is cost-effective in terms of quality-adjusted life-years (QALYs) as measured using the EQ-5D. There is some evidence that CBT-HA is cost-effective in terms of HAI outcomes and in those without serious personality disturbance. The large number of patients who had concurrent medical illnesses that had a disproportionate effect on costs complicated the economic evaluation.

Conclusions

Cognitive–behaviour therapy for health anxiety is a highly effective treatment for pathological health anxiety in patients attending medical clinics and its benefits are maintained over 5 years without reinforcement. Symptoms of anxiety and depression also improved with CBT-HA to a significantly greater extent than with standard care, and were also maintained over 5 years. There was no evidence that the treatment led to 'diagnostic overshadowing' of medical illness, and, among those who died, those who were allocated to standard care died earlier than those in the CBT-HA group. This supports recent evidence that untreated health anxiety is associated with premature mortality. The presence of personality abnormality is not a bar to a successful outcome. There was no evidence that CBT-HA was cost-effective in terms of QALYs, but concurrent medical illnesses obscure potential savings in costs and have a negative impact on quality of life. In terms of the HAI, CBT-HA has a > 50% probability of being cost-effective for almost all willingness-to-pay values, but the EQ-5D figures do not show the same advantages, probably because of considerable concurrent medical pathology that obscures gains made by psychological improvement. CBT-HA allows therapists with no previous experience to be trained relatively easily. It therefore has the potential to be used widely in general hospital settings under appropriate supervision, and so further joint mental and physical health care.

Trial registration

This trial is registered as ISRCTN14565822.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Chapter 1 Introduction to health anxiety

Health anxiety – and its older synonym, hypochondriasis – is a relatively common problem in both primary and secondary medical care settings.[2–4] It also places a substantial burden on health services,[5] as its central feature is sufficient fear of having a serious disease to lead to medical consultation, and, very commonly, this is followed by further investigations. This condition has only recently been recognised, despite its ubiquity and its ability to provoke considerable suffering. Even when the condition is recognised, concerns over litigation in hospital clinics may lead to expensive investigations being carried out unnecessarily. This may provoke further pathology when findings of marginal clinical significance are reported. The extra burden on services is particularly important in secondary medical care. Between 10% and 20% of all attenders at medical clinics have abnormal health anxiety[6,7] and patients often rotate between different clinics depending on the focus of their symptoms. The symptoms of abnormal health anxiety show little tendency to spontaneous resolution and persist for months in the absence of treatment.[6]

Potential benefits of psychological treatment and previous studies

The failure to detect this serious pathology is perhaps less surprising when there is, or at least has been until very recently, a general belief that there is no adequate treatment. Pharmacological management is generally unsatisfactory, but psychological treatment in the form of cognitive–behaviour therapy (CBT) has been shown to be effective both in primary care[8,9] and, more recently, in secondary care.[10] Although these trials suggested efficacy of this intervention, it is less clear if it has a significant impact on costs. Although the total costs were somewhat reduced in those receiving CBT in the only trial in secondary care, these manifested only in the 6 months after treatment had been completed.[10] It is also not known to what extent health anxiety is found in patients with existing medical disease and whether or not this can be successfully treated, as almost all published trials exclude those with definite physical illness.

The precursors to the cognitive–behaviour therapy for health anxiety in medical patients (CHAMP) trial were a series of research studies, mainly carried out at King's Mill Hospital in north Nottinghamshire. The first of these studies established, in a genitourinary medicine clinic setting, that health anxiety was relatively common, that it persisted in the absence of detection or intervention and that it led to more consultations with doctors.[6] The second suggested that the prevalence of health anxiety was somewhat higher (around 12%) in medical clinics such as cardiology and endocrinology clinics,[7] and the third was a randomised controlled trial of a modified form of CBT for health anxiety (CBT-HA) developed earlier by Salkovskis and Warwick[11] versus standard care in patients attending a genitourinary medicine clinic.[10] The last of these was the essential precursor to the CHAMP study. Since the trial began in 2008, there have been many more published trials but, as explained in full later in this report, these have all been concerned with somewhat different populations.

Chapter 2 Trial methods

Research objectives

The main objectives of the CHAMP trial were to examine the clinical value, cost and cost-effectiveness of the administration of CBT in health-anxious patients attending five medical clinics in secondary care. Specifically, we hypothesised that (1) between five and 10 sessions of health anxiety-directed CBT using the Salkovskis–Warwick model[11,12] are more effective than standard care in reducing health-anxious symptoms measured by the Health Anxiety Inventory (HAI)[13] 1 year after randomisation to the trial; and (2) the costs of the CBT and the control are equivalent; the end point for this outcome is the cost of health service interventions at 2 years adjusted for baseline values.

The secondary hypotheses were that, compared with the control condition (single interview), CBT-HA would lead to significantly greater improvement in health anxiety at 3, 6, 24 and 60 months measured using the HAI,[13] in self-rated generalised anxiety measured using the anxiety section of the Hospital Anxiety and Depression Scale (HADS),[14] in quality of life using the EuroQol-5 Dimensions (EQ-5D) measure of health-related quality of life[15] and in social functioning using the Social Functioning Questionnaire (SFQ),[16] all at 6, 12, 24 and 60 months.

In addition, we tested a number of secondary hypotheses. The first of these was that health anxiety-focused CBT (CBT-HA) would be less effective in patients who had additional comorbid pathology in the form of obsessional symptomatology [measured using the Short Obsessive–Compulsive disorder Screener (SOCS)].[17] We also hypothesised that personality status would have an impact on the effectiveness of treatment, and that those with dependent personalities [measured using the Dependent Personality Questionnaire (DPQ)][18] and other personality disorders[19] [measured using the Quick Personality Assessment Schedule (PAS-Q)],[20] which were subsequently converted into *International Statistical Classification of Diseases*, Eleventh Edition (ICD-11)[21] personality disorder categories,[22] would have a worse outcome with CBT-HA. We also expected that these comorbid disorders would be associated with increased costs.

The study also allowed prevalence estimates to be made for health anxiety in different age groups and in different medical clinics.

Patient and public involvement

We recognised at the outset of the study that one of the major problems in executing the trial was the relative lack of awareness of health anxiety in medical clinics. These clinics are busy places with clear tasks set for clinicians and, despite regular but fairly vague comments about the importance of mental pathology in patients who are attending, there is no requirement for mental health status to be assessed, with the possible exception of dementia.

With the help of a support group called Confederation of Health Anxiety Sufferers Supporting Increased Services (CHASSIS) we developed a strategy for identifying the patients who might have pathological health anxiety. In a previous study[7] we found that many patients with existing, and often successfully treated, medical pathology had a high level of health anxiety, and so excluding such patients was felt to be a mistake.

This led to the two-way strategy of combining feedback from clinics about potentially unsuitable attendees (by consultation with clinical staff) with screening of attenders using the short form of the HAI. As broaching the subject of health anxiety with people who were attending the clinic ostensibly for medical follow-up and consultation only was potentially counterproductive, we asked our CHASSIS group of sufferers with health anxiety to advise on the best way of introducing the subject of health anxiety. We chose 'worry about your health' as the core component of this after this consultation.

The CHASSIS group has also been active in disseminating the results of the CHAMP trial, most recently (at the time of writing) by attending a meeting of the All Party Mental Health Group in the House of Commons in December 2014.

Trial summary

The study was a pragmatic randomised controlled trial with two parallel arms and approximately equal randomisation of eligible patients to an active treatment group of 5–10 sessions of CBT or to a control group. During the course of the baseline assessment an explanatory interview was given about the nature of health anxiety; this was the only specific health-anxiety intervention in the control group, but there is some evidence that a simple explanation is of benefit in its own right.[11]

Settings

Patients attending cardiology, endocrinology, gastroenterology, neurology and respiratory medicine clinics in five general hospitals (King's Mill Hospital, north Nottinghamshire; St Mary's Hospital, London; Charing Cross Hospital, London; Chelsea and Westminster Hospital, London; and the Hillingdon Hospital, Middlesex) were considered for the study. A total of 107 consultants agreed to collaborate with the study and to allow their patients to be approached provided that they were not considered inappropriate for the study on account of the severity of their physical pathology.

Form of randomisation

After baseline assessment, randomisation was carried out by a computerised system [Open Clinical Data Management System (openCDMS), Centre for Health Informatics, University of Manchester, Manchester, UK] using block randomisation with no stratification in randomised blocks of four and six. The allocation was carried out by the UK Mental Health Research Network independently of CHAMP personnel.

Target population and procedure

Patients attending clinics of the collaborating consultants, apart from those who were specifically excluded, were approached while waiting for their outpatient appointments and, if they agreed, were given the short form of the HAI,[13] a rating scale of 14 questions that takes 5–10 minutes to complete. Those that scored at least 20 points on the scale were offered the opportunity to take part in the trial and given an information sheet about the study. If the patients agreed immediately, they were given an information sheet about the study and baseline assessments were made, provided that they satisfied the inclusion criteria and the *Diagnostic and Statistical Manual of Mental Disorders*-Fourth Edition (DSM-IV) diagnosis of hypochondriasis [derived from the Structured Clinical Interview for DSM-IV (SCID-IV) interview].[23] Those who were uncertain were approached later.

When each patient had satisfied the criteria for entry to the study, formal consent was obtained and baseline assessments completed. At the baseline assessment all patients received a standard explanation of

the nature and significance of health anxiety. After completion of the assessments, the research assistant entered and registered each patient to an online system (openCDMS) and this automatically led to the appropriate randomisation. The study co-ordinator was then informed of the details of the treatment arm allocation. Equal allocation was made to either (1) the active treatment group – between 5 and 10 1-hour sessions of CBT from a psychologist or research nurse at the clinic, backed up by a short take home manual; or (2) the standard care group, which received the normal care in the clinic.

The patients were recruited over a 21-month period beginning in October 2008 and ending in July 2010, and were followed up for 5 years. Because there were so many clinics running simultaneously, we required additional assessment help in recruitment. This was provided by Clinical Studies Officers of the North London and East Midlands hubs of the Mental Health Research Network, and proved to be invaluable.

Inclusion and exclusion criteria

Patients suitable for inclusion were those who satisfied the criteria for excessive health anxiety outlined above and who (1) were aged between 16 and 75 years, (2) were permanently resident in the area, (3) had a sufficient understanding of English to read and complete the questionnaires and (4) gave written consent for the interviews and audio-taping of 50% of treatment sessions, and for access to their medical records. The presence of existing medical pathology, provided that it was not new and required further investigation, was not a bar to treatment in the study, and as in preliminary work we had found that many patients with existing pathology have a high level of health anxiety.

Some patients who would otherwise satisfy the inclusion criteria above were excluded if (1) they were felt by their consultants to have a level of continuing major pathology that was too severe for them to take part in the study; (2) they were currently being actively investigated for significant pathology suspected by the clinician and for whom CBT might confuse or cause distress; (3) they had progressive cognitive impairment; or (4) they were currently under psychiatric care.

Assessments

The following assessments were carried out at baseline only:

- personality assessment using the PAS-Q,[20] followed by conversion to the ICD-11 personality levels[22] but also including the questions from the hypochondriasis subsection of the full schedule[19]
- the SOCS[17] (a set of seven questions that identify the likely presence of obsessive–compulsive disorder); and
- the DPQ,[18] an assessment of dependent personality traits (this was included because both dependent personality and obsessional symptoms are associated conditions that may handicap or complicate treatment).

The remaining clinical assessments, in addition to the main health anxiety measure (HAI) were generalised anxiety and depression (measured with the HADS[14]), as these symptoms are common in patients with hypochondriasis, quality of life (EQ-5D)[15] and social functioning (SFQ).[16] These assessments were given at baseline and at 6, 12, 24 and 60 months. To ensure the highest possible follow-up rate, patients were reminded of the next follow-up point at each assessment. The HAI was also given at 3 months by post or telephone with a research assistant.

Service use data for the economic evaluation were collected using the Adult Service Use Schedule (ADSUS).

Methods of overcoming bias

The independent central computerised system involved in randomisation (openCDMS) ensured no bias in allocation of treatments and also full baseline information, as it was only when all necessary data were entered that the patient was randomised. As this was a single-blind study, there was always the danger of disclosure of the form of treatment by the patient, therapist or other investigators in the study. This was minimised by (1) patients being asked by research assessors not to disclose their treatment to the research assessors, (2) the assessors and therapists working in different areas and (3) establishing a system whereby any assessor who was unwittingly informed about the nature of the treatment then ceased to assess that patient, and another research assessor was allotted for continued assessments.

Study interventions

Cognitive–behaviour therapy treatment arm

As the aim was to replicate the conditions of treatment that would be likely to prevail in the future if the trial found benefit from CBT, as much as possible it was aimed to give CBT within or close to the referring clinic, so that it was perceived by patients to be part of the clinic's function in combining help for mental and physical problems, instead of being a potentially stigmatised external psychiatric service.

At each clinic we therefore trained a psychologist, research nurse or equivalent health professional (G-grade or equivalent) to administer the treatment. Each patient was invited to receive between 5 and 10 sessions of CBT with additional adaptations for health anxiety developed by HT and PS, reinforced by three booklets to be handed to patients at treatment sessions (*Box 1*). Each therapist attended two workshops at the beginning of the study and received up to 3 months' training from the senior practitioners in the study, sometimes in vivo with two therapists being present in treatment sessions, before taking on the care of patients alone.

Because of the need for training, recruitment was planned to be slower in the first 3 months of the trial than in the later phases of the study. Following the initial period, therapists had fortnightly supervision from senior practitioners until the last patients had been recruited and treated. Therapists were also given a manual of CBT (written by PS and HT) developed for health anxiety. This was prepared in advance of training and used for refreshment during treatment.

Research assistants who had all been trained in the assessment procedures (by SC) carried out both baseline assessments and follow-up. The follow-up at 3 months concerned only the HAI, which was administered by post or telephone. Follow-ups from 6 months onwards were carried out by face-to-face interview with some patients but for those who preferred a telephone assessment this method was used. As the main clinical assessments were all self-ratings, this rarely presented a problem. The ADSUS is administered as a clinical interview, but the answers are all simple factual ones that readily allow the information to be gathered over the telephone.

BOX 1 Essentials of CBT-HA

- Recognition of fear of disease rather than actual disease.
- Dangers of internet browsing.
- Avoiding reassurance.
- Negative consequences of body monitoring and hypervigilance.
- Recognition that the awful possible explanations of symptoms are rare.
- Reading of three booklets summarising health anxiety.

Training and fidelity of intervention

Four of the applicants (PS, GS, DM and HS) were involved in the training of therapists in two all-day workshops, and also in the assessment of treatment fidelity, and HW, one of the originators of the treatment, also assessed the audio-taped interviews independently.

Approximately half of all treatment sessions were audio-recorded and tapes or discs of these sessions given to patients to help in their progress. Fidelity was tested using a health-anxiety modification of the Cognitive Therapy Rating Scale[24] (Health Anxiety Version), in which all therapists were assessed before they were regarded as competent. Those who did not reach an accepted grade had further training until they achieved competence. Manuals for the training of therapists and to aid patients in their treatment were also prepared. This issue is important, as better treatment fidelity with CBT has been associated with better treatment effects.[25,26]

Standard treatment arm

Patients allocated to the standard treatment arm continued their care in both primary and secondary care settings and were reminded that they would be followed up at regular intervals up to 5 years. No restrictions on treatment were given to this group as the study was a pragmatic trial and the follow-up period was long.

Sample size

We calculated sample sizes for both the primary outcome measure and the first secondary outcome measure, choosing the larger of the two for the study.

Based on the pilot study in a genitourinary medicine clinic,[10] we assumed that the true difference in the change of HAI score between CBT and control at 2 years is 5.00 points and that the standard deviation (SD) for the change of HAI score at 2 years is 7.58 points. With these assumptions, the study needed 122 patients to detect the above difference with 95% power at a two-sided 5% significance level. Taking into account 20% dropout by 24 months, the sample size was estimated to be 152 patients. It is also fair to add that when the study was set up there was no knowledge on what was a minimally significant clinical difference in the HAI score, and even now there is little work on this subject, but an improvement of 2 points on the scale appears to be clinically important (see *Chapter 5*, *Meaningful clinical difference in Health Anxiety Inventory scores*).

There remains no agreed approach to calculate the sample size required for an economic evaluation, particularly in areas such as health anxiety, in which the willingness to pay for improvements in outcomes is unknown. Based on the pilot study, we considered that the CBT intervention would be cost-effective if it improved HAI score and that it was no more costly than the control treatment. The sample size calculation for the economic evaluation was therefore based on the total costs over 24 months being equivalent.

With a sample size of 186 per group, the study had 80% power to reject the null hypothesis that the costs of the CBT and control are not equivalent (when the difference in mean costs is ≈£150) in favour of the alternative hypothesis that the means of the two groups are equivalent, assuming that the expected difference in means is 0 and the common SD is 580 (from pilot study data).

The sample size was thus powered by the first secondary outcome of the CHAMP study, estimated as 466 patients, assuming a 20% dropout by 24 months, leading to a total of 372 completing treatment and equal randomisation between groups. The sample size calculation uses a one-sided (non-inferiority) test. Thus, with 466 patients, or fewer if the dropout rate was less, the study was adequately powered to both

detect the assumed difference in the primary outcome and assess the equivalence in the secondary economic outcome between the CBT group and the control group.

Statistical analysis

All primary statistical analyses used the intention-to-treat principle using the statistical package SAS, version 9.3 (SAS Institute Inc., Cary, NC, USA). The numbers (with percentages) of losses to follow-up at 12, 24 and 60 months after randomisation will be reported and compared between the treatment arms with absolute risk differences [95% confidence intervals (CIs)]. Deaths were reported separately for each group. The Consolidated Standards of Reporting Trials (CONSORT) procedure was used for reporting flow through the trial.

The primary end point was analysed using a mixed model with time, treatment, and time × treatment interaction as fixed effects, baseline measurement as covariate and patient as random effect. The treatment differences at each time point together with the 95% CI were derived from the mixed model. Missing data were treated as missing at random in the mixed-model analysis. To assess the sensitivity of the result to missing values, the last observation carried forward strategy was used to compute the missing HAI score at the follow-up visits. Other assessments were analysed in a similar way. In addition, covariate-adjusted analysis was performed on the primary outcome analysis by mixed model, controlling for three pre-specified potential predictors for the primary end point (clinic type, site and age). In addition, the percentage of patients achieving normal levels of health anxiety (HAI score of ≤ 10 points) was compared using a generalised estimating equation model with visit, treatment, interaction between visits and treatment as fixed effect, baseline measurement of HAI score as covariate and patient as random effect (an exchangeable covariance structure).

