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A randomised controlled multicentre trial of treatments for adolescent anorexia nervosa including assessment of cost-effectiveness and patient acceptability – the TOuCAN trial

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Abstract

A randomised controlled multicentre trial of treatments for adolescent anorexia nervosa including assessment of cost-effectiveness and patient acceptability – the TOuCAN trial

SG Gowers,[1]*, AF Clark,[2] C Roberts,[3] S Byford,[4] B Barrett,[4] A Griffiths,[1] V Edwards,[5] C Bryan,[1] N Smethurst,[1] L Rowlands[1] and P Roots[6]

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Objective: To evaluate the clinical effectiveness and cost-effectiveness of inpatient compared with outpatient treatment and general (routine) treatment in Child and Adolescent Mental Health Services (CAMHS) against specialist treatment for young people with anorexia nervosa. In addition, to determine young people's and their carers' satisfaction with these treatments.
Design: A population-based, pragmatic randomised controlled trial (RCT) was carried out on young people age 12 to 18 presenting to community CAMHS with anorexia nervosa.
Setting: Thirty-five English CAMHS in the north-west of England co-ordinated through specialist centres in Manchester and Liverpool.
Participants: Two hundred and fifteen young people (199 female) were identified, of whom 167 (mean age 14 years 11 months) were randomised and 48 were followed up as a preference group.
Interventions: Randomised patients were allocated to either inpatient treatment in one of four units with considerable experience in the treatment of anorexia nervosa, a specialist outpatient programme delivered in one of two centres, or treatment as usual in general community CAMHS. The outpatient programmes spanned 6 months of treatment. The length of inpatient treatment was determined on a case-by-case basis on clinical need with outpatient follow-up to a minimum of 6 months.
Main outcome measures: Follow-up assessments were carried out at 1, 2 and 5 years. The primary outcome measure was the Morgan–Russell Average Outcome Scale (MRAOS) and associated categorical outcomes. Secondary outcome measures included physical measures of weight, height, body mass index (BMI) and % weight for height. Research ratings included the Health of the National Outcome Scale for Children and Adolescents (HoNOSCA). Self report measures comprised the user version of HoNOSCA (HoNOSCA-SR), the Eating Disorder Inventory 2 (EDI-2), the Family Assessment Device (FAD) and the recent Mood and Feelings Questionnaire (MFQ). Information on resource use was collected in interview at 1, 2 and 5 years using the Child and Adolescent Service Use Schedule (CA-SUS). Satisfaction was measured quantitatively using a questionnaire designed for the study and qualitative (free) responses on it. The questionnaire data were supplemented by qualitative analysis of user and carer focus groups.
Results: Of the 167 patients randomised, 65% adhered to the allocated treatment. Adherence was lower for inpatient treatment (49%) than for general CAMHS (71%) or specialist outpatient treatment (77%) ($p = 0.013$). Every subject was traced at both 1 and 2 years, with the main outcome measure completed (through contact with the subject, family members or clinicians), by 94% at 1 year, 93% at 2 years, but only 47% at 5 years. A validated outcome category was assigned for 98% at 1 year, 96% at 2 years and 60% at 5 years. There was significant improvement in all groups at each time point, with the number achieving a good outcome

being 19% at 1 year, 33% at 2 years and 64% (of those followed up) at 5 years. Analysis demonstrated no difference in treatment effectiveness of randomisation to inpatient compared with outpatient treatment, or, specialist over generalist treatment at any time point, when baseline characteristics were taken into account. Generalist CAMHS treatment was slightly more expensive over the first 2 years of the study, largely because greater numbers were subsequently admitted to hospital after the initial treatment phase. The specialist outpatient programme was the dominant treatment in terms of incremental cost-effectiveness. Specialist treatments had a higher probability of being more cost-effective than generalist treatments and outpatient treatment had a higher probability of being more cost-effective than inpatient care. Parental satisfaction with treatment was generally good, though better with specialist than generalist treatment. Young people's satisfaction was much more mixed, but again better with specialist treatment, including inpatient care.

Conclusion: Poor adherence to randomisation (despite initial consent to it), limits the assessment of the treatment effect of inpatient care. However, this study provides little support for lengthy inpatient psychiatric treatment on clinical or health economic grounds. These findings are broadly consistent with existing guidelines on the treatment of anorexia nervosa, which suggest that outpatient treatments should be offered to the majority, with inpatient treatment offered in rare cases, though our findings lend little support to a stepped-care approach in which inpatient care is offered to outpatient non-responders. Outpatient care, supported by brief (medical) inpatient management for correction of acute complications may be a preferable approach. The health economic analysis and user views both support NICE guidelines, which suggest that anorexia nervosa should be managed in specialist services that have experience and expertise in its management. Comprehensive general CAMHS might, however, be well placed to manage milder cases. Further research should focus on the specific components of outpatient psychological therapies. Although family-based treatments are well established, trials have not established their effectiveness compared with good-quality individual psychological therapies and the combination of individual and family approaches is untested. Further research is needed to establish which patients (if any) might respond to inpatient psychiatric treatment when unresponsive to outpatient care, the positive and negative components of it and the optimum length of stay.

Trial registration: NRR number (National Research Register) N0484056615; Current Controlled Trials ISRCTN39345394.

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List of abbreviations

AN	anorexia nervosa
BFST	Behavioural Family Systems Therapy
BMI	body mass index
CAMHS	Child and Adolescent Mental Health Services
CA-SUS	Child and Adolescent Service Use Schedule
CARER-SUS	Carer Service Use Schedule
CBT	cognitive behaviour therapy
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 4th Edition
EDE	Eating Disorder Examination
EDI-2	Eating Disorders Inventory second edition
EOIT	Ego-Oriented Individual Therapy
FAD-GF	Family Assessment Device–General Functioning
HoNOSCA-CR	clinician-rated Health of the Nation Outcome Scale for Children and Adolescents
HoNOSCA-SR	self-rated Health of the Nation Outcome Scale for Children and Adolescents
IBW	ideal body weight
ICER	incremental cost-effectiveness ratio
MFQ	Mood and Feelings Questionnaire
MRAOS	Morgan–Russell Average Outcome Scale
NICE	National Institute for Clinical Excellence (now National Institute for Health and Clinical Excellence)
RCT	randomised controlled trial
SD	standard deviation
TOuCAN	Treatment Outcome of Child and Adolescent Anorexia Nervosa

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

Executive summary

Background

Anorexia nervosa (AN) is a complex disorder generally developing in adolescence, with high rates of morbidity and occasional mortality. It often continues into adult life with a range of adverse physical and psychosocial outcomes. Although interventions to treat the disorder have been devised, evaluation of them has been limited. Inpatient psychiatric treatment is often employed, but this is expensive, has been poorly evaluated and never in randomised controlled trials involving adolescents using NHS facilities. Similarly, although treatment in specialist centres is often advocated, this is often confused with treatment in exclusive eating disorder inpatient units. No trials have examined the effectiveness or cost-effectiveness of specialist services for adolescents. Generic Child and Adolescent Mental Health Services (CAMHS) are well equipped to offer individual and family-based psychological therapies and may offer effective treatment for adolescent AN.

Objectives

The aim of the study was to determine if at 1, 2 and 5 years, young people treated in specialist services (inpatient and outpatient) enjoyed advantages over those attending general CAMHS. In addition, it aimed to evaluate whether inpatient management conferred advantages over outpatient treatment. The specific hypotheses were that:

- inpatient treatment would be more effective than outpatient treatment
- specialist treatment would be more effective than general treatment
- outpatient treatment would be more cost-effective than inpatient treatment
- specialist outpatient treatment would be more cost-effective than general CAMHS treatment
- carers would have higher expectations of treatment and would be more satisfied with it than young people with the disorder
- satisfaction would be higher with specialist treatment than with generalist treatment.

In addition we anticipated that:

- for the total series, few patients would fully recover by 1 year after the start of treatment, but overall outcomes would improve at the 2-year and 5-year time points
- for those remitting, relapse would be unusual during the course of the study.

To achieve these objectives a randomised controlled trial of inpatient management against a specialist outpatient programme and treatment as usual in general CAMHS was undertaken.

Method

A pragmatic randomised controlled trial was conducted on young people between the ages of 12 and 18 years presenting to community CAMHS with AN. Inclusion criteria comprised food restriction plus or minus compensatory behaviours; weight below 85% of that expected based on age and height; intense fear of gaining weight or undue influence of weight or shape on self-evaluation; primary or secondary amenorrhoea of at least 3 months in females, or menstruation only while on the contraceptive pill.

The only exclusion criteria employed were severe learning difficulties or the presence of severe chronic comorbid physical conditions affecting digestion or metabolism. No exclusions were made on grounds of clinical severity.

Setting

Thirty-five CAMHS in the north-west of England (total population 7.5 million), co-ordinated through specialist centres in Manchester and Liverpool, UK.

Interventions

Participants were randomised to either treatment as usual within community CAMHS, a specialist outpatient programme (delivered in two centres) comprising individual cognitive behaviour therapy,

dietary advice, parental counselling and feedback of self-report measures, or inpatient treatment within one of four specialist but not exclusive inpatient units. Outpatient treatment spanned a minimum of 6 months. Inpatient treatment was at the service's discretion with outpatient follow-up to a minimum of 6 months.

Baseline and outcome measures

Participants received a comprehensive baseline assessment and follow-up assessments at 1, 2 and 5 years. The main outcome measure was the Morgan–Russell Average Outcome Scale (MRAOS), a validated and frequently used measure for AN. This, and the Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA) (recently validated in a number of research trials), demonstrated good inter-rater reliability.

Secondary outcome measures included diagnosis and self-reported abnormal eating cognitions (Eating Disorders Inventory 2), mood (Mood and Feelings Questionnaire), family functioning (Family Assessment Device) and physical measures of weight, height and body mass index (BMI). Information on resource use was collected in interviews at 1, 2 and 5 years using the Child and Adolescent Service Use Schedule (CA-SUS). Participant and carer satisfaction was measured by a satisfaction questionnaire devised for this study and supplemented by qualitative data from user and carer focus groups.

Results

Of the 167 young people randomised, 67% adhered to allocated treatment, with lower adherence to inpatient management. Every subject was traced at both 1 and 2 years, (the main outcome point) with the main outcome measure completed by 94% at 1 year, 93% at 2 years but only 47% at 5 years. A valid outcome category was assigned for 98% at 1 year, 96% at 2 years and 60% at 5 years. There was significant improvement in all groups at each time point, with the number achieving a good outcome being 19% at 1 year, 33% at 2 years and 64% (of those followed up) at 5 years. Analysis by intention to treat demonstrated no difference in effectiveness (on the main outcome measure), for inpatient compared with outpatient treatment, or specialist over generalist treatment at any time point controlling for baseline characteristics; but specialist treatment had advantages with increasing time. Patients receiving inpatient treatment showed poor results, among those failing to make progress with outpatient treatment and transferring to it on clinical grounds.

Generalist treatment was slightly more expensive over the first 2 years, largely because greater numbers were subsequently admitted to hospital after the treatment phase. The cost-effectiveness analysis revealed that specialist outpatient services were dominant in terms of incremental cost-effectiveness (as they were more effective and less costly). Specialist outpatient services had a higher probability of being cost-effective than general CAMHS and outpatient services had a higher probability of being cost-effective than inpatient services.

The satisfaction study showed overall, good levels of satisfaction with young people being twice as likely to express positive as negative views of their treatment. Parents were much more satisfied, with five times as many expressing positive than negative views of treatment. Parents were consistently more satisfied than young people with each treatment but both parents and young people were more satisfied with specialist than general treatments, largely on account of their confidence in 'expertise' and their ability to forge a good relationship with an individual therapist, working either on an inpatient or outpatient basis.

Conclusions

Implications for health care

For moderately to severely ill adolescents with AN, outpatient services delivered by experienced, expert professionals, supported by medical management of physical complications as required, offer the most cost-effective treatments. Lengthy psychiatric inpatient treatment does little to add to positive outcomes and is cost-ineffective. Treatment in specialist services with experience and expertise in managing the condition is to be preferred owing to its cost-effectiveness and higher levels of satisfaction in both young people and carers. Where young people with AN are managed in community CAMHS, a consultation and advice link with a specialist service may enable the team to contain anxiety and reduce unnecessary hospital admissions, thereby leading to greater user satisfaction. This needs further investigation.

The findings are broadly consistent with the National Institute for Clinical Excellence [now National Institute for Health and Clinical Excellence (NICE)] guidelines on the treatment of AN. Although physical risk should not be underestimated and may require urgent and active intervention, this trial does not lend support to the advantages of managing this within a psychiatric service.

Recommendations for future research

Further research is recommended in the following areas.

Clarify the positive and negative aspects of inpatient care

Physical and psychological risk, parental anxiety and social and educational withdrawal often result in inpatient admission. The opportunities for intensive psychological therapies, general support, refeeding and respite from external stresses make specialist inpatient care a logical step. Satisfaction (particularly among parents) is quite good. However, research outcomes are consistently disappointing, suggesting that adverse effects are under-recognised. Some are likely to be associated with the specifics of inpatient care, such as reinforcement of feelings of ineffectiveness; some to do with difficulties negotiating discharge and continuity of care. These need further clarification.

Clarify the optimum length of stay for inpatient care

Some of the adverse effects of inpatient care may relate to 'institutionalisation', reinforcement of the sick role, or a deskilling effect on both young people and their carers. A study comparing brief stays to stabilise physical health and initiate normal eating, with longer more comprehensive treatment, would help to clarify these issues. Again, user views and a health economic component should be incorporated into such a study, given the high cost of inpatient care.

Evaluation of the efficacy and cost-effectiveness of individual psychological therapies

The current findings lent only modest support to the specialist programme used in this study comprising cognitive behaviour therapy with dietary therapy and parental counselling. As AN is a psychological disorder based on abnormal cognitions, further research is required to evaluate the effect of different approaches on the specific (weight and shape) and non-specific cognitions underlying the disorder. This research in adults is ongoing, but untested in (particularly younger) adolescents.

Evaluation of co-ordinated individual psychological therapies with family-based treatments

Since this project started, research into family-based treatments has been productive and indicated that these can be effective. However, they have not been adequately tested against individual approaches. For pragmatic as well as theoretical reasons, (supported by our user views), adolescents should receive individual therapies and involvement of the family. The specific components of combined therapies and how these should be co-ordinated to produce cognitive as well as behavioural change, requires further testing.

Trial registration

This trial is registered as NRR N0484056615 and ISRCTN39345394.

Chapter 1
Introduction

Anorexia nervosa in young people

Anorexia nervosa (AN) is a complex eating disorder, generally developing in adolescence or young adulthood but sometimes in late childhood. It is relatively rare at 12 years, but the prevalence rises with age, reportedly reaching about one in 200 adolescent girls at 16 years. The highest incidence rates are for females aged 15–19 years, who represent approximately 40% of all identified cases.[1] Incidence and prevalence rates of AN in males are more rarely reported, but it has been noted that where they are, the female to male ratio is around 11 : 1 overall[1] but it appears to be somewhat lower in adolescents,[2] with a more equal sex ratio at the younger end of the spectrum.

Anorexia nervosa appears to have become more common over recent decades, but the apparent increase could well be the result of greater help-seeking, better detection and changes in diagnostic practice rather than of any true increase in the incidence of the disorder.[3] The best evidence for this comes from Rochester, MN, USA.[4] This study suggested an increase in incidence of 36% in adolescent females every 5 years from 1950 to 1984. Anorexia nervosa is currently the most prevalent disorder within inpatient child and adolescent mental health services.[5]

It is thought that eating disorders may have changed over time, particularly in the increasing ratio of the purging form of AN to the restricting form. Anorexia nervosa used to be seen as a middle-class disorder of the white, western world. This is no longer the case, although uncertainties exist as to whether there has been a change in identification of cases in different cultures or whether the condition has spread to black and ethnic minority populations and to developing nations as they have taken on western culture and lifestyles.

Anorexia nervosa has the highest mortality rate of any psychiatric disorder in the UK; with patients with AN being 12 times more likely to die than women of a similar age in the general population.[6] The mortality rate among adolescents is low. Most deaths are either a direct result of medical complications or due to suicide.

Clinical features

Anorexia nervosa is a syndrome comprising a range of physical, psychological and behavioural features. These usually have an impact on social functioning and eventually their effects pervade most areas of the young person's life.

Four features are required to make a diagnosis:

- overevaluation of the importance of weight and shape (this is often expressed as an intense fear of becoming fat and is sometimes referred to as a distortion of body image)
- maintenance of an unduly low bodyweight [that is less than 85% of that expected, or a body mass index (BMI) below the second percentile for age]
- active control of weight by dietary restriction, exercise, vomiting or purging
- a widespread endocrine disturbance involving the hypothalamic–pituitary–gonadal axis (this is manifest as amenorrhoea in postpubertal females, as pubertal delay in pubescent females and as impotence and lack of sexual interest in males).

The central features are essentially the same in both sexes; those with AN judge their self-worth largely, or even exclusively, in terms of their shape and weight and their ability to control them. This results in a pursuit of weight loss and an intense fear of weight gain and fatness. Most of the other features are secondary to this cognitive abnormality and its consequences and there is a complex relationship between cognition, behaviour and the physical features. To the extent that this pursuit of a low weight is successful, weight control is seen as necessary rather than problematic. Successful dieting therefore tends to be viewed positively and, as a consequence, young people with AN generally have low motivation to change.

In AN a very low weight may be attained through severe and selective restriction of food intake

with self-induced vomiting and other forms of weight-control behaviour (such as the misuse of laxatives or diuretics) practised by a subgroup. Depressive and anxiety features, irritability, lability of mood, impaired concentration, loss of sexual interest and obsessional symptoms are frequently present. Typically these features get worse as weight is lost and improve to a large extent with weight restoration. Interest in the outside world also declines with the result that most become socially withdrawn and isolated. As bodyweight is maintained at least 15% below that expected, pubertal development is stunted or reversed. This results in either a delay in the menarche or secondary amenorrhoea in those who have completed puberty.

Negative physical outcomes such as failure to reach expected height, stunted breast development and reduced bone density are often reported. In the longer term, eating disorders may have an impact on pregnancy and motherhood. In those recovering from AN, fertility problems, spontaneous abortion, prematurity and small-for-gestational-age babies are regularly reported, as are elevated rates of infant mortality.[7,8]

A systematic review of 119 outcome studies of patients across the age range,[9] found high rates of anxiety disorders and affective disorders at long-term follow-up as well as substance misuse. Full long-term recovery was reported for 45.1%, a fair outcome for 35%, whereas 19.8% had a chronic course.

Treatment of anorexia nervosa

There has been surprisingly little research on the treatment of AN but most of this work has concerned adolescents.[10,11]. Recent systematic reviews[11–13] have drawn attention to the shortage of quality, adequately-powered treatment trials for anorexia nervosa. The National Institute for Clinical Excellence [now National Institute for Health and Clinical Excellence (NICE)] guidelines made treatment recommendations classified from A (the strongest) to C (the weakest), based on the strength of evidence. In considering the full range of psychological therapies, physical (including pharmacological) treatment and service settings, it was unable to make a single Grade A treatment recommendation across the age range.[11] Guidelines on the management of child and adolescent eating disorders are therefore based mainly on expert clinical opinion and cohort studies rather than on randomised clinical trials. A number of academic bodies have published consensus guidelines, some specifically in relation to the management of children and adolescents. There is much greater emphasis in these on physical rather than other aspects of management.

Physical management

In AN, guidelines refer to the potentially irreversible effects on physical growth and development and argue that the threshold for medical intervention in adolescents should be lower than in adults. Of particular importance, is the potential for permanent growth retardation if the disorder occurs before fusion of the epiphyses, and impaired bone calcification and mass during the second decade of life, predisposing to osteoporosis and increased fracture risk later in life. These features emphasise the importance of immediate medical management and ongoing monitoring by physicians who understand normal adolescent growth and development. There is a lack of consensus regarding oral feeding requirements. A weight gain of around 1 kg per week is generally recommended for inpatients and 0.5 kg per week for outpatients. After an initial safe weight has been achieved, the young person's food intake should be adjusted to ensure that growth is in keeping with normal weight and height trajectories. Weight restoration should use the least invasive procedures possible and should be provided within a caring age-appropriate setting. Nasogastric feeding should only be resorted to in the face of persistent refusal to eat normally. Strict behavioural regimes in which young people have to earn privileges through eating and weight gain are not desirable or acceptable because they militate against the therapeutic alliance and there is no evidence that these approaches work, other than by achieving short-term weight gain. In the long term, undue coercion may be perceived by the young person either as a recapitulation of abuse or neglect that they may have suffered previously, or it may reinforce low self-esteem and feelings of ineffectiveness, both of which are common antecedents of AN.

Pharmacological treatment

The use of psychotropic medication is not considered a first-line treatment for AN. A lack of studies and negative findings have led to the widely held view that the use of drugs is not justified in the first-line management and should be reserved

for cases complicated by comorbid diagnoses. However, a recent survey of seven specialist eating disorder services for children and adolescents in the UK,[14] showed that psychotropic medication is commonly prescribed (chiefly selective serotonin reuptake inhibitors antidepressants and major tranquillisers), and with apparently beneficial symptomatic benefit.

Psychological therapies

Although there are a considerable number of studies of psychological therapies in the recent eating disorder literature, a number of methodological issues make for difficulties in combining results in meta-analysis and reaching firm conclusions about the merits of different therapies. These include:

- heterogeneity within therapies of the same name
- the wide range of outcome measures used
- differences in timing of follow-up
- entry criteria
- other therapies given concurrently.

The NICE guideline concluded that there was limited evidence that a range of specific psychological treatments for AN with more therapeutic contact was superior to 'treatment as usual' (with a lower rate of contact) in terms of mean weight gain and the proportion of patients recovered. There was insufficient evidence from six small randomised controlled trials (RCTs) to suggest that any particular specialist psychotherapy [cognitive analytic therapy, cognitive behavioural therapy (CBT), interpersonal therapy, family therapy, or focal psychodynamic therapy] was superior to others.

Cognitive behavioural therapy

A number of cognitive behavioural models have been described for the development and maintenance of eating disorders (generally within the adult field); perhaps the most validated one being the model of Fairburn *et al.*[15] for bulimia nervosa, which has since been adapted to form a 'transdiagnostic' model of eating disorders.[16] This proposes that the restriction of food intake that characterises the onset of eating disorders has two main origins. The first is a need to feel 'in control' of life, which becomes displaced onto controlling eating. This need for control may be greatest in those who are constitutionally anxious, perfectionist or lacking in self-esteem. The second is an overevaluation of shape and weight in those who have been sensitised to their appearance, either by prior experiences (e.g. childhood obesity, parental concerns about eating) or by the changes in shape that occur during puberty. In both instances, the resulting dietary restriction and weight loss are highly reinforcing. Subsequently, other processes serve to maintain the eating disorder. In patients who are severely underweight, certain physical symptoms of starvation, particularly the preoccupation with food and eating, heightened fullness as the result of delayed gastric emptying, and social withdrawal have this effect.

A handful of small studies have examined the efficacy of CBT in AN in adults.[11] These suggest that it may be moderately effective, although there is insufficient evidence to recommend it over other therapies. Some suggest that CBT may be effective at the symptomatic level, e.g. in improving self-esteem, but studies lack power. More recently, Fairburn's Oxford group have trialled their transdiagnostic modification of the well-researched CBT for bulimia nervosa programme. This form of CBT is showing good results in older adolescents and adults presenting with a BMI above 15.

Family-based therapies

The psychosomatic conceptual model of Minuchin *et al.*[17] stimulated considerable interest in the use of family interventions in AN, particularly in adolescents. Initially the rationale was based on the notion of the 'anorexogenic family', but empirical study has failed to support the aetiological role of family dysfunction and the model fuels concern about blaming parents. Family interventions have therefore developed as treatments which mobilise family resources, whether delivered as 'conjoint' family therapy, separated family therapy (in which parents and the child or adolescent patient are seen separately) or 'parental counselling'. There have been a number of RCTs, although the results are somewhat inconsistent. To date, several studies have compared different forms of family intervention in child and adolescent AN, but only two have compared family therapy with forms of individual therapy.

Russell *et al.*[18] in a trial of patients whose weight had been restored in a specialist inpatient service before randomisation, found that for a small group of adolescents ($n = 21$) with short duration of illness, family therapy was superior to individual therapy. The findings in relation to those who had been ill for more than 3 years were inconclusive and the outcomes were generally poor. Robin *et*

al.[19] compared the effect of Behavioural Family Systems Therapy (BFST) with Ego-Oriented Individual Therapy (EOIT) in 37 adolescents with AN. Parents in the EOIT group received separate parental counselling. There was no significant difference between groups for weight gained or for psychological measures; however, the BFST group had a greater change in BMI over time, although this probably reflected different baseline values between groups. By the 1-year follow-up 94% of the BFST group had resumed menstruation compared with 66% of the EOIT group; however, 43% of the series had also been hospitalised when their weight fell below 77% ideal body weight (IBW).

Two further studies[20,21] at the Maudsley Hospital (Denmark Hill, London, UK) compared conjoint family therapy with separated family therapy in which patients were seen on their own and parents were seen separately by the same therapist. The overall results were similar in the two trials, with a trend towards a superior outcome for the separated form of therapy. A small subgroup with high maternal expressed emotion did markedly better with separated family therapy.

Multiple family group therapy

The apparent effectiveness of family interventions with children and adolescents with AN and the need to develop more intensive family-based interventions for those who require it, led to the development of this treatment approach. The therapy aims to help family members learn by identifying with members of other families with the same condition, by analogy.[22] It is generally delivered within a day-hospital programme, in which up to 10 families with a child with AN, attend a mixture of whole family group discussions, parallel meetings of parents and adolescents and creative activities. Preparation of lunch and communal eating is a central part of the programme. There is generally a 4- to 5-day block of therapy followed by a limited number of day attendances at approximately monthly intervals.[23,24] This treatment is at an early stage of evaluation, but preliminary findings suggest a high degree of acceptability and promising outcomes particularly in terms of a reduced need for hospitalisation.[23]

Service issues

Various treatment settings have been used to manage AN. The main ones being outpatient, day-patient or partial hospitalisation, and inpatient treatment; and within these settings a variety of interventions may be provided, physical, psychological or both. To complicate matters, patients may move from one setting to another, and within any one setting often more than one treatment is employed.

Inpatient treatment is used differently in different places; for example, it is common in some countries but unusual in others, and length of stay also varies markedly.[25] Such differences are not evidence-based because inpatient treatment has received scant research attention. For example, not only are the indications for hospitalisation not established, but the specific goals are not agreed nor is it known how best to achieve them. At best, there is modest evidence from cohort studies to support a focus on eating and an emphasis on weight regain. Comparisons of flexible behavioural programmes with more rigid ones have either yielded no significant differences in the rate of weight regain or have favoured the more flexible regimes. There is no evidence that drug treatment significantly enhances weight regain.

Whatever the place of inpatient and day-patient treatment, outpatient treatment is the mainstay of the treatment of AN. Outpatient treatment is the sole treatment for many patients, and even if patients receive inpatient or day-patient treatment, it is usually followed by outpatient treatment. The choice of setting used to treat young people with AN has tended to be based on clinical judgement and the availability of different models of service rather than research evidence. Debate about the merits of inpatient management frequently fails to distinguish between (often brief) medical admission and longer psychiatric admission, aimed at a combination of weight restoration, normal eating and psychological change. Most young people with AN can be managed on an outpatient basis, with inpatient care being only required for a minority, where there are serious complications related to comorbid diagnoses, or where there is high physical or psychiatric risk.[26] When admission is deemed necessary this may be to a paediatric ward, a general child or adolescent psychiatric unit, or to a specialist eating disorder service.

Research in the area of service provision is limited. There is one systematic review summarising what is known about the relative effectiveness of inpatient and outpatient care across the age range.[27] However, the review was based on only one small RCT with a 5-year follow-up, often referred to as the St Georges study,[28,29] plus a number of very varied cohort series, making it difficult to draw

meaningful conclusions. The main conclusions of the systematic review are that outpatient treatment for AN at a specialist tertiary referral eating disorder service was as effective as inpatient treatment in those not so severely ill as to warrant emergency intervention, and that outpatient care is in general cheaper than inpatient care.

It is widely believed that there are advantages in treating severe AN within a specialised tertiary eating disorder service compared with less specialised secondary services. Both competence and confidence tend to develop in settings where such treatment is a regular and ongoing activity.

