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Synopsis

Stepping into day treatment approach versus inpatient treatment for adults with anorexia nervosa: the DAISIES RCT

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Published February 2025
DOI: 10.3310/FTJP6744

Abstract

Background: A substantial proportion of anorexia nervosa patients require intensive treatments, commonly inpatient or day-patient treatment. The relative merits of these treatments for adults with anorexia nervosa are

This synopsis should be referenced as follows:
İnce B, Phillips MD, Dalton B, Irish M, Webb H, Mercado D, *et al*. Stepping into day treatment approach versus inpatient treatment for adults with anorexia nervosa: the DAISIES RCT. *Health Technol Assess* 2025;**29**(3):1–37. https://doi.org/10.3310/FTJP6744

unknown. Therefore, a trial investigating the clinical effectiveness and cost-effectiveness of inpatient treatment-as-usual versus a stepped-care day-patient approach in adults with anorexia nervosa (DAISIES) was commissioned. This trial terminated prematurely due to poor recruitment, mainly resulting from COVID-19's impact on service provision.
Objective: We describe the rationale, methods and available outcomes of the DAISIES trial. Reasons behind the trial's failure and implications for future research are investigated.
Design: A two-arm multicentre open-label parallel-group non-inferiority randomised controlled trial, evaluating the effectiveness, acceptability and cost-effectiveness of two intensive treatments for adults with severe anorexia nervosa.
Setting: Specialist eating-disorder services in the United Kingdom with inpatient and/or day-patient treatment facilities.
Participants: Adults (age 17 +) with severe anorexia nervosa (body mass index ≤ 16 kg/m^2) requiring intensive treatment and (optionally) their carers. Intended sample size: 386.
Interventions: Inpatient treatment-as-usual and a stepped-care day-patient treatment approach (with the option of initial inpatient treatment for medical stabilisation).
Main outcome measures: The primary outcome was body mass index at 12 months post randomisation. Qualitative interviews conducted during the trial included semistructured interviews to investigate patients', families' and clinicians' views on treatments.
Results: During the 16-month recruitment period (November 2020 to March 2022), 53 patients were approached. Of these, 15 were enrolled and randomly allocated to the inpatient treatment-as-usual (n = 7) or day-patient treatment (n = 8) treatment arms. All participants were female with a mean (standard deviation) age of 24.8 (9.1) years and a mean (standard deviation) body mass index of 14.4 (1.6) kg/m^2. Patients' body mass indexes had increased similarly in both groups at 12 months. Participants perceived the stepped-care day-patient treatment approach to be more acceptable than inpatient treatment-as-usual. Qualitative interviews with patients, carers and clinicians suggested valued (e.g. multidisciplinary provision of care) and disliked (e.g. perceived over-focus on weight gain) aspects of treatment. Investigation of the reasons behind the trial's failure revealed strong treatment preferences among patients as the most common reason for non-participation, alongside the impact of COVID-19 on service provision.
Limitations: The main trial questions could not be answered due to low participant numbers.
Conclusions: No conclusions can be drawn concerning the clinical and cost-effectiveness of inpatient treatment-as-usual or stepped-care day-patient treatment. The day-patient treatment approach was perceived more positively by patients and carers. Service-related (e.g. reduced clinician time for research), patient-related (e.g. treatment preferences) and wider systemic factors (e.g. reduced service capacity and patient throughput nationally during COVID-19) seem to have contributed to the failure of the DAISIES trial.
Future work: Despite the trial's failure, the need to investigate the effectiveness and experience of intensive treatments of adult anorexia nervosa remains. Alternative trial designs incorporating patient preferences and investigating community-based intensive treatment options have potential to improve acceptability and recruitment.
Funding: This synopsis presents independent research funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme as award number HTA 17/123/03.
A plain language summary of this synopsis is available on the NIHR Journals Library Website https://doi.org/10.3310/FTJP6744.

Introduction

Background to the DAISIES trial

Anorexia nervosa (AN) is a serious mental disorder associated with high levels of mortality and disability, physical and psychological morbidity, and impaired quality of life.[6–8] Approximately 30% of those with AN require intensive treatment at some point during their illness,[9] typically comprising specialist inpatient (IP) or day-patient treatment (DPT). The need for intensive treatment appears to be increasing; where hospital admission rates for other major mental disorders (e.g. schizophrenia, depression) have stabilised or decreased over the past two decades, eating disorder (ED) admissions have been increasing.[10–12]

Intensive treatments are recommended for those with severe AN whose physical and psychological health is significantly compromised or for those who do not improve through standard outpatient treatment (OPT) [National Institute for Health and Care Excellence (NICE)[13]]. IP treatment is widely considered the gold standard for patients with severe AN, offering intensive support around feeding and safety monitoring. It may also

give families a much-needed respite from looking after their relative. Patients may feel that they are part of a ready-made community of people with similar problems. However, especially if the admission is prolonged, as is common,[14] IP treatment may lead to patients becoming institutionalised, passive and disempowered and make it harder for them to translate gains made while in hospital into life in the community.[2,15]