Subgroup analyses were also carried out to determine if there was heterogeneity in any of the main groups identified for analysis.

Chapter 3 Results

Parts of this chapter have been reproduced with permission from Tyrer P, Wang D, Tyrer H, Crawford M, Cooper S. Dimensions of dependence and their influence on the outcome of cognitive behaviour therapy for health anxiety: randomized controlled trial. *Pers Ment Health* 2016;**10**:96–105.[27] Copyright © 2016 John Wiley & Sons, Ltd.

A total of 219 patients were allocated to CBT-HA and 225 to standard care. The CONSORT diagram for all phases in the trial is illustrated in *Figure 1*. Of the 444 patients (including those who had died), 416 (94%) were followed up at 3 months, 402 (91%) at 6 months, 386 (87%) at 12 months, 372 (84%) at 2 years and

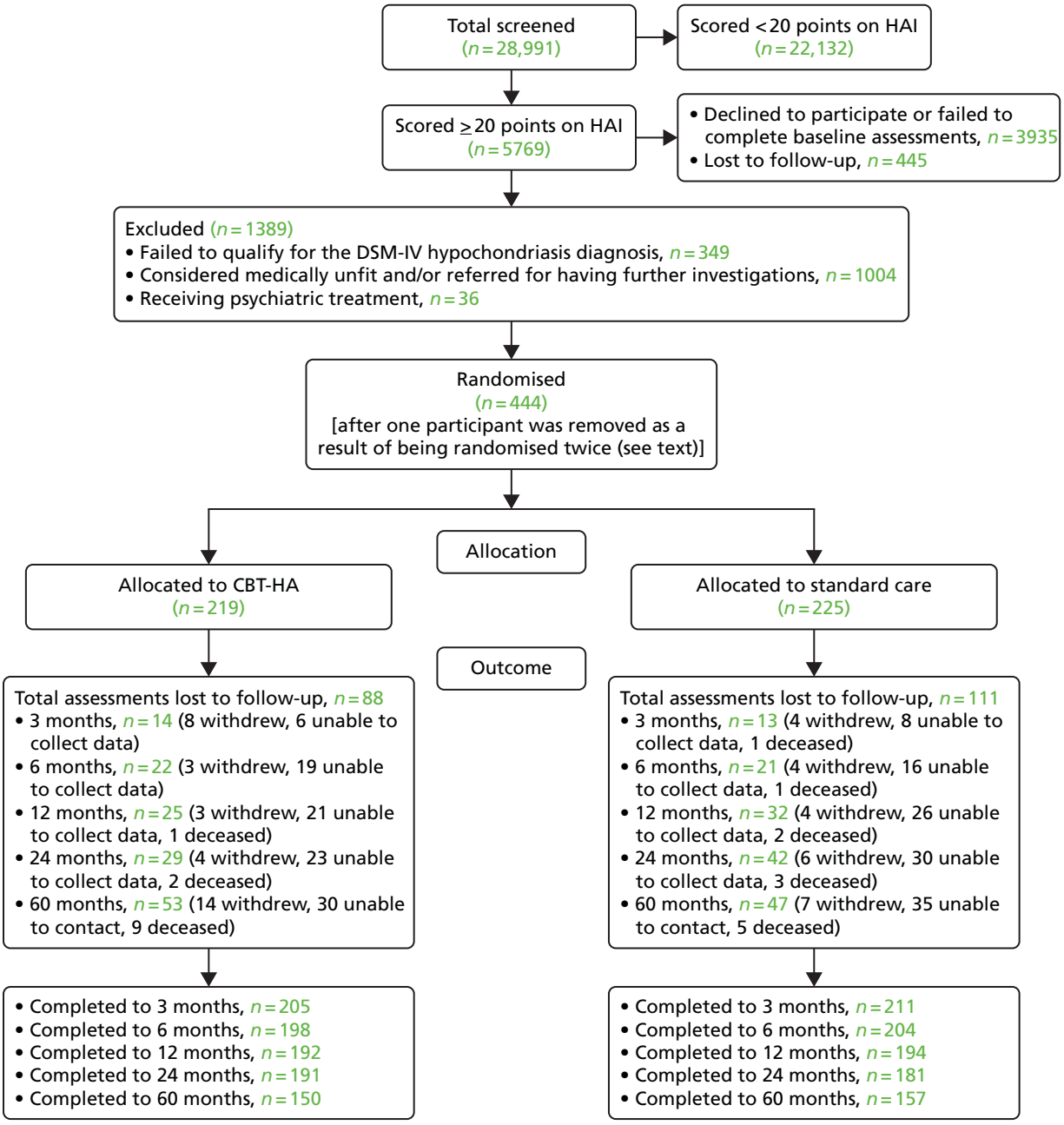

FIGURE 1 Consolidated Standards of Reporting Trials diagram (numbers assessed for some variables differ because of missing data). Reprinted from the *Lancet*, vol. 383, Tyrer P, Cooper S, Salkovskis P, Tyrer H, Crawford M, Byford S, *et al.* Clinical and cost-effectiveness of cognitive behaviour therapy for health anxiety in medical patients: a multicentre randomised controlled trial, pp. 219–25. Copyright (2014),[28] with permission from Elsevier.

308 (69%) at 5 years. The CONSORT details are notable in several respects. First, nearly 20% (2991) of all 5769 patients who completed the HAI scored ≥ 20 points and were therefore eligible to proceed to the next phase of the trial. After exclusions and refusals, only 444 were randomised. Possible explanations for this are given later in this report and, in particular, we suspect, but cannot confirm, that the sample that entered the trial was roughly a representative one. Second, although there were many reasons why high HAI scorers did not take part, only a minority ($n = 349$, 6%) were excluded because they did not have a DSM-IV diagnosis of hypochondriasis. The other finding worthy of note is that dropout rates were very similar in both groups, and at 5 years were greater in the CBT-HA group than in the standard care one. This is somewhat unusual in trials of psychological treatments, for which retention is usually greater in the psychological treatment arm.

The main baseline characteristics of the two treatment groups are shown in *Table 1*; the table shows that the two groups were essentially similar in important respects.

TABLE 1 Baseline characteristics of patients (intention-to-treat population)

	Treatment group		
Variable	CBT-HA ($N = 219$)	Standard care ($N = 225$)	All ($N = 444$)
Age (years)			
Mean (SD)	50.3 (13.6)	47.0 (13.4)	48.6 (13.6)
Gender, *n* (%)			
Female	113 (51.6)	123 (54.7)	236 (53.2)
Male	106 (48.4)	102 (45.3)	208 (46.8)
Ethnicity, *n* (%)			
White British	145 (67.8)	151 (68.0)	296 (67.9)
White other	26 (12.1)	18 (8.1)	44 (10.1)
Black/black British: African	6 (2.8)	9 (4.1)	15 (3.4)
Black/black British: Caribbean	5 (2.3)	7 (3.2)	12 (2.8)
Asian/Asian British	15 (7.0)	23 (10.4)	38 (8.7)
Asian/Asian British: other	8 (3.7)	8 (3.6)	16 (3.7)
Arab/Middle East	7 (3.3)	4 (1.8)	11 (2.5)
Chinese/Far East	2 (0.9)	2 (0.9)	4 (0.9)
Hospital, *n* (%)			
Chelsea and Westminster Hospital	26 (11.9)	23 (10.2)	49 (11.0)
Charing Cross Hospital	31 (14.2)	26 (11.6)	57 (12.8)
Hillingdon Hospital	56 (25.6)	63 (28.0)	119 (26.8)
King's Mill Hospital	70 (32.0)	74 (32.9)	144 (32.4)
St Mary's Hospital	36 (16.4)	39 (17.3)	75 (16.9)
Clinic type, *n* (%)			
Cardiology	53 (24.2)	57 (25.3)	110 (24.8)
Endocrinology	41 (18.7)	43 (19.1)	84 (18.9)
Gastroenterology	77 (35.2)	72 (32.0)	149 (33.6)
Neurology	20 (9.1)	22 (9.8)	42 (9.5)
Respiratory medicine	28 (12.8)	31 (13.8)	59 (13.3)
HAI score			
Mean (SD)	24.9 (4.2)	25.1 (4.5)	25.0 (4.4)

There were 24 deaths during the trial, 12 in each treatment group. All were from natural causes. The Kaplan–Meier plot of deaths showed a non-significant trend for lower mortality in the CBT-HA arm early in the trial (*Figure 2*). One patient in the standard care group had an episode of deliberate self-harm during follow-up. The 219 patients in the trial allocated to CBT-HA were seen by 11 therapists; assessment of the fidelity of therapists' treatment showed that all except one scored at an adequate competence level or higher, and this was confirmed by the independent assessor (HW). The therapist who failed to achieve this level saw five patients in the trial.

Primary outcome

The scores on the HAI showed greater improvement with CBT-HA than with standard care at all times of testing, with maximal differences at 6 months (*Table 2* and *Figure 3*).

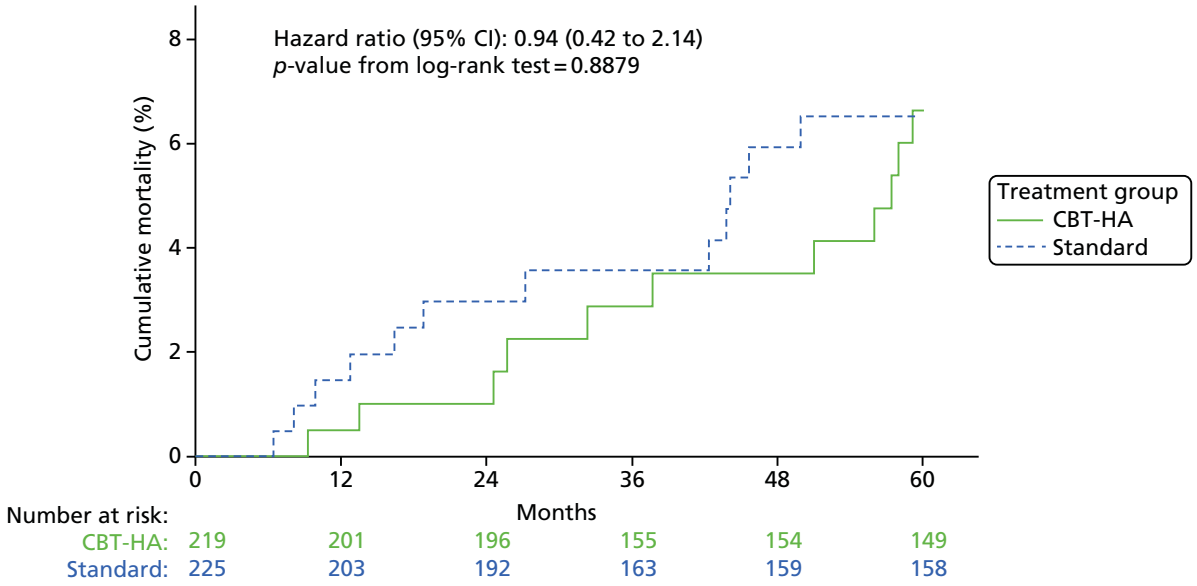

FIGURE 2 Kaplan–Meier plot of deaths over the 5-year period of the trial.

TABLE 2 Change in HAI scores over 5 years

	Observed value				Mixed-model analysis	
	CBT-HA		Standard care		Treatment difference (points) (95% CI)	*p*-value
Visit	*n*	Mean score (points) (SD)	*n*	Mean score (points) (SD)		
Baseline	219	24.88 (4.23)	225	25.12 (4.52)		
Improvement from baseline						
3 months	205	4.41 (7.63)	212	2.62 (6.17)	1.74 (0.38 to 3.11)	0.0123
6 months	197	7.11 (7.83)	204	2.33 (5.76)	4.83 (3.45 to 6.21)	< 0.0001
12 months	194	6.44 (7.47)	193	3.20 (6.54)	2.97 (1.57 to 4.37)	< 0.0001
24 months	190	5.90 (7.54)	183	3.66 (6.57)	2.01 (0.60 to 3.42)	0.0052
5 years	149	6.45 (8.57)	157	4.34 (7.75)	2.20 (0.70 to 3.70)	0.0040
Overall					2.75 (1.65 to 3.85)	< 0.0001

Adapted from the *Lancet*, vol. 383, Tyrer P, Cooper S, Salkovskis P, Tyrer H, Crawford M, Byford S, *et al.* Clinical and cost-effectiveness of cognitive behaviour therapy for health anxiety in medical patients: a multicentre randomised controlled trial, pp. 219–25. Copyright (2014),[28] with permission from Elsevier.

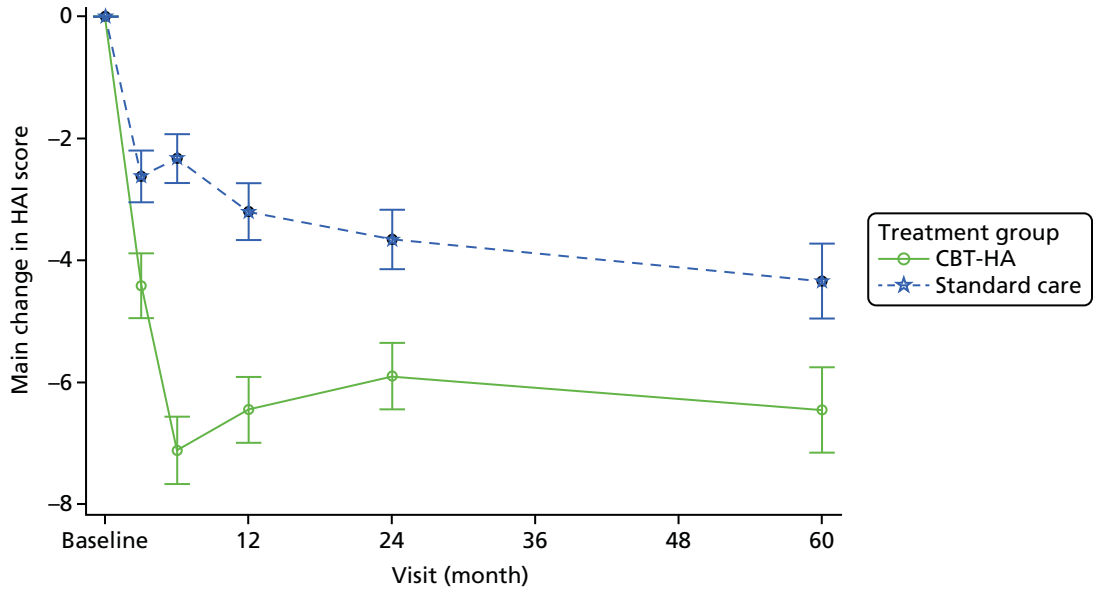

FIGURE 3 Change in HAI scores between CBT-HA and standard care (treatment as usual) over the 5-year period. Note: the change in HAI scores between the two treatments at 12 months is the primary outcome. Adapted from the *Lancet*, vol. 383, Tyrer P, Cooper S, Salkovskis P, Tyrer H, Crawford M, Byford S, *et al.* Clinical and cost-effectiveness of cognitive behaviour therapy for health anxiety in medical patients: a multicentre randomised controlled trial, pp. 219–25. Copyright (2014),[28] with permission from Elsevier.

Last observation carried forward analyses

The analysis using the last observation carried forward method for the primary outcome (HAI) showed very similar results. Because similar agreement was found with other outcomes they are not included in the report.

TABLE 3 Last observation carried forward analyses for primary outcome (change in HAI scores)

Comparison	Difference in score (points) (95% CI)	*p*-value
CBT-HA vs. standard care at 3 months	–1.72 (–3.03 to –0.41)	0.0099
CBT-HA vs. standard care at 6 months	–4.52 (–5.82 to –3.21)	< 0.0001
CBT-HA vs. standard care at 12 months	–2.93 (–4.24 to –1.63)	< 0.0001
CBT-HA vs. standard care at 24 months	–2.07 (–3.38 to –0.77)	0.0019
CBT-HA vs. standard care at 5 years	–2.06 (–3.36 to –0.75)	0.0021
CBT-HA vs. standard care at all times	–2.66 (–3.72 to –1.60)	< 0.0001

Secondary outcomes

Generalised anxiety and depression

Generalised anxiety and depression as recorded using the HADS anxiety (HADS-A) and depression (HADS-D) sections also showed significant differences between the two treatments over the 5-year period, with those for generalised anxiety (HADS-A) being maximal at 6 months (*Table 4* and *Figure 4*) and those for depression (HADS-D) being maximal at 5 years (*Table 5* and *Figure 4*).

Social functioning

There was very little difference between the scores on the SFQ between the two groups over the 5-year period. The scores at baseline indicated a moderate degree of social dysfunction (the normal population

TABLE 4 Change in HADS-A scores over 5 years

	Observed value				Mixed-model analysis	
	CBT-HA		Standard care			
Visit	*n*	Mean score (points) (SD)	*n*	Mean score (points) (SD)	Treatment difference (95% CI)	*p*-value
Baseline	219	12.56 (3.74)	225	12.25 (3.88)		
Improvement from baseline						
6 months	197	2.74 (4.41)	204	1.46 (3.89)	1.30 (0.48 to 2.11)	0.0019
12 months	194	2.80 (4.40)	193	1.67 (4.04)	1.02 (0.19 to 1.85)	0.0165
24 months	190	3.33 (4.57)	183	2.07 (4.35)	1.01 (0.17 to 1.86)	0.0186
5 years	150	5.56 (5.72)	158	4.54 (5.48)	0.71 (–0.20 to 1.61)	0.1245
Overall					1.01 (0.38 to 1.64)	0.0018

TABLE 5 Change in HADS-D scores over 5 years

	Observed value				Mixed-model analysis	
	CBT-HA		Standard care			
Visit	*n*	Mean score (points) (SD)	*n*	Mean score (points) (SD)	Treatment difference (95% CI)	*p*-value
Baseline	219	9.12 (4.34)	225	8.83 (4.58)		
Improvement from baseline						
6 months	197	2.74 (4.41)	204	1.46 (3.89)	0.75 (–0.09 to 1.58)	0.0797
12 months	194	2.80 (4.40)	192	1.67 (4.04)	0.75 (–0.10 to 1.60)	0.0821
24 months	189	3.33 (4.57)	181	2.07 (4.35)	0.63 (–0.23 to 1.49)	0.1521
5 years	150	5.56 (5.72)	157	4.54 (5.48)	1.41 (0.48 to 2.33)	0.0029
Overall					0.88 (0.25 to 1.52)	0.0065

Note
A negative score indicates an increase in depressive symptoms from baseline and this was shown in the standard care group at 5 years.

average is 4.6 points and a mean score of 7.7 points is found with patients attending general practice with common mental disorders.[13] The higher than expected SFQ scores were partly explained by comorbid medical pathology but also by personality status (see *Table 9*). Over the course of the study there was a modest improvement in social functioning in both groups (*Table 6*).