User satisfaction

A crucial issue in AN concerns the patient's attitude to the disorder. There is generally some ambivalence and at times determined opposition to treatment. Controversy also exists over the role of treatments given without the patient's consent. Patients may in certain circumstances be detained under the Mental Health Act (1983) but the NICE guideline expressed concern about the lack of clarity and openness around the treatment of young people when given on the basis of parental consent alone.[11]

Patient satisfaction has become increasingly important to the UK health-care industry and evaluation of the quality of health-care provision is essential for the improvement of services. However, there is a lack of clarity with regards to the definitions of service quality and satisfaction. Service quality and patient satisfaction are linked, indeed a South Korean study[30] recently found that 62% of the total variation in patient satisfaction was explained by service quality dimensions. Clearly when expectations of a service are greater than perceived performance, then quality will be judged as less satisfactory and dissatisfaction will be high. Those with eating disorders have been said to represent a unique group of health-care consumers among whom dissatisfaction tends to be high.[31] Furthermore, the source of negative commentary is often around activities and structures viewed as essential to traditional treatments.[32]

Economic aspects

As well as being associated with severe physical, psychological and social impairments and high levels of mortality,[11] AN places a significant cost-burden on young people, their families, health services and the wider society.[33,34] Inpatient admission for young people with AN is particularly disruptive to school, family and social life, and is an expensive option, yet evidence to support its cost-effectiveness is lacking.[11,35]

Rationale for the current trial

The recent research literature (confirmed during the course of the study by the NICE guideline) suggested that despite lengthy inpatient psychiatric treatment being commonly recommended as the 'gold standard' treatment for the condition,[36] there was little evidence to support this practice. The one small RCT of service setting showed no advantage of inpatient management over outpatient care for adults,[29] whereas our earlier cohort study[37] showed poor outcomes for adolescent inpatients. It seemed likely that inpatient management might be cost-ineffective. We were also aware of the low levels of satisfaction reported in some studies with inpatient management. Although, (in the course of this study) the NICE guideline recommended treatment in *specialist* settings, this has often been confused with treatment in *homogeneous* units in which all patients have the same condition. We therefore wished to explore the effectiveness of *specialist* services as described by the Eating Disorders section of the Royal College of Psychiatrists; that is, services with a dedicated, trained, multidisciplinary team treating a significant number of cases each year.

We report here a large population-based RCT of the three most common treatments available for adolescents with AN in the UK to compare the relative merits of inpatient psychiatric treatment and two forms of outpatient management, namely 'treatment as usual' in generic CAMHS, and a specialist multimodal multidisciplinary programme developed for the study.

Aims and objectives

The Treatment Outcome for Child and Adolescent Anorexia Nervosa (TOuCAN) trial aimed to compare the clinical effectiveness of inpatient against outpatient treatment and of generalist against specialist management, using a randomised design of three treatment approaches. The study also aimed to examine the cost-effectiveness of each approach, and user and carer satisfaction with each treatment. Subsidiary aims were to

measure the medium-term to long-term outcomes of the condition in a population-based cohort and identify predictors of outcome.

Hypotheses

The main hypotheses were:

Clinical

- The more intensive inpatient treatment would be more effective than outpatient treatment.
- Specialist treatment would be more effective than general CAMHS treatment.

Health economics

- Outpatient treatment (especially a specialist outpatient programme) would be more cost-effective than inpatient management.
- Specialist outpatient services would be more cost-effective than general treatment.

Satisfaction

- Carers (generally parents) would have higher expectations of treatment and would be more satisfied with it than young people with the disorder.
- Satisfaction would be higher with specialist treatment than with generalist treatment.

Subsidiary hypotheses

- For the total series, few patients would fully recover by 1 year after the start of treatment, but overall outcomes would improve at the 2-year and 5-year time points.
- For those in remission, subsequent relapse would be unusual during the course of the study.

Chapter 2
Methods

Trial procedures

Study population and participants

The trial took place in the north-west of England. The population (total 7.5 million) is served by 38 community CAMHS and four inpatient psychiatric units. The study aimed to recruit as complete a series as possible of consecutive cases of AN referred to community CAMHS. Thirty-five of the 38 CAMHS agreed to refer to the trial.

Inclusion criteria

Inclusion criteria were as follows:

Adolescents (male or female), age 12 to 18 years with a diagnosis of AN according to the *Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition* (DSM-IV) criteria modified for this age group as follows:

- food restriction +/– compensatory behaviours
- weight below 85% of that expected within 1 month of assessment, based on age and current height or previous height centile
- intense fear of gaining weight or undue influence of weight or shape on self-evaluation
- primary or secondary amenorrhoea for 3 months (in females), or menstruation only while on the contraceptive pill.

Exclusion criteria

Exclusion criteria were:

- those with severe learning difficulties
- presence of severe, chronic comorbid physical conditions affecting digestion or metabolism.

No exclusions were made on grounds of clinical severity, but the responsible clinician reserved the right to refer for acute medical management if required.

Recruitment and follow-up strategy

The CAMHS identified cases of probable AN and invited them to meet a representative of the research team. The researcher, supported by a clinician, then interviewed the young person (usually with a parental informant), confirmed the diagnosis and obtained informed consent to take part in the randomisation, along with completion of baseline measures. Those agreeing were sent an appointment at the allocated treatment facility closest to their home. The recruitment and consent strategy was approved by the north-west Multicentre Research Ethics Committee (ref no: MREC 99/8/21).

Follow-up interviews took place approximately 1, 2 and 5 years after baseline either at a local CAMHS or at the subject's home according to their preference. All interviews were carried out blind to treatment allocation by a research worker who had not been involved in recruitment and did not have access to the baseline database or recruitment file. Where the subject declined an interview, information was provided (with consent) by a relative (usually parent), a health-service professional involved in their care or (rarely) by telephone interview.

Randomisation and blinding

Treatment allocation was carried out by an independent randomisation service, by telephone, using stochastic minimisation controlling for sex, age above and below 16 years and BMI above and below 15.5.

Measures

Baseline

Interviewer-based measures

Clinical diagnosis (modified DSM-IV)

The use of the DSM-IV clinical diagnosis[38,39] as an entry criterion is described above.

Morgan–Russell Average Outcome Scale

The Morgan–Russell Average Outcome Scale (MRAOS)[40] adjusted for adolescents and used as a severity measure. This provides a quantitative score from 0 to 12 and a categorical measure (good, intermediate and poor), in which a good outcome represents weight restoration,

return of menstruation and absence of bulimia, a poor outcome represents continuing AN and an intermediate outcome represents weight restoration without resumption of normal hormone functioning or frequent engagement in bingeing or purging. It has been widely used in AN research.[18,21,28,40,41]

Health of the Nation Outcome Scale for Children and Adolescents

The 13-item clinician-rated measure Health of the Nation Outcome Scale for Children and Adolescents (HoNOSCA-CR)[42] yields a total severity and outcome score and has been shown to be reliable, valid and sensitive to change.[43,44] It has been used as the main outcome measure in treatment trials in adolescent mental health.[45]

Subject ratings

Eating Disorder Inventory-2

The Eating Disorder Inventory-2 is a self-rated questionnaire covering 12 domains of eating cognitions, behaviours and social functioning.[46] Total and subscale scores can be generated, with satisfactory validity and sensitivity to change.

HoNOSCA-SR

The adolescent self-rated (i.e. SR) version of HoNOSCA, covers the same 13 generic items as the clinician-rated measure.[47]

Family Assessment Device

The Family Assessment Device (FAD)[48] is a self-report questionnaire designed to evaluate family functioning based on the seven subscales of the McMaster model.

Recent Mood and Feelings Questionnaire

A 42-item questionnaire to rate depression, the recent Mood and Feelings Questionnaire (MFQ)[49] has good properties in clinical adolescent samples.[50]

Follow-up (1, 2 and 5 years)

The same measures were completed at follow-up, (the main outcome measure being the MRAOS) and with the addition of the Eating Disorder Examination (EDE) at 5 years.

Eating Disorder Examination

The EDE is a semi-structured interview that has been developed as a measure of the specific psychopathology of AN and bulimia nervosa.[53] It comprises five subscales covering eating, weight concern, shape concern, restraint and binge eating.

Satisfaction measures

Satisfaction questionnaires

Two questionnaires designed for the purpose of the study asked young people and their carers (independently) about any of the researched treatments they had received (randomised or not), at the 1-year and 2-year follow-up. They were asked to rate on a seven-point Likert scale (from very positive to very negative) their prior expectations of the treatment and subsequently (on the same scale) their satisfaction with it. Space was allocated for any further free comments about any treatment received.

Focus groups

All participants at 2-year follow-up were invited to attend focus groups in Chester or Manchester to expand on their experiences.

Sample size

The sample size was calculated using the main outcome measure, the MRAOS. Based on our previous findings,[40] an effect size of 1.5 units on this primary outcome was considered to be a clinically important difference. This also suggested a within-group standard deviation (SD) of 2.3 units on the MRAOS, a 2.5% two-sided significance level to adjust for two treatment group comparisons. Samples comprising 62 and 46 subjects per treatment arm would have 90% and 80% power, respectively, to detect this effect size. Initially, it was proposed to recruit 72 subjects per arm, but at a Health Technology Assessment review this was reduced to 57 subjects in each of the three groups. The study therefore had 80% power to detect a difference of this magnitude assuming an 85% follow-up rate.

Reliability of assessment measures:

Inter-rater reliability series involving 154 subjects and three ratings per subject were carried out within research site and between sites at baseline. For MRAOS the intraclass correlation coefficients were as follows: within-site: Manchester 0.93, Liverpool 0.97, between-sites: 0.96, and the inter-rater reliability was 0.93 at 1 year and 0.90 at 2 years. For HoNOSCA the intraclass correlations were: within-site: Manchester 0.83, Liverpool 0.98, between-sites: 0.87, and the inter-rater reliability was 0.89 at both 1 and 2 years.

Case ascertainment

Cases were diagnosed on clinical grounds by a qualified child and adolescent psychiatrist using the inclusion diagnostic criteria above. The researcher checked the recorded clinical features

against a checklist and essential features (e.g. low weight for height, presence of amenorrhoea, weight concern) were confirmed by completion of the global MRAOS, which includes these clinical features.

Treatments

Inpatient psychiatric treatment – four services

This was provided within the regional children's or adolescent psychiatric inpatient units. All four services had substantial experience and expertise in treating eating disorders. They were not however *exclusive* eating disorder services. In keeping with the national census findings,[5] AN often comprised the most prevalent diagnosis within the units. Treatment lasted 6 weeks in the first instance, extended as clinically indicated and determined by the treating service. The treatment was not manualised, but services met at the outset to identify core elements in treatment. They all used a multidisciplinary psychiatric approach with the aim of normalising eating, restoring healthy weight and facilitating psychological (cognitive) change. Each subject received both individual supportive or cognitive therapies and family therapy. All services had staff who were trained and experienced in family therapy, but not necessarily family interventions specifically for eating disorders. There was a high expectation of early behavioural change and services employed a weight restoration programme with an expected weight increase of 800–1000 g per week. Patients were ambulant and attended the unit school subject to medical stability. Nasogastric feeding was rarely employed and the services aimed to avoid coercive treatment practices.

Specialised outpatient treatment – two services

This programme was manualised and devised for the trial. It comprised an initial motivational interview, individual CBT plus parental feedback (12 sessions), parental counselling with the patient (minimum four sessions, increasing to eight for younger patients), dietary therapy (four sessions, with parental involvement as required), and multimodal feedback (weight, self-report and clinician-rated questionnaire) and monitoring (four sessions). The treatment was designed to last 6 months. The CBT programme and parental counselling were provided by a trained member of the eating disorder team, with good experience of behavioural management of eating disorders and addressing the typical cognitions. They had pilot experience of the manualised treatment, but they represented a range of disciplines and their formal training in CBT was variable and sometimes only at foundation level. The same therapist provided feedback to the patient every 6 weeks, reviewing the physical and self-report questionnaire data. The aim was to demonstrate an association between weight gain and *reduced* self-reported psychopathology, to motivate the patient to take the next steps to recovery. Dietetic therapy was provided by a trained dietician working as a fully integrated member of the team. This treatment has been described in detail[52] along with the rationale behind it.[55] Checks of treatment fidelity were made at weekly joint meetings between the clinical and research teams. Travel times to the specialist services were generally under 90 minutes, by either car or public transport.

Treatment as usual in general community CAMHS

This was not a manualised treatment, but comprised the usual first-line treatment approach that young people in the UK receive. The 35 services provided (generally) a multidisciplinary, family-based approach, with variable dietetic, individual supportive therapy and paediatric (medical) liaison. As the study aimed to compare the specialised treatment with 'treatment as usual', the latter was not prescriptive and the outpatient arms were not matched for intensity; however, the duration of therapy was set at 6 months.

Data analytic strategy and methods

Comparison of randomised treatment groups

Statistical analysis of the three randomised treatment groups was based on the intention-to-treat principle subject to the availability of data. Clinical outcome was measured at 1, 2 and 5 years. Preliminary analysis investigated the pattern of missing outcome data comparing baseline characteristics of subjects with and without follow-up data.

Longitudinal modelling of treatment effects for quantitative outcomes

Statistical analysis of continuous clinical outcome measures combined the data from the 1-, 2- and 5-year assessments in a longitudinal analysis using a linear mixed model.[56] Unlike some forms of longitudinal analysis, such as repeated measures analysis of variance, a linear mixed model does not require complete follow-up data for all subjects. In

a longitudinal analysis of trial data the treatment effect, by which one means a difference between randomised groups, can be a *treatment group with time interaction*, that is the difference between treatment groups changes over time during the follow-up period. Alternatively, there may be a constant difference in the mean value of the outcome measure throughout the follow-up period, sometimes called the *main effect of treatment*. As a result of the unequal spacing (1, 2, 5 years) the *assessment number,* rather than the time to follow-up assessment, was included as the time covariate. This was chosen to prevent the 5-year assessment having undue influence on the analyses. Hence, the time effect was assessed by the *assessment number* with the treatment-group interaction term and the main effect by the covariate for treatment group.

Where there is evidence of an assessment with treatment-group interaction, the covariate of treatment group cannot be easily interpreted because the treatment effect is changing between assessments. In this case, the separate analysis for each assessment (1, 2 or 5 years) provides a method of interpretation. Hence, where there is an interaction, the *p*-value for the cross-sectional analysis at the 1-, 2- and 5-year assessments has been given in the relevant summary table. If there is no evidence of an assessment with treatment-group interaction, the model was refitted without the interaction term to estimate the main effect of treatment, and a *p*-value has not been given for the cross-sectional analysis. The distributional assumptions of the model were checked using normal probability plots for assessment and subject level residuals.

Analysis of diagnostic outcome category

Diagnostic outcome category (poor, intermediate, good) was modelled using ordinal logistic regression with the same covariates.[57] In this case, the longitudinal data analysis was carried out estimating the marginal effect of treatment rather than the subject-specific effect using a standard ordinal logistic regression with robust standard errors.

Baseline covariates

For the analysis of each variable, the baseline values of that measure, and the variables in minimisation (age at randomisation, gender, age, baseline MFQ and baseline MRAOS) were included as covariates in the model.

Multiplicity

One issue in quantitative studies is multiplicity, as the result of either multiple groups or multiple outcome measures. An option is to adjust *p*-values or significance levels for this. Such procedures can be highly conservative, particularly with multiple outcomes because these tend to be correlated.

Where more than two treatment groups are employed, various comparisons can be made between treatment groups. With three treatment groups there are six possible contrasts that can be made. Following the studies objectives, two contrasts were considered to be of primary interest, first a comparison of outpatient treatments with inpatient treatment and second a comparison of specialist treatments with routine CAMHS treatment.

Sample size used a significance level of 2.5% to allow for multiplicity. A Bonferroni correction has not therefore been made to *p*-values, but readers may wish to use a 2.5% significance level instead of the conventional 5% level.

Baseline predictors of clinical outcome and service use

Secondary analyses investigated baseline predictors of clinical outcome measures and service use. Clinical outcome measures considered were:

- % weight for height
- self-reports of morbidity [Eating Disorders Inventory second edition (EDI-2) total score, MFQ, HoNOSCA-SR]
- researcher-assessed morbidity (MRAOS, HoNOSCA-CR)
- family functioning [FAD-General Functioning (-GF)]
- separate analyses were carried out for 1-, 2- and 5-year follow-up data.

Service use measures considered were:

- hospital admissions within 2 years
- time until first hospital admission
- number of hospital admissions
- number of inpatient days for admitted patients
- still in treatment at 1 and 2 years.

The following baseline variables were considered as potential predictors:

- age of patient at outset of study
- gender

- length of history of eating disorder (< 15 months, ≥ 15 months)
- diagnostic subtype (restrictor, binge–purger)
- site (Mersey/north-west)
- % weight for height
- self-reports of morbidity (EDI-2 total score, MFQ, HoNOSCA-SR)
- research-assessed morbidity (MRAOS, HoNOSCA-CR)
- family functioning (FAD-GF).

One approach to identifying predictor variables is to apply backward stepwise selection procedures to a pool of candidate variables. A limitation of this method is that the estimated coefficients of any selected variable may overestimate the effect of that variable. Correlations between variables, mean that the coefficients of variables finally selected for the model may include the causal effect of other variables that have been excluded from the model. (Suppose two variables A and B predict outcome Y, and suppose that A is a stronger predictor of Y than B. If A and B are correlated and if B is dropped from the model, the coefficient for A may increase because it may now include some of the effect of B.)

Two analyses are therefore presented. The first gives the coefficients of a model where the variables have been selected by backward stepwise selection. The second gives the corresponding coefficient for the selected variables from the full-model, including all covariates, to give an indication of the overprediction caused by stepwise selection.

For quantitative clinical outcome measures, standardised beta-coefficients are given as a measure of the effect of a variable. These express the effect on a dimensionless scale thereby enabling comparison of effect between different predictor variables. For binary outcome variables, the adjusted odds is given. For ordered categorical outcome variables, the adjusted odds common odds ratios are given. These are estimated using binary or ordinal logistic regression models. The adjusted hazard ratio, estimated using a Cox proportional hazard model, is used for modelling time until admission.

Inclusion of highly correlated predictor variables can give contradictory results symptomatic of overfitting the data. Some predictor variables were strongly correlated. For example EDI-2 total score, MFQ and HoNOSCA-SR at baseline were quite strongly correlated, with correlation coefficients ranging from 0.69 to 0.80. Where there is correlation between predictor variables, models with different variables may have very similar fit. For example when EDI-total score at 1 year was considered, models including either MFQ or EDI-total score at baseline had very similar values of r-squared. Results of the predictor analyses should therefore be interpreted with care. Hence, inclusion of any one of MFQ, EDI or HoNOSCA-SR is perhaps best interpreted as suggesting any self-assessed morbidity is important, rather than as a prediction due to specific measure of morbidity.

Economic evaluation methods

Perspective and data collection

At the 2-year follow-up, the economic evaluation took a broad service-providing perspective, including costs to the health, social services, education, voluntary and private sectors. Resource use data were collected in interview at the 1- and 2-year follow-up assessments using the Child and Adolescent Service Use Schedule (CA-SUS), developed by the authors in previous research with young people and adapted for the purpose of the current study.[58–60] Information on hospital contacts were collected from clinical records to avoid patients un-blinding research assessors in follow-up interviews. In addition, the use of primary and secondary hospital and community health-care services (including NHS, private and voluntary sectors) by the young person's primary carer were collected at the 1- and 2-year follow-ups using the Carer Service Use Schedule (CARER-SUS), which was developed and used by the authors previously in similar research.[46]

At the 5-year follow-up, a brief version of the CA-SUS was used to collect resource use information on the participant's use of services for the 3-year period between the 2-year and final 5-year follow-up interviews. The CA-SUS was limited to use of key resources (high cost and/or high probability of use) anticipated to be relatively easy to recall over this period of time, including hospital services, information on accommodation and employment and use of benefits. The decision to focus on key services was taken: (1) to reduce the problem of inaccurate recollection of less significant service contacts and (2) because the relative expense of these key services is likely to over-ride any differences in less resource-intensive services; hence, although absolute costs may be underestimated, relative costs are unlikely to be greatly affected. The brief CA-SUS was completed by participant self-report in the final follow-up interview.

Unit cost calculation

All unit costs were for the financial year 2003–4. A summary of the unit costs applied is provided in *Table 1*. Local unit costs were applied to hospital data and data on schools attended. Nationally applicable unit costs were applied to services that make a much smaller contribution to total costs, such as community health and social services and medication. Trust-specific costs for NHS hospital contacts, including the trial interventions, were sourced from NHS reference costs.[61] Unit costs for inpatient stays and outpatient appointments in private sector services were collected through direct personal communication with each facility. Community health and social services costs were taken from national publications.[62] The costs of mainstream and specialist schooling came from a number of sources including various OFSTED reports (the inspectorate and regulatory body for schools in England – see www.ofsted.gov.uk) and published documents.[63] The cost of medications was calculated using the British National Formulary.[64] Where necessary, unit costs were inflated to 2003–4 costs using the Hospital and Community Health Services inflation indices.[61] For the economic evaluation carried out at the 2-year follow-up, costs in the second year were discounted at a rate of 3.5%, as recommended by NICE.[65] The rate was varied from 0% to 6% in sensitivity analysis. For the economic analyses carried out at the 5-year follow-up point, costs are presented in 2003–4 prices.

TABLE 1 *TOuCAN unit costs for 2003–4*

Service	Unit cost (£)	Source
Hospital		
Inpatient (night)	195.00–520.00	Department of Health (2004)[59]
Outpatient (appointment)	31.00–307.00	
Day patient (attendance)	89.00–381.00	
Accident and emergency (attendance)	97.00	
Community		
General practitioner (per minute contact)	1.73	Curtis and Netten (2004)[60]
Practice nurse (per minute contact)	0.42	
Dietician (per minute contact)	0.87	
District nurse (per minute contact)	0.78	
Health visitor (per minute contact)	1.08	
Community paediatrician (per minute contact)	1.73	
Community nurse (per minute contact)	0.42	
Clinical psychologist (per minute contact)	0.68	
Counsellor (per minute contact)	0.55	
Family therapist (per minute contact)	0.55	
Dentist (per examination)	6.49	
School doctor (per minute contact)	1.73	
School nurse (per minute contact)	0.42	
Social worker (per minute contact)	0.53	
Foster care (per night)	66.00	
Education		
Day school (per day)	15.50–19.94	Curtis and Netten (2004)[60], Independent Schools Council (2004)[61]
Boarding school (per day)	27.00	
Hospital school (per day)	129.60	
Home tuition (per hour)	34.34	
School counsellor (per minute contact)	0.55	
Education welfare officer (per minute contact)	0.45	

Economic evaluation at 2-year follow-up

Economic analyses were carried out on an intention-to-treat basis using a statistical analysis plan drawn up before the analysis of the data. The primary analysis was of total costs over 2 years for the sample of young people with complete service use data who entered the RCT.

Differences in service use are reported descriptively and are not compared statistically to avoid problems associated with multiple testing, and because the focus of the economic evaluation was on costs and cost-effectiveness. As is common in such data sets, costs were not normally distributed. Analyses compared mean costs in the three groups using analysis of covariance with covariates for prespecified baseline characteristics: site (Liverpool and Manchester), gender, age at baseline, baseline BMI and baseline MRAOS score. Because of the non-normal distribution of the data, the robustness of the parametric tests was confirmed using bootstrapping,[66] as recommended by Barber and Thompson.[67] The primary analysis was of the sample of young people with complete service use data; the impact of dropout was assessed by comparing the baseline characteristics of patients who had missing data with those of patients who had full economic data.

Cost-effectiveness was assessed through the calculation of incremental cost-effectiveness ratios (ICERs)—the additional costs of one intervention compared with another, divided by the additional effects of one intervention compared with another,[68] in this case using the MRAOS measure of effectiveness. When more than two strategies are compared, as is the case in this study, ICERs are calculated using rules of dominance and extended dominance.[69] In this approach, strategies are ranked by cost, from the least expensive to the most expensive, and if a strategy is more expensive and less effective than the previous strategy, it is said to be dominated and is excluded from the calculation of ICERs. Hence, this process compares strategies in terms of observed differences in costs and effects, regardless of the statistical significance of the difference.

Uncertainty around the cost and effectiveness estimates was represented by plotting cost-effectiveness acceptability curves.[68,70]. Repeat resampling from the costs and effectiveness data (bootstrapping) was used to generate a distribution of mean costs and effects for the three treatments. These distributions were used to calculate the probability that each of the treatments is the optimal choice, subject to a range of possible maximum values (a ceiling ratio, λ) and that a decision-maker might be willing to pay for a unit improvement in MRAOS score. The cost-effectiveness acceptability curves are presented by plotting these probabilities for a range of possible values of the ceiling ratio and so they incorporate (1) the uncertainty that exists around the estimates of mean costs and effects as a result of sampling variation and (2) the uncertainty regarding the maximum cost-effectiveness ratio that a decision-maker would consider acceptable.[71]

Missing data were explored in three sensitivity analyses using the following data: (1) hospital cost data collected from clinical records and available for a larger sample of young people than full economic data from the CA-SUS; (2) hospital cost data collected from records plus missing non-hospital cost data imputed using the last value carried forward approach for participants with missing year 2 data; and (3) hospital cost data collected from records plus mean imputation by randomised group of missing non-hospital cost data.

Economic evaluation at 5-year follow-up

No analysis of cost-effectiveness between randomised groups was carried out using the 5-year data because of the substantial amount of further treatments received in this period and the small sample sizes. However, differences in the use of hospital services between randomised groups are explored. Use of accommodation and rates of employment over the 3-year period between 2-year and final follow-up are reported descriptively for the cohort as a whole, including both randomised and preference groups.

Total hospital costs for the full cohort (randomised plus preference) over the 5-year follow-up period (1-year plus 2-year plus 5-year data) were calculated, and a regression analysis was carried out to explore baseline characteristics that predict high or low costs in terms of use of hospital services over the full 5-year follow-up period. To identify possible predictors, we examined studies that had previously explored the impact of baseline characteristics on service use and costs in adolescents with mental health problems,[45,72] although we did not identify any relevant papers in

eating disorders. The list of possible predictors was then developed and discussed with the TOuCAN research team.

Univariate associations between each of the specified predictors and total hospital costs over 5 years were explored first in a linear regression. For continuous variables, although analyses were carried out on continuous data, results are presented in two groups split at the median. Multiple regression was then used to reduce the variable set to those factors independently associated with costs. The multiple regression initially included all variables that had significant univariate associations with cost, discarding from the model all variables that were no longer found to be important. Variables that did not have a univariate association were then added and retained if they added significantly to the model, or otherwise discarded. The model arrived at was checked to ensure that no variables excluded would add significantly to it.[73] A significance level of around 10% was used though not strictly applied.

Chapter 3
Results

Baseline characteristics

Demographic characteristics of randomised subjects

Subjects were aged between 11 years 11 months and 17 years 11 months, mean age 14 years 11 months. One hundred and fifty-three (92%) were female; 127 (78%) experienced the restricting subtype, 40 (24%) and had the binge–purging subtype of AN. Mean length of history was 13 months. One hundred and four (64.3%) lived with both biological parents, 32 with mother (19.2%) and six (3.6%) with the father. Eleven (6.6%) lived with mother and stepfather and 13 (7.8%) in other arrangements (one case not known). There were no significant differences between the samples recruited from the Manchester site ($n = 80$) and the Liverpool site ($n = 87$).

Clinical features

Table 2 and *Table 3* show the presenting features of the three randomised treatment arms and the preference group. They were generally a moderately to severely ill group (mean weight for height 80.0%, lowest 59.9%). Eight cases had a weight for height above the diagnostic threshold for AN. Of these, four were included because they lost significant weight in the 4 weeks following assessment, or they had previously attained a greater height percentile, suggesting stunting of growth. While four others with borderline weights were included because they fulfilled the other criteria plus significant (> 15% and generally > 20%) weight loss with amenorrhoea. Five cases were sporadically menstruating, but at < 85% weight for height.

There were no significant differences between groups on any variable including length of history. For the EDI, MFQ, FAD and HoNOSCA a higher score indicates greater difficulty, whereas the Morgan–Russell Scales indicate greater clinical severity by a lower score. Characteristics of all four groups were similar, although the non-randomised preference group was slightly older, contained more patients with a longer history of eating disorder and tended to have worse morbidity at baseline with a lower % weight for height and MRAOS.