Influence of obsessional symptoms on outcome

Scores on the SOCS scale were dichotomised at the level of 6 points, as recommended by the original and subsequent authors.[17,29] The results showed that patients with higher SOCS scores had somewhat lesser improvement in HAI scores with CBT-HA over the 5-year period (*Figure 5*) and that at 5 years the difference between CBT-HA and standard care was not significant (see *Table 13*).

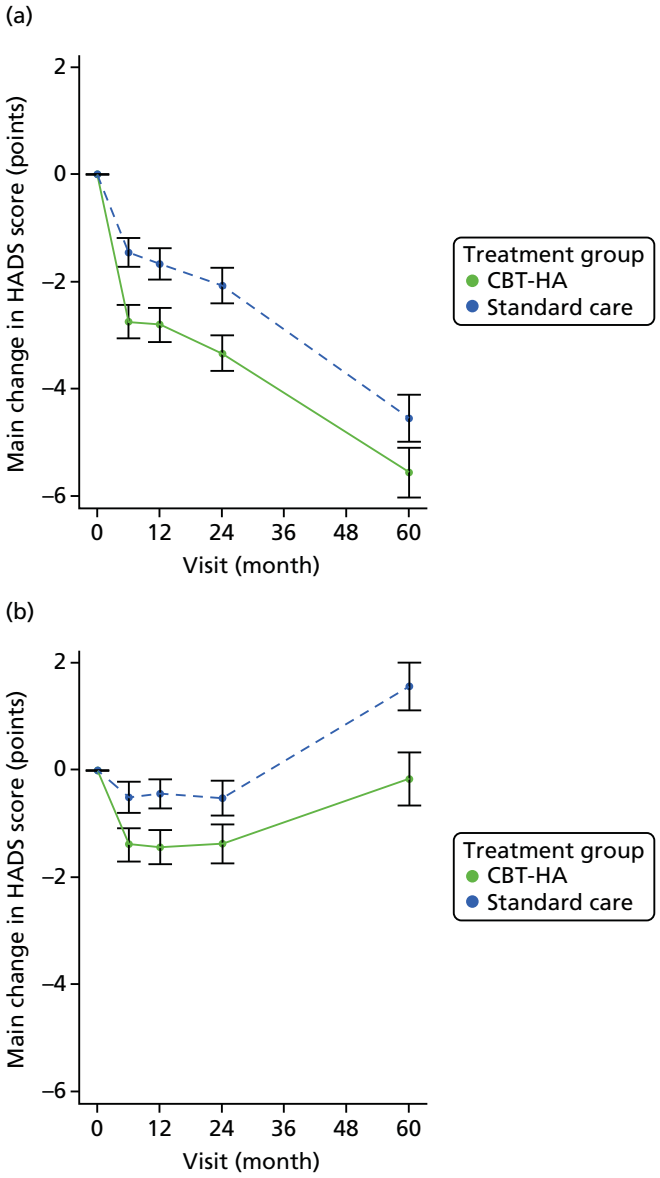

FIGURE 4 Changes in the anxiety and depression sections of the HADS over 5 years. (a) HADS anxiety total score; and (b) HADS depression total score.

TABLE 6 Change in SFQ scores over 5 years

	Observed value				Mixed-model analysis	
	CBT-HA		Standard care		Treatment difference (points) (95% CI)	*p*-value
Visit	*n*	Mean score (points) (SD)	*n*	Mean score (points) (SD)		
Baseline	219	8.52 (2.07)	225	8.59 (2.00)		
Improvement from baseline						
6 months	197	0.32 (1.71)	204	0.33 (1.77)	0.02 (–0.47 to 0.50)	0.9508
12 months	194	2.21 (1.75)	192	2.30 (1.69)	–0.09 (–0.58 to 0.41)	0.7335
24 months	190	0.70 (1.93)	182	0.58 (1.85)	0.12 (–0.38 to 0.63)	0.6355
5 years	150	1.20 (4.88)	157	1.27 (4.56)	–0.06 (–0.62 to 0.50)	0.8367
Overall					–0.00 (–0.32 to 0.32)	0.9908

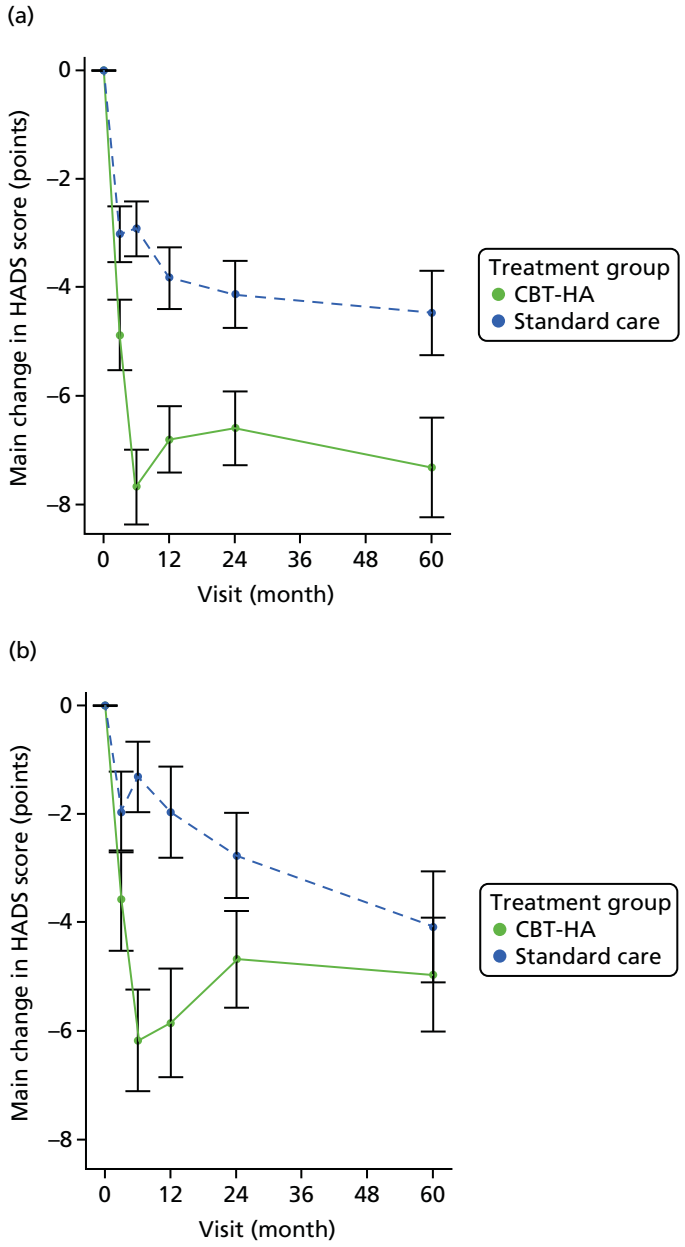

FIGURE 5 Mean change in HAI score by initial scores on the SOCS, with scores dichotomised at the recommended score of 6. (a) SOCS score of ≤ 6 points; and (b) SOCS score of ≥ 6 points.

Influence of personality status on outcome

Personality assessment was carried out using the PAS-Q,[20] derived from its parent instrument,[30] which records both the severity and the type of personality disorder with an algorithm to identify the *International Statistical Classification of Diseases*, Tenth Edition (ICD-10)[31] personality disorders, including dependent personality disorder. SC trained all raters in advance on a standard course. During the progress of the study the Working Group for the Reclassification of Personality Disorder in ICD-11 completed its initial work on a classification based on severity criteria (April 2010).[22] The PAS-Q data were subsequently reclassified to the ICD-11 severity equivalents. Good reliability between assessors in this exercise was achieved.[32]

Using the ICD-11 classification, only 63 (14.2%) had no personality dysfunction but 197 (44.3%) had personality difficulty (a subthreshold condition not qualifying for disorder). Only three people assessed had severe personality disorder and so they were included with the moderate group. No differences in patient characteristics at baseline were identified and there was an even spread of male/female and a similar age profile between the ICD-11 personality groups (*Table 7*). However, there were significant differences in symptoms of health anxiety and generalised anxiety, depression and social functioning at baseline; participants with moderate to severe personality disorder had significantly higher scores than those with no personality disturbance (see *Table 7*). There were no differences in total cost at baseline apart from somewhat greater costs for each increment of personality severity.

The outcome data over follow-up by ICD-11 classification are detailed in *Table 8* and *Figure 6*. Contrary to our hypotheses, the results show that those with no personality dysfunction showed no benefit from CBT-HA at any time point in the study; overall standard care was superior ($p < 0.05$). For all other groups the picture was different. For participants with personality difficulty and mild personality disorder, there was evidence of strong gains from CBT-HA at all time points compared with standard care ($p < 0.001$), and these were maintained at 5 years, especially in those with mild personality disorder. For participants with moderate and severe personality disorder, the initial benefit was not retained at 2 years, resulting in a weaker relationship over follow-up ($p < 0.05$), and by 5 years benefit was lost. Improvement in social function was similar in all groups except in those with no personality dysfunction ($p < 0.02$ in favour of standard care) and in those of mild personality disorder at 5 years, whose SFQ scores were significantly lower in the CBT-HA group (*Figure 7*). Clinical symptomatology increased and social dysfunction was

TABLE 7 Patient characteristics, outcomes and cost at baseline by personality status

	Personality status				
Variable	0 (*N* = 63)	1 (*N* = 197)	2 (*N* = 142)	3–4 (*N* = 42)	*p*-value
Sex, *n* (%)					
Female	29 (46.0)	109 (55.3)	76 (53.5)	22 (52.4)	0.642
Male	34 (54.0)	88 (44.7)	66 (46.5)	20 (47.6)	–
Age (years)					
Mean (SD)	48.6 (14.8)	49.5 (13.6)	47.5 (13.6)	47.9 (11.3)	0.592
Minimum to maximum (range)	18.3 to 73.9	17.3 to 74.3	17.0 to 75.5	21.7 to 72.4	–
HAI score					
Mean (SD)	24.0 (3.2)	24.8 (4.5)	25.2 (4.3)	26.9 (4.9)	0.006
HADS-A score					
Mean (SD)	10.1 (3.6)	12.1 (3.7)	13.4 (3.6)	14.0 (3.6)	< 0.001
HADS-D score					
Mean (SD)	6.7 (3.7)	8.2 (4.1)	10.0 (4.4)	12.4 (4.7)	< 0.001
SFQ score					
Mean (SD)	5.9 (3.4)	8.6 (4.0)	11.3 (4.4)	12.7 (3.8)	< 0.001
Total cost (preceding 6 months)					
Mean (SD)	2405.2 (2526.3)	2601.8 (2837.2)	2668.1 (2887.1)	2692.5 (2708.3)	0.954

TABLE 8 Summary changes from baseline in the CBT-HA group compared with standard care in ICD-11 personality groups over 2 years

Variable	Difference between CBT-HA and standard care (95% CI)			
	ICD-11 personality level 0 (*N* = 63)	ICD-11 personality level 1 (*N* = 197)	ICD-11 personality level 2 (*N* = 142)	ICD-11 personality level 3–4 (*N* = 42)
HAI score				
3 months	2.12 (–1.41 to 5.64)	–1.62 (–3.56 to 0.31)	–3.24** (–5.57 to –0.92)	–3.76 (–8.24 to 0.71)
6 months	–1.29 (–4.9 to 2.31)	–4.80*** (–6.77 to –2.84)	–5.51*** (–7.85 to –3.16)	–8.13** (–12.59 to –3.66)
12 months	0.47 (–3.11 to 4.05)	–3.55** (–5.54 to –1.57)	–3.32** (–5.69 to –0.96)	–4.42 (–8.99 to 0.14)
24 months	1.45 (–2.12 to 5.03)	–2.98** (–4.98 to –0.97)	–2.96* (–5.35 to –0.56)	–0.31 (–4.93 to 4.31)
At all time points	0.69 (–2.23 to 3.6)	–3.24*** (–4.84 to –1.64)	–3.76*** (–5.78 to –1.74)	–4.16* (–7.99 to –0.33)
HADS-A score				
6 months	1.45 (–0.5 to 3.39)	–1.47* (–2.64 to –0.29)	–1.71* (–3.05 to –0.36)	–2.03 (–4.7 to 0.65)
12 months	2.68 (0.75 to 4.62)	–1.70** (–2.89 to –0.51)	–1.42* (–2.78 to –0.06)	–1.32 (–4.05 to 1.41)
24 months	2.21* (0.25 to 4.16)	–1.81** (–3.01 to –0.60)	–1.00 (–2.38 to 0.38)	–1.00 (–3.77 to 1.77)
At all time points	2.11** (0.51 to 3.71)	–1.66*** (–2.62 to –0.70)	–1.38* (–2.56 to –0.20)	–1.45 (–3.79 to 0.89)
HADS-D score				
6 months	2.17* (0.11 to 4.24)	–1.33* (–2.49 to –0.17)	–1.1 (–2.49 to 0.28)	–1.42 (–4.32 to 1.48)
12 months	1.79 (–0.27 to 3.85)	–1.27* (–2.45 to –0.09)	–0.69 (–2.10 to 0.71)	–2.64 (–5.62 to 0.33)
24 months	3.29** (1.22 to 5.36)	–0.69 (–1.88 to 0.49)	–1.84* (–3.27 to –0.41)	–2.06 (–5.08 to 0.96)
At all time points	2.42** (0.62 to 4.21)	–1.10* (–2.06 to –0.13)	–1.21* (–2.41 to –0.02)	–2.04 (–4.55 to 0.47)
SFQ score				
6 months	2.32* (0.19 to 4.45)	–0.42 (–1.57 to 0.73)	–0.31 (–1.68 to 1.06)	–1.89 (–4.54 to 0.77)
12 months	1.52 (–0.61 to 3.64)	–0.08 (–1.25 to 1.09)	–0.66 (–2.05 to 0.73)	–1.91 (–4.64 to 0.82)
24 months	2.88** (0.75 to 5.01)	–0.19 (–1.37 to 0.98)	–1.49* (–2.9 to –0.08)	–0.88 (–3.65 to 1.89)
At all time points	2.24* (0.41 to 4.07)	–0.23 (–1.19 to 0.73)	–0.82 (–1.97 to 0.33)	–1.56 (–3.83 to 0.71)

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.
Positive score differences for symptoms indicate greater improvement in CBT-HA groups except for social functioning (SFQ scores). (Thus, in those with no personality disturbance, social functioning was significantly worse after CBT-HA than standard care.)
ICD-11 level 0 = no personality disturbance, ICD-11 level 1 = personality difficulty, level 2 = mild personality disorder, level 3–4 = moderate and severe personality disorder.
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greater with each increment of personality pathology, and although the results were most marked in those with health anxiety they were also found with generalised anxiety and depressive symptoms (see *Table 7*).

Costs were lower in patients treated with CBT-HA for all levels of personality disturbance apart from moderate and severe personality disorder, when costs were greater (*Table 9*).

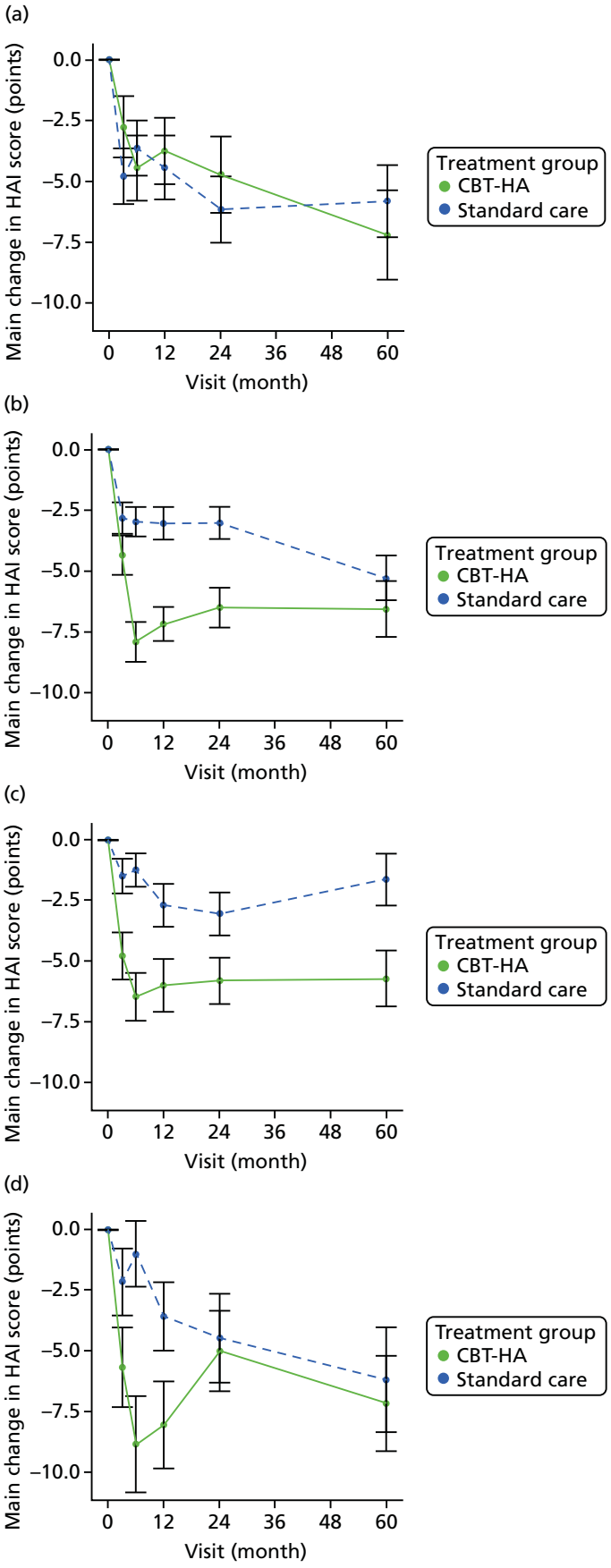

FIGURE 6 Differential outcome of patients over 5 years treated by CBT-HA and standard care groups separated by ICD-11 personality status at baseline (see *Table 8* for significance of differences). (a) No personality dysfunction; (b) personality difficulty; (c) mild personality disorder; and (d) moderate/severe disorder.

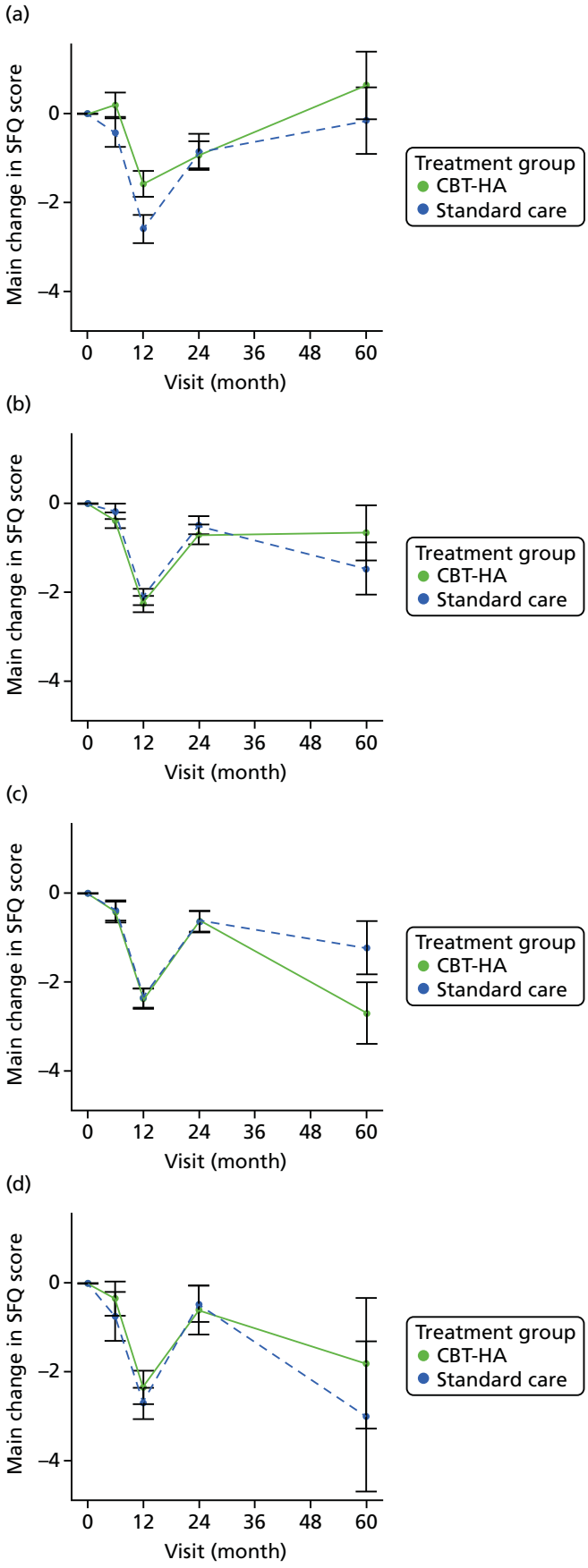

FIGURE 7 Change in social functioning separated by ICD-11 personality status in CBT-HA and standard care groups over a 5-year period. (a) No personality dysfunction; (b) personality difficulty; (c) mild personality disorder; and (d) moderate/severe disorder.

TABLE 9 Total costs over 24 months' follow-up by randomised group and personality status

	Treatment group					
	Standard care		CBT-HA		Total	
ICD-11 personality status	Mean	SD	Mean	SD	Mean	SD
No personality disorder, 0 ($n = 49$)	7565.45	9840.9	6204.83	5731.1	6926.79	8121.8
Personality difficulty, 1 ($n = 153$)	8436.81	8835.34	8166.55	9302.32	8297.26	9050.66
Mild personality disorder, 2 ($n = 106$)	7754.32	10021.78	6819.05	5558	7277.86	8037.21
Moderate and severe personality disorder, 3 ($n = 31$)	5363.28	3266.24	6529.42	3876.78	5927.54	3563.55

Note
Significantly greater improvement in social functioning with standard care (level 0 dysfunction) and with CBT-HA (level 2: mild personality disorder).
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Effect of personality: dependent personality traits

Dependent personality status was also assessed dimensionally in the same way as the ICD-11 severity levels (range 0–24) using the DPQ.[18] A previous epidemiological study in general practice[33] had identified the range of scores associated with disability with 0–6 (no personality dysfunction), 7–11 (personality difficulty), 12–16 (mild personality disorder) and ≥ 17 (moderate personality disorder) linking to ICD-11 severities. The DPQ does not allow severe dependent personality disorder to be identified because none of its questions address self-harm or aggression, even though these may sometimes be present in association with dependent personality.[34]

As with the main study using ICD-11 diagnostic criteria for all personality disorders, most patients in the study had some degree of dependent personality disturbance at baseline, with women having more dependent traits than men (*Table 10*). The generalised anxiety and depression scores were higher in those who were more dependent, although this was not the case for the HAI scores, and there was significantly greater social dysfunction in higher scorers (see *Table 10*). The mean number of treatment sessions was higher in those with more dependent personality dysfunction ($p < 0.005$) (*Table 11*).

TABLE 10 Patient characteristics and clinical ratings at baseline by dependent personality score

	Dependent personality dysfunction				
Variable	0 ($N = 76$)	1 ($N = 186$)	2 ($N = 141$)	3 ($N = 41$)	*p*-value
Age (years), mean (SD)	50.64 (13.03)	49.88 (13.61)	46.48 (12.89)	46.56 (15.62)	0.0507
Female, *n* (%)	29 (38.2)	100 (53.8)	85 (60.3)	22 (53.7)	0.0206
HAI score, mean (SD)	24.31 (4.18)	24.85 (4.38)	25.29 (4.50)	25.95 (4.14)	0.1957
HADS-A score, mean (SD)	10.46 (3.53)	11.97 (3.81)	13.45 (3.62)	14.41 (2.86)	< 0.0001
HADS-D score, mean (SD)	7.70 (4.55)	8.46 (4.44)	9.42 (3.71)	12.12 (5.22)	< 0.0001
SFQ score, mean (SD)	8.28 (4.41)	8.70 (4.35)	9.65 (4.09)	12.88 (4.91)	< 0.0001

0 = no dependent personality dysfunction; 1 = dependent personality difficulty; 2 = mild dependent personality disorder; and 3 = moderate dependent personality disorder.
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TABLE 11 Sessions of CBT-HA separated by dependent personality group

	Dependent personality dysfunction group				
Statistics	**0**	**1**	**2**	**3**	***p*-value**
n	47	86	65	21	0.0046
Mean	5.40	5.28	6.49	8.62	
SD	4.174	3.794	3.857	5.390	
Minimum	0.00	0.00	0.00	0.00	
Median	5.00	5.00	8.00	7.00	
Maximum	21.00	15.00	14.00	22.00	

0 = no dependent personality dysfunction; 1 = dependent personality difficulty; 2 = mild dependent personality disorder; and 3 = moderate dependent personality disorder.
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Of the 444 patients, 47 had an ICD-10 diagnosis of dependent personality disorder, seven with dependent disorder alone and 18 in conjunction with other personality disorders. Agreement between the DPQ and the PAS-Q groups was significant but relatively low (weighted kappa 0.16; $p < 0.01$).

Contrary to the initial hypotheses, patients treated with CBT-HA who had greater levels of dependence showed superior improvement in health-anxiety scores to those receiving standard care at all times of testing, and this was equally strong after 5 years (*Table 12*). The score differences were of greater magnitude in those with moderate dependent personality disorder, among whom, at 5 years, the mean score of 13.9 was fairly close to the normal level in the population (around 11)[18] (see *Table 12*). Generalised anxiety and depression scores (HADS) were also significantly more improved in those who received CBT-HA than in those who received standard care. Social function showed no significant differences between the allocated treatments separated by dependence groups (see *Table 12*).

TABLE 12 Summary results from mixed-model analysis of changes from baseline in the CBT-HA group compared with the standard care group by dependent personality score

Outcome (CBT-HA group vs. standard care group)	Dependent personality dysfunction			
	0 (*n* = 76)	**1 (*n* = 186)**	**2 (*n* = 141)**	**3 (*n* = 41)**
HAI score				
3 months				
Difference (95% CI)	–0.81 (–4.92 to 3.31)	–1.03 (–3.05 to 0.99)	–3.23 (–5.62 to –0.84)	–1.37 (–5.60 to 2.87)
p-value	0.6998	0.3168	0.0082	0.5244
6 months				
Difference (95% CI)	–3.82 (–7.93 to 0.29)	–4.33 (–6.40 to –2.26)	–5.20 (–7.62 to –2.78)	–6.52 (–10.7 to –2.30)
p-value	0.0683	< 0.0001	< 0.0001	0.0027
12 months				
Difference (95% CI)	–2.80 (–7.03 to 1.43)	–2.30 (–4.37 to –0.24)	–3.32 (–5.76 to –0.89)	–4.91 (–9.33 to –0.49)
p-value	0.1938	0.0291	0.0076	0.0296

continued

TABLE 12 Summary results from mixed-model analysis of changes from baseline in the CBT-HA group compared with the standard care group by dependent personality score (*continued*)

Outcome (CBT-HA group vs. standard care group)	Dependent personality dysfunction			
	0 ($n = 76$)	1 ($n = 186$)	2 ($n = 141$)	3 ($n = 41$)
24 months				
Difference (95% CI)	0.47 (–3.83 to 4.78)	–2.02 (–4.13 to 0.09)	–3.26 (–5.70 to –0.82)	–1.90 (–6.35 to 2.55)
p-value	0.8292	0.0601	0.0090	0.3996
5 years				
Difference (95% CI)	–4.60 (–9.13 to –0.08)	–1.26 (–3.46 to 0.94)	–1.65 (–4.32 to 1.03)	–4.08 (–8.71 to 0.55)
p-value	0.0463	0.2608	0.2273	0.0837
Overall				
Difference (95% CI)	–2.31 (–5.66 to 1.03)	–2.19 (–3.80 to –0.58)	–3.33 (–5.28 to –1.38)	–3.76 (–7.29 to –0.23)
p-value	0.1748	0.0078	0.0008	0.0372
HADS-A score				
6 months				
Difference (95% CI)	–1.75 (–3.83 to 0.34)	–1.22 (–2.53 to 0.08)	–1.08 (–2.49 to 0.33)	–2.41 (–5.00 to 0.18)
p-value	0.0997	0.0658	0.1330	0.0676
12 months				
Difference (95% CI)	–0.80 (–3.00 to 1.40)	–0.57 (–1.87 to 0.73)	–1.21 (–2.63 to 0.21)	–2.87 (–5.65 to –0.09)
p-value	0.4745	0.3907	0.0957	0.0433
24 months				
Difference (95% CI)	–0.79 (–3.02 to 1.43)	–0.90 (–2.25 to 0.44)	–1.09 (–2.51 to 0.34)	–1.89 (–4.69 to 0.92)
p-value	0.4828	0.1884	0.1345	0.1843
5 years				
Difference (95% CI)	–0.80 (–3.18 to 1.58)	–0.72 (–2.12 to 0.69)	–0.98 (–2.57 to 0.60)	–1.53 (–4.49 to 1.43)
p-value	0.5095	0.3147	0.2230	0.3064
Overall				
Difference (95% CI)	–1.03 (–2.63 to 0.56)	–0.85 (–1.83 to 0.12)	–1.09 (–2.21 to 0.03)	–2.17 (–4.20 to –0.15)
p-value	0.2031	0.0871	0.0572	0.0352
HADS-D score				
6 months				
Difference (95% CI)	–0.45 (–2.74 to 1.83)	–0.41 (–1.74 to 0.91)	–1.36 (–2.78 to 0.07)	–1.47 (–4.00 to 1.07)
p-value	0.6950	0.5409	0.0626	0.2543
12 months				
Difference (95% CI)	–0.05 (–2.46 to 2.35)	–0.41 (–1.73 to 0.91)	–1.23 (–2.67 to 0.21)	–2.26 (–5.01 to 0.49)
p-value	0.9644	0.5429	0.0929	0.1062
24 months				
Difference (95% CI)	2.16 (–0.27 to 4.59)	–0.65 (–2.02 to 0.71)	–1.87 (–3.32 to –0.43)	–1.56 (–4.34 to 1.22)
p-value	0.0808	0.3482	0.0111	0.2686
5 years				
Difference (95% CI)	–4.09 (–6.68 to –1.51)	–0.87 (–2.30 to 0.56)	–0.83 (–2.44 to 0.77)	–1.52 (–4.49 to 1.45)
p-value	0.0021	0.2317	0.3083	0.3120

TABLE 12 Summary results from mixed-model analysis of changes from baseline in the CBT-HA group compared with the standard care group by dependent personality score (*continued*)

Outcome (CBT-HA group vs. standard care group)	Dependent personality dysfunction			
	0 ($n = 76$)	1 ($n = 186$)	2 ($n = 141$)	3 ($n = 41$)
Overall				
Difference (95% CI)	–0.61 (–2.42 to 1.20)	–0.59 (–1.57 to 0.40)	–1.32 (–2.46 to –0.18)	–1.70 (–3.42 to 0.01)
p-value	0.5069	0.2414	0.0229	0.0519
SFQ score				
6 months				
Difference (95% CI)	–0.17 (–1.46 to 1.12)	0.26 (–0.53 to 1.06)	–0.10 (–0.91 to 0.71)	–0.85 (–2.38 to 0.67)
p-value	0.7946	0.5138	0.8094	0.2683
12 months				
Difference (95% CI)	–0.26 (–1.63 to 1.11)	0.30 (–0.49 to 1.10)	0.15 (–0.67 to 0.97)	–1.01 (–2.66 to 0.64)
p-value	0.7090	0.4546	0.7231	0.2263
24 months				
Difference (95% CI)	–0.47 (–1.86 to 0.92)	–0.04 (–0.86 to 0.78)	0.02 (–0.80 to 0.85)	–0.79 (–2.46 to 0.88)
p-value	0.5067	0.9323	0.9556	0.3480
5 years				
Difference (95% CI)	0.40 (–1.12 to 1.92)	–0.00 (–0.89 to 0.89)	–0.14 (–1.11 to 0.83)	–0.56 (–2.39 to 1.27)
p-value	0.6041	0.9998	0.7772	0.5431
Overall				
Difference (95% CI)	–0.12 (–1.05 to 0.80)	0.13 (–0.37 to 0.64)	–0.02 (–0.56 to 0.53)	–0.81 (–1.87 to 0.26)
p-value	0.7906	0.6052	0.9507	0.1357

Differences in outcome by site, clinic and age

These outcomes were considered relevant in the covariate-adjusted analyses and are summarised here, but it is important to emphasise that there were no particular hypotheses linked to these outcomes and randomisation did not take account of these. The five sites covered a mix of urban, suburban and rural areas, including two main teaching hospitals (St Mary's Hospital and Charing Cross Hospital), two hospitals linked to teaching hospitals (Hillingdon and Chelsea and Westminster) and one district general hospital (King's Mill Hospital). Four of the clinics concerned (cardiology, endocrinology, gastroenterology and respiratory medicine) had been identified previously as having at least 12% of attenders with a high level of health anxiety,[7,35] and during the course of the study another clinic type, neurology, was added.

The differences between sites are shown in *Figure 8*. In general, the non-teaching hospitals showed the largest differences between the patients receiving CBT-HA and those receiving standard care. There is no obvious explanation for this difference except in terms of therapist type (see *Subgroup analyses*). There were also differences in HAI outcome by clinic. Patients seen in cardiology clinics showed the largest differences between those who received CBT-HA and those receiving standard care, maximal at 5 years (*Figure 9*), and respiratory medicine patients showed the least differences between groups (with no benefit after the first 6 months of treatment).

Older patients derived greater benefit from CBT-HA compared with standard care than younger patients. This was not an expected finding and possible reasons for it are discussed later in this report.

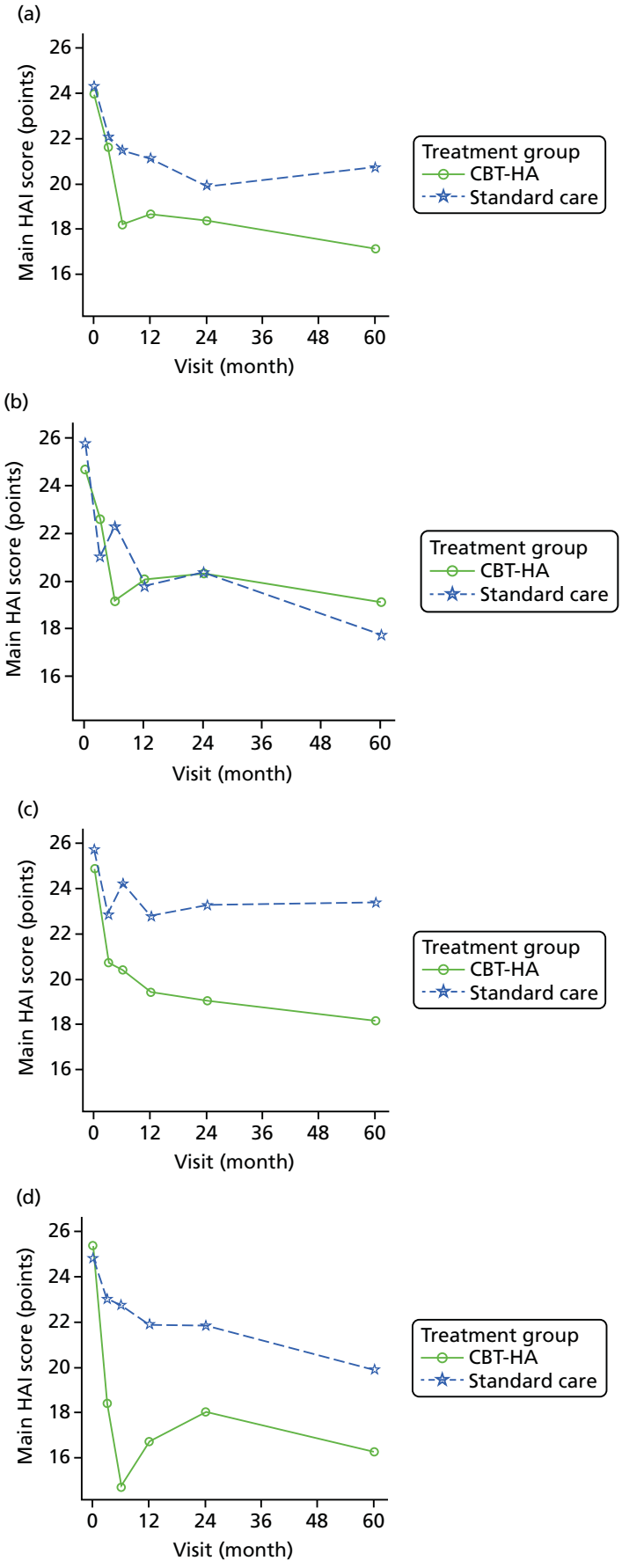

FIGURE 8 Differences in outcome by HAI scores separated by site. (a) Chelsea and Westminster; (b) Charing Cross Hospital; (c) Hillingdon Hospital; (d) King's Mill Hospital; and (e) St Mary's Hospital. (*continued*)

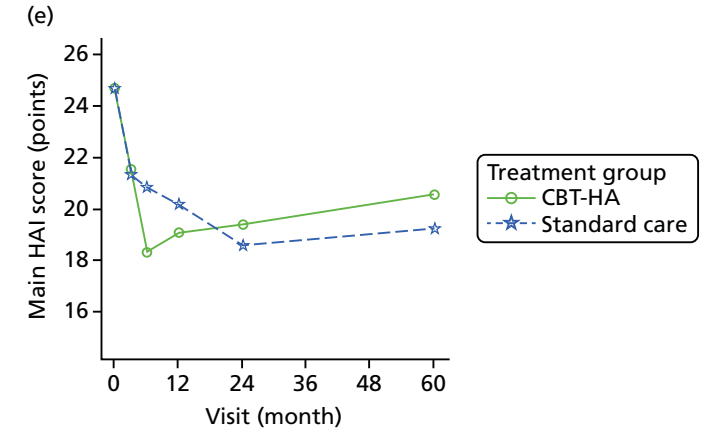

FIGURE 8 Differences in outcome by HAI scores separated by site. (a) Chelsea and Westminster; (b) Charing Cross Hospital; (c) Hillingdon Hospital; (d) King's Mill Hospital; and (e) St Mary's Hospital.