Adherence to treatment allocation and withdrawals

Despite all randomised subjects agreeing to randomisation at the point of giving signed informed consent, adherence to allocated

TABLE 2 *Categorical baseline characteristics by treatment group: frequency (%)*

	General CAMHS ($n = 55$)	Specialist outpatient ($n = 55$)	Specialist inpatient ($n = 57$)	Preference ($n = 48$)
Site				
Mersey	29 (53)	25 (45)	33 (58)	31 (65)
North-west	26 (47)	30 (55)	24 (42)	17 (35)
Female	51 (93)	51 (93)	51 (89)	46 (96)
Subtype				
Restrictor	44 (80)	42 (76)	41 (72)	35 (73)
Binge–purger	11 (20)	13 (24)	16 (28)	13 (27)
History (months)				
< 15	36 (65)	34 (62)	41 (72)	19 (40)
> 15	18 (33)	16 (29)	13 (23)	26 (54)
Not known	1 (2)	5 (9)	3 (5)	3 (6)

TABLE 3 *Quantitative baseline characteristics by treatment group*

	General CAMHS			Specialist outpatient			Specialist inpatient			Preference		
	Mean	**(SD)**	***n***	**Mean**	**(SD)**	***n***	**Mean**	**(SD)**	***n***	**Mean**	**(SD)**	***n***
Age (years)	14.97	(1.40)	55	15.09	(1.22)	55	14.88	(1.46)	57	15.40	(1.76)	48
Morgan–Russell Scales												
A (Food intake)	3.09	(1.63)	55	3.36	(1.99)	55	3.30	(1.74)	57	2.67	(2.16)	48
B (Menstruation)	1.00	(2.41)	48	0.80	(2.14)	50	0.87	(2.52)	46	0.74	(2.00)	43
C (Mental state)	5.31	(2.18)	55	5.24	(1.87)	55	5.47	(1.95)	57	5.33	(2.08)	48
D (Psychosexual state)	5.53	(2.65)	55	5.84	(2.82)	55	6.57	(2.87)	56	5.64	(3.26)	45
E (Socioeconomic state)	7.84	(1.98)	55	7.21	(2.99)	55	8.11	(2.17)	57	7.17	(2.68)	48
MRAOS (average of all scales)[a]	4.67	(1.27)	55	4.56	(1.46)	55	5.05	(1.46)	57	4.38	(1.59)	48
Weight for height (%)	78.80	(7.86)	55	77.14	(8.10)	55	78.16	(8.08)	57	74.82	(9.30)	48
Body mass index	15.48	(1.60)	55	15.25	(1.58)	55	15.29	(1.65)	57	14.85	(1.78)	48
EDI-2 total	88.48	(51.36)	52	86.52	(47.53)	54	89.61	(44.52)	56	89.76	(45.76)	41
MFQ total	32.36	(16.12)	53	30.09	(14.70)	54	32.55	(14.60)	56	32.20	(14.67)	44
FAD-GF	2.13	(0.59)	52	2.12	(0.53)	54	2.08	(0.49)	56	2.08	(0.58)	41
HoNOSCA												
Clinician-rated	20.04	(5.72)	55	20.71	(7.50)	55	20.04	(5.63)	57	20.98	(5.94)	48
Self-rated	16.46	(9.95)	54	17.40	(9.88)	53	15.64	(9.54)	53	15.70	(9.89)	43

a Primary outcome measure at baseline.

treatment was only 67% and varied between groups (*Figure 1*). To a large extent this lack of adherence is in the nature of the condition and the attitude of patients with AN to treatment. Explanation of the failure of adherence was as follows:

- *Inpatient treatment adherence rate* = 28/59 (49.1%) (defined as a minimum 4-week inpatient stay). In most cases, those failing to adhere agreed initially to admission and then bargained their way out by achieving a small weight gain in the short time between randomisation and admission. Mean length of stay for those admitted was 15.2 weeks.
- *Specialist outpatient adherence rate* = 41/57 (76.5%) (defined as a minimum of six attendances). Of the remainder, 10 changed their mind and opted for general CAMHS treatment (generally because of travelling distance), three were admitted before treatment could start and one dropped out of all treatment.
- *General CAMHS adherence rate* = 38/57 (71.1%) [defined as attending general CAMHS and no other treatment (beyond possibly specialist second opinion) in the initial 6-month phase]. Two of the remainder had no treatment, four opted for specialist outpatient treatment, while 11 were referred to an alternative by clinician preference (10 inpatient, one specialist outpatient).

Clinical outcomes

Tracing and completion of follow-up assessments

The main outcome point determined at the start of the trial was 2 years. To this point, every subject was traced, with the main outcome measures completed as follows: diagnostic outcome and outcome category 164 (98%) at 1 year, 160 (96%) at 2 years; MRAOS 157 (94%) at 1 year, 155 (93%) at 2 years; BMI/weight for height 154 (92%) at 1 year, 150 (90%) at 2 years; HoNOSCA 154 (92%) at 1 year, 155 (93%) at 2 years. These were achieved by face-to-face interview in 129 (79%) at 1 year and 121 (75%) at 2 years. Outcome data

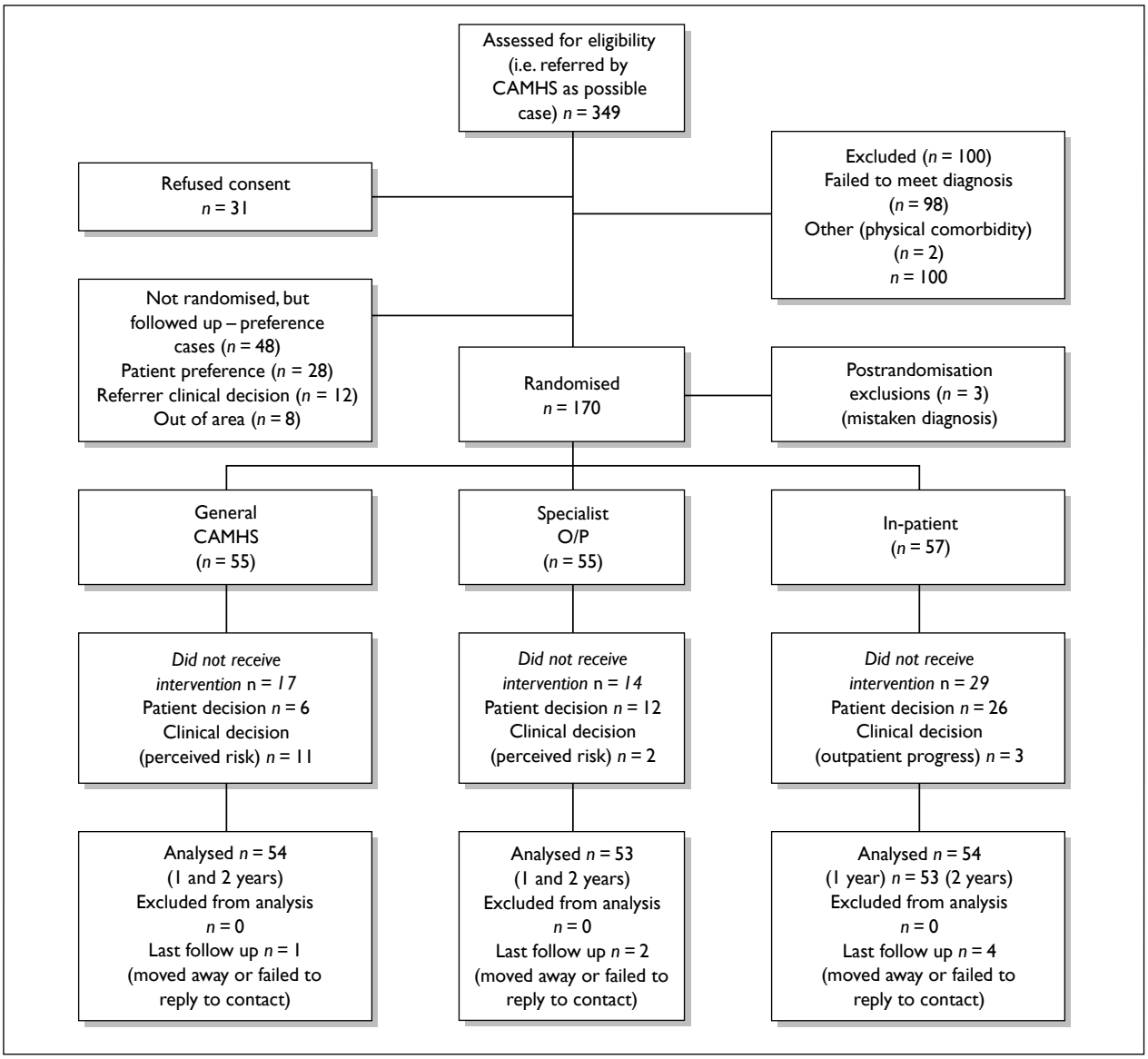

FIGURE 1 *TOuCAN trial – recruitment.*

were obtained by telephone interview or interview with a health professional informant with recent knowledge of the case in 34 (20%) at 1 year and 40 (24%) at 2 years. The remaining four at 1 year and six at 2 years were all traced (alive) but little or no information was obtained on their health status.

At 5 years, the rate of completion of follow-up was much lower, largely because of refusals to take part, but also because subjects were not traced. In large part, this was likely to be because the mean age of subjects at 5 years was 20 years. Many would have left home to attend higher education and they were no longer likely to be persuaded by parents to take part. The number followed up at 5 years was: diagnostic outcome and outcome category 97 (60%), MRAOS 81 (47%). Similar levels of follow-up were seen for HoNOSCA-CR and % weight for height. Lower levels of follow-up were observed for patient-completed outcomes (MFQ, EDI-2 and HoNOSCA-SR). For the MFQ the follow-up rate at 1, 2 and 5 years was 81%, 77% and 43%, respectively. Two patients died during the course of the study (and are included at the relevant time point as having a poor outcome) – one died by 2 years of an apparently unrelated physical illness, the other at 5 years of a drug overdose.

Baseline characteristics of patients with and without follow-up are given in *Table 4* and *Table 5*. The proportion of subjects with follow-up assessments for the primary outcome were similar between treatment groups for the year 1 and year 2 assessments, but at 5 years a smaller proportion

TABLE 4 *Baseline characteristics of subjects with and without the primary outcome measure for each follow-up assessment (randomised cases only): categorical measures*

			Year 1		Year 2		Year 5	
		(*n*)	Followed up	(%)	Followed up	(%)	Followed up	(%)
Site	Mersey	(87)	84	97%	81	93%	46	53%
	North-west	(80)	73	91%	74	93%	33	41%
Gender	Male	(14)	13	93%	13	93%	4	29%
	Female	(153)	144	94%	142	93%	75	49%
Type	Restrictor	(127)	119	94%	117	92%	61	48%
	Binge–purger	(40)	38	95%	38	95%	18	45%
History	< 15 months	(111)	104	94%	103	93%	58	52%
	≥ 15 months	(47)	44	94%	43	91%	18	38%
Treatment arm	General CAMHS	(55)	53	96%	52	95%	19	35%
	Specialised outpatient	(55)	52	95%	51	93%	31	56%
	Specialised inpatient	(57)	52	91%	52	91%	29	51%

of subjects in the general CAMHS treatment group (35%) were followed up, compared with specialist outpatient treatment (58%) and specialist inpatient treatment (53%). Quantitative characteristics of the groups were similar, although at 5 years followed up subjects tended to have a lower baseline HoNOSCA-SR, and a higher MRAOS, i.e. were slightly healthier at baseline.

All groups made substantial mean improvements in terms of weight, global measures and self-reported psychopathology by 1 year, with further significant improvement by 2 years. *Table 6* and *Table 7* summarise the quantitative outcomes at 1, 2 and 5 years. By intention-to-treat there are no statistically significant differences between the three groups at 1 year or 2 years. In particular, the mean values on the MRAOS were remarkably similar across the treatments. Confidence intervals are also presented for the comparison of inpatient treatment with outpatient and for general CAMHS treatment with specialist treatment for 1 year, 2 years and 5 years.

Mixed Model Analysis of Quantitative Outcome

As outlined in the analysis plan, two comparisons were made between the three randomised groups. First, between inpatient treatment and outpatient treatment (general CAMHS and specialist) and second between general CAMHS and specialist treatment (outpatient and inpatient).

Comparison of inpatient with outpatient treatment

Table 6 and *Table 7* summarise the outcome for the quantitative outcome measures and give confidence intervals for the two planned comparisons.

When a linear mixed model was fitted including the assessment point (1, 2, 5 years) with treatment–group interaction, there were no interactions between assessment and treatment for the primary outcome measure (MRAOS), nor for the secondary outcome measures (*Table 8*) for this comparison. When the model was refitted without an interaction there was no main effect of inpatient treatment for MRAOS or the secondary measures. In a further analysis, not presented here, there was no treatment by site interaction. No further subgroup analyses of potential moderators have been carried out.

The analyses suggest no advantage for inpatient over outpatient treatment.

Comparison of specialist treatment with general CAMHS

In the comparison of specialist services with general CAMHS, there was no interaction between assessment and treatment in the linear mixed

TABLE 5 *Baseline characteristics of subjects with and without the primary outcome measure for each follow-up assessment (randomised cases only): quantitative measures*

	Without follow-up			With follow-up		
	Mean	**SD**	***n***	**Mean**	**SD**	***n***
Year 1						
Age (years)	14.86	1.50	10	14.99	1.35	157
MRAOS (average of all scales)	4.30	1.38	10	4.79	1.41	157
Weight for height (%)	80.00	7.19	10	77.91	8.05	157
EDI-2 total	88.22	70.07	9	88.22	46.19	153
MFQ total	2.12	0.54	9	2.11	0.54	153
FAD–general functioning	32.22	15.34	9	31.64	15.13	154
HoNOSCA-CR	21.70	6.04	10	20.17	6.33	157
HoNOSCA-SR	19.78	12.73	9	16.30	9.57	151
Year 2						
Age (years)	14.35	1.41	12	15.03	1.35	155
MRAOS (average of all scales)	4.25	1.42	12	4.80	1.41	155
Weight for height (%)	77.07	8.86	12	78.11	7.95	155
EDI-2 total	61.00	40.52	11	90.20	47.49	151
MFQ total	2.15	0.52	11	2.11	0.54	151
FAD– general functioning	28.55	16.68	11	31.90	15.01	152
HoNOSCA-CR	22.75	7.64	12	20.06	6.17	155
HoNOSCA-SR	17.18	10.21	11	16.45	9.76	149
Year 5						
Age (years)	14.86	1.39	88	15.11	1.32	79
MRAOS (average of all scales)	4.65	1.47	88	4.89	1.34	79
Weight for height (%)	77.79	7.87	88	78.31	8.17	79
EDI-2 total	86.37	49.84	86	90.30	44.98	76
MFQ total	2.18	0.50	86	2.04	0.57	76
FAD–general functioning	32.51	15.04	86	30.74	15.19	77
HoNOSCA-CR	20.85	5.89	88	19.59	6.71	79
HoNOSCA-SR	18.33	10.08	84	14.47	9.03	76

model analyses for the primary outcome measure except for the secondary outcome measures % weight for height and FAD-GF. In both cases, the direction of the interactions suggested that the outcome for specialist treatments tended to improve relative to general CAMHS over time. There was an increased effect of specialist treatment relative to general CAMHS between consecutive assessments of 2.80 (95% CI 0.31 to 5.29 $p = 0.027$). At the 1-year and 2-year follow-ups the general CAMHS treatment gave slightly better (but non-significant) outcomes than the two specialist treatments for % weight for height.

Patients in the specialist treatments reported better outcomes at 5 years than those on CAMHS treatment ($p = 0.02$, see *Table 7*). For FAD-GF specialist treatments reported a better outcome at 5 years, but this finding was not statistically significant. It should be noted, that the proportion of subjects followed up to 5 years is low and varied between treatment arms [general CAMHS 36% (20/57), specialist outpatient 58% (31/57), specialist inpatient 42% (24/59)], so that differences between treatments at 5 years may therefore be based on selection effects with the follow-up influenced by randomisation; as the reduced follow-up in the CAMHS arm may arise because of the reduced contact of trial subjects with specialist services.

When the model was refitted without an interaction there was a significant main effect of specialist

TABLE 6 *Summary statistic and intention-to-treat analysis of 1-year and 2-year outcomes for Morgan–Russell Scales*

		General CAMHS			Specialist outpatient			Specialist inpatient			Inpatient–Outpatient		Specialist–General	
Assessment		**Mean**	**(SD)**	***n***	**Mean**	**(SD)**	***n***	**Mean**	**(SD)**	***n***	**Diff.[a]**	**(95% CI)**	**Diff.[a]**	**(95% CI)**
A (Food intake)	Baseline	3.09	(1.63)	55	3.36	(1.99)	55	3.30	(1.74)	57				
	1 year	7.78	(2.65)	53	7.43	(2.77)	52	6.98	(2.95)	52	−0.77	(−1.73 to 0.18)	−0.53	(−1.46 to 0.41)
	2 years	7.88	(2.75)	52	8.11	(2.63)	51	7.49	(3.25)	52	−0.55	(−1.58 to 0.47)	−0.11	(−1.11 to 0.89)
	5 years	8.42	(3.25)	19	8.28	(3.20)	31	9.19	(2.96)	29	0.72	(−0.75 to 2.19)	0.78	(−0.86 to 2.42)
B (Menstruation)	Baseline	1.00	(2.41)	48	0.80	(2.14)	50	0.87	(2.52)	46				
	1 year	5.62	(5.25)	47	5.42	(5.06)	45	6.04	(5.50)	45	0.68	(−1.26 to 2.62)	0.22	(−1.68 to 2.12)
	2 years	7.24	(5.46)	42	7.14	(5.41)	42	7.52	(5.17)	42	0.66	(−1.31 to 2.63)	0.32	(−1.61 to 2.25)
	5 years	9.43	(4.60)	14	9.90	(3.71)	21	10.29	(3.41)	14	0.73	(−1.73 to 3.18)	0.81	(−1.64 to 3.26)
C (Mental state)	Baseline	5.31	(2.18)	55	5.24	(1.87)	55	5.47	(1.95)	57				
	1 year	7.32	(2.91)	53	7.31	(2.93)	52	7.00	(2.84)	52	−0.57	(−1.52 to 0.37)	−0.32	(−1.24 to 0.60)
	2 years	8.00	(3.17)	52	8.08	(2.83)	51	8.00	(3.17)	52	−0.27	(−1.28 to 0.75)	−0.08	(−1.07 to 0.90)
	5 years	9.47	(2.74)	19	9.68	(2.88)	31	10.76	(2.17)	29	1.27	(0.01 to 2.53)	1.02	(−0.37 to 2.40)
D (Psychosexual state)	Baseline	5.53	(2.65)	55	5.84	(2.82)	55	6.57	(2.87)	56				
	1 year	7.76	(3.28)	52	7.86	(3.56)	51	7.61	(3.38)	51	−0.16	(−1.27 to 0.95)	−0.13	(−1.23 to 0.96)
	2 years	8.19	(3.49)	52	8.84	(3.21)	51	8.70	(3.47)	52	0.06	(−1.08 to 1.20)	0.49	(−0.62 to 1.60)
	5 years	10.56	(2.36)	19	9.80	(3.10)	31	10.80	(2.32)	29	0.86	(−0.44 to 2.15)	0.09	(−1.33 to 1.51)
E (Socioeconomic state)	Baseline	7.84	(1.98)	55	7.21	(2.99)	55	8.11	(2.17)	57				
	1 year	9.30	(2.65)	53	8.61	(3.19)	52	9.40	(2.19)	52	0.11	(−0.80 to 1.01)	−0.35	(−1.30 to 0.60)
	2 years	9.58	(2.71)	52	9.30	(2.73)	51	9.34	(2.77)	52	−0.35	(−1.30 to 0.60)	−0.33	(−1.26 to 0.60)
	5 years	10.32	(1.64)	19	9.68	(2.50)	31	10.51	(1.95)	29	0.57	(−0.49 to 1.63)	−0.10	(−1.26 to 1.06)
MRAOS (Average of all scales)	Baseline	4.67	(1.27)	55	4.56	(1.46)	55	5.05	(1.46)	57				
	1 year	7.61	(2.22)	53	7.34	(2.27)	52	7.50	(2.43)	52	−0.09	(−0.88 to 0.70)	−0.26	(−1.03 to 0.50)
	2 years	8.25	(2.61)	52	8.36	(2.38)	51	8.25	(2.58)	52	−0.20	(−1.07 to 0.68)	0.00	(−0.85 to 0.84)
	5 years	9.60	(2.01)	19	9.44	(2.26)	31	10.34	(1.81)	29	0.87	(−0.12 to 1.85)	0.46	(−0.62 to 1.53)

a Statistical analysis adjusted from baseline age, sex, site and baseline mood and feelings score.

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TABLE 7 *Summary statistic and intention-to-treat analysis of 1-year and 2-year secondary outcomes*

		General CAMHS			Specialist outpatient			Specialist inpatient			Inpatient–Outpatient		Specialist–General		
Assessment		**Mean**	**(SD)**	***n***	**Mean**	**(SD)**	***n***	**Mean**	**(SD)**	***n***	**Diff[a]**	**(95% CI)**	**Diff[a]**	**(95% CI)**	***p*-value**
Weight for height (%)	Baseline	78.80	(7.86)	55	77.14	(8.10)	55	78.16	(8.08)	57					
	1 year	90.89	(13.34)	50	88.15	(10.63)	52	86.67	(9.90)	52	−2.24	(−5.93 to 1.46)	−2.33	(−6.00 to 1.35)	0.21
	2 years	94.17	(12.98)	46	90.10	(9.78)	50	90.45	(13.35)	51	−1.74	(−5.85 to 2.38)	−2.85	(−7.00 to 1.30)	0.18
	5 years	88.71	(10.43)	20	96.01	(12.00)	31	95.65	(12.14)	24	4.31	(−1.69 to 10.31)	7.64	(1.45 to 13.83)	0.02
EDI-2 total	Baseline	88.48	(51.36)	52	86.52	(47.53)	54	89.61	(44.52)	56					
	1 year	69.38	(53.32)	45	57.64	(54.02)	44	60.60	(52.91)	43	−1.09	(−18.44 to 16.26)	−4.28	(−21.39 to 12.83)	
	2 years	60.98	(51.97)	40	52.50	(49.15)	42	40.33	(36.36)	43	−12.15	(−28.98 to 4.68)	−11.71	(−28.53 to 5.11)	
	5 years	56.09	(44.44)	22	51.76	(45.53)	25	42.00	(35.66)	25	−11.56	(−32.30 to 9.17)	−10.07	(−31.43 to 11.29)	
FAD-General	Baseline	2.13	(0.59)	52	2.12	(0.53)	54	2.08	(0.49)	56					
functioning	1 year	1.97	(0.57)	46	2.08	(0.55)	45	1.95	(0.49)	43	−0.08	(−0.25 to 0.10)	0.05	(−0.12 to 0.22)	0.57
	2 years	2.02	(0.65)	41	1.99	(0.59)	39	1.99	(0.52)	42	0.05	(−0.16 to 0.26)	−0.01	(−0.21 to 0.20)	0.93
	5 years	2.03	(0.65)	22	1.92	(0.45)	24	1.85	(0.55)	23	−0.13	(−0.42 to 0.16)	−0.16	(−0.46 to 0.13)	0.27
MFQ total	Baseline	32.36	(16.12)	53	30.09	(14.70)	54	32.55	(14.60)	56					
	1 year	23.85	(17.71)	46	19.28	(16.70)	46	18.16	(15.65)	43	−3.11	(−8.82 to 2.61)	−3.64	(−9.19 to 1.92)	
	2 years	24.19	(20.18)	42	17.14	(15.14)	42	15.83	(14.51)	42	−3.36	(−9.45 to 2.74)	−5.71	(−11.61 to 0.19)	
	5 years	22.32	(17.32)	22	18.08	(15.45)	25	14.00	(11.70)	25	−7.24	(−14.92 to 0.45)	−7.23	(−15.15 to 0.68)	
HoNOSCA															
Clinician-rated	Baseline	20.04	(5.72)	55	20.71	(7.50)	55	20.04	(5.63)	57					
	1 year	15.02	(9.09)	53	16.84	(9.69)	49	14.19	(7.40)	52	−1.29	(−4.18 to 1.60)	0.51	(−2.32 to 3.33)	
	2 years	13.75	(9.76)	52	13.69	(8.92)	51	14.25	(9.14)	52	0.96	(−2.14 to 4.07)	0.44	(−2.60 to 3.47)	
	5 years	9.11	(7.04)	19	10.55	(8.22)	31	6.72	(4.87)	29	−3.38	(−6.69 to 0.07)	−1.07	(−4.70 to 2.56)	
Self-rated	Baseline	16.46	(9.95)	54	17.40	(9.88)	53	15.64	(9.54)	53					
	1 year	10.53	(10.03)	45	11.70	(9.03)	44	8.62	(8.15)	42	−1.55	(−4.75 to 1.65)	0.92	(−2.20 to 4.04)	
	2 years	9.97	(9.84)	37	8.88	(8.11)	43	7.65	(8.58)	43	−0.42	(−3.56 to 2.73)	−0.92	(−4.13 to 2.29)	
	5 years	6.74	(4.15)	19	7.34	(8.09)	29	4.38	(4.78)	24	−2.68	(−5.61 to 0.26)	−1.31	(−4.31 to 1.68)	

a Statistical analysis adjusted from baseline age, sex, site and baseline mood and feelings score.

TABLE 8 *Summary of longitudinal mixed model analyses*

	Coefficient	95% CI	*p*-value
MRAOS			
Inpatient–Outpatient			
Treatment with session interaction	0.12	(−0.60 to 0.83)	0.752
Treatment main effect[b]	0.15	(−0.86 to 1.16)	0.770
Specialist–Generalist			
Treatment with session interaction	0.42	(−0.09 to 0.94)	0.104
Treatment main effect[b]	−0.01	(−0.67 to 0.64)	0.965
% Weight for height			
Inpatient–Outpatient			
Treatment with session interaction	−0..86	(−4.37 to 2.64)	0.629
Treatment main effect[b]	−0.46	(−5.57 to 4.66)	0.862
Specialist–Generalist			
Treatment with session interaction[a]	2.80	(0.31 to 5.29)	0.027
Treatment main effect	−2.16	(−5.47 to 1.115)	0.200
EDI-2 total			
Inpatient–Outpatient			
Treatment with session interaction	−4.51	(−19.10 to 10.09)	0.545
Treatment main effect[b]	0.24	(−19.87 to 20.35)	0.981
Specialist–Generalist			
Treatment with session interaction	−2.95	(−12.72 to 6.82)	0.553
Treatment main effect[b]	−10.26	(−23.39 to 2.87)	0.126
FAD-GF			
Inpatient–Outpatient			
Treatment with session interaction	0.102	(−0.094 to 0.297)	0.309
Treatment main effect[b]	−0.080	(−0.31 to 0.15)	0.494
Specialist–Generalist			
Treatment with session interaction[a]	−0.13	(−0.26 to 0.00)	0.047
Treatment main effect	−0.01	(−0.16 to 0.14)	0.929
MFQ			
Inpatient–Outpatient			
Treatment with session interaction	0.09	(−5.77 to 5.96)	0.975
Treatment main effect[b]	0.72	(−6.07 to 7.52)	0.835
Specialist–Generalist			
Treatment with session interaction	−1.68	(−5.60 to 2.24)	0.400
Treatment main effect[b]	−5.94	(−10.35 to −1.54)	0.008
HoNOSCA-CR			
Inpatient–Outpatient			
Treatment with session interaction	0.82	(−1.76 to 3.39)	0.534
Treatment main effect[b]	−1.29	(−4.92 to 2.35)	0.488
Specialist–Generalist			
Treatment with session interaction	−1.55	(−3.36 to 0.26)	0.094
Treatment main effect[b]	−0.19	(−2.54 to 2.17)	0.876

TABLE 8 *Summary of longitudinal mixed model analyses (continued)*

	Coefficient	95% CI	*p*-value
HoNOSCA-SR			
Inpatient–Outpatient			
Treatment with session interaction	1.17	(−1.37 to 3.71)	0.367
Treatment main effect[b]	−1.46	(−4.89 to 1.97)	0.404
Specialist–Generalist			
Treatment with session interaction	−1.14	(−2.89 to 0.61)	0.202
Treatment main effect[b]	−0.63	(−2.94 to 1.68)	0.593

a Suggestion of interaction between sessions and treatment – see Table 4 for separate cross-sectional analyses.
b Treatment main effect is averaged across sessions because there is no interaction between sessions and treatment

treatment compared with general CAMHS treatment for MFQ. Averaging across follow-up assessments MFQ was 5.94 points (95% CI 1.56 to 10.35, $p = 0.008$) lower (better outcome) in specialist services than general CAMHS. This difference is also apparent in *Table 7* with the difference between specialist treatment and general CAMHS being 3.6, 5.7 and 7.2 at 1, 2 and 5 years follow-up, respectively. There were no other differences between groups.