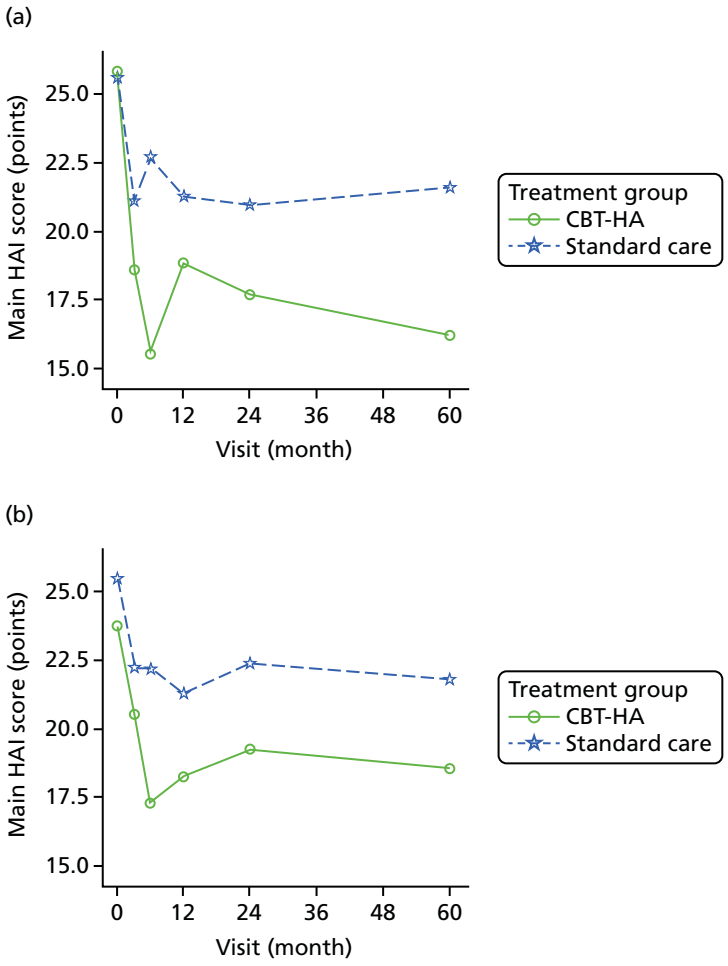

FIGURE 9 Differences in outcome by HAI scores separated by clinic type. (a) Cardiology; (b) endocrinology; (c) gastroenterology; (d) neurology; and (e) respiratory medicine. (*continued*)

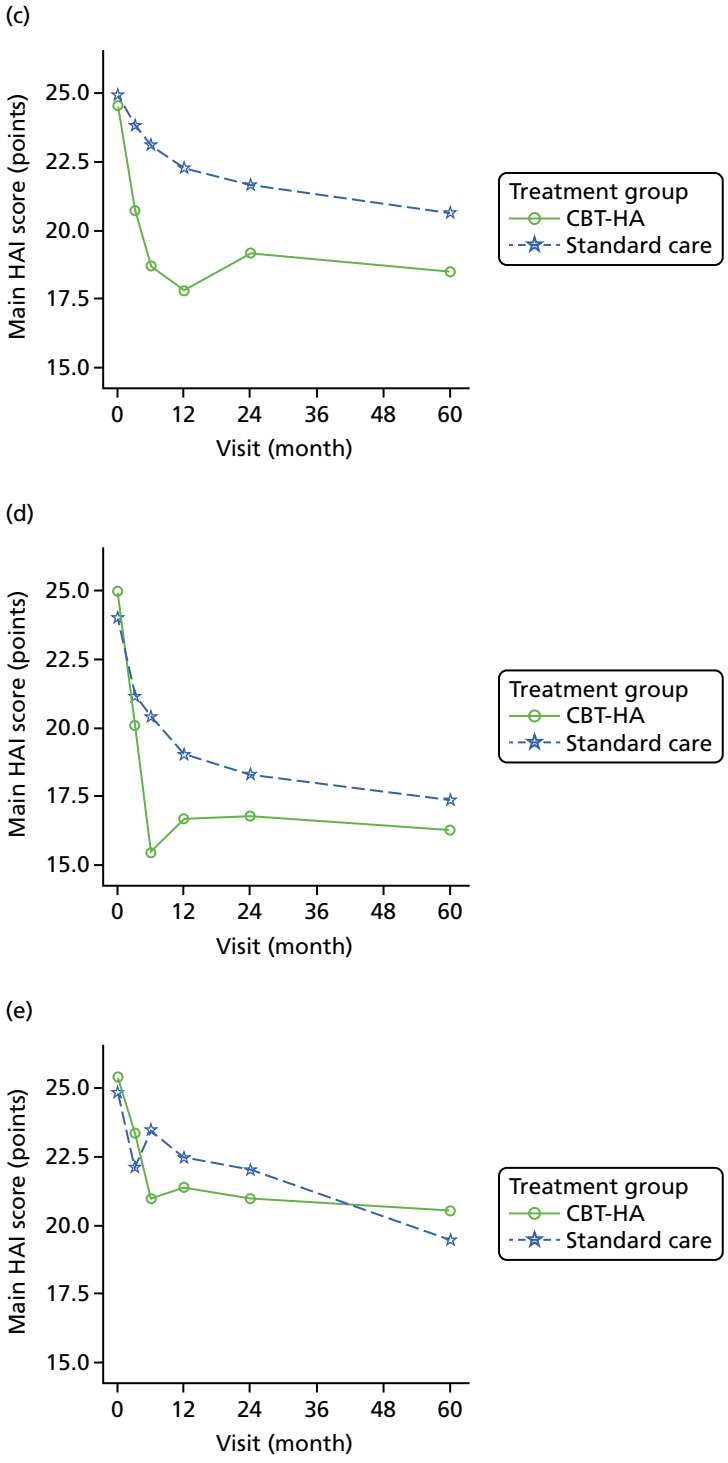

FIGURE 9 Differences in outcome by HAI scores separated by clinic type. (a) Cardiology; (b) endocrinology; (c) gastroenterology; (d) neurology; and (e) respiratory medicine.

Subgroup analyses

There were several subgroup analyses that showed generally similar findings. The subgroup analysis to examine the heterogeneity of the variables of interest is shown for the primary outcome, the HAI, in *Table 13*. There were no significant interactions, suggesting that the data were consistent and robust. The only variable approaching heterogeneity was the study site. King's Mill Hospital had a better outcome than the other sites over the period of the study; this was also the site where the nurses were the main therapists.

TABLE 13 Subgroup analysis of heterogeneity from the mixed model. Analysis of HAI score change from baseline

	Mixed-model result				
	CBT-HA	Standard care			
Variable	*n*, mean (SD)	*n*, mean (SD)	Difference (95% CI)	*p*-value	*p*-value from interaction test
Age group (years)					
≤ 49	63, 6.68 (8.36)	79, 5.69 (7.06)	1.78 (–0.46 to 4.01)	0.1197	0.2051
> 49	86, 6.28 (8.76)	79, 2.98 (8.21)	2.78 (0.77 to 4.79)	0.0067	–
Hospital					
Charing Cross Hospital	20, 5.10 (9.81)	19, 6.58 (8.64)	–3.32 (–7.50 to 0.86)	0.1186	–
Chelsea and Westminster Hospital	14, 6.93 (6.47)	15, 3.12 (6.39)	3.60 (–1.10 to 8.30)	0.1321	0.0669
Hillingdon Hospital	43, 6.33 (8.47)	46, 2.37 (7.09)	3.56 (0.83 to 6.29)	0.0107	–
King's Mill Hospital	45, 8.89 (7.62)	53, 4.85 (7.49)	4.78 (2.15 to 7.42)	0.0004	–
St Mary's Hospital	27, 3.35 (9.50)	25, 5.88 (9.06)	–1.66 (–5.32 to 2.00)	0.3718	–
Clinic					
Cardiology	33, 8.73 (7.93)	38, 3.56 (8.62)	5.21 (2.08 to 8.34)	0.0012	0.4715
Endocrinology	28, 4.89 (6.82)	30, 3.70 (6.30)	1.39 (–2.06 to 4.83)	0.4286	–
Gastroenterology	57, 5.77 (9.02)	55, 4.78 (7.73)	1.45 (–1.07 to 3.98)	0.2591	–
Neurology	13, 9.08 (9.05)	17, 5.53 (8.19)	1.15 (–3.52 to 5.82)	0.6274	–
Respiratory medicine	18, 4.97 (9.87)	18, 4.53 (8.27)	–0.13 (–4.39 to 4.12)	0.9507	–
SOCS score					
≤ 6 points	94, 7.32 (8.93)	103, 4.47 (7.87)	2.73 (0.87 to 4.58)	0.0040	0.4376
> 6 points	55, 4.97 (7.76)	55, 4.09 (7.59)	1.31 (–1.23 to 3.84)	0.3112	–
DPQ score					
≤ 15 points	127, 6.51 (8.86)	140, 4.57 (7.78)	2.02 (0.41 to 3.64)	0.0140	0.5229
> 15 points	22, 6.09 (6.75)	18, 2.50 (7.52)	3.30 (–0.62 to 7.22)	0.0983	–
PAS-Q					
0	20, 5.02 (9.46)	17, 4.59 (7.61)	0.25 (–4.24 to 4.74)	0.9118	0.2902
1	79, 6.27 (8.84)	97, 4.05 (7.81)	2.30 (0.35 to 4.25)	0.0207	–
2	39, 8.10 (7.77)	33, 4.03 (8.26)	3.83 (0.62 to 7.03)	0.0194	–
3	11, 4.55 (7.66)	11, 7.36 (5.95)	–0.93 (–6.81 to 4.94)	0.7537	–

Outcome by therapist type

When the CHAMP trial started it was hoped that sufficient excess treatment costs might be available to fund dedicated therapists at all sites in the study; this was not possible, but at one site (King's Mill Hospital) a subvention grant allowed two general nurses (SM and YL-S) to be employed for approximately 80% of their time in giving CBT-HA. In other centres somewhat less funding was obtained for other therapists, mainly trainee psychologists, but also other health professionals, including a dietitian, to be employed on a mainly part-time basis.

Apart from the nurses and the dietitian, the other therapists had at least some knowledge of the principles of CBT before the trial began and some had practised, but none had been trained in, CBT-HA. All therapists were involved in the initial 2-day workshop and, once trained at this standard level, received supervision from established trainers at each site.

The results, also reported elsewhere,[36] showed that although the patients treated by all three therapist groups (nurses, assistant psychologists and graduate workers) showed superior HAI outcomes after 6 months, the nurses group showed the largest benefit across the initial 2-year period (*Figure 10* and *Table 14*). After 2 years, 23.5% of patients in standard care had improved to a score of 15 on the HAI (mild but not pathological health anxiety), whereas the proportions in the three therapist CBT-HA groups were 28.9% (assistant psychologists), 34% (graduate workers) and 44.3% (nurses) (*Table 15*).

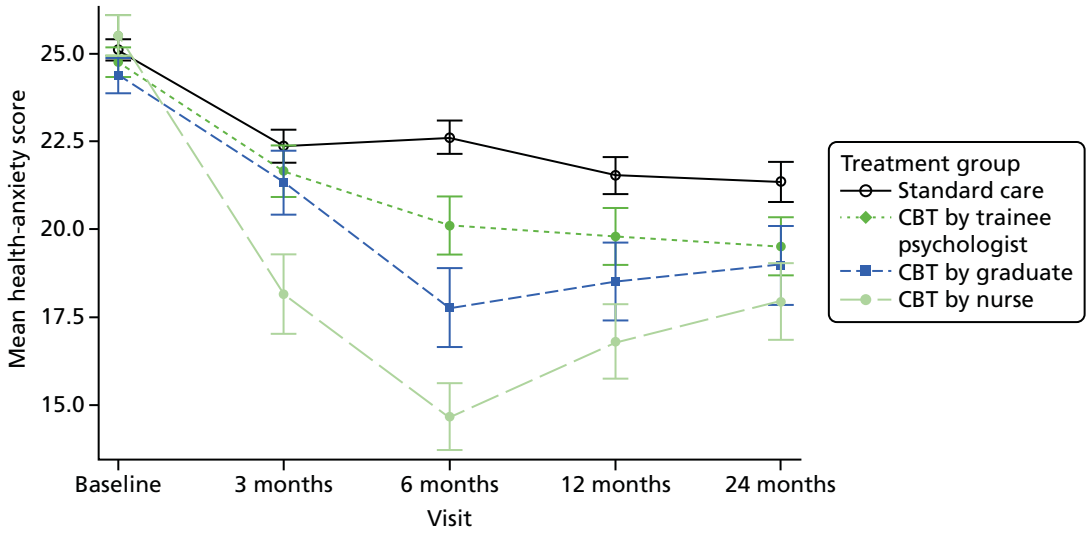

FIGURE 10 Mean differences in HAI scores between the outcomes of 219 patients with health anxiety treated by nurses ($n = 66$), graduate workers ($n = 66$) and assistant psychologists ($n = 87$) over 2 years. Reprinted from the *International Journal of Nursing Studies*, vol. 52, Tyrer H, Tyrer P, Lisseman-Stones Y, McAllister S, Cooper S, Salkovskis P, *et al.* Therapist differences in a randomised trial of the outcome of cognitive behaviour therapy for health anxiety in medical patients, pp. 686–94. Copyright (2015),[36] with permission from Elsevier.

TABLE 14 Comparison of health-anxiety outcome using the HAI, separated by therapist group in 444 randomised patients

	HAI score (points), *n* of patients, mean score (SD)					Difference between nurses and other groups
Visit	Standard care	CBT by assistant psychologists	CBT by graduates	CBT by nurses	All	Mean (95% CI); *p*-value
Baseline	225, 25.12 (4.52)	87, 24.76 (3.91)	66, 24.38 (4.15)	66, 25.53 (4.67)	225, 25.12 (4.52)	–
3 months	212, 22.37 (6.71)	82, 21.65 (6.62)	59, 21.33 (6.97)	64, 18.15 (9.07)	212, 22.37 (6.71)	4.10 (6.1 to 3.1); $p < 0.0001$
6 months	204, 22.62 (6.81)	78, 20.13 (7.26)	56, 17.77 (8.42)	63, 14.67 (7.53)	204, 22.62 (6.81)	4.93 (7.0 to 2.9); $p < 0.0001$
12 months	193, 21.54 (7.45)	75, 19.80 (6.96)	57, 18.53 (8.31)	62, 16.81 (8.31)	193, 21.54 (7.45)	3.24 (5.3 to 1.2); $p < 0.002$
24 months	183, 21.35 (7.67)	76, 19.51 (7.22)	53, 18.98 (8.14)	61, 17.95 (8.63)	183, 21.35 (7.67)	2.49 (4.5 to 0.5); $p < 0.02$
All periods						3.7 (5.4 to 2.0); $p < 0.0001$

Reprinted from the *International Journal of Nursing Studies*, vol. 52, Tyrer H, Tyrer P, Lisseman-Stones Y, McAllister S, Cooper S, Salkovskis P, *et al.* Therapist differences in a randomised trial of the outcome of cognitive behaviour therapy for health anxiety in medical patients, pp. 686–94. Copyright (2015),[36] with permission from Elsevier.

TABLE 15 Proportions of patients separated by therapist type showing significant improvement (HAI score of ≤ 15 points) after 1 year

Therapist group	Number of patients (%) with HAI scores of ≤ 15 points	Odds ratio of improvement (CBT-HA vs. standard care): all times (significance)	95% CI
Standard care			
3 months	31 (14.6)	–	–
6 months	30 (14.7)		
12 months	42 (21.8)		
24 months	43 (23.5)		
CBT-HA: assistant psychologists			
3 months	16 (19.5)	1.58 ($p = 0.05$)	0.99 to 2.51
6 months	24 (30.8)		
12 months	19 (25.3)		
24 months	22 (28.9)		
CBT-HA: graduates			
3 months	10 (16.9)	2.05 ($p = 0.005$)	1.25 to 3.36
6 months	24 (42.9)		
12 months	24 (42.1)		
24 months	18 (34.0)		
CBT-HA: nurses			
3 months	28 (43.8)	3.16 ($p < 0.0001$)	1.97 to 5.06
6 months	40 (63.5)		
12 months	33 (53.2)		
24 months	27 (44.3)		

Reprinted from the *International Journal of Nursing Studies*, vol. 52, Tyrer H, Tyrer P, Lisseman-Stones Y, McAllister S, Cooper S, Salkovskis P, *et al.* Therapist differences in a randomised trial of the outcome of cognitive behaviour therapy for health anxiety in medical patients, pp. 686–94. Copyright (2015),[36] with permission from Elsevier.

Chapter 4 Economic evaluation

Perspective

The economic evaluation took a health and social care perspective, which included the costs of the CBT intervention, other health-care costs and other community health and social services. In addition, we completed the sensitivity analysis from a societal perspective, to include all resources in the health and social care perspective plus productivity losses.

Identification of resources

The calculation of costs was separated into three stages: identification, measurement and valuation of resources.

We identified relevant resources based on the results of our pilot study[10] and in discussion with study clinicians and patient representatives. Resource use was collected in the following domains:

- delivery of CBT-HA
- use of NHS secondary care services
- inpatient stays
- day-case procedures
- outpatient appointments
- accident and emergency attendances
- use of NHS primary care services
- General practitioner [(GP) in practice, at home or by telephone]
- community nurse (practice nurse, district nurse, health visitor, midwife)
- community mental health services
- community medical services (walk-in clinic)
- community medical professional (physiotherapist, chiropodist)
- use of all medication
- use of social care and voluntary sector services
- social worker
- voluntary sector advice worker
- housing services
- service-provided accommodation
- productivity losses measured as absenteeism.

Measurement of resources

The identified resources were measured using the following methods.

The CBT-HA therapists recorded information on attendance and non-attendance at treatment sessions together with the duration of each session. These data were extracted for analysis from trial records.

The computerised records of the host hospital trusts (Sherwood Forest Hospitals NHS Foundation Trust, Imperial College Healthcare NHS Trust, Chelsea and Westminster Hospital NHS Foundation Trust and The Hillingdon Hospitals NHS Foundation Trust) were examined and accident and emergency attendances,

inpatient stays, day-patient procedures and outpatient appointments were extracted for analysis by hospital trust-based information specialists co-ordinated by AP.

Other service use data for the economic evaluation were collected using the ADSUS, based on previous economic evaluations in adult mental health populations[37] and on the data collected in the pilot study.[10] The ADSUS was completed at baseline, at 6, 12 and 24 months and at the 5-year follow-up. At baseline, the ADSUS covered the previous 6 months and at each of the follow-up interviews, service use since the previous interview was recorded so that the entire period from baseline to final follow-up was covered. The ADSUS records the number and duration of contacts with a range of health and social service professionals and medications taken.

The number of days taken off work because of ill health was collected with the relevant questions from the World Health Organization Health and Work Performance Questionnaire.[38]

Valuation of resources

The cost of the CBT-HA intervention was estimated using the bottom-up approach set out by the Personal Social Services Research Unit at the University of Kent.[39] The salary cost for the therapist was based on that of an experienced nurse or therapist (Agenda for Change Band 6),[40] onto which employer costs (National Insurance and pension contribution) were added. Overhead costs were then added to include building costs, administrative and managerial costs and capital costs. An hourly cost was calculated on the working time assumptions set out in the Unit Costs of Health and Social Care,[41] and then weighted to account for the therapist spending time on non-patient-facing activities. In addition, the final cost per hour included an allowance for the cost of time spent by the therapist in supervision and the cost of supervisor time.

For each type of other service use, an appropriate unit cost was identified. All unit costs were for the financial year 2009–10 and costs with their sources are listed in full in *Table 16*. When necessary, unit costs were inflated to 2009–10 costs using the Hospital and Community Health Services inflation index or the Retail Price Index as appropriate.[41] Costs in the second, third, fourth and fifth years were discounted at a rate of 3.5% per annum as recommended by the National Institute for Health and Care Excellence (NICE).[44]

TABLE 16 Unit costs applied to service use data

Service	Unit	Cost (£)
Medication[42]	Per daily dose	Various
Inpatient[43]	Per night	382–726
Outpatient[43]	Per appointment	39–989
Diagnostic procedure[43]	Per procedure	1–553
Accident and emergency[43]	Per attendance	103
Ambulance[43]	Per trip	222
GP surgery[41]	Per minute of patient contact	2.40
GP home[41]	Per home visit minute	4.00
GP telephone[41]	Per minute of patient contact	2.40
Community medical professionals[41]	Per minute of contact	0.37–1.13
Community social care professionals[41]	Per minute of contact	0.42–2.63

The cost of productivity losses was calculated using the human capital approach, when each day off work is valued at the daily salary for that individual.[45]

Calculation of quality-adjusted life-years

Quality-adjusted life-years (QALYs) were calculated on the basis of the EQ-5D health state classification instrument[46] and the health states were assigned a utility score using responses from a representative sample of adults in the UK.[47] QALYs were then calculated as the area under the curve defined by the utility values at baseline and at the 6-, 12-, 24- and 60-month follow-ups. We assumed that changes in utility score over time followed a linear path.[48] QALYs in the second to fifth years were discounted at a rate of 3.5% as recommended by NICE[44] and all analyses were adjusted for baseline utility scores to take into consideration the impact of baseline differences on the area under the curve.[49]

Data analysis

For the economic evaluation the base case was a complete-case analysis.

We report the mean average resource use by randomised groups at 24 months' and 5 years' follow-up, as well as the percentage of people in each randomised group who have had at least one contact with each service. No between-group statistical comparisons are made in order to avoid the problems of multiple comparisons and because the focus of the economic evaluation is on cost and cost-effectiveness.

Our hypothesis was that the cost of the CBT intervention would be recouped through a reduction in the use of health and social care services. We tested this through a non-inferiority (equivalence) test, with a pre-specified equivalence test of £150. The equivalence was declared between active and control groups if the 95% CI fell between –£150 and £150. These analyses were adjusted for baseline differences in cost.

Cost-effectiveness was considered for two outcomes: QALYs and the HAI score. Cost-effectiveness was initially explored through the calculation of incremental cost-effectiveness ratios (ICERs), a ratio of differences in cost by differences in outcomes between the CBT-HA and standard care groups. ICERs are a useful decision-making tool when there is no uncertainty around the costs and outcomes used in the ratio. Here, the ICERs are based on four sample means; therefore, the uncertainty around the ICER was explored.

Cost-effectiveness planes were produced by the production of bootstrapped regressions (5000 replications) of study group on total costs and HAI score or QALYs, with covariates for baseline costs or outcomes as appropriate. The coefficients of group differences were then plotted on to a graph.

Replications in the north-east quadrant suggest that CBT-HA is more effective and more costly than standard care, replications in the south-east quadrant suggest that CBT-HA is more effective and less costly than standard care, replications in the south-west quadrant suggest that CBT-HA is less effective and less costly than standard care and replications in the north-west quadrant suggest that CBT-HA is more costly and less effective than standard care.

Knowledge of uncertainty around incremental cost-effectiveness is not sufficient for decision-making, which will depend on the how much society is willing to pay for improvements in outcomes. Cost-effectiveness acceptability curves (CEACs) were therefore constructed, and these show the likelihood that CBT is cost-effective for different values a decision-maker is willing to pay for improvements in outcome.[50] All analyses were adjusted for baseline costs and for baseline HAI and EQ-5D scores as appropriate.

We completed a number of sensitivity analyses. First, we used the Stata® (StataCorp LP, College Station, TX, USA) impute command (a regression-based single imputation) to impute missing costs at 24 months and 5 years. Second, we undertook an analysis of differences in costs, including the estimates of the cost of productivity losses.

Results

At 24 months, full ADSUS and hospital records data were available for 172 participants in the CBT-HA group and 170 in the standard care group (77% of those randomised). At 5 years, full ADSUS and hospital records data were available for 149 participants in the CBT-HA group and 157 in the standard care group (69% of those randomised). For total costs over 5 years we needed data from the 24-month and 5-year interviews and there were 141 participants in the CBT-HA group and 133 in the standard care group who met this criterion (62%). We were able to collect hospital service use for 442 randomised participants (99%).

We examined the cost data in order to examine the impact of highly influential observations, which, as defined by Weichle *et al.*,[51] were those that were above the 99th centile and when removed would have resulted in major changes to the results. Following this, two observations were identified and were removed from the main analysis as recommended.

Resource use

Service use over 24 months' follow-up is detailed in *Table 17*. There were no between-group differences in service use and no evidence that CBT-HA reduced service use over this period, as the use of some hospital and community services remained high.

Use of service-provided accommodation such as hotels, refuges and emergency accommodation (e.g. bed and breakfast) was low, being accessed by 2–4% of the sample over the 24 months.

TABLE 17 Service use over 24 months' follow-up

	Treatment group					
	CBT ($n = 172$)			Standard care ($n = 170$)		
Service	Mean	SD	%	Mean	SD	%
Service-provided accommodation	0.13	0.87	2.33	0.27	1.49	3.53
Inpatient number of nights[a,b]	2.57	7.09	32	2.18	8.07	29
Outpatient number of appointments[a,b]	13.08	13.64	99	12.88	16.84	99
Accident and emergency number of attendances[a,b]	1.22	4.14	37	0.87	1.37	41
GP[a]	13.33	11.12	97.67	14.61	16.26	97.65
Community medical professionals[a]	10.15	13.54	93.02	9.76	13.84	84.71
Community social service professionals[a]	5.01	27.08	21.51	6.09	30.85	22.94
Community mental health services[a]	0.05	0.32	2.33	0.29	1.78	5.29
Community other professionals[a]	0.43	1.52	11.05	1.39	6.65	11.76

a Self-reported in the ADSUS.
b From hospital trust records.

Hospital outpatient appointments were attended by 99% of the study participants and the average number of appointments was 13. Around one-third of the study participants were admitted as inpatients and the average length of stay among the whole sample was between two and three nights. Attendance at accident and emergency departments was low.

The use of GPs and community medical services such as community nursing, physiotherapy, pharmacy and walk-in centres was common. Almost all participants (up to 98%) had at least one contact with a GP and the average number of appointments was between 13 and 16. Interestingly, the use of community mental health services was low; only 2–5% of participants had any contact with a community mental health professional.

In some areas, the use of services between 2 and 5 years continued the pattern set at 24 months, as detailed in *Table 18*. For example, around one-third of the sample in both groups had an inpatient stay. However, there was a 20% drop in the percentage of participants having at least one outpatient appointment and, as a yearly average, the number of appointments was lower. Similarly, over the 2–5-year period there were, on average, only five GP appointments, compared with 14 over the first 24 months.

Over the 5-year follow-up period, almost all inpatient stays were medical admissions and there were no admissions to mental health units. Similarly, almost all non-trial outpatient appointments were to medical specialties rather than to a mental health professional. In common with the numbers at 24 months, the use of community mental health services was very low.

Total cost

The mean cost of the CBT-HA intervention in the intervention group was £421.51 per patient (range 0–2383) for an average of six sessions.

Table 19 shows total costs per patient over 24 months' follow-up. For all cost categories, total costs were lower for the CBT-HA group than for the control group. Overall, total health and social care costs, including the cost of the intervention, were lower in the CBT-HA group (mean £7314) than in the control group (mean £7727). In analyses adjusted for baseline cost, however, the adjusted mean difference between the two groups was £156 (95% CI –£1446 to £1758; $p = 0.848$). Although equivalence was not achieved, there was no evidence of a significant difference in cost between the CBT-HA and standard care groups.

TABLE 18 Resource use between 2 and 5 years' follow-up, showing mean, SD and the percentage of the randomised group with at least one contact

	Treatment group					
	CBT-HA ($n = 149$)			Standard care ($n = 157$)		
Resource use	Mean	SD	%	Mean	SD	%
Inpatient number of nights[a]	3.05	9.52	29	3.85	17	30
Outpatient number of appointments[a]	11.5	14.97	78	12.01	15.27	78
Accident and emergency number of attendances[a]	1.81	3.22	53	1.43	2.64	48
GP[b]	5.15	6.61	88	5.72	6.83	91
Community medical professionals[b]	13.99	33.41	72	13.74	34.14	71
Community social service professionals[b]	2.27	16.5	9	2.39	16.47	8
Community mental health services[b]	0.53	3.08	6	1.24	4.37	14
Community other professionals[b]	0.43	2.65	7	0.39	2.63	4

a From hospital trust records.
b Self-reported in the AD-SUS.

TABLE 19 Total costs (£) over 24 months' follow-up by randomised group

	Treatment group						
	CBT ($n = 172$)		Standard care ($n = 170$)				
Individual cost item	Mean	SD	Mean	SD	Adjusted coefficient	95% CI (adjusted, bootstrapped)	*p*-value
CBT-HA	421.51	308.25	0.00	0.00	–	–	–
Service-provided accommodation	134.52	1025.45	235.83	1640.25	–	–	–
Hospital services	3946.81	5583.89	4223.31	6353.28	–	–	–
Community services	774.02	1153.36	891.53	1639.54	–	–	–
Medication	2037.33	2760.75	2376.74	4487.03	–	–	–
Total	7314.20	7429.58	7727.40	8970.80	155.86	–1446.20 to 1757.93	0.848

The total cost for the 5-year follow-up is detailed in *Table 20*. The second row of the table reports costs in years 3, 4 and 5 as £5055 in the CBT-HA group and £4835 in the standard care group. The adjusted mean difference in cost is –£557, thus rejecting the null hypothesis that costs are equivalent at follow-up. Taking the costs between randomisation and 24 months and 2 and 5 years together gives the total costs over 5 years' follow-up. These are also listed in *Table 19*. In total, costs were £12,591 in the CBT-HA group and £13,335 in the standard care group. The regression adjusted for baseline costs also showed that these costs were not equivalent [coefficient = 545, 95% CI (–2375 to 3466); $p = 0.713$]. The direction of the difference in costs changes when the adjustment is made for baseline costs.

Outcomes

The EQ-5D tariff over the 5-year follow-up is detailed in *Table 21* and shown graphically in *Figure 11*. Utility scores are very similar between groups over follow-up. When QALYs were calculated, these were 1.09 in both the CBT-HA group and the standard care group at 24 months, and 2.75 in the CBT-HA group and 2.64 in the standard care group at 5 years; this small difference at 5 years is not significant.

The EQ-5D visual analogue scale (VAS) scores are also presented in *Table 21* and *Figure 12*. Again the results are generally similar between groups and, while there are some differences in VAS score at 24 months, the difference is not significant and not sustained at 5 years.

TABLE 20 Total cost (£) over 5 years' follow-up

	Treatment group						
	CBT		Standard care				
Cost	Mean	SD	Mean	SD	Adjusted mean difference	95% CI	*p*-value
Years 1 and 2 ($n = 342$)	7314.20	7429.58	7727.40	8970.80	155.86	–1446.20 to 1757.93	0.848
Years 3, 4 and 5 ($n = 303$)	5054.56	6581.72	4834.74	6908.10	557	–919.82 to 2034.65	0.458
Total cost ($n = 271$)	12,590.58	14,290.00	13,334.94	14,402.05	545	–2374.78 to 3466.02	0.713

TABLE 21 The EQ-5D, three-level version tariff, visual analogue scale score and QALYs over the 5-year follow-up

EQ-5D variables and QALYs by visit	Treatment group				Adjusted mean difference	95% CI	*p*-value
	CBT		Standard care				
	Mean	SD	Mean	SD			
EQ-5D tariff							
Baseline ($n = 442$)	0.49	0.35	0.47	0.35	–	–	–
6 months ($n = 401$)	0.52	0.4	0.52	0.36	–	–	–
12 months ($n = 386$)	0.57	0.37	0.56	0.37	–	–	–
24 months ($n = 371$)	0.57	0.38	0.55	0.37	–	–	–
5 years ($n = 308$)	0.56	0.4	0.54	0.4	–	–	–
QALYs							
24 months ($n = 347$)	1.09	0.63	1.09	0.6	–0.002	–0.09 to 0.09	0.964
5 years ($n = 303$)	2.75	1.55	2.64	1.58	0.09	–0.16 to 0.33	0.482
EQ-5D VAS							
Baseline ($n = 434$)	50.92	22.51	51.47	21.34	–	–	–
6 months ($n = 389$)	56.91	25.78	52.71	23.75	–	–	–
12 months ($n = 376$)	58.00	23.44	57.12	23.62	–	–	–
24 months ($n = 363$)	59.94	25.43	55.67	23.63	4.27	–0.80 to 9.34	0.098
5 years ($n = 307$)	56.2	24.02	55.62	25.69	–0.58	–5.02 to 6.17	0.840

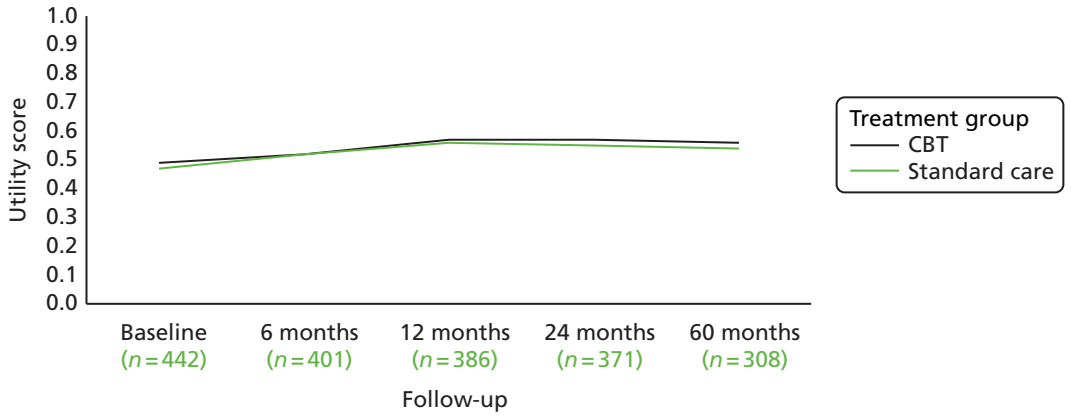

FIGURE 11 Mean EQ-5D tariff by randomised group.

Cost-effectiveness analysis

In adjusted analyses, the ICER for QALYs was £14,169 (the difference in cost, £156, divided by the difference in QALYs, 0.011), which highlights that additional QALYs can be gained only with additional expenditure. The scatterplot and CEAC in *Figures 13* and *14* demonstrate that there is substantial uncertainty around the mean values used in the ICER. In *Figure 13*, the bootstrapped replications of costs and outcomes fall almost equally across all four quadrants of the cost-effectiveness plane, suggesting that there is no clear evidence on the cost-effectiveness of either CBT-HA or standard care. The CEAC in *Figure 14* suggests that CBT-HA is not cost-effective for the usually accepted values that a decision-maker would be willing to pay for improvements in outcomes.

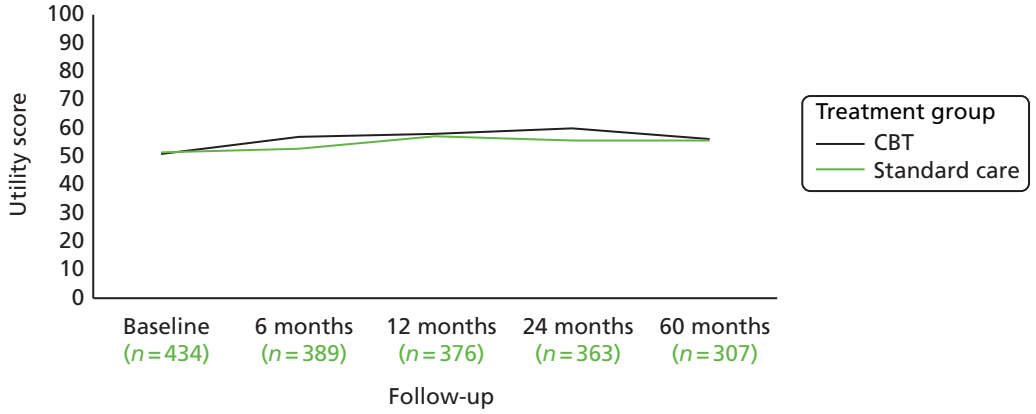

FIGURE 12 Mean EQ-5D VAS by randomised group.