There was no treatment by site interaction and no other subgroup analyses were carried out.

Diagnostic outcome category

Table 9 and *Figure 2* show the diagnostic outcome category at years 1, 2 and 5. These are based on the categories employed in the Maudsley studies[18,21,37] employing a high threshold for assigning recovery. A good outcome indicates a full recovery from AN (weight above 85% of expected, return of menstruation, bingeing/purging no greater than once per month). A poor outcome was indicated if weight was not above 85% or the young person was still being treated as an inpatient for AN. The intermediate category comprises those whose weight had risen to within the normal range, but without return of menstruation, with bingeing–purging at a frequency greater than monthly, or considerable residual concerns about weight and shape scored on Morgan–Russell scale A. At 1 year, 18% had fully recovered, 38% still had diagnostic AN. By 2 years there was an overall good outcome for 33%, but 27% still had the condition.

Table 10 summaries the longitudinal marginal model analysis using robust standard errors. There were no statistically significant differences between inpatient and outpatient treatments. In the comparison of specialist treatment with general CAMHS treatment there was slight evidence of a time with treatment interaction ($0 = 0.66$). From *Table 10* it can be seen that general CAMHS did better than specialist treatments at 1 year (Common Odds Ratio 0.56, 95% CI 0.29 to 1.01 $p = 0.05$), having fewer poor outcomes, whereas at 5 years the Common Odds Ratio tended to favour specialist treatment (1.54, 95% CI 0.61 to 3.93) although not significantly ($p = 0.39$). There was no treatment by site interaction and no other subgroup analyses were carried out.

Clinical course

On the whole, patients made a steady improvement over the 5 years. *Table 11* shows the movement between outcome category by each of the four groups between 2-year and 5-year outcomes. Overall, the outcome category is known for 131 subjects at both the 2-year and 5-year time points. Of 54 with a good outcome at 2 years, only two had a poor outcome at 5 years (one with AN and one who had died). Only eight with a good outcome at 2 years had slipped back into an intermediate outcome, suggesting that when full recovery is achieved, relapse is relatively unlikely. This pattern is seen for each of the treatment groups with no notable differences between them. Meanwhile, the outcome at 5 years for the 28 in the poor category at 2 years is much more mixed, with equal numbers having recovered as remain with AN at 5 years (10 in each category).

TABLE 9 *Diagnostic outcome category with ordinal logistic regression analysis; estimates of the effect of inpatient treatment compared with outpatient treatment and general CAMHS compared with specialist treatment*

	General CAMHS	Specialist outpatient	Specialist inpatient			
	n = 55	*n* = 55	*n* = 57	Odds ratio	95% CI	*p*-value
1 year						
Poor	13	24	26	Inpatient–Outpatient		
	24%	44%	46%	0.70	(0.37 to 1.34)	
Intermediate	31	22	18			
	57%	41%	32%	Specialist–General		
Good	10	8	12	0.54	(0.29 to 1.01)	0.05
	19%	15%	21%			
Followed up	54	54	56			
Alive but no further info.	1	1	1			
2 year						
Poor	14	12	17	Inpatient–Outpatient		
	26%	23%	32%	0.86	(0.45 to 1.64)	
Intermediate	20	28	17			
	37%	53%	32%	Specialist–General		
Good	20	13	19	0.84	(0.45 to 1.56)	0.58
	37%	25%	36%			
Followed up	54	53	53			
Alive but no further info.	1	1	3			
No info.	0	1	1			
5 year						
Poor	5	2	3	Inpatient–Outpatient		
	18%	6%	9%	1.56	(0.61 to 4.02)	
Intermediate	6	13	8			
	21%	37%	24%	Specialist–General		
Good	17	20	22	1.52	(0.59 to 3.93)	0.39
	61%	57%	67%			
Followed up	28	35	33			
Alive but no further info.	6	3	7			
No info.	21	17	17			

Adjusted for sex, % weight for height, age, site, Morgan–Russell total and MFQ.
Info., information.

The course of every patient through the four assessment points for the main outcome measure (MRAOS) is shown in *Figure 8* in Appendix 1 to the last assessment point achieved for that patient. It can be seen that in general (though not exclusively) the trends of the graphs are generally upwards with time. Similarly, *Figure 9* in Appendix 2 shows individual patient progress in terms of percentage weight for height.

Adherence to treatment allocation and outcome

The trial aimed to compare randomisation to specialist inpatient treatment and specialist outpatient treatment with randomisation to general CAMHS treatment. However, as we have discussed, adherence to the allocated treatment was poor for the inpatient arm. In the first year of the trial,

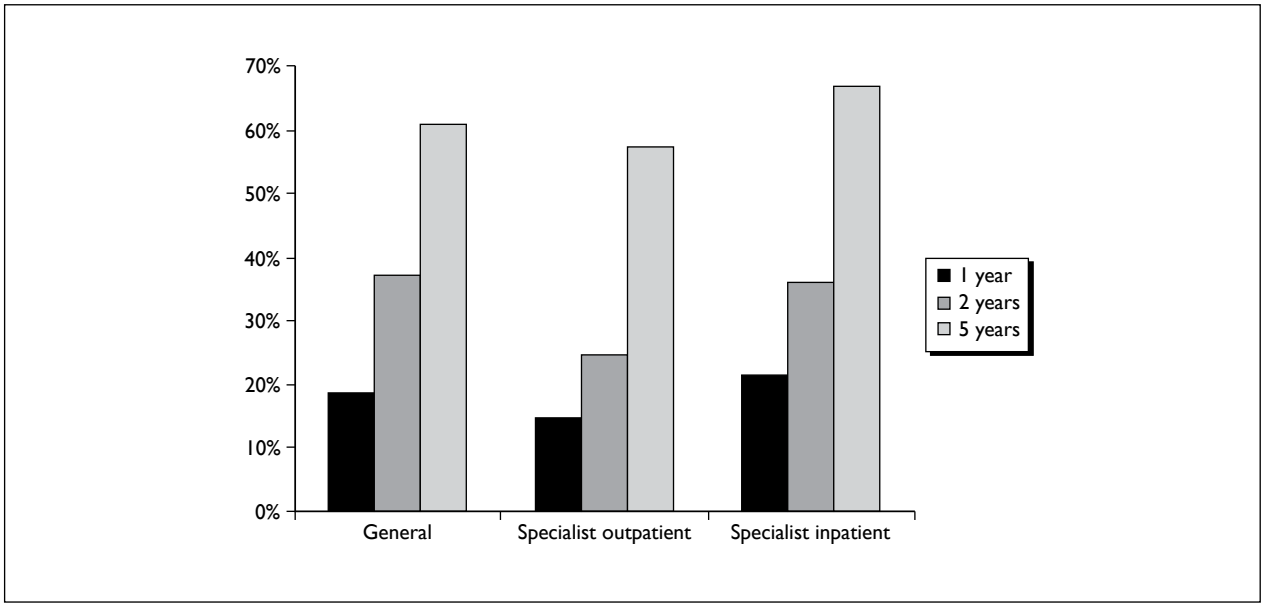

FIGURE 2 *Percentage good outcome (cases with known outcome).*

TABLE 10 *Summary of longitudinal ordinal logistic regression analysis of diagnostic outcome category*

	Odds ratio	95% CI	*p*-value
Inpatient–Outpatient			
Treatment with session interaction	0.91	(0.48 to 1.73)	0.769
Main effect	1.16	(0.54 to 2.48)	0.705
Specialist–General			
Treatment with session interaction	1.57	(0.97 to 2.52)	0.064
Main effect	0.78	(0.47 to 1.29)	0.327

specialist inpatient treatment at one of the four centres was received by 49% (28/59) of subjects randomised to this treatment and 20% (23/110) of those randomised to general CAMHS or specialist treatment. Assuming that there are no subjects who will always opt for the opposite of their randomly assigned treatment, one can argue that only 29% of patients (49% minus 20%) accepted randomisation to specialist inpatient treatment because 20% would have received this irrespective of random allocation and 53% (29/59) did not receive it.

Of those patients randomised to specialist outpatient treatment at the two specialist outpatient centres, 75% (41/57) received specialist outpatient treatment, whereas only 18% (20/112) of patients randomised to either general CAMHS or specialist inpatient received this. Hence, randomisation to specialist outpatient treatment was more likely to be determined by randomisation than specialist inpatient treatment, with 57% (75% minus 18%) accepting randomisation of this option. Allocation to specialist outpatient treatment led to 77% of the sample receiving some form of specialist treatment whereas only half of those assigned to specialist inpatient treatment received it.

Adherence to allocated treatment did have a significant bearing on outcome, though a number of issues, including those above, mean that caution is advised in interpreting the findings.

Examining the outcome of those allocated to *inpatient treatment* reveals that adherence to this treatment was poor (49%, 28 out of 59) and so in theory this might have compromised the effectiveness of this intervention. At baseline, *Table 12* demonstrates that, on the measures used, there was little difference between the two subgroups (adherers and non-adherers), though those who

TABLE 11 *Comparison of diagnostic outcomes at 2 and 5 years by treatment group and overall*

	2 years											
5 years	**Poor**	**(%)**	**Inter.**	**(%)**	**Good**	**(%)**	**Not known**	**(%)**	**No info.**	**(%)**	**Total**	**(%)**
General CAMHS												
Poor	3	(21)	2	(10)	0	(0)	0	(0)	–	–	5	(9)
Intermediate	2	(14)	2	(10)	2	(10)	0	(0)	–	–	6	(11)
Good	1	(7)	6	(30)	9	(45)	1	(100)	–	–	17	(31)
Alive – no further information	2	(14)	1	(5)	3	(15)	0	(0)	–	–	6	(11)
No information	6	(43)	9	(45)	6	(30)	0	(0)	–	–	21	(38)
Total	14		20		20		1		–	–	55	
Specialist outpatient												
Poor	0	(0)	1	(4)	1	(8)	0	(0)	0	(0)	2	(4)
Intermediate	2	(17)	9	(32)	2	(15)	0	(0)	0	(0)	13	(24)
Good	5	(42)	6	(21)	9	(69)	0	(0)	0	(0)	20	(36)
Alive – no further information	0	(0)	3	(11)	0	(0)	0	(0)	0	(0)	3	(5)
No information	5	(42)	9	(32)	1	(8)	1	(100)	1	(100)	17	(31)
Total	12		28		13		1		1		55	
Specialist inpatient												
Poor	2	(12)	1	(6)	0	(0)	0	(0)	0	(0)	3	(5)
Intermediate	4	(24)	2	(12)	2	(11)	0	(0)	0	(0)	8	(14)
Good	2	(12)	7	(41)	12	(63)	1	(33)	0	(0)	22	(39)
Alive – no further information	3	(18)	2	(12)	2	(11)	0	(0)	0	(0)	7	(12)
No information	6	(35)	5	(29)	3	(16)	2	(67)	1	(100)	17	(30)
Total	17		17		19		3		1		57	
Patient preference												
Poor	5	(45)	1	(5)	1	(6)	0	(0)	–	–	7	(15)
Intermediate	0	(0)	5	(26)	2	(12)	0	(0)	–	–	7	(15)
Good	2	(18)	9	(47)	12	(71)	0	(0)	–	–	23	(48)
Alive – no further information	0	(0)	1	(5)	0	(0)	0	(0)	–	–	1	(2)
No information	4	(36)	3	(16)	2	(12)	1	(100)	–	–	10	(21)
Total	11		19		17		1		–	–	48	
Total												
Poor	10	(19)	5	(6)	2	(3)	0	(0)	0	(0)	17	(8)
Intermediate	8	(15)	18	(21)	8	(12)	0	(0)	0	(0)	34	(16)
Good	10	(19)	28	(33)	42	(61)	2	(33)	0	(0)	82	(38)
Alive – no further information	5	(9)	7	(8)	5	(7)	0	(0)	0	(0)	17	(8)
No information	21	(39)	26	(31)	12	(17)	4	(67)	2	(100)	65	(30)
Total	54		84		69		6		2		215	

Inter., intermediate; Info., information.

were admitted were on average 6 months younger and showed a reduced food intake (Morgan–Russell Scale A).

For the *two outpatient treatment arms* there was a notably better outcome for those who fully adhered to treatment compared with those failing to adhere or later transferring away from the allocated treatment. Specifically, for general CAMHS treatment, only one out of 17 admitted for inpatient treatment had a good outcome at 1 year, whereas for the specialist outpatient programme, none of the 14 who initially failed to adhere to the allocated programme had a good outcome, nor any of 14 subsequently admitted to inpatient treatment (*Table 13*). At 2 years, of 17 allocated to CAMHS who were admitted to hospital, two had a good outcome whereas for the specialist outpatient programme, 13 found their way into inpatient management, of whom only one had a good outcome.

Below, a predictor model is developed for prediction of admission in year 1 among subjects not randomised to inpatient treatment. This can be applied to subjects randomised to inpatient treatment to estimate the probability that each subject would have been admitted. *Figure 3* illustrates the probability of admission according to initial adherence to randomisation to admission. Without randomisation, those subjects who initially adhere to allocation to hospital treatment had a high probability of receiving inpatient treatment. Thirty-eight per cent of adherers would have been admitted whereas only 24% of non-adherers would have been admitted (Wilcoxon $p = 0.007$). Initial adherers to hospital treatment had a higher propensity to receive it, suggesting that they had a different prognosis. *Tables 12* and *13* cannot therefore be interpreted as providing a valid comparison of inpatient and outpatient treatment and should be interpreted with caution.

Table 13 demonstrates the relatively better outcome of non-adherers in terms of outcome category. By 2 years, there is a general improvement from the 1-year time point, but this is more marked for those who declined admission. There remains a better outcome on the main outcome measure for those declining admission compared with those who were admitted, even controlling for baseline variables (*Table 12*).

At 1-year follow-up, those not admitted were doing significantly better on the MRAOS (mean difference 2.0, 95% CI 0.8 to 3.2, $p = 0.001$) and virtually all self-report measures of psychopathology, including mood (all change scores controlled for baseline values).

Inpatient admission appears to be associated with continuing high rates of core abnormal cognitions, such as body dissatisfaction and drive for thinness, whereas those who declined admission made improvements in these areas, suggestive of early cognitive improvement in this subgroup.

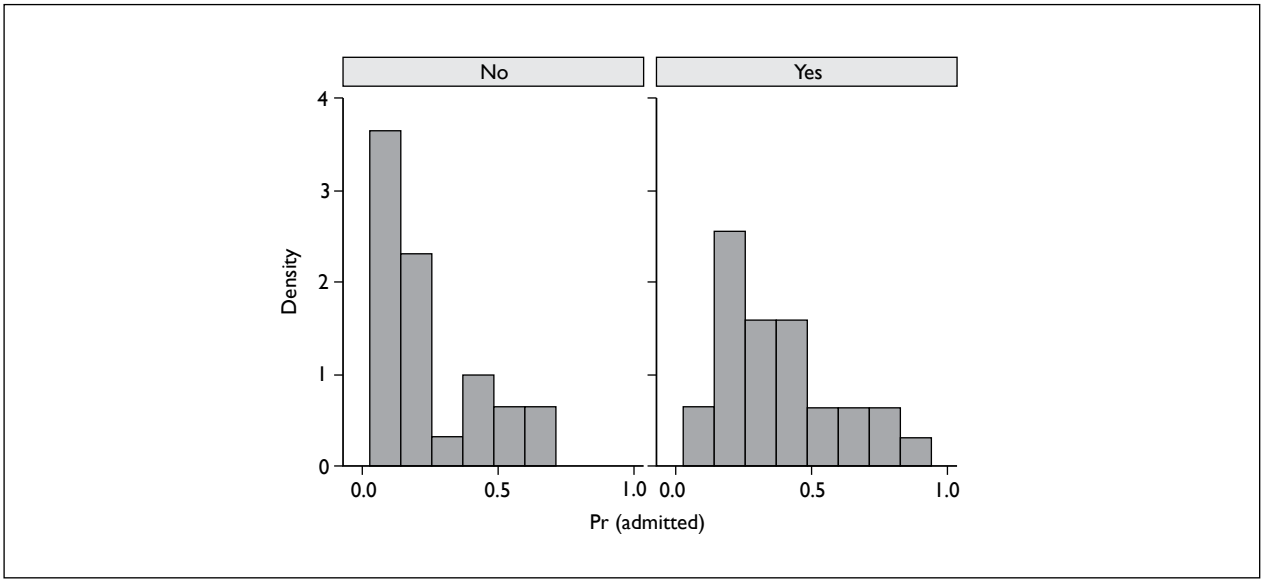

FIGURE 3 *Graphs by initial adherence.*

TABLE 12 *Outcomes of inpatients adhering to treatment and those refusing admission, postrandomisation*

	Baseline					1 year			
	Adherers (*n* = 28)		Non-adherers (*n* = 29)			Adherers (*n* = 26)		Non-adherers (*n* = 26)	
Outcome measure	**Mean**	**(SD)**	**Mean**	**(SD)**	***p***	**Mean**	**(SD)**	**Mean**	**(SD)**
Body mass index (BMI)	14.8	(1.8)	15.8	(1.4)	0.026	17.2	(2.2)	17.9	(2.1)
% Weight for height	76.5	(8.3)	79.7	(7.6)	0.134	85.8	(9.6)	87.5	(10.3)
EDI-2									
Drive for thinness	11.0	(7.1)	11.1	(7.5)	0.985	9.6	(8.4)	4.5	(5.6)
Body dissatisfaction	14.1	(8.9)	16.3	(7.5)	0.317	15.0	(11.4)	8.7	(8.6)
Total	89.9	(47.0)	89.3	(42.7)	0.962	74.6	(55.0)	48.5	(49.0)
MFQ Total	33.9	(13.8)	31.3	(15.5)	0.509	24.5	(17.0)	12.7	(12.3)
HoNOSCA									
Clinician-rated	21.0	(6.7)	19.1	(4.3)	0.224	17.2	(7.0)	11.4	(6.7)
Self-rated	17.3	(10.2)	13.8	(8.6)	0.177	12.3	(8.8)	5.3	(6.0)
Morgan–Russell Scales									
Scale A (Food intake)	2.7	(1.5)	3.9	(1.8)	0.009	5.8	(2.9)	8.1	(2.6)
Scale B (Menstruation)	0.7	(2.0)	1.0	(3.0)	0.645	4.6	(5.3)	7.3	(5.5)
Scale C (Mental state)	5.0	(1.8)	5.9	(2.0)	0.071	5.8	(2.8)	8.1	(2.3)
Scale D (Psychosexual)	6.6	(3.3)	6.5	(2.4)	0.870	6.7	(3.7)	8.4	(2.9)
Scale E (Socioeconomic state)	7.8	(2.2)	8.4	(2.1)	0.336	8.4	(2.1)	10.4	(1.8)
Average outcome (Average of all scales)	4.8	(1.5)	5.3	(1.4)	0.127	6.3	(2.5)	8.6	(1.8)

a Adjusted for baseline.

Predictors of outcome

The TOuCAN project provides a large population-based cohort of adolescents with AN, representative of those presenting to UK CAMHS. Irrespective of the RCT component of the study it provides an opportunity to examine prognostic variables and in particular (given the aim of the trial to explore the value of different forms of service provision) those related to service usage.

The following variables were selected for this analysis: gender, age, subtype, length of history, site, % weight for height, MRAOS, HoNOSCA, HoNOSCA-SR, EDI-2 total, MFQ and FAD-GF.

Table 14 shows that a number of these variables are correlated at baseline, notably the global measures (MRAOS and HoNOSCA). It should be noted that the MRAOS–HoNOSCA correlation is negative, given that these items are scored in opposite directions to indicate severity. There is also a strong correlation between the self-report items (EDI-2, MFQ and HoNOSCA-SR).

Table 15 shows the baseline variable selected to predict outcome at each of the time points by outcome variable. Only significant predictors are given. For example, in terms of the main outcome measure (MRAOS), this outcome at 1 and 2 years is predicted by the baseline MRAOS, but at 5 years it is best predicted by weight for height at baseline (i.e. higher weight at baseline predicts better outcome on MRAOS at 5 years). The EDI-2 negatively predicts 5-year outcome on this measure [i.e. a lower (healthier) EDI score at baseline predicts healthier MRAOS score at 5 years]. Percentage weight for height is predicted best by baseline weight for height at each of the time points, i.e. extreme thinness at presentation is a predictor of thinness 5 years later. It is also of note that there is consistency in assessment of family functioning across the four time points. It

			2 years						
Difference between non-adherers and adherers			Adherers (n = 25)		Non-adherers (n = 27)		Difference between non-adherers and adherers		
Diff.[a]	95% CI	*p*	Mean	(SD)	Mean	(SD)	Diff[a]	95% CI	*p*
0.02	(–1.07 to 1.11)	0.97	18.3	(3.0)	19.0	(2.6)	0.39	(–1.20 to 1.97)	0.63
–0.06	(–5.15 to 5.04)	0.98	88.9	(14.4)	91.9	(12.4)	1.82	(–5.79 to 9.44)	0.63
–4.47	(–8.65 to –0.28)	0.04	3.5	(4.1)	4.6	(6.1)	1.45	(–1.59 to 4.49)	0.34
–6.78	(–12.31 to –1.24)	0.02	8.4	(9.2)	8.6	(9.3)	–0.82	(–6.09 to 4.45)	0.76
–21.99	(–52.31 to 8.33)	0.15	43.1	(33.2)	38.2	(39.3)	–4.66	(–25.7 to 16.4)	0.66
–10.28	(–19.03 to –1.52)	0.03	20.1	(14.2)	12.3	(14.1)	–7.10	(–15.2 to 1.00)	0.08
–5.27	(–9.07 to –1.47)	0.01	16.8	(9.9)	11.9	(7.9)	–3.48	(–8.17 to 1.21)	0.14
–5.67	(–10.71 to –0.63)	0.03	9.3	(9.7)	6.2	(7.3)	–1.59	(–6.41 to 3.24)	0.51
1.61	(0.10 to 3.13)	0.04	6.5	(3.5)	8.4	(2.8)	1.62	(–0.25 to 3.48)	0.09
3.24	(–0.24 to 6.72)	0.07	6.2	(5.5)	9.0	(4.5)	2.67	(–0.50 to 5.84)	0.10
1.89	(0.49 to 3.28)	0.01	7.0	(2.9)	8.9	(3.2)	1.03	(–0.57 to 2.63)	0.20
1.66	(–0.20 to 3.52)	0.08	8.0	(3.8)	9.3	(3.1)	1.31	(–0.60 to 3.22)	0.17
1.90	(0.81 to 2.98)	0.001	9.1	(2.9)	9.6	(2.7)	0.35	(–1.21 to 1.92)	0.65
2.02	(0.83 to 3.22)	0.001	7.4	(2.6)	9.0	(2.3)	1.46	(0.05 to 2.87)	0.04

should be noted also that for quantitative variables, the effects, as measured by the standardised beta coefficient, were mainly small (approximately 0.2), and so the effects are quite weak.

Baseline predictors of service usage

As only 18% of cases had fully recovered by 1 year and clinical judgement was used to determine treatment beyond the initial 6 months of the trial; we were interested to explore what predicted non-randomised admission to hospital and the use of inpatient beds within the first 2 years, irrespective of treatment allocation and predictors of still being in treatment 1 and 2 years after assessment. *Table 16* shows some of the categorical features of those 102 patients admitted to hospital. Admission was more likely in the Manchester site, for binge–purgers and for those with a longer history of illness. *Table 17* shows that those admitted had a lower presenting MRAOS and % weight for height and higher self-rated measures of psychopathology. *Table 18* provides the statistical analysis showing that % weight for height and self-rated mood were powerful predictors of admission, and that weight for height and EDI-2 total score predicted a shorter time to admission and a greater number of admissions. *Table 19* and the associated scatter plot (*Figure 4*) show that there is a modest but significant association between presenting MRAOS and number of inpatient days in the first 2 years. This illustrates that 15 subjects spent more than 1 year in the first 2 years in hospital, all with a presenting MRAOS of less than four.

At 1 year, 130 cases were still in treatment and at 2 years this number was 64. *Table 20* shows the categorical breakdown of these cases, *Table 21* shows the baseline values of those who are in treatment at the two time points and *Table 22* the baseline predictors of still being in treatment. In

TABLE 13 *Categorical outcomes at 1 and 2 years for adherers and non-adherers*

	1 year				2 years			
	Good	**Intermediate**	**Poor**	**Not known (alive)**	**Good**	**Intermediate**	**Poor**	**Not known (alive)**
General CAMHS								
Adherers								
Full	8	19	4		15	12	3	1
Subsequently admitted	0	3	4		0	0	7	
Total (*n* = 38)	8	22	8		15	12	10	1
Non-adherers								
Treated as outpatient	1	2	1	1	2	2	1	
Treated as inpatient	1	6	3		2	6	2	
Untreated	0	1	1		1	0	1	
Total (*n* = 17)	2	9	5	1	5	8	4	
Total	10 (18%)	31 (56%)	13 (24%)	1(2%)	20(36%)	20(36%)	14 (26%)	1 (2%)
Specialist outpatient								
Adherers								
Full	8	12	11		11	15	5	
Subsequently admitted	0	3	7		0	7	2	1
Total (*n* = 41)	8	15	18		11	22	7	1
Non-adherers								
Treated as outpatient	0	6	3		1	5	3	
Treated as inpatient	0	1	3	1	1	1	2	1
Total (*n* = 14)	0	7	6	1	2	6	5	1
Total	8 (15%)	22 (40%)	24 (44%)	1 (2%)	13(24%)	28(51%)	12 (22%)	2 (4%)
Inpatient								
Adherers (*n* = 28)	3	9	15	1	6	9	11	2
Non-adherers (*n* = 29)	9	9	11		13	8	6	2
Total	12 (21%)	18 (32%)	26 (46%)	1 (2%)	19(33%)	17 (30%)	17 (30%)	4 (7%)

Ordinal logistic regression, 1 year $p = 0.22$; 2 years $p = 0.89$.