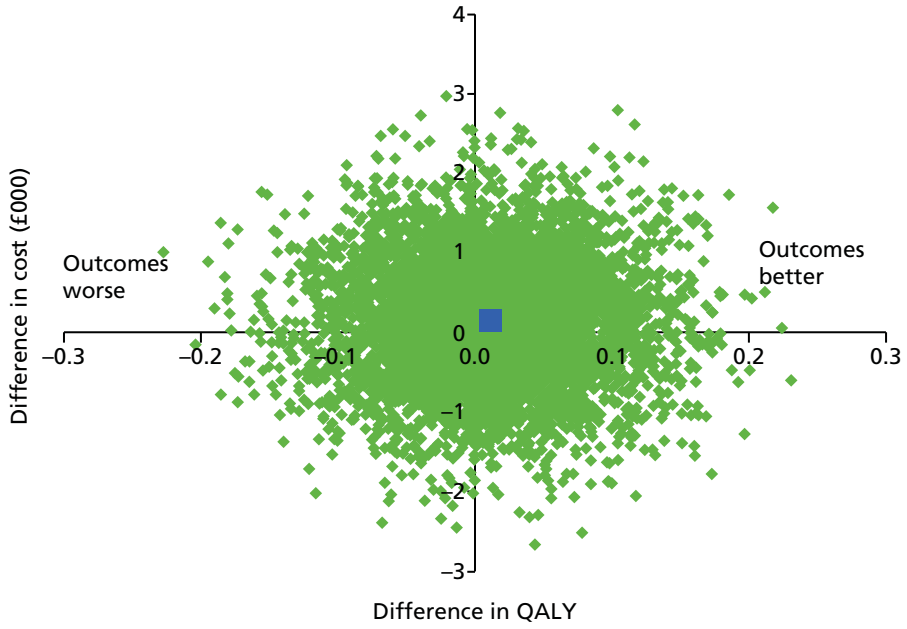

FIGURE 13 Cost-effectiveness plane showing bootstrapped cost and QALY pairs at the 24-month follow-up.

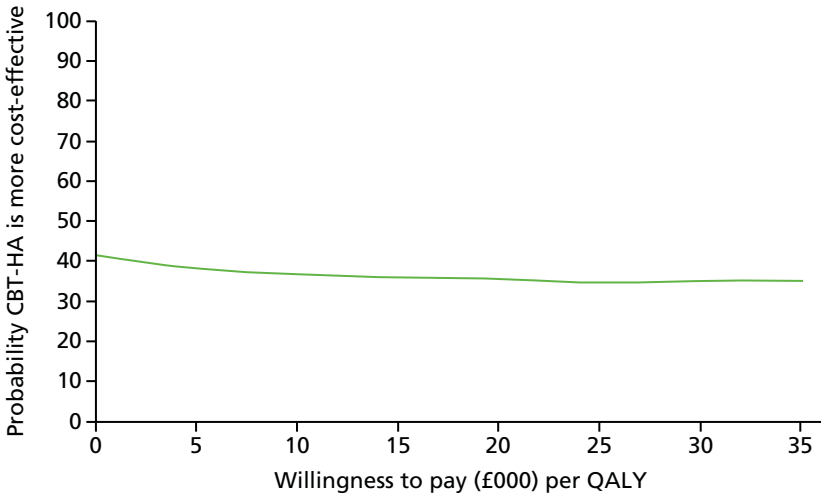

FIGURE 14 Cost-effectiveness acceptability curve showing the probability that CBT-HA is more cost-effective than standard care in terms of QALYs at the 24-month follow-up.

The ICER for the HAI, adjusted for baseline costs, was £55.86 (the difference in cost, £156, divided by the difference in HAI score, 2.79 points). The adjusted scatterplot in *Figure 15* shows replications in the north-west and south-west quadrants. Here, these quadrants represent better outcomes in the CBT-HA group because a higher score on the HAI denotes worse anxiety. There is clear evidence that CBT-HA improves outcomes, but the picture regarding costs is uncertain. The CEAC in *Figure 16* reflects this uncertainty, demonstrating that, at a willingness to pay for an improvement in HAI score of zero points, there is only a 44% probability of CBT-HA being cost-effective. However, if willingness to pay per point change in HAI score increases to values over £53, there is a > 50% probability that CBT-HA is cost-effective.

Over 5 years, costs are, on average, lower in the CBT-HA group than in the standard care group and outcomes in terms of QALYs and HAI scores are better. In these cases ICERs are not the most useful decision-making tool, as negative values can produce a positive ICER; we therefore leave them to one side

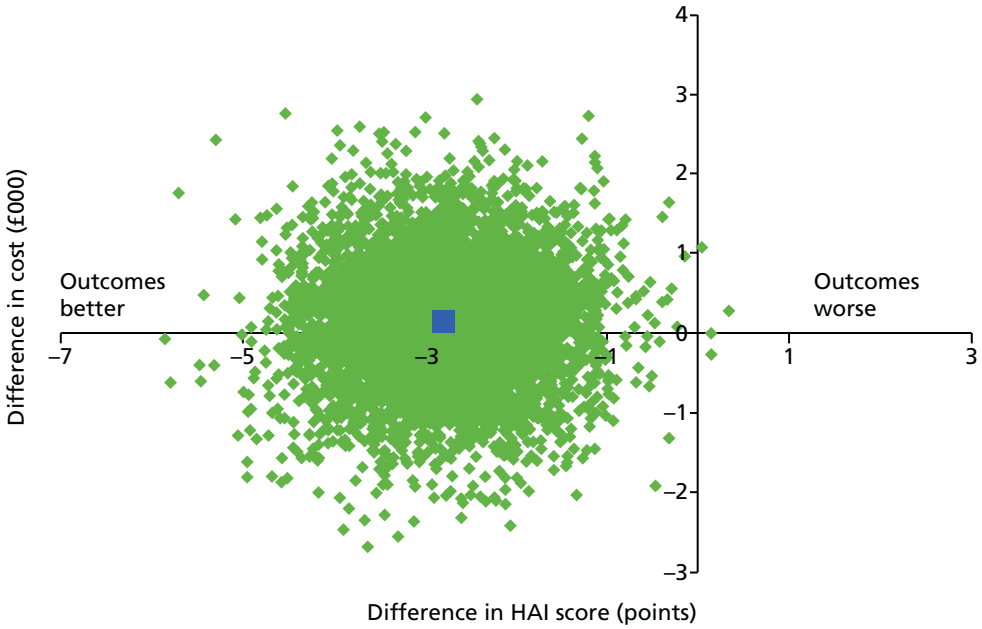

FIGURE 15 Cost-effectiveness plane showing bootstrapped cost and HAI score pairs at the 24-month follow-up.

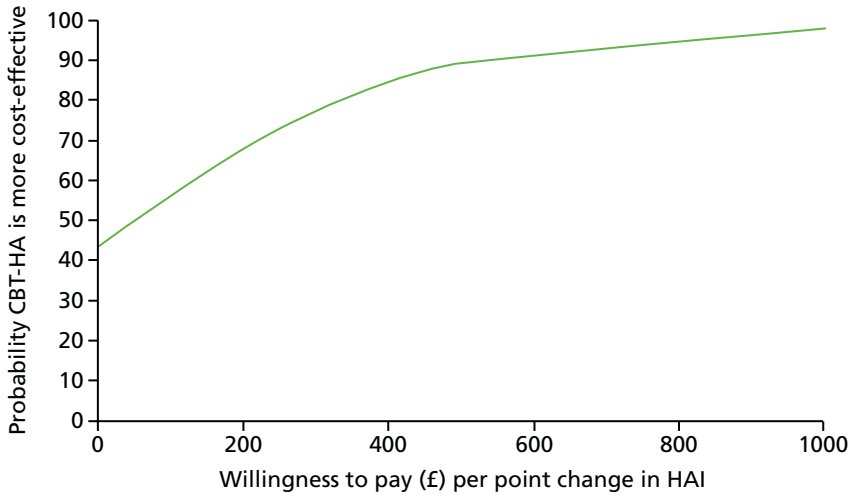

FIGURE 16 Cost-effectiveness acceptability curve showing the probability that CBT-HA is more cost-effective than standard care in terms of health anxiety at the 24-month follow-up.

in order to concentrate on the scatterplots and CEACs presented in *Figures 17–20*. The scatterplot in *Figure 17* shows that the bootstrapped replications mainly fall to the right of the *y*-axis in the north-east and south-east quadrants, where outcomes are better but costs are either higher or lower. This finding is reflected in the CEAC for QALYs in *Figure 18*, which shows that there is little evidence that CBT-HA is cost-effective in terms of QALYs.

For the HAI score at 5 years, the bootstrapped replications in *Figure 19* fall between the south-west and north-west quadrants (again these quadrants represent better outcomes in the CBT-HA group because a higher score on the HAI denotes worse anxiety). The related CEAC in *Figure 20* generally supports the cost-effectiveness of CBT-HA, particularly for willingness-to-pay values for a unit change in HAI scores of > 100 points.

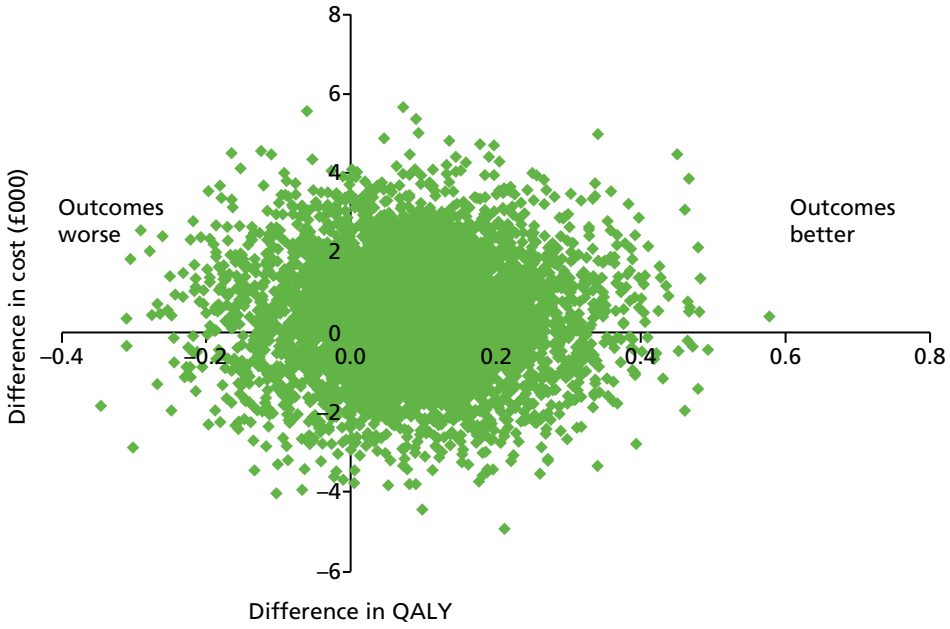

FIGURE 17 Cost-effectiveness plane showing bootstrapped cost and QALY pairs at the 5-year follow-up.

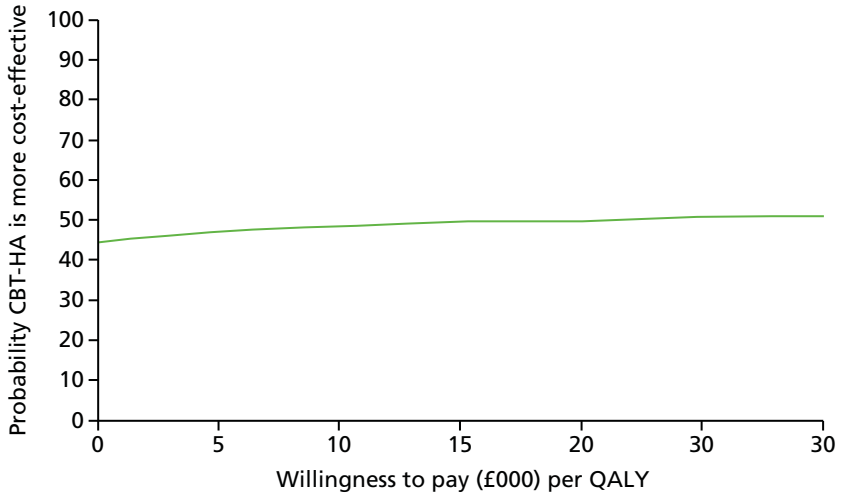

FIGURE 18 Cost-effectiveness acceptability curve showing the probability that CBT-HA is more cost-effective than standard care in terms of QALYs at the 5-year follow-up.

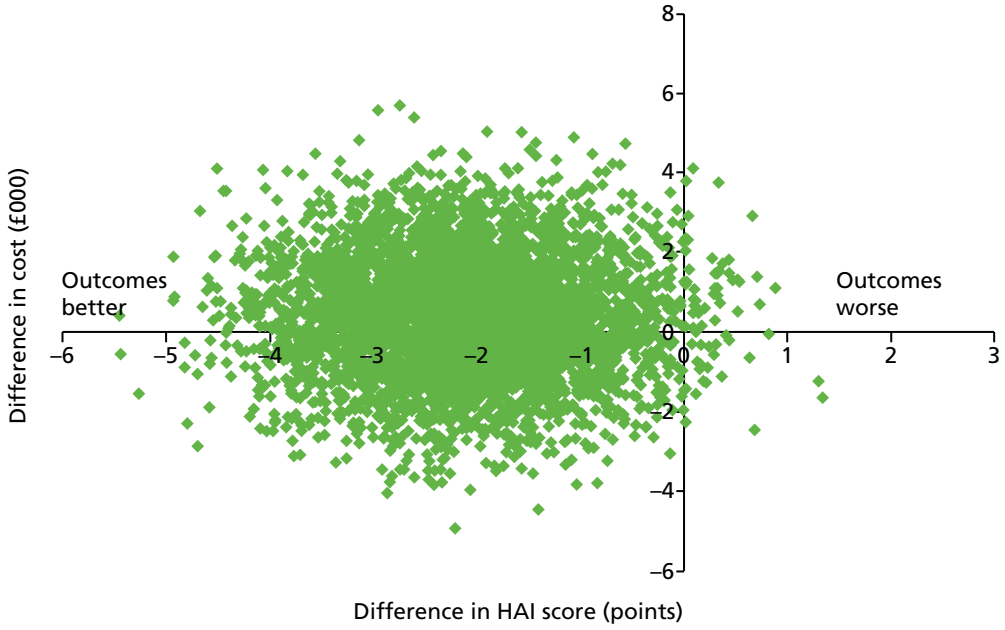

FIGURE 19 Cost-effectiveness plane showing bootstrapped cost and HAI score pairs at the 5-year follow-up.

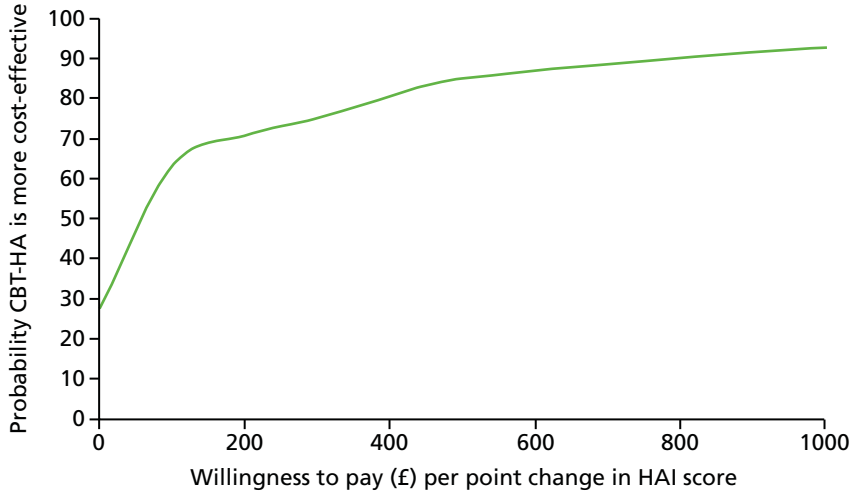

FIGURE 20 Cost-effectiveness acceptability curve showing the probability that CBT-HA is more cost-effective than standard care in terms of health anxiety at the 5-year follow-up.

Sensitivity analysis

Imputation of missing data and the inclusion of productivity losses did not alter the finding that costs were not equivalent, as detailed in *Table 22*.

TABLE 22 Sensitivity analysis

	Treatment group						
	CBT		Standard care		Adjusted mean difference		
Cost variable	Mean	SD	Mean	SD		95% CI	*p*-value
Multiple imputation of total cost ($n = 444$)	14,095.49	9780.85	14,748.15	10,648.14	–368.80	–1793.76 to 1056.17	0.611
Total costs plus productivity losses ($n = 258$)	14,437.41	16,379.47	14,455.54	15,488.24	1438.87	–2050.26 to 4927.99	0.417

Chapter 5 Discussion

The CHAMP trial is the first large-scale trial of CBT-HA in secondary care. Although there has been increasing evidence of the clinical benefits of this treatment in primary care,[52–56] particularly during the period of this trial, the added value of this treatment in secondary care in terms of cost-effectiveness is still uncertain, and explains the major argument for long-term follow-up. As our data showed that the benefit of CBT-HA extends far beyond the duration of treatment this has important implications.

Identification and classification of health anxiety

When the CHAMP trial started in 2008, health anxiety had uncertain status in international diagnostic systems. It was regarded as a synonym for hypochondriasis, although there was a suspicion among researchers that it was not exactly the same condition. Because of this uncertainty we also required patients to satisfy the diagnostic requirements of the DSM-IV for hypochondriasis, and so all who progressed to randomisation had this formal label, which placed patients in the somatoform disorder group.

Since then there have been new international classifications developed and a new diagnosis, illness anxiety (diagnostic code 300.7), was introduced to the fifth American classification *Diagnostic and Statistical Manual of Mental Disorders*-Fifth Edition. This is very similar to health anxiety, as it incorporates excessive concern and monitoring of health, fear of developing or having a physical disease, bodily checking and high levels of anxiety, but an absence of marked somatic symptoms.[57] This last requirement serves to separate illness anxiety from what used to be called 'medically unexplained symptoms', but have been relabelled somatic symptom disorders. Because of the apparent close links between illness anxiety and these other conditions, illness anxiety is placed in the somatic symptom group, but paradoxically has introduced the requirement that 'marked somatic symptoms' must be absent. In the experience of therapists in the CHAMP trial, somatic symptoms of anxiety are very common.