TABLE 14 *Correlation coefficients between predictor variables at baseline*

	Gender	Age	Subtype	History	Site	% Weight for height	Morgan–Russell total	HoNOSCA-CR	HoNOSCA-SR	EDI-2 Total	MFQ Total	FAD-GF
Gender	1.000											
Age	0.095	1.000										
Subtype	−0.019	0.085	1.000									
History	0.000	0.222	0.090	1.000								
Site	0.019	−0.277	0.148	−0.060	1.000							
% Weight for height	−0.117	−0.176	0.174	−0.019	0.034	1.000						
Morgan–Russell total	−0.177	0.176	0.136	0.079	−0.163	0.366	1.000					
HoNOSCA-CR	0.077	−0.021	0.201	0.028	0.076	−0.131	**−0.580**	1.000				
HoNOSCA-SR	0.077	−0.053	0.388	0.043	0.194	0.125	−0.343	**0.613**	1.000			
EDI-2 Total	0.113	0.080	0.264	0.047	0.012	0.277	−0.193	0.383	**0.682**	1.000		
M & FQ Total	0.138	0.035	0.278	−0.040	0.053	0.175	−0.206	0.411	**0.666**	**0.784**	1.000	
FAD-GF	0.060	0.036	0.200	0.003	0.075	0.071	−0.106	0.224	0.376	0.409	0.345	1.000

TABLE 15 *Baseline predictors of outcome measure at 1, 2 and 5 years*

			Reduced model[a]		Full model[b]	
Outcome	**Year**	**Baseline**	**Beta**	***p*-value**	**Beta**	***p*-value**
Morgan–Russell Scales	1	Morgan–Russell	0.290	<0.001	0.302	0.014
Global Score	2	Morgan–Russell	0.246	<0.001	0.209	0.045
	5	Weight for height	0.343	<0.001	0.290	0.005
		EDI-2 Total	–0.400	<0.001	–0.461	0.004
Weight for height (%)	1	Weight for height	0.329	<0.001	0.366	0.000
	2	Weight for height	0.335	<0.001	0.351	0.000
	5	Weight for height	0.273	0.004	0.266	0.005
EDI-2 Total	1	MFQ Total	0.380	<0.001	0.221	0.075
		Weight for height	0.237	0.002	0.161	0.068
		History	0.193	0.005	0.158	0.037
		Morgan–Russell	–0.156	0.025	–0.281	0.011
		Age	0.153	0.036	0.105	0.186
	2	EDI-2 Total	0.391	<0.001	0.237	0.093
	5	EDI-2 Total	0.472	<0.001	0.480	0.012
		Weight for height	–0.224	0.023	–0.151	0.252
FAD-GF	1	FAD	0.506	<0.001	0.534	0.000
		Morgan–Russell	–0.225	0.008	–0.174	0.097
		HoNOSCA-CR	–0.190	0.025	–0.145	0.169
		History	0.170	0.012	0.139	0.066
	2	FAD	0.451	<0.001	0.433	<0.001
	5	FAD	0.371	<0.001	0.383	0.001
		Morgan–Russell	–0.274	0.003	–0.370	0.020
MFQ Total	1	MFQ Total	0.412	<0.001	0.331	0.009
		Morgan–Russell	–0.176	0.012	–0.238	0.026
		History	0.206	0.003	0.161	0.036
	2	MFQ Total	0.389	<0.001	0.210	0.116
	5	EDI-2 Total	0.384	<0.001	0.435	0.028
		Weight for Height	–0.258	0.011	–0.291	0.036
HoNOSCA-CR	1	HoNOSCA-SR	0.296	<0.001	0.245	0.055
		Morgan–Russell	–0.154	0.034	–0.163	0.129
	2	HoNOSCA-SR	0.379	0.001	0.404	0.002
	5	EDI-2 Total	0.427	<0.001	0.343	0.040
		Weight for height	–0.289	0.002	–0.225	0.054
HoNOSCA-SR	1	HoNOSCA-SR	0.340	0.005	0.316	0.017
		Morgan–Russell	–0.156	0.039	–0.316	0.006
	2	HoNOSCA-SR	0.404	<0.001	0.357	0.012
	5	HoNOSCA-SR	0.326	<0.001	0.339	0.025
		Age	0.273	0.002	0.245	0.027
		Morgan–Russell	–0.206	0.023	–0.179	0.174

a Backward stepwise selection of variable.
b Full model including all covariates.

TABLE 16 *Frequency of admission by baseline characteristic*

	Frequency	%
Gender		
Male	9/16	56%
Female	93/193	47%
Type		
Restrictor	71/162	44%
Binge–purger	31/53	58%
History		
< 18 months	64/142	45%
≥ 18 months	38/73	52%

Table does not include subjects randomised to inpatient treatment and includes the preference patients.

TABLE 17 *Proportion of subjects that were admitted by baseline characteristic at admission*

Baseline characteristic	Not admitted			Admitted		
	Mean	SD	*n*	Mean	SD	*n*
Age	15.17	1.32	89	15.10	1.64	69
MRAOS	4.95	1.31	89	4.02	1.43	69
Weight for height	78.8	7.1	89	74.7	9.6	69
EDI-2 Total	79.0	43.2	85	100.7	51.9	62
FAD-GF	2.07	0.55	85	2.18	0.58	62
MFQ Total	27.8	14.5	89	36.8	14.5	62
HoNOSCA-CR	18.9	6.4	89	22.7	5.8	69
HoNOSCA-SR	14.2	8.5	87	19.8	10.8	63

Table does not include subjects randomised to inpatient treatment and includes the preference patients.

TABLE 18 *Baseline predictors of hospital admissions*

	Reduced model			Full model		
Admission	**Odds ratio**	**95% CI**	***p*-value**	**Odds ratio**	**95% CI**	***p*-value**
Site	2.768	(1.308 to 5.855)	0.008	3.545	(1.406 to 8.939)	0.007
Weight for height	0.916	(0.873 to 0.961)	< 0.001	0.914	(0.857 to 0.975)	0.007
MFQ Total	1.056	(1.029 to 1.085)	< 0.001	1.031	(0.988 to 1.076)	0.161
Time to first admission	**Hazard ratio**	**95% CI**	***p*-value**	**Hazard ratio**	**95% CI**	***p*-value**
Site	3.630	(1.821 to 7.237)	< 0.001	3.899	(1.706 to 8.913)	0.001
Weight for height	0.905	(0.865 to 0.947)	< 0.001	0.907	(0.853 to 0.963)	0.002
EDI-2 Total	1.013	(1.006 to 1.020)	< 0.001	1.009	(0.997 to 1.022)	0.128
Number of inpatient admissions	**Common odds**	**95% CI**	***p*-value**	**Common odds**	**95% CI**	***p*-value**
Site	2.062	(1.056 to 4.027)	0.034	2.234	(0.995 to 5.013)	0.051
Weight for height	0.919	(0.880 to 0.959)	< 0.001	0.944	(0.895 to 0.996)	0.036
EDI-2 Total	1.012	(1.005 to 1.019)	0.001	1.005	(0.993 to 1.017)	0.458

Table does not include subjects randomised to inpatient treatment and includes the preference patients.

TABLE 19 *Predictors of inpatient days within first 2 years*

	Reduced model			Full model		
Inpatient days	**Common odds ratio**	**95% CI**	***p*-value**	**Common odds ratio**	**95% CI**	***p*-value**
MRAOS	0.667	(0.484 to 0.918)	0.013	0.652	(0.371 to 1.146)	0.138

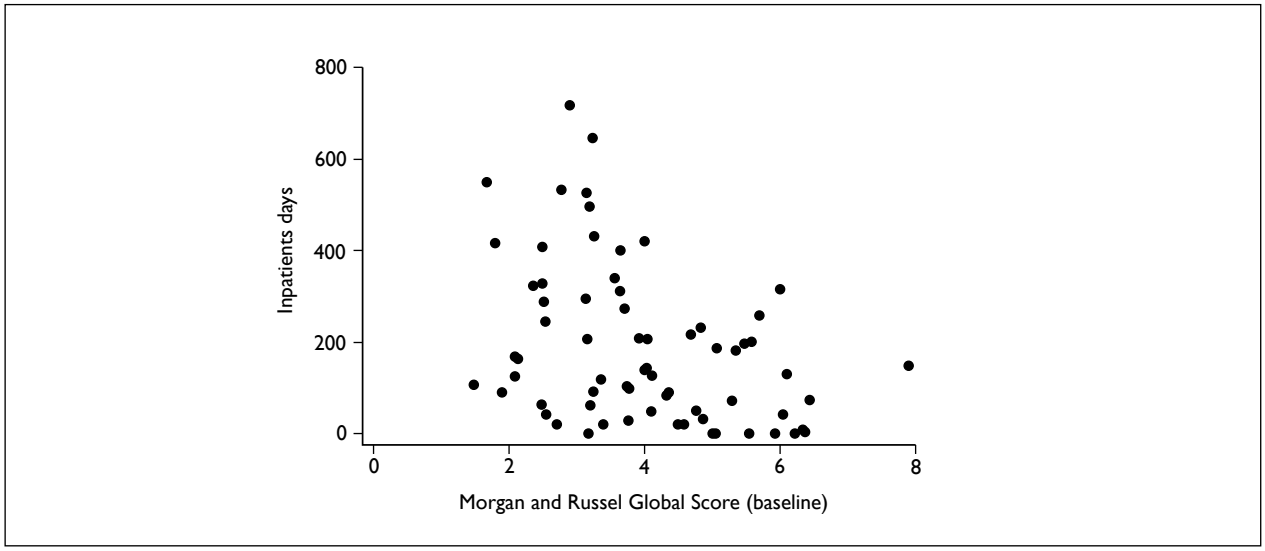

FIGURE 4 *Predictors of inpatient days within first 2 years from MRAOS.*

TABLE 20 *In treatment at 1 and 2 years by patient characteristics*

	1 year		2 years	
	n	**%**	***n***	**%**
Site				
Mersey	58/116	50%	31/115	27%
North-west	55/96	57%	31/96	32%
Gender				
Male	8/16	50%	3/16	19%
Female	105/196	54%	59/195	30%
Type				
Restrictor	92/160	58%	49/159	31%
Binge–purger	21/52	40%	13/52	25%
History				
< 18 months	78/142	55%	45/141	32%
≥ 18 months	35/70	50%	17/70	24%

TABLE 21 *Quantitative characteristics at baseline according to treatment at 1 and 2 years*

	1 year						2 years					
	No			Yes			No			Yes		
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*
Age	15.37	1.35	99	14.79	1.52	113	15.27	1.40	149	14.53	1.52	62
MRAOS	5.20	1.40	99	4.23	1.34	113	4.91	1.39	149	4.12	1.46	62
Weight for height	78.5	7.6	99	76.4	9.0	113	78.0	8.0	149	75.7	9.3	62
EDI-2 Total	83.3	47.4	95	93.4	46.8	106	86.3	46.8	143	95.7	47.5	57
FAD-GF	2.07	0.55	95	2.13	0.55	106	2.11	0.53	143	2.10	0.59	57
MFQ Total	28.6	14.4	96	34.8	14.9	108	31.0	14.7	145	34.3	15.3	58
HoNOSCA-CR	18.8	6.0	99	21.7	6.1	113	20.0	6.2	149	21.3	6.3	62
HoNOSCA-SR	14.4	9.2	94	18.0	10.0	107	15.7	9.4	141	18.0	10.6	59

TABLE 22 *Baseline predictors of being in treatment at 1 and 2 years*

	Reduced model			Full model		
	Odds ratio	95% CI	*p*-value	Odds ratio	95% CI	*p*-value
1 year						
Age	0.805	(0.648 to 1.001)	0.051	0.774	(0.599 to 1.001)	0.051
Subtype	0.429	(0.201 to 0.916)	0.029	0.402	(0.171 to 0.945)	0.037
MRAOS	0.642	(0.505 to 0.816)	<0.001	0.740	(0.532 to 1.029)	0.073
MFQ Total	1.034	(1.010 to 1.059)	0.005	1.042	(1.004 to 1.083)	0.032
2 years						
Age	0.661	(0.521 to 0.840)	0.001	0.700	(0.536 to 0.914)	0.009
Weight for height	0.947	(0.909 to 0.986)	0.008	0.961	(0.915 to 1.008)	0.105
EDI-2 Total	1.009	(1.002 to 1.016)	0.018	1.008	(0.995 to 1.020)	0.232

particular, those who were the thinnest and had the highest self-rated cognitions on the EDI-2 at presentation were likely to be still in treatment at 2 years.

Economic evaluation results

Economic evaluation at 2 years

Data availability

Full economic data for the 2-year follow-up period were available for 135 young people (81%), 47 in the inpatient group, 45 in the specialist outpatient group and 43 in the general CAMHS group. A comparison of baseline characteristics (site, age, gender, BMI and MRAOS) revealed no significant differences between those included in the economic evaluation and those who were missing and there was no difference overall in missing data between the three treatment groups. Length of follow-up varied somewhat (range 99 to 118 weeks); however, there was no significant difference in length of follow-up between the three treatment groups on average (mean 105 weeks in the inpatient and general CAMHS groups and 106 in the specialist group).

Resource use

The mean number of contacts the young people had with all services over the 2-year follow-up period is detailed in *Table 23*. Service use differed little between the randomised groups except for use of hospital inpatient and outpatient services. The general CAMHS group spent more time in hospital and had a greater number of outpatient attendances on average than the specialist

TABLE 23 *Use of resources during the 2-year follow-up period: mean per young person*

Service	General CAMHS (*n* = 43) Mean (SD)	Specialist outpatient (*n* = 45) Mean (SD)	Specialist inpatient (*n* = 47) Mean (SD)
Secondary health services			
Inpatient nights	89 (159)	55 (114)	73 (124)
Outpatient appointments	31 (24)	26 (22)	23 (20)
Day patient contacts	1 (5)	1 (7)	4 (12)
Accident and emergency	0 (1)	1 (2)	0 (1)
Community health and social services			
General practitioner	6 (8)	7 (9)	7 (9)
Practice nurse	1 (4)	3 (10)	2 (5)
Medication	63%	58%	60%
Dietician	0 (0)	0 (0)	0 (3)
District nurse	0 (0)	0 (2)	0 (0)
Health visitor	0 (0)	0 (0)	0 (1)
Community paediatrician	0 (3)	0 (0)	0 (1)
Community psychiatric nurse	1 (5)	1 (7)	0 (1)
Clinical psychologist	0 (0)	0 (1)	1 (8)
Counsellor	0 (1)	0 (2)	0 (1)
Family therapist	0 (2)	0 (0)	1 (8)
Dentist	0 (0)	0 (1)	0 (0)
School doctor	0 (0)	0 (0)	0 (2)
School nurse	1 (2)	1 (2)	1 (6)
Social worker	0 (1)	1 (4)	1 (2)
Foster care	2 (13)	0 (0)	0 (0)
Eating disorders association	0 (0)	0 (1)	0 (1)
Family therapy	0 (0)	0 (1)	0 (1)
Education			
State day school months	12 (10)	10 (9)	11 (9)
Independent day school months	1 (5)	2 (6)	1 (4)
Independent boarding school months	0 (2)	0 (0)	0 (1)
Hospital school months	2 (4)	1 (2)	1 (3)
Home tuition months	1 (4)	1 (3)	0 (1)
School counsellor	0 (0)	1 (7)	1 (7)
Education welfare officer	0 (1)	0 (1)	0 (0)

outpatient or inpatient groups and the specialist outpatient group spent the least amount of time in hospital. Exploring hospital contacts over the 1-year, 2-year and 5-year follow-up periods revealed a reduction in the use of hospital services over time: a larger proportion of days were spent in hospital in the first year (inpatient group 64 days, specialist outpatient 35 days, general CAMHS 67 days) than the second year (inpatient group 12 days, specialist outpatient 20 days, general CAMHS 24 days). By 3–5 years, the average number of inpatient days per annum fell further (inpatient group 5 days, specialist outpatient 9 days, general CAMHS 8 days) (see *Table 29*). When study participants in one of the outpatient groups received inpatient treatment, this generally

occurred after assigned treatment had ended. Details of adherence to treatment have been discussed and are given in *Tables 12* and *13*.

Although the hospital contacts reported in *Table 23* include all medical specialties, the vast majority of contacts were psychiatric (73% of inpatient admissions and 90% of inpatient days) or paediatric (20% of admissions and 10% of inpatient days). Other medical specialties used by the young people (9% of admissions and 0.2% of inpatient days) included gastroenterology, general medicine, haematology, intensive care unit, obstetrics, orthopaedics, plastic surgery and urology.

Time spent by the young people in education was similar across the three groups with evidence of substantial periods out of education in this sample; on average, participants spent a significant proportion of the 2-year follow-up period not in education (approximately 10 out of the 24 months follow-up).

Use of resources by the young person's primary carer is reported in *Table 24*. Very few differences between randomised groups are evident.

Costs

Mean total costs over the 2-year follow-up are detailed in *Table 25*. Analysis of covariance demonstrated that there were no statistically significant differences between the three groups. In terms of observed differences, the specialist outpatient group was consistently cheaper than the other two groups and the general CAMHS group was the most expensive of the three. The bootstrapped results differed little from the analyses using the raw data and are therefore not reported here. Hospital costs constitute the greatest proportion of total costs (93% in each group), with relatively few community health and social services being used. In *Table 26*, the individual service contributions to total costs over the 2-year follow-up are reported. It shows that inpatient and outpatient hospital costs make up 81% and 10% of total costs respectively and that the remaining costs constitute a much smaller proportion of total costs.

Figure 5 illustrates change in costs over time, over the 2-year follow-up. It shows the total cost per participant separated by year and clearly demonstrates that the majority of the costs were incurred in the first year after entry to the study, with much lower costs incurred in the second year.

Mean total costs of health services used by the young person's primary carer are reported in *Table 27*. Overall the primary carers of the specialist outpatient group cost slightly less than those of the inpatient and general CAMHS groups, but this difference was not statistically significant.

Cost-effectiveness analysis

The cost-effectiveness analysis at the 2-year follow-up point employed the rules of dominance and found that the specialist outpatient treatment (bootstrapped mean cost per patient £26,797; bootstrapped mean MRAOS effect 8.35) dominates the inpatient group (£34,371; 8.26) and the general CAMHS group (£40,520; 8.26) because

TABLE 24 *Use of health and community resources by primary carer over 2-year follow-up period: mean per carer*

	General CAMHS (*n* = 14)	**Specialist outpatient (*n* = 20)**	**Specialist inpatient (*n* = 16)**
Service	**Mean**	**Mean**	**Mean (SD)**
Secondary-care services			
Inpatient nights	1 (2)	0 (2)	0 (2)
Outpatient appointments	2 (3)	2 (3)	4 (7)
Day patient attendances	0 (0)	0 (0)	0 (1)
Accident and emergency	0 (0)	0 (1)	0 (0)
Primary-care services			
General practitioner	8 (13)	4 (5)	7 (8)
Practice nurse	1 (1)	2 (3)	1 (2)
Counsellor/therapist	1 (4)	4 (15)	5 (18)
Medication (%)	64%	40%	56%

TABLE 25 *Total cost per young person over the 2-year follow-up period (£)*

	General CAMHS ($n=43$)			Specialist outpatient ($n=45$)			Specialist inpatient ($n=47$)			ANOVA[a]
Sector	**Mean (SD)**	**Min**	**Max**	**Mean (SD)**	**Min**	**Max**	**Mean (SD)**	**Min**	**Max**	***p*-value**
Secondary health care	37,746 (62,046)	68	269,236	24,724 (46,231)	103	244,043	32,015 (51,541)	69	280,580	0.456
Primary health care	245 (361)	0	2078	385 (873)	0	4325	380 (640)	4	2773	0.503
Education	2654 (2228)	0	12,093	1595 (1456)	0	6393	2098 (2115)	0	8783	0.088
Other community services[b]	150 (806)	0	5244	35 (104)	0	445	37 (110)	0	513	0.504
Total 2-year cost	40,794 (63,652)	1483	274,838	26,738 (46,809)	462	244,174	34,531 (52,439)	86	282,508	0.426
Total cost per week	386 (600)	14	2603	253 (442)	4	2288	325 (487)	1	2588	0.423

a Analysis of variance adjusted for site, sex, age at baseline, baseline BMI and baseline MRAOS score.
b Includes community social, voluntary and private sector services.

TABLE 26 *Individual service contributions to total costs at 2-year follow-up*

Service	% of total costs	Cumulative %
Inpatient	81.34	81.34
Outpatient	10.33	91.67
State day school	3.03	94.70
Hospital school	2.67	97.37
Day patient	0.76	98.13
General practitioner	0.38	98.52
Independent day school	0.37	98.89
Medication	0.28	99.17
Accident and Emergency	0.15	99.32
Community psychiatric nurse	0.12	99.44

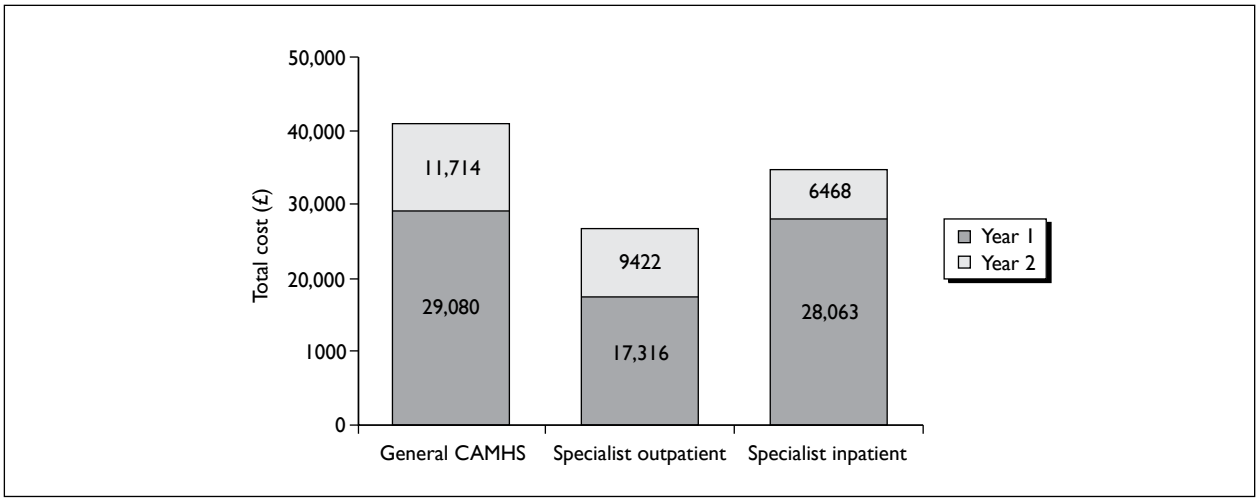

FIGURE 5 *Total cost per young person by year.*

TABLE 27 *Total health and community service costs per primary carer over 2-year follow-up period (£)*

	General CAMHS (*n* = 14)	Specialist outpatient (*n* = 20)	Specialist inpatient (*n* = 16)	ANOVA[a]
Service	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	***p*-value**
Community health services	297 (670)	196 (514)	223 (382)	
Hospital services	258 (335)	218 (311)	440 (805)	
Medication	152 (424)	77 (113)	87 (252)	
Total cost	707 (840)	491 (772)	750 (1199)	0.68

a Analysis of variance adjusted for site, sex, age at baseline, baseline BMI and baseline MRAOS score.

it is both cheaper and more effective. The cost-effectiveness acceptability curve in *Figure 6* illustrates the uncertainty associated with the costs and effects of the three treatments at 2 years. It demonstrates that if decision-makers were willing to pay nothing for a unit increase in MRAOS score, then there would be a 80% chance of specialist outpatient services being the most cost-effective strategy, 16% for inpatient services and only 6% for general CAMHS. The probability of specialist outpatient services being the most cost-effective strategy decreases with increasing levels of willingness to pay for gains in effectiveness. This levels out at around 47%, but remains higher than the other two strategies over the full range of willingness-to-pay values shown, and beyond.

Figure 6 suggests that the probability of our first hypothesis being true is high, i.e. that specialist outpatient services are more cost-effective than general outpatient services. *Figure 7* depicts the cost-effectiveness acceptability curve for the second hypothesis – that outpatient services (specialist combined with general CAMHS) are more cost-effective than inpatient services. It shows that there is a greater probability of outpatient services being more cost-effective than inpatient services for the full range of values of willingness to pay.

Sensitivity analyses explored the impact of missing data on the results of the cost-effectiveness analysis. Similar relationships between the three arms of the study were found, with specialist outpatient services having a higher probability of being cost-effective than the other groups over a wide range of willingness-to-pay values, using both last-value-carried-forward and mean imputation techniques. At a zero level of willingness to pay for effectiveness gains, the probability of being the most cost-effective option ranged between 72 and 80% for specialist outpatient services, 13 and 14% for inpatient services and 7 and 16% for general CAMHS. The probability of general CAMHS being the most cost-effective option remains low for all values of willingness to pay. The probability of inpatient services being the most cost-effective option increases as willingness to pay increases, whereas the probability for specialist outpatient services falls. At values of willingness to pay over £100,000, the probability for inpatient services overtakes that for specialist outpatient services but only for the last-value-carried-forward imputation. In all other missing data sensitivity analyses, the specialist outpatient service dominates across the full range of values of willingness to pay.

The cost of education received by study participants was included to explore the additional costs associated with greater disruption as a result of longer admissions to hospital or greater illness severity, such as hospital school attendance or home tuition. However, it is also the case that

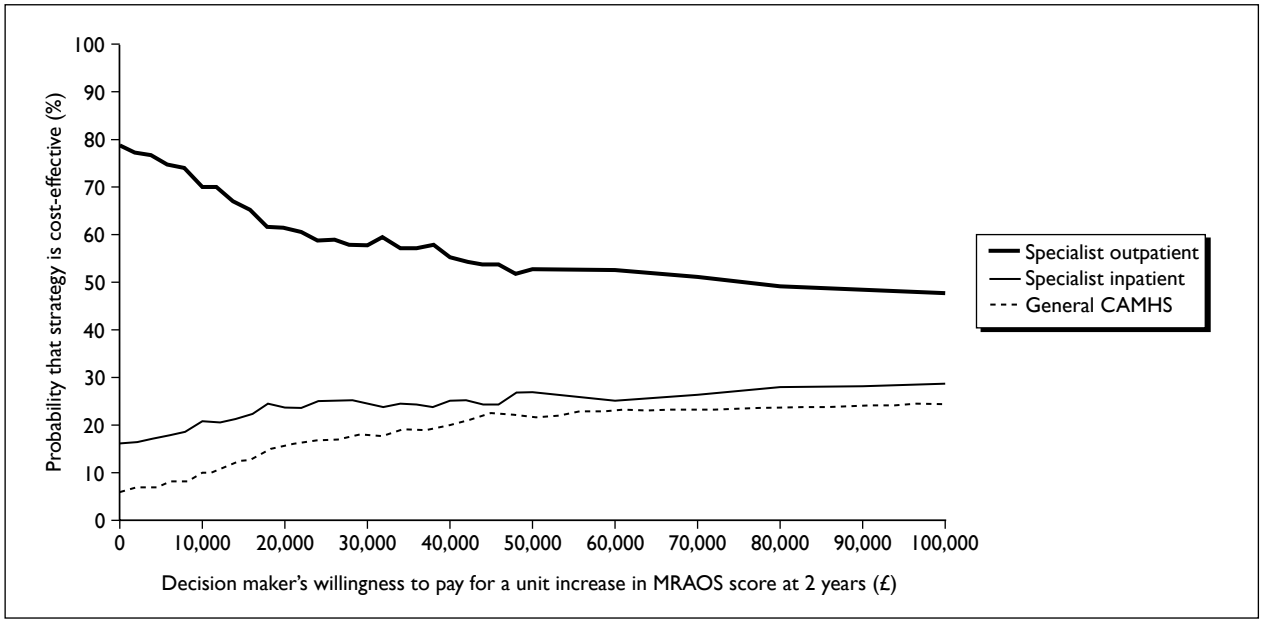

FIGURE 6 *Cost-effectiveness acceptability curve for MRAOS score – three arms.*

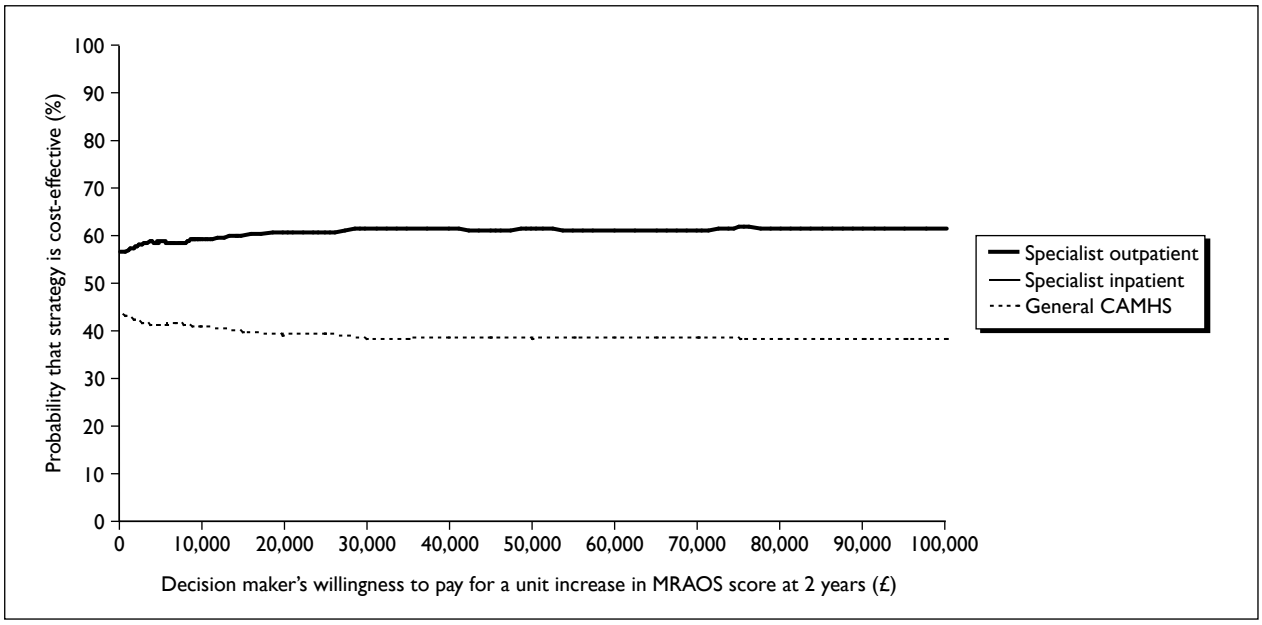

FIGURE 7 *Cost-effectiveness acceptability curve for MRAOS score—inpatient versus outpatient.*

education may be more expensive because a young person has better attendance (a good outcome). For this reason, we undertook a further sensitivity test, which excluded the cost of education. This analysis left the results of the base-case cost-effectiveness analysis unchanged.

Economic evaluation at 5 years

Data availability

Full economic data for the 5-year follow-up period were available for 102 young people (49%). Of those cases randomised, full economic data were available for 71 (41%), 23 in the inpatient group, 28 in the specialist outpatient group and 18 in the general CAMHS group. A comparison of baseline characteristics (site, age, gender, BMI and MRAOS) revealed some differences between those included in the 5-year analysis and those who were missing. Although there was no difference overall in missing data between the three treatment groups, those in the preference arm were more likely to have been followed up than those in the randomised groups. In addition, the young people for whom data were available at follow-up were slightly older than those for whom data were missing. Length of follow-up varied (range 131–223 weeks); however, there was no significant difference in length of follow-up between the three treatment groups on average (mean 168 weeks in the inpatient group, 165 weeks in the general CAMHS group and 166 weeks in the specialist outpatient group).

Accommodation and employment

The type of accommodation and employment status of the young people 3–5 years after baseline is detailed in *Table 28*. During this period, the young people tended to live at home with their parents or independently and there was little use of supported accommodation or residential care.

Almost two-thirds of the participants were employed at some point during the 3 years of follow-up, for an average of 17 months. Self-reported time off work due to illness was low, at only 10 days on average, whereas the average length of time on benefits was 3 months.

TABLE 28 *Accommodation and employment status of young people 3–5 years after baseline*

Service (n = 102)	Mean (SD)
Domestic accommodation (months)	27 (11)
Independent living (months)	8 (11)
Residential care (months)	0 (1)
Supported accommodation (months)	0 (2)
Hostel (months)	0 (1)
Currently employed (%)	61%
Months employed	17 (14)
Days off sick	10 (28)
Months on benefits	3 (9)

Hospital use and cost

Use and total cost of hospital services during the 3–5 years after baseline for the randomised groups is detailed in *Table 29*. There appear to be some quite substantial differences in the use of hospital services between randomised groups, for example the mean number of inpatient nights in both the specialist outpatient and general CAMHS groups is much higher than that in the inpatient group. In addition, the mean number of day-patient attendances in the specialist outpatient group is far higher than attendances in the inpatient and general CAMHS group. Closer inspection of the data reveals that these differences are the result of a skewed dataset where a small number of young people in each group made substantial use of hospital services. For example, two young people in the specialist outpatient group spent very long periods of a year or more in inpatient services and one young person in the specialist outpatient group attended a day-patient service on 730 occasions. Despite these differences in service use, there are no overall differences in total costs between the randomised groups at 5 years. This is largely because of the higher unit costs of inpatient and day-patient attendances at private facilities, which were observed more often in the general CAMHS and inpatient groups than in the specialist outpatient group.

Regression analysis

Variables examined in the regression analysis are reported in *Table 30*. Univariate analysis revealed that higher total costs were significantly associated with lower baseline percentage weight for height ratio, lower MRAOS score, higher MFQ scores and higher HoNOSCA-CR, all in the anticipated direction (i.e. higher costs associated with greater morbidity). Weight for height ratio remained the only variable significantly and independently related to cost in multiple regression analysis (*Table 31*). The results demonstrate that for a unit reduction in the weight for height ratio, total costs over the full 5-year follow-up period increased by £4024. The regression model was able to account for less than 10% of the variation in total costs (adjusted $R^2 = 0.080$), suggesting substantial unexplained variation in this group of young people.

TABLE 29 *Hospital use and cost – young people 3–5 years after baseline*

	General CAMHS (*n* = 18)	Specialist outpatient (*n* = 28)	Specialist inpatient (*n* = 23)
	Mean (SD)	**Mean (SD)**	**Mean (SD)**
Service use			
Inpatient nights	25 (106)	28 (89)	14 (62)
Outpatient appointments	6 (11)	14 (29)	5 (11)
Day-patient attendances	1 (3)	26 (138)	10 (50)
Accident and emergency	1 (1)	1 (5)	0 (1)
Costs (£)			
Inpatient nights	13,758 (58,233)	10,874 (35,128)	8867 (41,561)
Outpatient appointments	1005 (2153)	2263 (5339)	652 (1860)
Day-patient attendances	376 (1553)	2356 (12,399)	5743 (27,523)
Accident and emergency	63 (125)	142 (473)	42 (117)
Total costs	15,203 (61,275)	15,636 (46,545)	15,304 (69,083)

TABLE 30 *Univariate associations with cost over 5 years*

	n	Mean cost (£)	*p*-value
Sex			
Male	6	25,105	0.520
Female	96	56,013	
Age			
≤ 15 years	71	48,118	0.915
> 15 years	31	68,113	
ED type			
Restrictor	75	57,037	0.676
Binge–purger	27	46,303	
Length of history of eating disorder			
≤ 15 months	62	44,776	0.280
> 15 months	38	70,401	
Percentage weight for height			
≤ 78	51	74,913	0.002
> 78	51	33,478	
MRAOS			
≤ 5	51	84,106	0.003
> 5	51	24,285	
MFQ score			
≤ 25	42	25,363	0.104
> 25	57	75,978	
HoNOSCA-CR			
≤ 19	53	26,543	0.014
> 19	49	84,105	
Home situation			
Living with both parents	72	52,850	0.854
All other home situations	30	57,425	

TABLE 31 *Multivariate associations with cost over 5 years*

Variable	Coefficient[a]	(95% CI)	*p*-value
Percentage weight for height ratio[b]	−4024	(−65,773 to −1475)	0.0002

a Adjusted $R^2 = 0.080$.
b The coefficient indicates the decrease in cost over 5 years per unit increase in the variable.

Chapter 4
User and carer satisfaction

Method

All 215 participants and their parents (randomised and non-randomised) were contacted at 1 year for a full clinical assessment. At this point they were given a satisfaction questionnaire to return anonymously by post. This asked them to rate their prior expectations of any treatment they had received (randomised or not) on a seven-point Likert scale (from very positive, to very negative). It then asked them their subsequent level of satisfaction with each treatment received over the course of the year. Participants were also invited to give free comments about any aspect of the services they had received. Many subjects received further treatment during year 2 of the trial. If this included one of the three treatment options not received in year 1, their views on this were elicited, by way of further quantitative ratings and comments by questionnaire at the 2-year follow-up. The quantitative (Likert scale) ratings were collated and simple frequencies were compared across treatment groups.

The qualitative evaluation comprised an analysis of the free comments from the questionnaire supported by data derived from a subsequent series of focus groups.

The authors were familiar with the eating disorder satisfaction literature but a process for data analysis was chosen that aimed to minimise the effect of any preconceptions. The free comments were analysed with the aim of establishing common satisfaction themes through a series of steps, following the established qualitative methodologies described by Mason.[74] First, the comments were collected and coded according to treatment option and whether by parent or child. Then comments from one of the two sites (n approximately 200) were reviewed separately by the three authors who proposed their own series of themes (open coding). These themes were then extensively discussed between coders, resulting in a consensus and a provisional set of agreed themes.

The printed comments were then reduced to individual elements, coded by whether they were positive or negative about the service in question and collated according to the provisional themes. The comments allocated to each theme were reread and the themes were modified several times until there was agreement on the minimum number that reflected the content of the comments. The rest of the data were then allocated according to these themes (focused coding) with no new themes emerging from these data.

In the second qualitative stage, focus groups for parents and adolescents were arranged in the two main sites to further explore the themes and identify any other important issues that were not highlighted in the questionnaires. Purposive sampling was used to select a varied group of participants, receiving each of the treatments but only a relatively small number ($n = 21$) were able to take part. Incidental expenses were offered.

A questioning route was developed for the focus groups that included general questions about satisfaction and specific questions related to the themes we had identified from the questionnaires and that allowed time for other themes to be raised by participants, following prescribed conventions.[75]

The sessions were audio-taped, transcribed, coded and analysed for thematic content in a similar manner to the questionnaire data.[74] Themes were developed, the materials in the focus group were aggregated and the themes were reviewed and modified several times. Other members of the research team then reviewed the themes and the illustrative quotes to reach a consensus that they could be justified from the transcribed material.

To ascertain the independent validity of the themes, an external researcher was given a structured recoding task to match all 430 comments from the questionnaires and focus groups to a list of 10 themes or identify additional themes not covered.

Results

The questionnaire response rate was 76% (160 out of 215) for adolescents and 71.8% (150 out of 215) for parents. The rate of response by treatment

group was proportional to the numbers receiving it, suggesting that there was no response bias by treatment received. As some participants received more than one treatment, the total number giving an opinion of each treatment option exceeded the number of participants in the trial. For the purposes of analysis, the three negative categories and the three positive categories were collapsed for both expectation and satisfaction.

Prior expectation

Parents had very positive expectations of all treatment options, significantly higher than those of their children (see *Table 32*). There were no statistically significant differences in parental expectations between treatments but adolescents' expectations of general CAMHS treatment were lower than of the more specialist options.

Satisfaction

Parents reported being generally satisfied with all treatments but were significantly more satisfied with specialist outpatient treatment than with general CAMHS (*Table 32*), inpatient treatment showing intermediate levels of satisfaction. However, overall satisfaction levels were notably lower than their very high prior expectations.

Adolescents had more mixed experiences of treatment, with significantly lower overall levels of satisfaction than parents. Many young people rated the treatments negatively. However, as with their parents, adolescents appeared more satisfied with specialist outpatient treatment than general CAMHS but this finding was not statistically significant. Whereas parents' expectations appeared unrealistically high, the adolescents' expectations seemed borne out by their subsequent experience.

Qualitative results

General

Most of the questionnaire respondents added at least one comment. In total 375 responses from the questionnaires were analysed as follows:

- adolescent inpatient = 40
- adolescent general CAMHS = 67
- adolescent specialist outpatient = 64
- adolescent other treatment = 14
- parent inpatient = 48
- parent general CAMHS = 66
- parent specialist outpatient = 65
- parent other treatment = 19.

Some responses incorporated more than one comment and were therefore split, yielding a total of 430 comments.

There were slightly more positive than negative comments. The 10 most common themes relating to treatment satisfaction are presented in *Table 33*; 71% of the comments fitted into these themes. A large number of the remainder comprised general appraisals of services (repeating the Likert scale ratings) or comments about the outcome of treatment. The independent rater's validity check revealed a very high level of agreement for the major themes and resulted in even more examples of comments about clinician expertise being identified. An extra theme emerged from this exercise of the perceived value of developing insight into the condition.

Themes highlighting differences between treatment groups

The importance of expertise (48 comments)

> 'I think the trouble with CAMHS is that they do have a working knowledge of adolescence and mental health disorders but not necessarily with the anorexia side of it…Yeah I mean they tried their best but…' [parents' focus group]

The highest number of negative comments and some of the most strongly worded comments were related to this theme and were almost exclusively made in relation to a perceived lack of expertise in general CAMHS. We wondered why specialist knowledge should be so important, if the things that were most frequently identified as helpful were generic skills that should be found in all services. In the focus groups it appeared that a combination of these qualities was considered essential. Therapists needed to gain the trust of parents and young people by demonstrating their familiarity and understanding of what people with eating disorders may go through.

> 'The most helpful aspect of the treatment was that my daughter trusted the people she was working with and was therefore more ready to follow their advice. I think she trusted them because they were experienced and sympathetic' [parent questionnaire]

This expertise also needs to be used sensitively (or expertly). It was not appreciated if it was conveyed in the form of too much direct advice giving or comparison with previous patients:

TABLE 32 *Expectation and satisfaction with treatment*

Inpatient				General CAMHS				Specialist outpatient			
Adolescent (*n* = 46)		Parent (*n* = 48)		Adolescent (*n* = 83)		Parent (*n* = 83)		Adolescent (*n* = 82)		Parent (*n* = 74)	
Expectation (*n* = 46)	Satisfaction (*n* = 40)	Expectation (*n* = 47)	Satisfaction (*n* = 44)	Expectation (*n* = 80)	Satisfaction (*n* = 80)	Expectation (*n* = 77)	Satisfaction (*n* = 76)	Expectation (*n* = 80)	Satisfaction (*n* = 78)	Expectation (*n* = 69)	Satisfaction (*n* = 68)
11	12	1	7	29	30	7	19	20	17	3	8
6	3	1	6	23	8	4	10	13	11	2	4
29	25	45	31	28	42	66	47	47	50	64	56

Expectation: Parents versus adolescents: $\chi^2 = 76.54$, df = 2, $p < 0.01$; parents by group χ^2 not significant. Adolescents by group $\chi^2 = 13.2$, df = 2, $p < 0.05$.
Satisfaction: Parents versus adolescents $\chi^2 = 7.72$, df = 2, $p < 0.05$; parents by group $\chi^2 = 7.42$, df = 2, $p < 0.05$. Adolescents by group $\chi^2 = 4.8$, df = 2, $p = 0.09$.

TABLE 33 *Treatment satisfaction themes – from questionnaires*

Theme	Number of comments
1. Importance of an individual relationship	101
2. Importance of expertise	48
3. Parental involvement in treatment	39
4. Communication with parents and other agencies	28
5. Mixing with other patients	22
6. Importance of dietary therapy	19
7. Access and flexibility of treatment	12
8. Delay or lack of intensity of treatment	10
9. Too much focus on psychological factors (motivation or talking)	10
10. Too much focus on weight	7

> 'They say "Yeah well I've seen one girl who did this and did this and now she's better so now you can do it" but I'm not her' [adolescent focus group]

Availability of dietetic therapy (19 comments)

The only professional role the importance of which was repeatedly singled out was the dietician's. This was highly valued and there was some concern when this service was not available. Both of the specialist services involved had dedicated specialist dietetic input. This is often not available for CAMHS teams without such high patient flows.

Themes highlighting differences between parents and young people

Overall parents made more comments related to service delivery issues, availability of services, communication, access and flexibility, and in the focus groups raised major concerns about the difficulties of getting the eating disorder recognised in primary care.

Family therapy and parental involvement (39 comments)

Parent and family support was very often highlighted.

> As parents we did get a lot of support and helpful advice on how to cope and manage our daughter's illness [parent questionnaire]

Parents greatly valued family work and wanted to be kept informed and to be able to ask questions. There was unease about being excluded from some aspects of treatment because of confidentiality issues or a perceived need to protect the therapeutic relationship. On the other hand, there was an appreciation that some degree of separation from parents had its place in helping the young person to talk. In the focus groups there was strong advocacy for parent support groups and strong views that siblings were not well catered for.

Young people appreciated the need for family work but were not as enthusiastic about it as their parents. In the focus groups it was apparent that young people thought it vital that their parents receive support themselves but found the joint sessions to be challenging and often unhelpful.

Contrary to our preconception that some forms of family therapy might be perceived as blaming of parents, there were no comments about this. This issue was specifically addressed in the focus groups where a number of parents reported that they valued professionals actively helping them to disabuse themselves of feeling guilty that their child had AN.

> You think it yourself 'did I do something wrong?' as a parent…I think all parents do with a lot of illnesses but I think they were very clear here that it's a lot of issues, it's a lot of things, it's complex, it's genetic, it's personality it's partly this…you haven't to blame yourself [parents' focus group]

Common themes across treatment groups

Many of the satisfaction comments applied to all treatment options.

Importance of an individual therapeutic relationship (101 comments)

The most prominent theme that emerged was the important impact of individual therapeutic relationships. Around 80% of these comments spoke in positive terms about the helpfulness of specific clinicians.

> It was good to go and talk to a specialist who understood my feelings and fears. [A]'s understanding and friendliness was very useful to me and it was good that she listened [adolescent questionnaire]

More than 50 comments named clinicians who were appreciated, mostly for generic interpersonal

and psychotherapeutic skills such as listening, understanding, seeing the whole person and forming a good relationship with them.

Themes eliciting polarised views

Mixing with other inpatients (22 comments)

An area where there were strongly polarised views among both young people and parents, was the helpfulness, or otherwise, of mixing with other patients in inpatient units. There were many comments about this in the questionnaires, which were explored further in the focus groups. Some extolled the benefits of mixing with non-eating-disordered patients to gain broader perspectives, share common difficulties and obtain distance from other patients with eating disorders. Others had very negative views on the stress of being on a mixed unit with young people with serious mental disorders and felt the influence of other eating-disordered patients was supportive.

Focus on weight and physical issues (seven comments)

We had expected, on the basis of the existing literature, to find a number of comments about there being too much focus on weight and other physical factors. There were only seven comments to this effect and in contrast there were 10 comments about there being too much focus on psychological issues such as motivation.

Chapter 5
Summaries of findings

Summary of clinical trial

The TOuCAN trial was successful in recruiting in excess of the required number of cases as calculated by the power estimate. As such, this trial represents the largest RCT of AN carried out to date; successfully recruiting the vast majority of new cases known to CAMHS during the recruitment phase. It is a population-based pragmatic, effectiveness RCT based on the range of NHS treatments available in the north-west of England and probably typical of the rest of the country. One of these treatments (the specialist outpatient programme) was manualised, with fidelity checks; the other two arms represented treatment 'as usual' in generic CAMHS and the four regional inpatient units.

Tracing and follow-up were also satisfactory and almost complete to the 2-year time point but less so at 5 years. Reliable and robust outcome measures were used.

Adherence to treatment allocation was less than optimal, reflecting the real world of services and in particular attitudes of patients with AN and their families to treatment. Nevertheless, the data collected and its analysis are adequate to answer the clinical hypotheses:

- Inpatient treatment is not more clinically effective than outpatient treatment.
- Specialist treatment was not found in this study to be more effective than general CAMHS treatment – at least in the short term but it may possibly be in the longer term.

The subanalysis of those allocated to inpatient treatment, examining adherence, suggests poorer outcomes for those actually admitted, even taking into account the baseline levels of measured psychopathology. However, these findings should be treated cautiously given that the two subgroups (adhering and not), may differ on significant but unmeasured variables such as motivation and ability to respond to the assessment interview in the immediate days before admission was available.

The analysis of prognostic indicators reveals that baseline levels of morbidity (chiefly the main outcome measure – MRAOS) and degree of thinness (percentage weight for height) are powerful predictors of service use and medium-term to long-term outcome. Self-reported eating psychopathology at baseline is also a notable predictor of long-term outcome based on the main outcome measure.

Anorexia nervosa is often a chronic disorder in which a number of young people are still ill with the condition at 5-year follow-up. However, it is not primarily a remitting and relapsing disorder, with those who managed to achieve recovery tending to stay well.

Summary of economic analysis

This study represents the first economic evaluation of alternative strategies for the treatment of AN using primary data collected from an RCT.

At 2 years, the specialist outpatient group were the least costly and the general CAMHS group was the most costly, although these results were not statistically significant. These findings were robust to sensitivity analysis of the discount rate and in analyses of missing data. Observed differences in total mean cost per patient were almost entirely the result of differences in the length of time spent in hospital.

The majority of inpatient admissions took place during the first year and there was substantial cross-contamination of groups. For example, although not randomised to psychiatric inpatient services, the general CAMHS group spent almost as much time in hospital as the inpatient group. This finding suggests that general CAMHS were less successful at maintaining the young people in the community than the specialist outpatient services.

With the exception of CAMHS, participants used very few community health and social services. The number of months in education was similar across the groups on average, though the relatively low mean number of months in this adolescent population highlighted the significant proportion

of time participants spent out of education, presumably as a result of their illness.

The annual service costs of caring for this group of young people, £17,000, are substantial and much higher than the cost of conditions generally treated in the community – for example, conduct disorder with annual service cost estimates varying between £1300 and £3200.[58,72] However, the annual cost is similar to the cost of a cohort of young people with mental health problems that led to them being treated in child and adolescent psychiatric inpatient wards, estimated to be £24,000 per admission.[76] The slightly higher costs in this case were the result of longer mean lengths of stay, on average.

The results of the cost-effectiveness analysis reveal that specialist outpatient services were the dominant treatment option in terms of incremental cost-effectiveness, as they were more effective and less costly. The cost-effectiveness acceptability curves, which consider associated uncertainty, support this finding. In terms of our hypotheses, the data suggest that specialist outpatient services have a higher probability of being cost-effective than general CAMHS and that outpatient services (specialist combined with general) have a higher probability of being cost-effective than inpatient services.

By the 5-year follow-up, hospital-use information was available for less than half of the randomised cases, and the skewed nature of the data (because of a small number of young people with lengthy hospital or day-case admissions) makes it difficult to reach conclusions on differences in resource use and costs. Some clear findings do emerge however. First, the trend in reductions in hospital use between years 1 and 2 was maintained over the longer term with, on average, much lower use of hospital services by 5 years follow-up. Second, there were no differences in average total cost per young person between randomised groups.

Univariate regression analysis at 5-years demonstrated that more severe cases of anorexia nervosa at baseline, including those with lower percentage weight for height and lower MRAOS scores (poorer health), cost significantly more in terms of hospital costs over the 5-year follow-up. In addition, those with more severe mental health problems, as measured by the MFQ and the HoNOSCA-CR, cost significantly more in terms of hospital costs over the 5-year follow-up. However, when these variables were included in a multiple regression analysis, only weight for height remained significant, suggesting that thinness at baseline was the most important factor predicting high costs in terms of hospital services over 5 years.

Summary of satisfaction study

This study provided a wealth of information from both users and carers in relation to their experience of the range of treatment approaches.

Overall, levels of satisfaction with services were good with young people being twice as likely to express positive as negative views of their treatment. Parents were much more satisfied with about five times as many expressing positive as negative views of treatment. Parents were consistently more satisfied than young people with each treatment, but both parents and young people were more satisfied with specialist than general treatments. The satisfaction of both young people and their parents was largely based on their confidence in 'expertise' and forging a good relationship with an individual therapist working on either an inpatient or an outpatient basis.

Chapter 6
Conclusions

- Lengthy inpatient psychiatric treatment, although commonly employed for adolescent AN, offers no advantage over good-quality outpatient care and is more expensive.
- Treatment in specialist services offers little advantage over good-quality multidisciplinary care delivered in generic CAMHS with a family approach, although both young people and their parents prefer it.
- Treatment in a specialist outpatient programme is likely to be the most cost-effective treatment approach for adolescent AN, chiefly because it reduces the need for later inpatient care.
- The traditional model of stepped care from outpatient to inpatient care for those who fail to respond is not supported by this trial, as transfer from outpatient to inpatient care after the study period generally yielded poor outcomes.
- As AN is associated with serious physical and psychological risk, inpatient admission is probably unavoidable because approximately 50% of patients expecting to be treated as outpatients were admitted in the first 2 years of the study. This trial was unable to reach conclusions about the best setting or length of admission, for such unplanned admissions.
- Anorexia nervosa in adolescents is commonly a chronic condition lasting a number of years, in which any one episode of care is unlikely to result in a complete cure.
- Nevertheless, at 2 years from presentation to CAMHS only 26% have the full syndrome, whereas 33% have gone into remission, often with recovery lasting to 5 years.
- Achieving a very low weight (as a % of expected weight) in the early stages of the illness and severity, as measured by a global assessment measure for eating disorders comprising psychosocial as well as physical aspects, is a good predictor of long-term outcome as well as use of services.
- Achieving a very low weight (as a % of expected weight) in the early stages of the illness is also a good predictor of long-term total costs.
- Young people and to some extent their parents have low expectations that generic CAMHS will meet their treatment needs and they want treatment in specialist centres, delivered by staff with expertise in managing the condition.
- Young people's experience of treatment is mixed but they tend to be satisfied with treatment in specialist services. Parents are generally quite satisfied, particularly with specialist care, even when outcomes are poor.
- There are a number of areas in which there is a lack of consensus among service users about aspects of care which are valued and disliked. Examples include the balance in emphasis between physical and psychological aspects of care and the desirability or otherwise of mixing with other young people with eating disorders.

Discussion

This pragmatic treatment trial has attempted to address the issues posed by the brief concerning the merits of different models of care for adolescent AN. Specifically, little was previously known of the relative clinical effectiveness and cost-effectiveness of different service settings or young people's and their parents' satisfaction with these.[11] The brief was an important one because of the extremely high cost of inpatient care,[35,61] when stays commonly last several months and when AN makes a major demand on adolescent inpatient services.[5] The facility to offer long-term psychiatric (as opposed to medical) treatment in the UK has often been highly valued, clinical intuition suggesting that more intensive treatments should be more effective than briefer, non-specialist treatment for a condition that is often chronic and has a high morbidity and mortality.

Previous cohort and treatment studies[28,37,41] have raised questions about the value of inpatient care, but without a randomised allocation to inpatient care it has been difficult to evaluate the benefits of admission over and above outpatient management; although the one systematic review concluded that outpatient treatment in a specialist eating disorder service was as effective as inpatient treatment in those not so severely ill as to warrant emergency admission. Furthermore, these reviewers estimated the costs of outpatient treatment to be approximately one-tenth the cost of inpatient treatment.[27]

Not surprisingly, given the ambivalence of young people with AN to treatment and the large personal and family investment required of those admitted to inpatient care, adherence to this arm of the trial was unavoidably less than optimal. In addition, given the often chronic nature of the condition, it was not possible to keep patients treatment-free between the treatment and follow-up phases. It might be argued that a 6-month follow-up assessment point would have been useful to assess the trial interventions before the picture became blurred by subsequent treatment. However, we deliberately avoided doing this as recommendations in this field[11] suggest 2 years as a minimum useful follow-up point and because it is well known that inpatient gains are often short-lived (for example in the St George's and Maudsley trials[28,41]) and so such an assessment point would be likely to favour this treatment arm.

Nevertheless, this trial has reached some important conclusions, particularly given the recruitment design, which was highly inclusive, population-based and used readily available CAMHS. This study is much larger than those reported in the literature to date and includes around four-fifths of incident cases known to child and adolescent mental health services in the north-west of England over a 3-year period. We achieved a high follow-up rate with demonstrably reliable outcome measures.

The findings challenge a number of notions about care for this disorder. In particular, psychiatric inpatient treatment does not confer advantages over outpatient care, and is associated with a lower probability of being cost-effective than the combined outpatient groups. Although adherence to inpatient care was only 50%, the subanalysis reveals that rather than the outcome of this arm being adversely affected by a lack of adherence, in fact, the overall (intention-to-treat) outcomes are improved by the better outcomes of those declining admission once offered it. The subanalysis of those accepting or declining admission within the inpatient arm should, however, be interpreted with caution. It may be that the decision to accept randomised admission is based on a number of negative prognostic variables, rather than it reflecting on the inpatient treatment itself. Based on the predictive model for admission developed among patients not admitted, one can see that those adhering to admission had a higher probability of admission based on baseline characteristics. Possibly some unmeasured variables such as motivation or family resources may have accounted for the difference in response.

This finding does not deny the necessity of emergency medical management of physical complications in an inpatient setting, which may on occasions be life-saving, but our results do suggest that inpatient management is rarely associated with comprehensive recovery, as opposed to improvement or stability within the condition.

The finding that specialist care offers few advantages requires clarification. In some respects the findings mirror the results from the New Zealand trial,[77] in which an adult (and probably less severely unwell) series did as well with non-specific supportive clinical management as with two specialist psychological therapies. As with this trial, it is important not to underestimate the quality of the 'control' or generic intervention. General CAMHS (as opposed to adult Community Mental Health Teams, for example) commonly offer psychological therapies (often based on CBT) and family-based treatments in the context of a developmental perspective – an approach which suits this condition well. However, the greater success of specialist outpatient services at maintaining young people in the community resulted in a poorer performance in terms of cost-effectiveness for general CAMHS. This relative cost-effectiveness of specialist care may be the result of the inexperience of managing AN in the CAMHS teams and the resulting anxiety which may have led to the more frequent hospital admissions and costs of this treatment. This anxiety may in turn have transmitted itself to the families involved, leading to lower levels of satisfaction.