The ICD-11 classification group has chosen differently; it has opted to place health anxiety in the obsessional group of disorders, as there is a degree of overlap between the excessive checking behaviour of the health-anxious patient and obsessional behaviour,[58] and this is also noted in the CHAMP study. There is considerable dissatisfaction with the somatic group of psychiatric disorders, even after these revisions,[59] and the CHAMP trial results suggest that health anxiety is primarily an anxiety disorder, not a somatic one. This suggestion is made as the results of the HADS-A scale paralleled those of the HAI throughout the 5 years of study, and when health anxiety reduced so did generalised anxiety. A similar recommendation that health anxiety is fundamentally an anxiety disorder has also been made on the basis of its links to other disorders.[60]

Representativeness of sample

It could be argued that, as < 10% of those who were originally identified with a high level of health anxiety took part in the trial, those who did participate were unrepresentative. This cannot be answered definitively, as we had no data apart from the HAI scores on those who did not participate, but we were not surprised by the relatively low uptake of invitee participation in the trial. Patients were approached at ordinary outpatient clinics and were not seeking any form of intervention for health anxiety. As they were attending medical clinics, it is reasonable to suppose that patients were seeking medical advice and not expecting to be invited to take part in a psychological treatment.

If we had adopted other ways of recruiting, such as asking consultants to refer patients, we do not think that we would have recruited so many participants. Although the staff in some hospitals are conscious of the importance of health anxiety – several were noted in our study – they are currently in a minority, and most medical staff do not regard the psychological aspects of their patients as a priority when their main tasks are to treat and exclude organic disease. In this respect, the study population was very different from those in other recent trials of internet-delivered or group treatment of health anxiety,[52–55] as clearly those populations recognised the problem of health anxiety and were seeking help for it.

Differences from recent studies

Since the CHAMP trial was started in 2008 there has been one meta-analysis and five other trials published of CBT and related psychological treatments in health anxiety,[52–56,61] all of which showed positive results in favour of the CBT-linked psychological intervention. There were some important differences between the populations treated in these studies and those in the CHAMP trial that need to be highlighted. All of these other publications described populations that had consulted or responded to advertisements from professionals who were providing treatment for health anxiety (i.e. the patients understood fully that they had health anxiety and wanted treatment for it). Patients in the CHAMP study were not seeking treatment and > 90% of those who screened positively for health anxiety (HAI score of $\geq$ 20 points) did not proceed to randomisation, largely because of refusal rather than exclusion criteria. This is not really surprising, as the people approached in medical clinics had a predominantly medical consultation mindset, with the expectation that, whatever the nature of any worries that might beset them, these would be answered by doctors in the clinic, not external psychological sources.

The mean scores for the HAI (≈25 points at baseline) in CHAMP were also considerably lower than the equivalent scores in these other studies (≈40 points), and this explains why many of these other studies refer to 'severe health anxiety' in their titles. The population in CHAMP was not a highly handicapped one (except when there was associated significant medical pathology), and it is possible that the long-term benefits shown with CBT-HA in this group were achieved because of this lesser handicap. Put another way, once people had 'seen the light' and realised that health anxiety was an important part of their problem, it did not require a great deal of intervention to make this benefit semi-permanent. The additional evidence that this was achieved with benefits to generalised anxiety and depression over 5 years shows the degree of overlap between health anxiety and other common mental disorders.

This supposition is also supported by the improvement shown in the patients allocated to standard care. Over the course of 5 years the maximal improvement (60%) was shown in the first 3 months (see *Figure 3*), suggesting that even the relatively short and bland explanation of health anxiety during the baseline assessment was enough to give a degree of insight into the subject and yield some benefit.

Meaningful clinical difference in Health Anxiety Inventory scores

It is not known what constitutes a meaningful clinical difference (MCD) in scores on either the long or short form of the HAI. In very large trials it is possible to find statistically significant differences that are not clinically meaningful because the differences are so small. In our original sample size calculations we suggested that a difference of 5 points in treatment groups was meaningful, but this was based on limited evidence.

Previous studies of anxiety using the HADS have suggested that a reduction in the HADS-A score of 0.7 points or a reduction in the total scale score of 1.32 points is clinically meaningful[62,63] and, if we take a conservative estimate of 1 point for a MCD for the HADS-A and 0.7 points for the HADS-D, this roughly equates to a MCD of 2 points on the HAI. On this basis, the differences between treatments at all assessment points after baseline suggest that CBT-HA is clinically effective as well as statistically superior to standard care.

Relevance of findings of personality status

The findings with regard to personality status were of particular interest in this study because they contradicted previous robust findings with regard to the outcome of depression and, to a lesser extent, anxiety.[62–65] The main studies, backed up by a substantial meta-analysis, showed that patients with comorbid depressive and personality disorder had an odds ratio of > 2 in having a worse symptomatic outcome than those who had depression alone.[64,65] It was expected that these findings would extend to health anxiety and a previous cohort study had found that those with hypochondriacal personality characteristics, possibly of sufficient severity to be called hypochondriacal personality disorder, had a much worse outcome than those without this disorder.[66]

All studies in this subject carried out previously were with patients who had generalised anxiety or depression. The CHAMP study findings of greater improvement with CBT-HA than standard care, extending over 5 years, in those with personality difficulty and mild personality disorder, findings not shown with other personality groups, are striking. The additional evidence that this difference in improvement also extended to social functioning, and that standard care led to better social function in those with no personality dysfunction, adds to the impact of these findings.

However, there was an important difference between the assessment of personality in CHAMP and those of other studies. Currently personality disorder is diagnosed dichotomously in classification systems: patients either do or do not have personality disorder. The ICD-11 system of classification[67] uses a single dimension of classification consistent with research evidence; of the two levels of personality disturbance that showed persistent preferential improvement with CBT-HA, one, personality difficulty, is classified as a 'non-disorder', and the other, mild personality disorder, is included among the personality disorders. Using the older dichotomous system of classification, the differences between outcomes would have been attenuated, but not to the extent that the previous findings of a poorer outcome in personality-disordered patients would be replicated.

The high proportion of patients with at least some level of personality disturbance (80%) may appear surprising but is also consistent with other data.[68–71] People with high levels of health anxiety and, to a lesser extent, generalised anxiety, often have personalities that are strong in avoidant, anxious and dependent characteristics, and this impairs both relationships and functioning, and adds to symptomatology (see *Table 17*). The evidence that this does not handicap patients' responses to CBT-HA, in either the short or longer term, is encouraging. Whether or not the difference in response by personality level is sufficiently strong to suggest that personality assessment should be undertaken in ordinary practice is beyond the scope of this study, but there are cogent arguments in its favour.[70,71]

It is not clear why those with no personality dysfunction did not respond to CBT-HA or why this treatment seemed to impair social functioning. One possible explanation is that this group had appropriate rather than pathological anxiety, and so the introduction of CBT-HA was regarded not only as unnecessary, but also as irritating or annoying.

Implications for health services

Our findings indicate that excessive health anxiety is common and, if untreated, tends to persist, which supports previous evidence from several sources.[6,72,73] Therefore, it appears that the natural course of health anxiety is quite different from that of generalised anxiety disorder, which tends to pursue a fluctuating path depending on circumstances. Possible reasons for health anxiety persisting without much improvement include the reinforcing aspects of reassurance and medical consultation, and these tend to continue in the absence of any appropriate management.

At the time of writing, in most parts of the UK this management can be accessed only through the Improving Access to Psychological Therapies (IAPT) programme but, although practitioners in the services were initially trained to have skills in CBT for depression and anxiety, the IAPT services have extended these to include health anxiety. However, the numbers potentially benefiting from therapy, possibly one in five of all medical outpatients, are far beyond the capacity of an external service to serve. It may appear too strong a claim, but the number of people with major health-anxiety concerns in general hospitals is both sufficiently large and undetected to be called a silent epidemic.[74] There is a growing realisation that better integration of medical and mental health services is necessary in general hospitals[75] and that it would be a great advantage to develop skills within the general hospital to identify and treat patients with health anxiety, alongside the provision of normal care. The evidence from the CHAMP study that general nurses, when appropriately trained, were highly suitable practitioners of CBT-HA, suggests that an obvious way forward would be to train interested nurses in general hospitals in the principles of treatment and to raise awareness of the nature of health anxiety among their fellow professionals.

Comment was made after the first major CHAMP publication that the intervention could not be regarded as cost-effective because of the high degree of screening needed to recruit patients.[76] We argue that if health-anxiety literacy in medical clinics were greater, there would be no need for screening, and until this time comes it would be perfectly reasonable for the HAI or a similar scale to be given to patients when first registering at a medical outpatient clinic, at very low cost. In this way, patients who present recurrently with anxiety about problems that appear to have no physical cause would be identified in the clinic and an appropriate response made.

Long-term benefit of cognitive–behaviour therapy for health anxiety

The benefit of CBT-HA in reducing health anxiety appears to be long lasting. This finding was unexpected, not least as most interventions for anxiety and depression using CBT tend to diminish over time and are seldom present over 1 year after completing therapy.[77–81] There is no doubt that CBT is effective in treating both generalised anxiety and depression (these benefits often go together),[80] but the evidence that these benefits extend beyond 1–2 years is very weak, partly because so many trials have waiting list controls that curtail comparison of groups over long periods.[79,80] There is one exception to this: the CoBalT study of CBT for depression showed continuing benefits of CBT 40 months after randomisation.[81] There is no equivalent for generalised anxiety.

The evidence that these benefits were maintained with gains at 2 years being just as strong at 5 years deserves discussion. There could be at least three reasons for this: first, the failure of those in standard care to improve beyond the initial gains at 3 months could have been a consequence of their continued concerns and consultations about their health, which only reinforced their symptoms. Second, in those who received CBT-HA in this particular population, the acquisition of insight into the presence of health anxiety, together with a relatively straightforward set of learnt procedures to overcome it, may have been a powerful restitutional force that kept people well (other general advice, including avoidance of internet browsing for health problems, may also have been of benefit). The third reason relates to psychological help-seeking – in most studies of psychological treatment for anxiety and depression the patients are seeking treatment, and if they do not receive it from one source they get it from another. In the words of a study of collaborative care, those in control populations ‘catch up’ on those who have more specific interventions over the course of time[82] because they eventually receive the care that is needed.

The population with health anxiety in CHAMP was not help-seeking and so ‘catching up’ was not an issue for them. Before being involved in the CHAMP study, patients felt that it was quite in order for them to continue to express concerns about their health to their physicians and no further intervention was necessary. Therefore, there was no attempt from those in the control group to seek further assistance and, indeed, there was no evidence of crossover to CBT-HA or other related therapies in the standard care group over the 5-year period.

In view of the maintenance of benefit of CBT-HA after 5 years, the project group is now carrying out an 8-year follow-up. This will also examine costs again to see if the continued savings between 2 and 5 years are extended.

Interpretation of the economic evaluation

In terms of cost-effectiveness, our data suggest that the picture is more complex than our original hypothesis that successful CBT-HA would reduce health anxiety and, therefore, unnecessary service use would result in lower costs. The results of the cost-effectiveness analysis therefore require careful interpretation. Our original hypothesis was that savings would offset the additional costs of the CBT intervention elsewhere in the health system, resulting in equivalent costs between groups. We found evidence of offset but did not find hypothesised equivalence, nor did we find any noticeable or significant difference in cost between groups, except in personality status. As a consequence, it is right to state that the CHAMP trial did not find clear evidence of cost-effectiveness. These issues will be considered in the following section.

The inability to demonstrate equivalence and cost-effectiveness has its root in two key characteristics of the data and the patient group: that there is considerable variation in costs and that the costs are multifaceted. Variation in costs is not unusual in cost data; however, the variation in this group was substantial enough that it was necessary to remove two outliers from the main analysis as they met the criteria for influential outliers. The multifaceted nature of the costs needs to be unpacked a little. If we take costs back to service use, it allows us to try and explain what exactly this phenomenon might be. *Table 17* shows that levels of hospital and GP use were considerable, and that use of these services continued in both randomised groups throughout follow-up. Given that we believe that the patient group is one with substantial medical pathology, it is perhaps unsurprising that use of these medical services remained high despite a noted and consistent reduction in health anxiety in the CBT-HA group. Thus, any reductions in service use as a result of changes in behaviour following successful CBT-HA are lost in the noise of all other medical service use.

A previous study of the cost-effectiveness of CBT-HA compared with control treatment was carried out in Sweden using internet-guided treatment.[83] This showed that the total costs were only a little higher (< 15%) than those of health care in this population, suggesting that future studies could rely on health-care costs alone.

There are a number of limitations of the economic evaluation, which resulted from both the duration of the analysis and the patient group. In terms of the duration of the analysis, collecting service use data over long periods generates a number of challenges. For the follow-up interviews up to 12 months, the ADSUS asked participants to recall their service use only for the previous 6 months. At the 24-month interview recall was for 12 months, and at the 5-year interview recall was for 3 years. We acknowledge that the accuracy of recall over long periods is limited and we sought to limit the impact of this in two ways. First, the list of services that we asked participants to recall was short and limited to services provided in the community. Second, we did not ask participants to recall use of hospital services and instead extracted these from hospital trust computer databases. In addition, we were able to extract hospital use data from the trial host hospital trust databases only, and it is likely that participants accessed services from other hospitals from which we were not permitted to access information. It is important to note that there is nothing to suggest that recall bias is not equally distributed across the whole cohort. If this were so, the randomised group differences are valid. However, recall bias may provide an explanation for the apparent reduction in community service use at 5 years.

Another important limitation was the choice of outcome measure for the economic evaluation. Our results suggest that it is likely that CBT-HA is cost-effective in terms of health anxiety and that the probability of it being cost-effective increases with positive values on the willingness to pay for an improvement in outcome. The difficulty with this is that the willingness-to-pay value for a change in HAI score is unknown,

so it is therefore not possible to make clear statements in terms of policy-making. Regarding the economic outcomes, there were no noticeable improvements in quality of life as measured with the EQ-5D. One explanation for the inability of the EQ-5D to pick up the improvement in the CBT-HA group that was found with the HAI outcome links back to a key characteristic of the patient group; rather than being a group of individuals with health anxiety and medically unexplained symptoms, they are in many cases individuals with health anxiety and substantial medical pathology. These problems would inevitably have an impact on an individual's quality of life. The EQ-5D contains only one domain on depression/anxiety and it is likely that study participants would continue to score highly in the other domains of the EQ-5D, making any differences in anxiety as a result of the intervention difficult to capture. It is also possible that the health-anxiety intervention did not have an impact on depression and, thus, there could be no impact on the EQ-5D scores in this way either. Future studies in health anxiety should consider a different measure of quality of life.

It does remain possible and important, however, to reach conclusions based on the evidence we have collected on the costs of health anxiety in medical patients. The first is that, in terms of the HAI score as an outcome, CBT-HA has a > 50% probability of being cost-effective for almost all willingness-to-pay values. The second is that, counter to this, there is no evidence that CBT-HA is cost-effective in terms of QALYs as measured using the EQ-5D.

Chapter 6 Recommendations for further research

We have identified pathological health anxiety as a highly prevalent problem in medical clinics and have developed a treatment that is clinically effective and possibly cost-effective. The work has posed many new areas for research.

- Is the degree of health anxiety in patients attending all medical clinics clearly pathological? It is reasonable to argue that, when someone is medically ill, they should be more concerned about their health than at other times, and it could be argued that such anxiety is normal. The persistence of therapeutic value in the CHAMP study suggests that such anxiety is indeed pathological, as it would be likely to wax and wane in line with medical pathology. There is also evidence that worry over health leads to premature mortality[84] and that cardiac anxiety is associated with later major cardiac pathology.[85] This may be of particular relevance to cardiology as, in the CHAMP study, the beneficial effects were maximal at 5 years.
- What are the main reasons for poor recruitment of patients to receive psychological treatments, especially CBT, for the treatment of health anxiety? We have speculated about this in the report, but formal studies, probably qualitative in nature, are needed to explore this more fully.
- Are general or specialised nurses in medical specialties better able to deliver CBT-HA in medical settings or is this work suitable for trained IAPT therapists, as current government strategy suggests?
- Is there a good argument for a staged care strategy for health anxiety in medical settings? The improvement made by the standard care group in the first 3 months suggested that being made aware of health anxiety was of benefit. In such a staged strategy it would seem appropriate for the first stage to be carried out by nurses or other staff in the medical clinics concerned.
- Why is it that older patients have a better outcome than younger ones? Is it likely to be related to comorbid pathology? It is reasonable to postulate that in the presence of any form of medical pathology health anxiety is likely to be activated, and the better response in older patients might be related to better understanding of heath-anxiety generation.
- Is there a better way of measuring cost-effectiveness of psychological treatments in the presence of significant medical illness, when the costs of the latter far exceed those of the psychological intervention (taking into account its likely savings)? This, to some extent, may be determined by other studies in different populations, especially in primary care, when expensive medical costs are absent. One study followed the principles of CBT-HA and combined it with web-based video interaction with therapists instead of face-to-face contact[86] and this is likely to report shortly.
- Are the prevalence and incidence of health anxiety increasing as a consequence of cyberchondria (excessive use of the internet for health advice)?

The CHAMP study is continuing to a final follow-up after 8 years and it is hoped that some of these questions can at least be partially addressed in this last phase of the study.

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Contributions of authors

The trial was initiated by **Peter Tyrer** and **Helen Tyrer**, who, with **Paul Salkovskis**, **Michael J Crawford**, **Simon Dupont**, **John Green**, **David Murphy**, **Steven Reid**, **Sarah Byford** and **Barbara Barrett**, designed the structure of the trial.

Duolao Wang and **Barbara Barrett** were involved primarily in developing the statistical analysis plan.

Sylvia Cooper was the trial co-ordinator and organiser of the recruitment strategy.

Georgina Smith, **Rachel Evered**, **Yvonne Lisseman-Stones**, **Sharon McAllister** and **Jessica Nagar** were the main therapists.

Rahil Sanatinia co-ordinated the acquisition of personality data for ICD-11 conversion.

Sharandeep Bhogal, **Shaeda Nourmand**, **Valentina Lazarevic**, **Gemma Loebenberg**, **Stephanie Kings**, **Antoinette McNulty**, **Kofi Kramo**, **Katherine Whittamore** and **Gemma Walker** were the main research assistants.

Aaron Philip assisted with the co-ordination and checking of hospital data, **Hilary Warwick** helped with assessment of treatment fidelity, and **Sarah Byford** and **Barbara Barrett** carried out the economic analysis.

All authors read and approved the final manuscript.

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Data sharing statement

The full data set for this study can be obtained from the corresponding author.

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