It is also of note that the specialist outpatient arm was the only manualised treatment and also incorporated fidelity checks. This may have added to its effectiveness and these components are essential in comparing findings across different studies.

Our study suggested that there was a reasonably high level of satisfaction for each of the treatment groups in this trial, by parent and, to a lesser extent, patient perspective. The overall response rate (over 72%) would appear good for a satisfaction measure, but we are unable to say whether non-responders would have been less satisfied over all, or with one particular treatment option. As in a Norwegian study,[78] this was in spite of the clinical outcomes. When expectations of a service are greater than perceived performance, then quality will be judged as less satisfactory and dissatisfaction will be high. Although definitions of satisfaction vary, satisfaction has been defined

as being about 'the appraisal of the extent to which the care provided has met the individual's expectations and preferences'.[79] In our study, parental expectations were very high, rendering them liable to dissatisfaction when the experience was less than anticipated.

The literature often reveals negative experiences of inpatient treatment. A postal survey of members of the Eating Disorders Association[78] revealed mixed experiences, with slightly more respondents feeling this made the situation worse than found it very helpful. These findings were largely replicated in a Norwegian survey that showed patients were relatively satisfied with outpatient individual and group therapies (and to a lesser extent with family therapy) and dissatisfied with inpatient treatment.[81] This survey showed that patients particularly valued therapist expertise, results duplicated in a survey of 300 patients from the Netherlands.[80]

The most reported theme in our series – the importance of a relationship with an individual professional – replicates findings from previous research in the eating disorder field and within mental health more generally. Good generic psychotherapeutic skills are seen as very important by service users. All three treatment modalities in the study generally aimed to provide these and there was no perception that therapy was overly focused on physical aspects.

General CAMHS compared unfavourably with specialist outpatient and inpatient services, mainly because of a perceived lack of expertise with eating disorders. It may be that when parents and adolescents are accessing specialist services, they feel reassured that they are in the right hands because of the 'specialist' status even if they are not making significant clinical progress. This view was borne out by the quantitative data, which suggested that adolescents had lower expectations of CAMHS, than other treatments, though strikingly 86% of parents had positive expectations of CAMHS treatment. During the TOuCAN study, a survey of the local CAMHS teams found that the average number of AN presentations to CAMHS was around two or three cases a year. It may well be that generic clinicians do not become familiar with working with what can be a particularly demanding condition and at particularly worrying stages of the treatment; professionals without experience of eating disorders may therefore find it harder to maintain the positive aspects of their therapeutic relationship. Experienced specialists working with colleagues with similar expertise may be more able to maintain warmth, hope and positivity in the face of uncertain outcomes and the chronic nature of the condition, and also possibly avoid the hospital admissions which drive up costs. Greater patient flows also enable specialist services to incorporate dietetics and creative therapies into their treatment programmes.

It is encouraging that unlike previous reports, we did not find that families reported feeling blamed by services for the condition of their daughter or son. In fact they greatly valued the support that they received and their involvement in treatment. A strong message was given in the focus groups about the impact of eating disorders on siblings. This should encourage services to continue to offer parental and family therapies in keeping with NICE recommendations.

Limitations of the trial

It could be argued that the inpatient services in the study were not truly *specialised* because they were not *exclusive* eating disorder facilities. However, all four units had extensive experience and tradition of treating such cases. Indeed 17 cases entered other (often exclusive) specialist inpatient services in the follow-up period of the study and nevertheless, had (generally) poor outcomes at 2 years.

The present study was devised before the more recent positive outcomes of family-based treatment[81] were published and it is of note that our findings suggest poorer outcomes. We had been impressed by the preliminary outcomes of CBT-Enhanced[16] in addressing the core psychopathology of eating and weight concerns, and questioned the power of family-based treatment to address these as opposed to behavioural aspects of the condition.

The outcome of our individual CBT was poorer than reported for family-based treatment – a direct comparison is required on a similar population to clarify this further.

In the cost-effectiveness analysis, despite substantial observed differences in costs between groups, the differences did not reach statistical significance at 2 years. This may be because of inadequate sample sizes for the economic evaluation because sample size calculations were based on the primary outcome measure, the MRAOS. Calculations on the basis of cost or cost-effectiveness were not feasible

at the design stage because of the lack of any relevant published cost data, but it is possible that a sample calculated in this way may have required a much larger sample. Although acknowledging this limitation, the use of a decision-making approach to the economic evaluation provides probabilistic evidence of the cost-effectiveness of the alternative treatment strategies, given the data currently available. Larger trials may be considered in the future, but this must be balanced against the cost of additional research in a disease area where low prevalence rates necessitate large and resource intensive multicentre evaluation.

Analysis of patients excluded because of missing economic data at both 2 and 5 years did not suggest any bias; patients included in the economic evaluation did not differ significantly from those excluded and there was no evidence to suggest any bias in missing data between the three treatment groups. On the whole, exploration of missing data in sensitivity analysis supported the results of the main analysis.

This study was able to demonstrate the value of economic evidence as a decision-making tool in situations where clinical differences between treatments are minimal. However, the value of the results presented is more limited in a broader decision-making context because of the lack of a generic, preference-based measure of outcome. NICE guidelines, for example, require evidence of cost-effectiveness (to be presented in terms of cost per quality-adjusted life-year) to allow comparison across diverse disease areas to support the allocation of scarce societal health and personal social services resources.[65] Future studies should consider the inclusion of such measures so as to place services for adolescents with AN within this broader decision-making context.

Implications for health care

For moderately to severely ill adolescents with AN, outpatient services delivered by experienced, expert professionals, supported by medical management of physical complications as required, offer the most cost-effective treatments. Lengthy psychiatric inpatient treatment does little to add to positive outcomes and is cost-ineffective. Treatment in specialist services, with experience and expertise in managing the condition, is to be preferred because of its cost-effectiveness and higher levels of both young people's and carer's satisfaction. Where young people with AN are managed in community CAMHS, a consultation and advice link with a specialist service may enable the CAMHS to contain anxiety and reduce unnecessary hospital admissions, thereby leading to greater user satisfaction. This needs further investigation.

The findings are broadly consistent with the NICE guidelines on the treatment of AN. Although physical risk should not be underestimated and may require urgent and active intervention, this trial does not lend support to the advantages of managing this within a psychiatric service.

Recommendations for future research

Further research is recommended in the following areas.

Clarify the positive and negative aspects of inpatient care

Physical and psychological risk, parental anxiety and social and educational withdrawal often result in inpatient admission. The opportunities for intensive psychological therapies, general support, refeeding and respite from external stresses make specialist inpatient care a logical step. Satisfaction (particularly among parents) is quite good. However, research outcomes are consistently disappointing, suggesting that adverse effects are under-recognised. Some are likely to be associated with the specifics of inpatient care, such as reinforcement of feelings of ineffectiveness; some to do with difficulties negotiating discharge and continuity of care. These need further clarification.

Clarify the optimum length of stay for inpatient care

Some of the adverse effects of inpatient care may relate to 'institutionalisation', reinforcement of the sick role, or a deskilling effect on both young people and their carers. A study comparing brief stays to stabilise physical health and initiate normal eating, with longer more comprehensive treatment, would help to clarify these issues. Again user views and a health economic component should be incorporated into such a study, given the high cost of inpatient care.

Evaluation of the efficacy and cost-effectiveness of individual psychological therapies

The current findings lent only modest support to the specialist programme used in this study comprising CBT with dietary therapy and parental counselling. As AN is a psychological disorder based on abnormal cognitions, further research is required to evaluate the effect of different approaches on the specific (weight and shape) and non-specific cognitions underlying the disorder. This research in adults is ongoing, but untested in (particularly younger) adolescents.

Evaluation of co-ordinated individual psychological therapies with family-based treatments

Since this project started, research into family-based treatments has been productive and indicated that these can be effective. However, they have not been adequately tested against individual approaches. For pragmatic as well as theoretical reasons, (supported by our user views), adolescents should receive individual therapies and the family should be involved. The specific components of combined therapies and how these should be co-ordinated to produce cognitive as well as behavioural change, requires further testing.

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Contributions of authors

Simon G. Gowers was the principal investigator and designed the study and was lead author of the report. Andrew F. Clark led the research at the Manchester site and contributed to writing and editing the report. Chris Roberts, lead statistician, helped in the statistical design, analysis and report writing and editing. Sarah Byford and Barbara Barrett were responsible for health economic design, analysis, report writing and editing. Alison Griffiths, Vanessa Edwards, Claudine Bryan and Nicola Smethurst were project trial managers and contributed to clinical support, data management, tracing and report editing. Laura Rowlands, a project trial manager, helped with clinical support, data management, tracing, the satisfaction study and the report editing and Peter Roots lead the satisfaction study and contributed to editing the report.

Publications

Gowers SG, Clark A, Roberts C, Griffiths A, Edwards V, Bryan C, *et al*. Clinical effectiveness of treatment for anorexia nervosa in adolescents – Randomised controlled trial. *Br J Psychiatry* 2007:**191**;427–35.

Byford S, Barrett B, Roberts C, Clark A, Edwards V, Smethurst N, *et al*. Economic evaluation of a randomised controlled trial for anorexia nervosa in adolescents. *Br J Psychiatry* 2007:**191**;436–40.

Roots P, Rowlands L, Gowers S. User satisfaction with services in a randomized controlled trial of adolescent anorexia nervosa. *Eur Eat Disord Rev* 2009:**17**;331–37.

References

1. van Hoeken D, Seidell J, Hoek H. Epidemiology. In Treasure J, Schmidt U, Van Furth E, editors. *Handbook of eating disorders*. 2nd edn. Chichester: Wiley; 2003. pp. 11–34.

2. Doyle J, Bryant-Waugh R. Epidemiology. In Lask B, Bryant-Waugh R, editors. *Anorexia nervosa and related eating disorders in childhood and adolescence*. 2nd edn. Hove: Psychology Press; 2000. pp. 41–63.

3. van Son GE, van Hoeken D, Bartelds AIM, van Furth EF, Hoek HW. Time trends in the incidence of eating disorders: a primary care study in the Netherlands. *Int J Eat Disord* 2006;**39**:565–9.

4. Lucas AR, Beard CM, O'Fallon WM, Kurland LT. 50-year trends in the incidence of anorexia nervosa in Rochester, Mn–a population-based study. *Am J Psychiatry* 1991;**148**:917–22.

5. O'Herlihy A, Worrall A, Lelliott P, Jaffa T, Hill B, Banerjee S. Distribution and characteristics of in-patient child and adolescent mental health services in England and Wales. *Br J Psychiatry* 2003;**183**: 547–53.

6. Keel PK, Dorer DJ, Eddy KT, Franko D, Charatan DL, Herzog DB. Predictors of mortality in eating disorders. *Arch Gen Psychiatry* 2003;**62**:179–83.

7. Zipfel S, Reas DL, Thornton C, Olmsted MP, Williamson DA, Gerlinghoff M, *et al*. Day hospitalization programs for eating disorders: A systematic review of the literature. *Int J Eat Disord* 2002;**31**:105–17.

8. Key A, Mason H, Bolton J. Reproduction and eating disorders: a fruitless union. *Eur Eat Disord Rev* 2000;**8**:81–91.

9. Steinhausen HC. The outcome of anorexia nervosa in the 20th century. *Am J Psychiatry* 2002;**159**: 1284–93.

10. Commission on Adolescent Eating Disorders Eating disorders. In Evans DL, Foa EB, Gur RE, Hendin H, O'Brien CP, Seligman MEP, *et al*. editors. *Treating and Preventing Adolescent Mental Health Disorders*. New York: Oxford University Press; 2005. pp. 257–332.

11. National Collaborating Centre for Mental Health (NCCMH). *Core interventions in the treatment and management of anorexia nervosa, bulimia nervosa, and binge eating disorder*. London: British Psychological Society/Gaskell; 2004.

12. Gowers SG, Bryant-Waugh R. Management of child and adolescent eating disorders: the current evidence base and future directions *J Child Psychol Psychiatry* 2004;**45**:65–83.

13. Treasure J, Schmidt U. Anorexia nervosa: *Clin Evid* 2002;**7**:824–33.

14. Gowers S, Claxton M, Rowlands L, Inbasagaran A, Wood D, Yi I, *et al*. Drug prescribing in child and adolescent eating disorder services (CAMH). *Child Adolesc Ment Health* 2005;**10**:170–8.

15. Fairburn CG, Marcus MD, Wilson GT. Cognitive-behavioral therapy for binge eating and bulimia nervosa: a comprehensive treatment manual. In Fairburn CG, Wilson GT, editors. *Binge eating: nature, assessment and treatment*. New York, NY: Guilford Press. 1993; pp. 361–404.

16. Fairburn C, Cooper Z, Shafran R. Cognitive behaviour therapy for eating disorders; a 'transdiagnostic' theory and treatment. *Behav Res Ther* 2003;**41**:509–28.

17. Minuchin S, Baker L, Rosman BL, Liebman R, Milman L, Todd TC. Conceptual model of psychosomatic illness in children: family organization and family therapy. *Arch Gen Psychiatry*,1975;**32**:1031–8.

18. Russell GF, Szmukler GI, Dare C, Eisler I. An evaluation of family therapy in anorexia nervosa and bulimia nervosa. *Arch Gen Psychiatry* 1987;**44**:1047–58.

19. Robin A, Siegel PT, Moye AW, Gilroy M, Dennis AB, Sikand A. A controlled comparison of family versus individual therapy for adolescents with anorexia nervosa. *J Am Acad Child Adolesc Psychiatry* 1999;**38**:1482–9.

20. Le Grange D, Eisler I, Dare C, Russell GFM. Evaluation of family therapy in anorexia nervosa: a pilot study. *Int J Eat Disord* 1992;**12**:347–59.

21. Eisler I, Dare C, Hodes M, Russell GFM, Dodge E, Le Grange D. Family therapy for adolescent anorexia nervosa: the results of a controlled comparison of two family interventions. *J Child Psychol Psychiatry* 2000;**41**:727–36.

22. Asen KE. Developments in multiple family therapy. *J Family Ther* 2002;**24**:3–16.

23. Scholtz M, Asen E. Multiple family therapy with eating disordered adolescents. *Eur Eat Disord Rev* 2001;**9**:33–42.

24. Dare C, Eisler I. A multi-family group day treatment programme for adolescent eating disorder. *Eur Eat Disord Rev* 2000;**8**:4–18.

25. Gowers SG, Edwards V, Fleminger S, Massoubre C, Wallin U, Canalda G, *et al*. Treatment aims and philosophy in the treatment of adolescent anorexia nervosa in Europe. *Eur Eat Disord Rev* 2002;**10**: 271–80.

26. Nicholls D, Bryant-Waugh R. Children and young adolescents. In Treasure J, Schmidt U, Van Furth E, editors. *Handbook of eating disorders*. 2nd edn. Chichester: Wiley; 2003. pp. 415–34.

27. Meads C, Gold L, Burls A. How effective is outpatient compared to inpatient care for treatment of anorexia nervosa? A systematic review. *Eur Eat Disord Rev* 2001;**9**:229–41.

28. Crisp AH, Norton KWR, Gowers SG, Halek C, Levett G, Yeldham D, *et al*. A controlled study of the effect of therapies aimed at adolescent and family psychopathology in anorexia nervosa. *Br J Psychiatry* 1991;**159**:325–33.

29. Gowers S, Norton K, Halek C, Crisp AH. Outcome of outpatient psychotherapy in a random allocation treatment study of anorexia nervosa *Int J Eat Disord* 1994;**15**:165–79.

30. Cho WH, Lee H, Kim C, Lee S, Choi K-S. The impact of visit frequency on the relationship between service quality and outpatient satisfaction: a South Korean study. *Health Serv Res* 2004;**39**: 13–33.

31. Bell L. What can we learn from consumer studies and qualitative research in the treatment of eating disorders? *Eat Weight Disord* 2003;**8**:181–7.

32. Swain-Campbell NR, Surgenor LJ, Snell DL. An analysis of consumer perspectives following contact with an eating disorders service. *Aust NZ J Psychiatry* 2001;**35**:99–103.

33. Simon J, Schmidt U, Pilling S. The health service use and cost of eating disorders. *Psychol Med* 2005;**35**:1543–53.

34. Striegel-Moore RH, Leslie D, Petrill SA, Garvin V, Rosenheck RA. One-year use and cost of inpatient and outpatient services among female and male patients with an eating disorder: evidence from a national database of health insurance claims. *Int J Eat Disord* 2000;**27**:381–9.

35. Romeo R, Byford S, Knapp M. Economic evaluations of child and adolescent mental health interventions: a systematic review. *J Child Psychol Psychiatry* 2005;**46**:919–30.

36. Crisp AH. *Anorexia nervosa; let me be*. 2nd edn. London: Lawrence Erlbaum Associates; 1995.

37. Gowers SG, Weetman J, Shore A, Hossain F, Elvins R. The impact of hospitalisation on the outcome of adolescent anorexia nervosa. *Br J Psychiatry* 2000;**45**:138–41.

38. North C, Gowers SG. Anorexia nervosa, psychopathology and outcome. *Int J Eat Disord* 1999;**26**:386–91.

39. American Psychiatric Association. *Diagnostic and Statistical Manual for Mental Disorders-Fourth Edition* (DSM-IV). Washington, DC: American Psychiatric Association; 1994.

40. Morgan HG, Hayward AE. Clinical assessment of anorexia nervosa. The Morgan–Russell Outcome Assessment Schedule. *Br J Psychiatry* 1988;**152**: 367–74.

41. Eisler I, Dare C, Russell GFM, Szmukler G, Le Grange D, Dodge E. Family and individual therapy in anorexia nervosa. A 5-year follow-up. *Arch Gen Psychiatry* 1997;**56**:1025–30.

42. Gowers SG, Harrington R, Whitton A, Lelliott P, Wing J, Beevor A, *et al*. A brief scale for measuring the outcomes of emotional and behavioural disorders in children: HoNOSCA. *Br J Psychiatry* 1999;**174**:413–16.

43. Garralda ME, Yates P, Higginson I. Child and adolescent mental health service use; HoNOSCA as an outcome measure. *Br J Psychiatry* 2000;**177**:54–8.

44. Yates P, Garralda ME, Higginson I. The PCS and HoNOSCA as measures of child mental health service intakes. *Br J Psychiatry* 1999;**174**:417–23.

45. Goodyer I, Dubicka B, Wilkinson P, Kelvin RG, Roberts C, Byford S, *et al*. A randomised controlled trial of cognitive behavioural therapy in adolescents with major depression treated by selective serotonin reuptake inhibitors. *Health Technol Assess* 2008;**12**(14).

46. Garner DM. *Eating Disorder Inventory–2*. Odessa, FL: Psychological Assessment Resources; 1991.

47. Gowers SG, Levine W, Bailey-Rogers S, Shore A, Burhouse E. The use of a routine self report outcome measure (HoNOSCA-Sr) in two adolescent mental health services. *Br J Psychiatry* 2002;**180**:266–9.

48. Epstein N, Bishop D, Levin S. The McMaster Family Assessment Device. *J Marital Fam Ther* 1983;**9**: 171–80.

49. Angold A, Costello EJ, Messer SC, Pickles A, Winder F, Silver D. The development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. *Int J Methods Psychiatr Res* 1995;**5**:237–49.

50. Wood A, Kroll L, Moore A, Harrington R. Properties of the mood and feelings questionnaire in adolescent psychiatric outpatients: a research note. *J Child Psychol Psychiatry* 1995;**36**:327–34.

51. Bryant-Waugh R, Cooper P, Taylor C, Lask B. The use of the eating disorder examination with children: a pilot study. *Int J Eat Disord* 1996;**19**: 391–8.

52. Gowers S, Smyth B. The impact of a motivational assessment interview on initial response to treatment in adolescent anorexia nervosa. *Eur Eat Disord Rev* 2004;**12**:87–93.

53. Gowers SG. Evidence based research in CBT with adolescent eating disorders. *Child Adolescent Mental Health* 2006;**11**:9–12.

54. Diggle PJ, Liang KY, Zeger SL. *Analysis of longitudinal data*. Oxford: Oxford Scientific Publications; 1994.

55. McCullagh P. Regression models for ordinal data (with discussion) *JRSS Series B* 1980;**42**:109–42.

56. Byford S, Harrington R, Torgerson D, Kerfoot M, Dyer E, Harrington V, *et al*. Cost-effectiveness analysis of a home-based social work intervention for children and adolescents who have deliberately poisoned themselves. Results of a randomised controlled trial. *Br J Psychiatry* 1999;**174**:58–64.

57. Harrington RC, Peters P, Green J, Byford S, Woods J, McGowan R. Randomised comparison of the effectiveness and costs of community and hospital based mental health services for children with behavioural disorders. *BMJ* 2000;**321**:1047–50.

58. Barrett B, Byford S, Chitsabesan P, Kenning C. Mental health provision for young offenders: service use and cost. *Br J Psychiatry* 2006;**188**:541–6.

59. Department of Health. *NHS reference costs*. London: Department of Health; 2004.

60. Curtis L, Netten A. *Unit costs of health and social care*. Canterbury: University of Kent; 2004.

61. Independent Schools Council. *ISC census*. London: Independent Schools Council; 2004.

62. British Medical Association, Royal Pharmaceutical Society of Great Britain. *British national formulary 47*. London: BMJ Books/Pharmaceutical Press; 2004.

63. National Institute for Clinical Excellence. *Guide to the methods of technology appraisal*. London: NICE; 2004.

64. Efron B, Tibshirani R. *An introduction to the bootstrap*. New York, NY: Chapman and Hall; 1993.

65. Barber JA, Thompson SG. Analysis and interpretation of cost data in randomised controlled trials: review of published studies. *BMJ* 1998;**317**:1195–200.

66. Van Hout BA, Al MJ, Gordon GS, Rutten FH. Costs, effects and cost-effectiveness ratios alongside a clinical trial. *Health Econ* 1994;**3**:309–19.

67. Johannesson M, Weinsten MC. On the decision rules of cost-effectiveness analysis. *J Health Econ* 1993;**12**:459–69.

68. Fenwick E, Claxton K, Sculpher M. Representing uncertainty: the role of cost-effectiveness acceptability curves. *Health Econ* 2001;**10**:779–87.

69. Fenwick E, Byford S. A guide to cost-effectiveness acceptability curves. *Br J Psychiatry* 2005;**187**:106–8.

70. Clark A, O'Malley A, Woodham A, Barrett B, Byford S. Children with complex mental health problems: needs costs and predictors over one year. *Child and Adolescent Mental Health* 2005;**10**:170–8.

71. Byford S, Barber JA, Fiander M, Marshall S, Green J. Factors that influence the cost of caring for patients with severe psychotic illness: report from the UK700 trial. *Br J Psychiatry* 2001;**178**:441–7.

72. Mason J. *Qualitative researching*. 2nd edn. New York, NY: Sage Publications Ltd; 2002.

73. Krueger RA, Casey M. *Focus groups – a practical guide for applied research*. 3rd edn. New York: Sage Publications; 2000.

74. Green J, Jacobs B, Beecham J, Dunn G, Kroll L, Tobias C, *et al*. Inpatient treatment in child and adolescent psychiatry–an exploratory prospective study of health gain and costs. *J Child Psychol Psychiatry* 2007;**48**:1259–69.

75. McIntosh VVW, Jordan J, Carter FA, Luty SE, McKenzie JM, Bulik CM, *et al*. Three psychotherapies for anorexia nervosa: a randomised controlled trial. *Am J Psychiatry* 2005;**162**: 741–7.

76. Halvorsen I, Heyerdahl S. Treatment perception in adolescent onset anorexia nervosa: retrospective views of patients and parents. *Int J Eating Disord* 2007;**40**:629–39.

77. Brennan PF. Patient satisfaction and normative decision theory. *J Am Med Inform Assoc* 1995;**2**: 250–9.

78. Newton T, Robinson P, Hartley P. Treatment for eating disorders in the United Kingdom. Part II. Experiences of treatment: a survey of members of Eating Disorders Association. *Eur Eat Disord Rev* 1993;**1**:10–21.

79. Rosenvinge JH, Khulefelt Klusmeier A. Treatment for eating disorders from a patient satisfaction perspective. *Eur Eat Disord Rev* 2000;**8**:293–300.

80. De la Rie S, Noordenbos G, Donker M, van Furth E. Evaluating the treatment of eating disorders from the patient's perspective. *Int J Eat Disord* 2006;**39**:667–78.

81. Lock J, Agras WS, Bryson S, Kraemer HC. A comparison of short- and long-term family therapy for adolescent anorexia nervosa. *J Am Acad Child Adolesc Psychiatry* 2005;**7**:632–39.

Appendix 1

Case-by-case 2-year course – general (MRAOS)

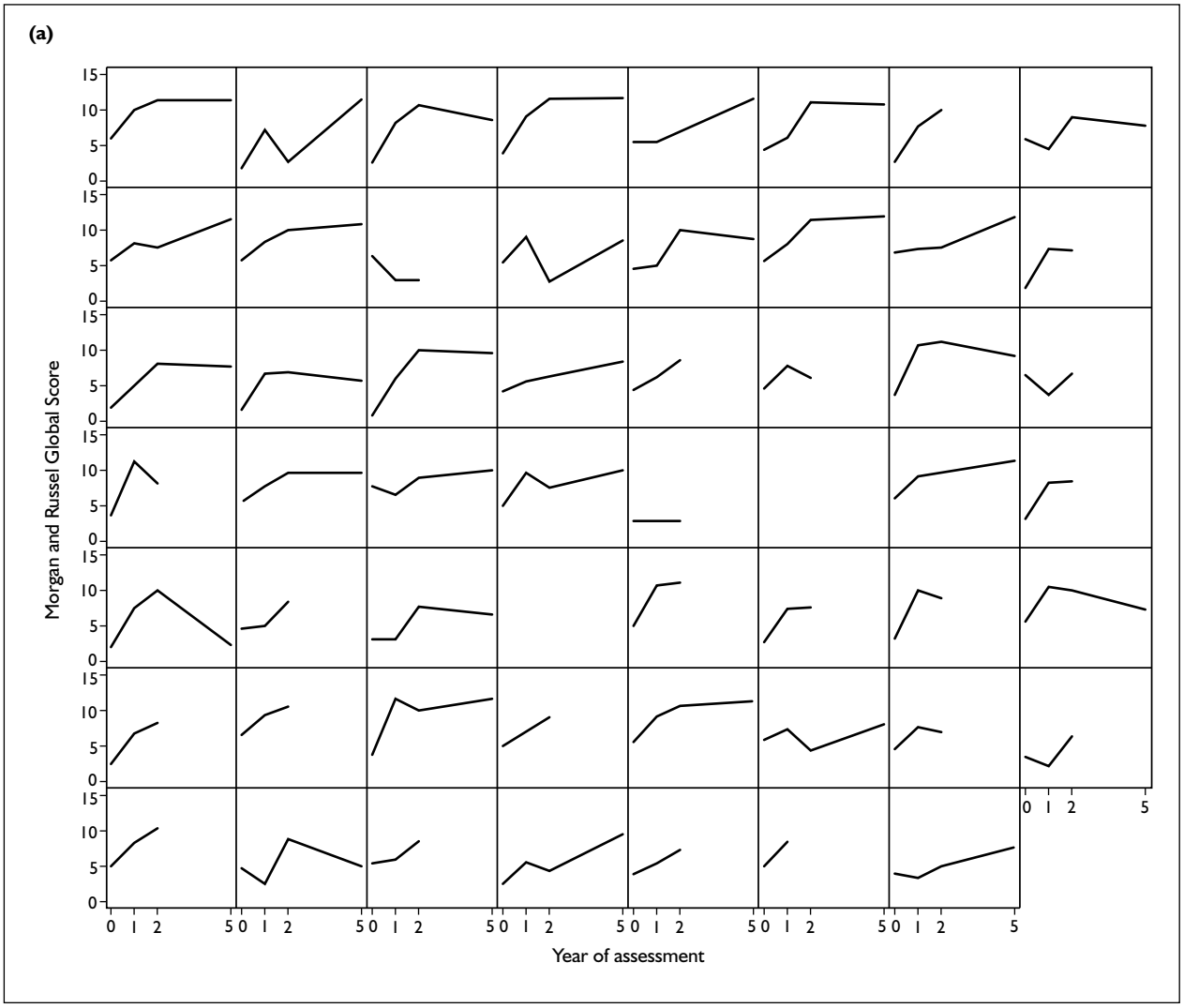

FIGURE 8 *Individual longitudinal profiles for Morgan and Russell Average Outcome Score by treatment. a, general CAMHS; b, specialist outpatient; c, specialist inpatient; and d, preference.*

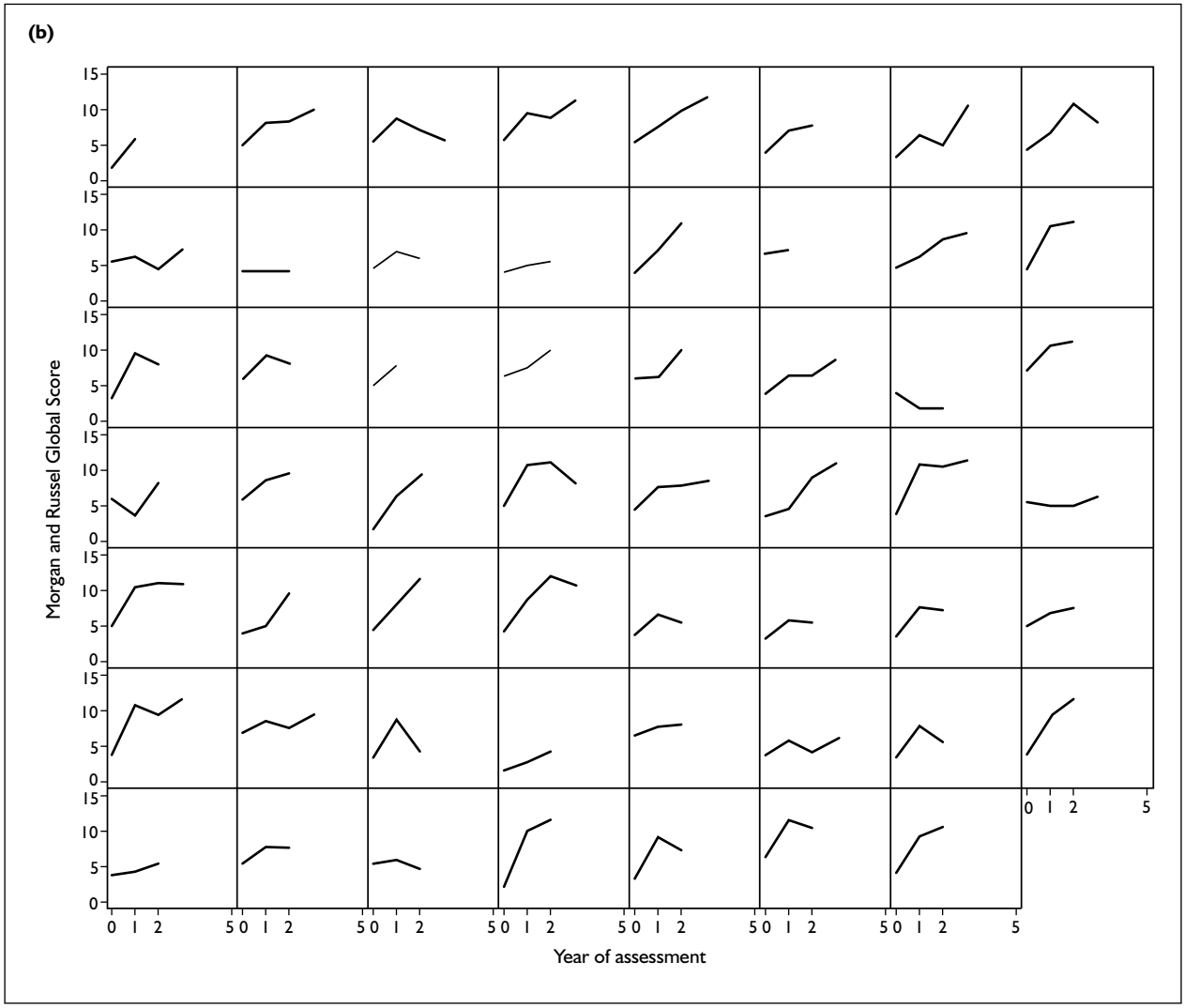

FIGURE 8 *Individual longitudinal profiles for Morgan and Russell Average Outcome Score by treatment. a, general CAMHS; b, specialist outpatient; c, specialist inpatient; and d, preference. (continued)*

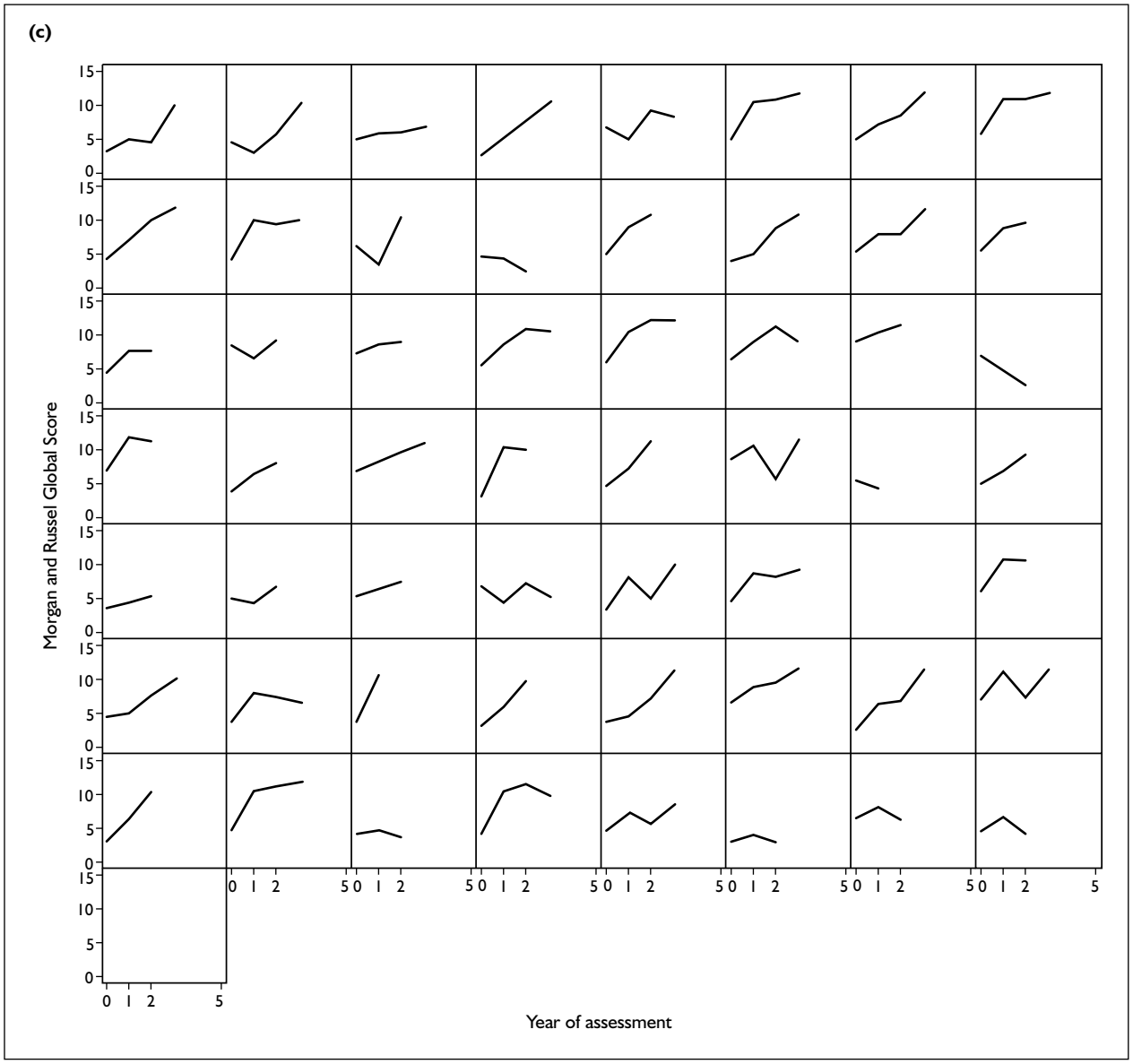

FIGURE 8 *Individual longitudinal profiles for Morgan and Russell Average Outcome Score by treatment. a, general CAMHS; b, specialist outpatient; c, specialist inpatient; and d, preference. (continued)*

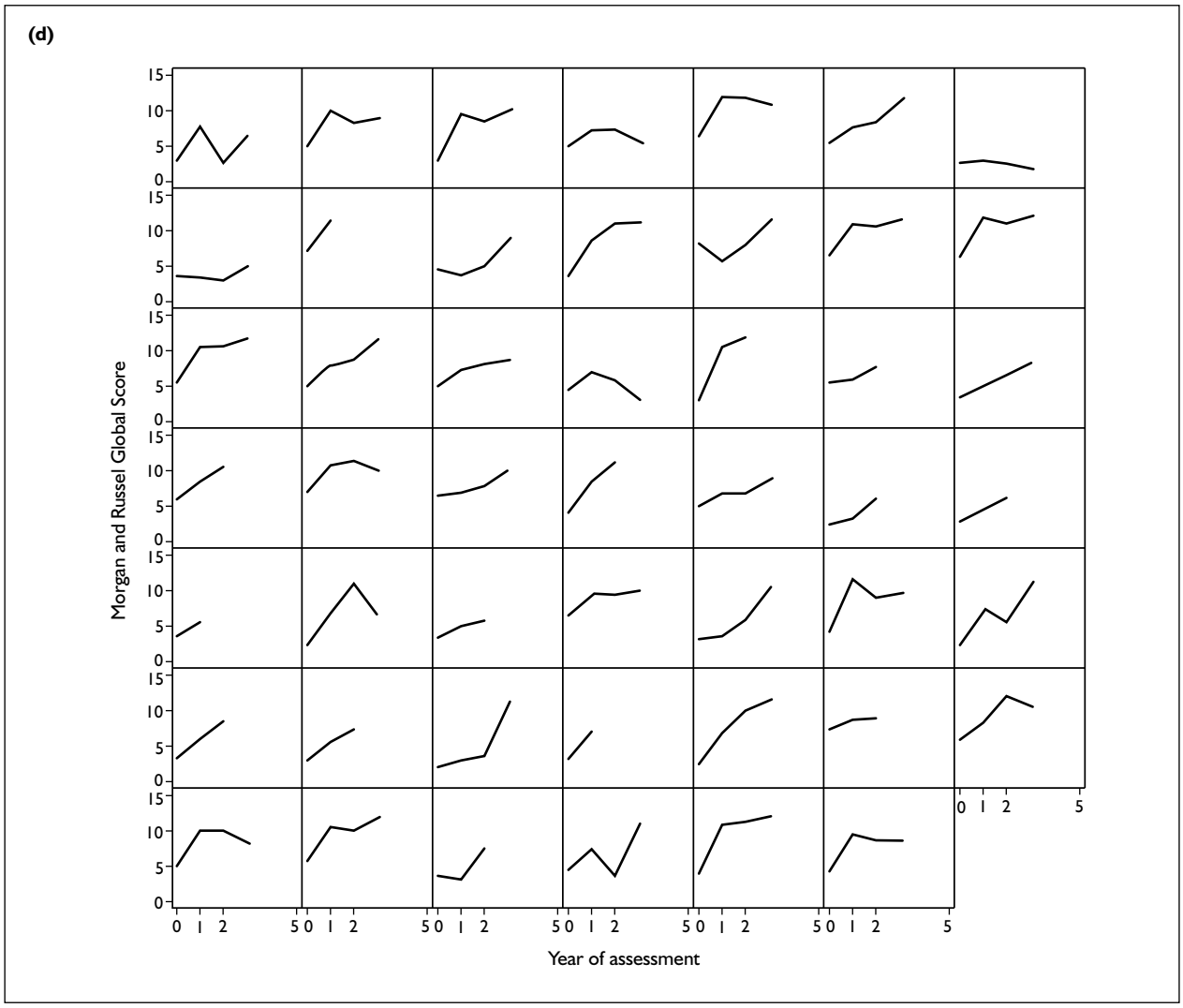

FIGURE 8 *Individual longitudinal profiles for Morgan and Russell Average Outcome Score by treatment. a, general CAMHS; b, specialist outpatient; c, specialist inpatient; and d, preference. (continued)*

Appendix 2

Case-by-case 2-year course – percentage weight for height

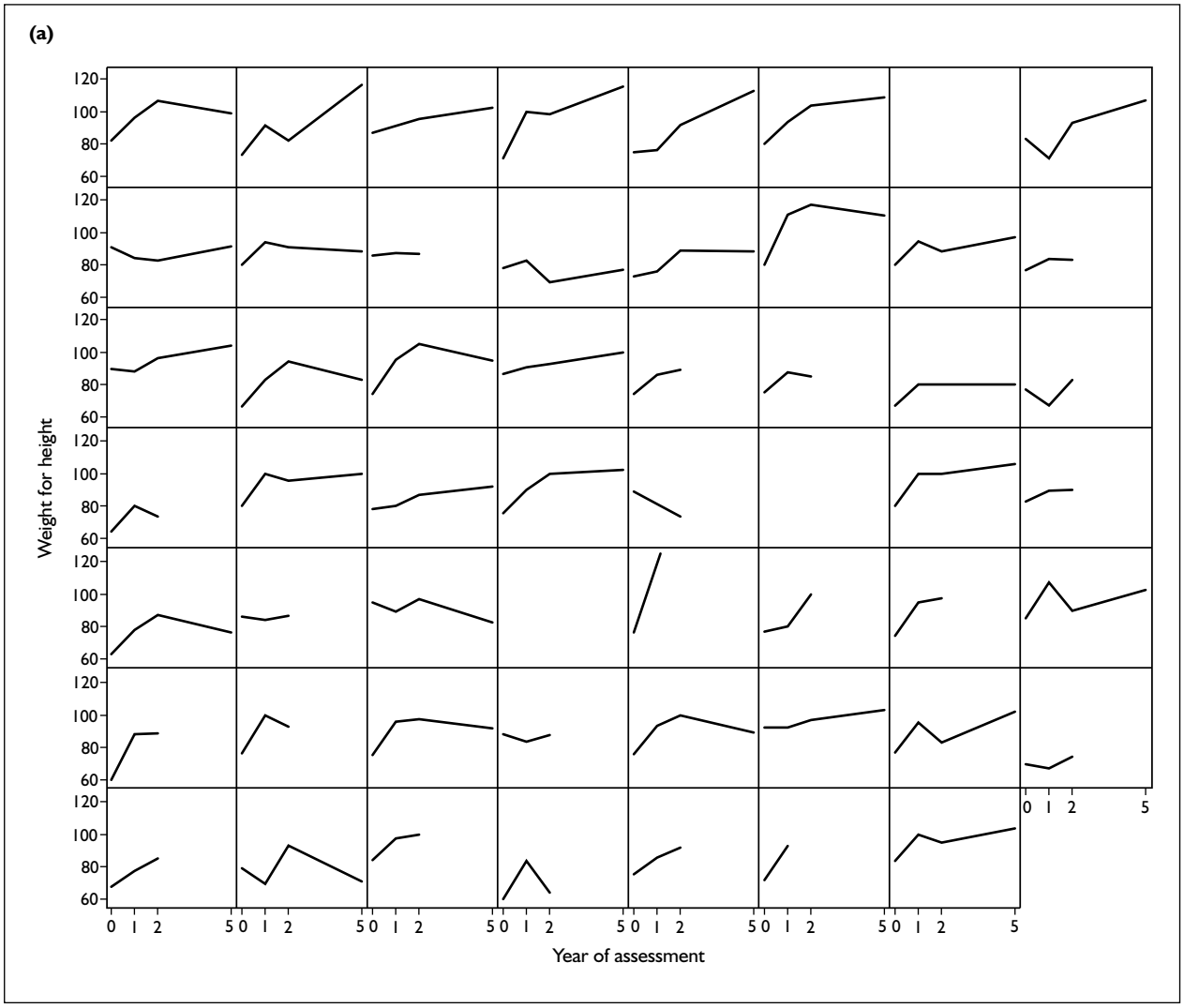

FIGURE 9 *Individual longitudinal profiles for % weight for height by treatment. a, general CAMHS; b, specialist outpatient; c, specialist inpatient; and d, preference.*

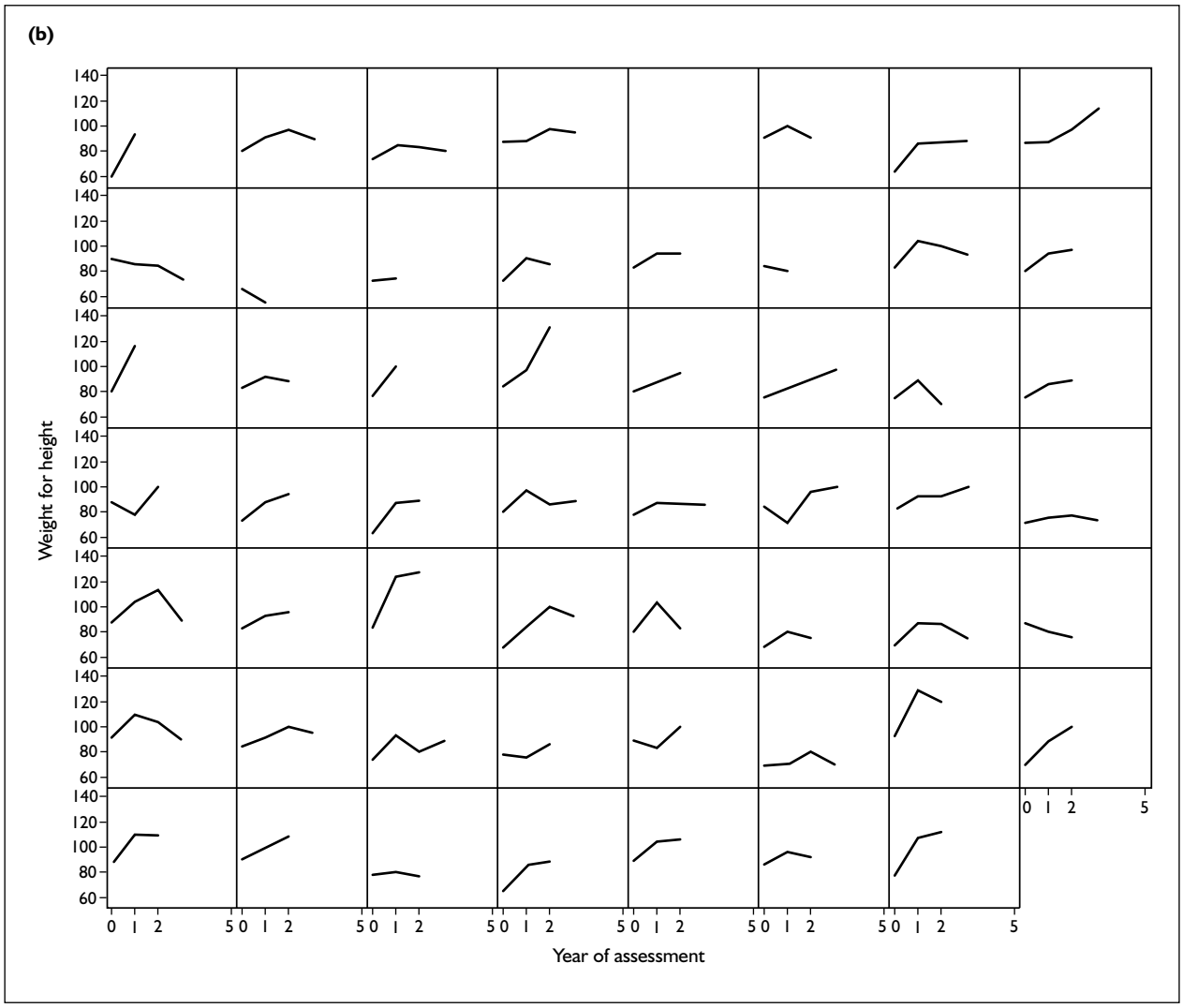

FIGURE 9 *Individual longitudinal profiles for % weight for height by treatment. a, general CAMHS; b, specialist outpatient; c, specialist inpatient; and d, preference. (continued)*

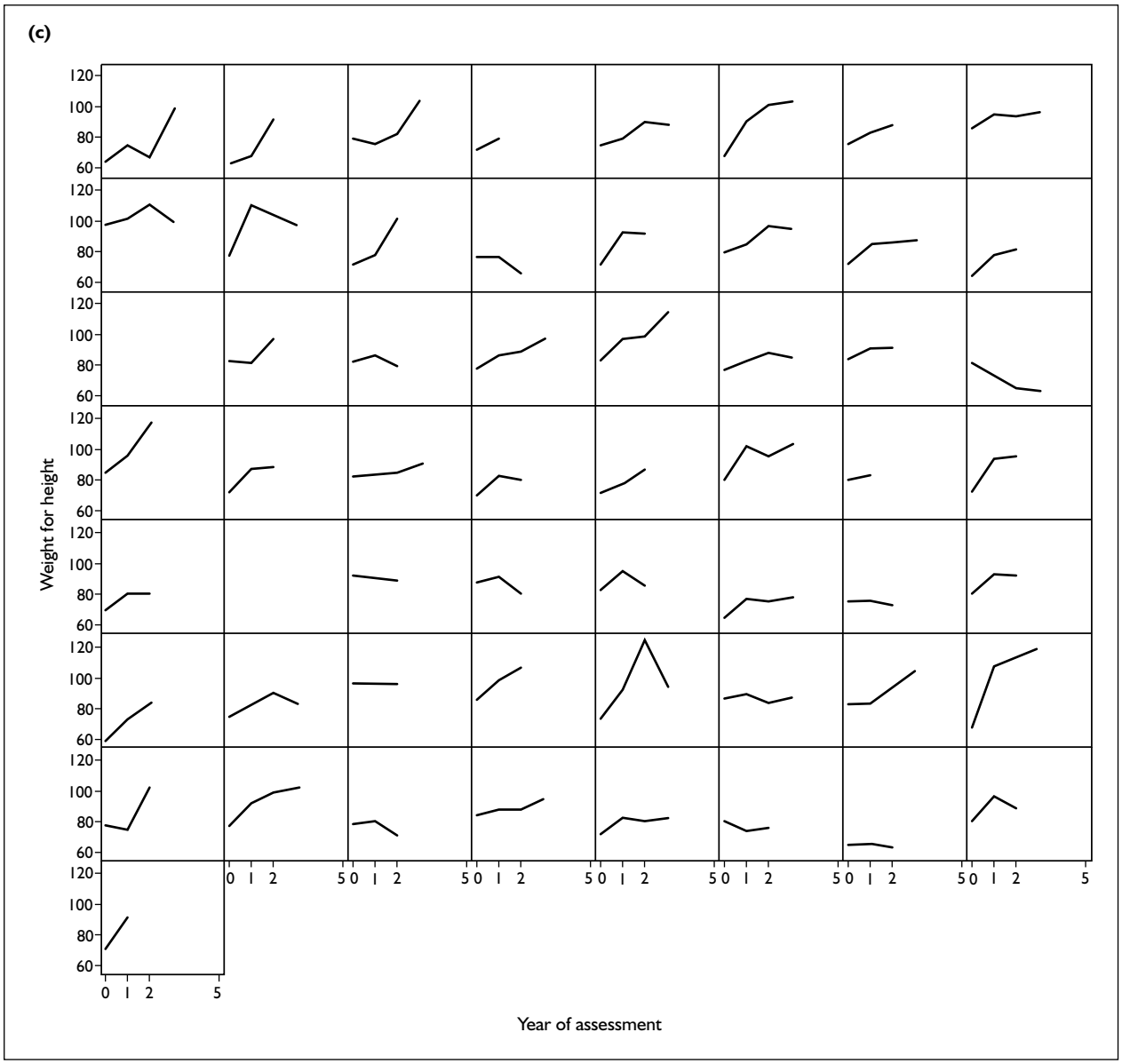

FIGURE 9 *Individual longitudinal profiles for % weight for height by treatment. a, general CAMHS; b, specialist outpatient; c, specialist inpatient; and d, preference. (continued)*

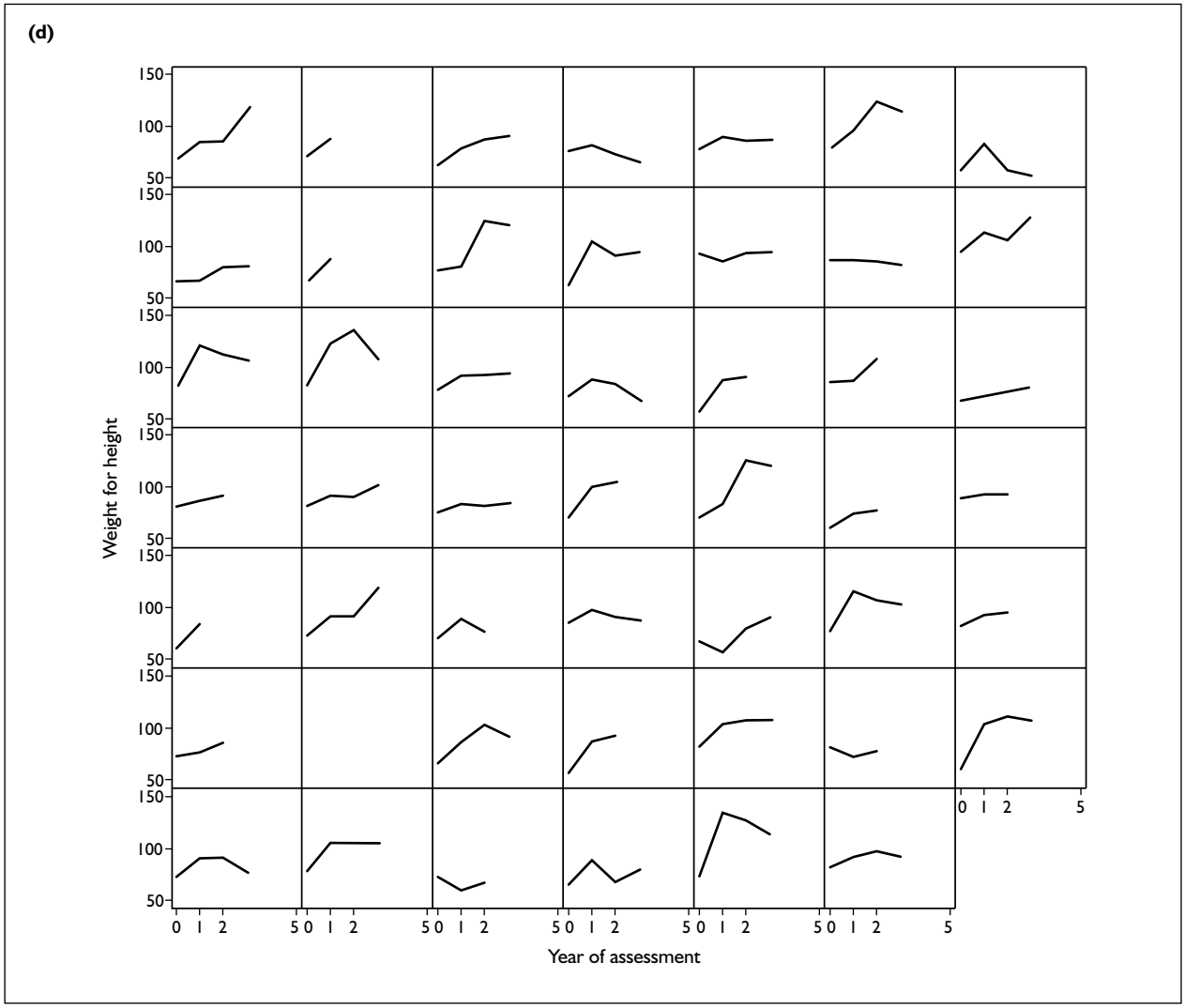

FIGURE Individual *longitudinal profiles for % weight for height by treatment. a, general CAMHS; b, specialist outpatient; c, specialist inpatient; and d, preference. (continued)*

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

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

We look forward to hearing from you.

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