A potential alternative to IP treatment for patients with severe AN is DPT. Often this is used as a step-down treatment after an initial period of IP treatment for medical stabilisation.[16–18] A stepped-care DPT approach allows for the flexible delivery of personalised care tailored according to patient risk and progress, and for patients to retain better links with their family and friends. It may also help patients realise that they need to be actively involved in their recovery, and by doing so may make them more resilient against relapse. Likewise, this approach may also help carers feel more empowered to support the person at home. However, having intensive support for only part of the week may make it harder to achieve substantial weight gain, necessary for recovery, and daily travel to treatment may pose practical challenges for patients living far away. DPT may also increase burden on families. Ultimately, the risk and benefit ratio will vary case by case, and it is currently unknown whether treatment outcomes from these approaches are comparable.

To date, only one large-scale randomised controlled trial (RCT) has compared IP to a stepped-care DPT approach. The ANDI trial, involving adolescents with first-episode AN in Germany, showed that stepping down to DPT after a 3-week IP admission is safe and non-inferior to IP for weight restoration.[19] Additional studies have compared IP to DPT (without stepped care) for those with AN: one small RCT reporting no difference between IP and DPT,[20] one case-controlled study reporting the superiority of IP over DPT for adults,[21] and one observational retrospective study in adolescents reporting the superiority of DPT over IP in terms of weight gain and psychosocial outcomes at discharge.[22] Despite some promising results, evidence for clinical outcomes for IP and DPT is therefore limited. In addition to these outcomes, system-level impact (e.g. cost-effectiveness) is also an important consideration. Generally, AN has one of the highest treatment costs of any psychiatric disorder, largely driven by the high cost of IP treatment,[23–25] as well as protracted average length of stays across both IP (M = 76.4 days) and day-patient (DP) (M = 86.3 days) treatment settings.[14] While the costs of IP treatment are greater than those of DPT, the question of which is more cost-effective remains unclear.[19,22,26]

In summary, relatively little is known about the comparative clinical effectiveness and cost-effectiveness of a stepped-care DPT approach compared to IP treatment-as-usual (IP-TAU) for treating severe AN. If at least a proportion of patients needing intensive treatment could be treated as DPT, or be stepped down into DPT from initial IP treatment earlier than commonly practised, this could have significant cost savings and other benefits for patients and families (e.g. better connection with one's community). The clinical effectiveness and cost-effectiveness of a 'stepping into day treatment' approach versus IP-TAU for AN in adult specialist ED services (DAISIES trial) aimed to compare these two intensive treatment approaches in a two-arm multi-centre open-label parallel-group non-inferiority RCT in adults with severe AN or related disorders in the NHS of the UK.

Trials and tribulations

Set-up of the DAISIES trial began in January 2020, and recruitment opened in November 2020. The timeline of the trial coincided with the onset of the COVID-19 pandemic in the UK. Against a backdrop of rising admissions to specialist ED services in the absence of appropriate rises in funding pre-pandemic,[12,27] further increases in admissions, referrals and symptom severity were seen during the pandemic, both in the UK and internationally.[28,29] Parallel to this increased burden, intensive ED services across the UK either decreased in capacity or closed in response to infection-control restrictions, including those which were agreed to be the recruiting sites of the trial. Ultimately, the trial was prematurely terminated in March 2022 by the funder due to poor recruitment.

Premature terminations of clinical trials are not uncommon; estimates suggest that up to 25% of clinical trials are prematurely terminated, mostly due to poor recruitment.[30–33] Early termination of a trial represents an undesirable return on research resource investment and has ethical implications for participants who believed they would be contributing socially useful data;[34] despite this, the majority of terminated trials are unpublished,[31,32] preventing lessons from being learnt. Disseminating the results of and reasons behind terminated trials is therefore important in informing future research. Given the pronounced need for intensive treatment and relative scarcity of trials on intensive treatment approaches for AN, we felt it imperative that the difficulties faced during the DAISIES trial were fully explored and subsequently disseminated. Thus, we pursued qualitative research with trial stakeholders [e.g. clinicians, members of the Trial Steering Committee (TSC)] surrounding the trial's implementation, and informal dissemination of researcher-identified areas of difficulty.

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Synopsis

This synopsis summarises the extant work conducted for the DAISIES trial, including the initial design and plan for the research, the available quantitative results, and the results of three separate qualitative process evaluation analyses conducted during different stages of the trial. A narrative description of difficulties encountered during the trial will also be presented, as well as the results of a qualitative examination of implementation difficulties. All synthesised publications can be found in *Publications*.

Objectives

The original objectives of the DAISIES trial were to:

1. establish whether a stepped-care DPT approach is non-inferior to IP-TAU in relation to improving body mass index (BMI) at 12 months post randomisation (primary outcome)
2. compare the two care pathways in terms of AN symptoms, comorbid symptoms and psychosocial outcomes at different time points (superiority assessment)
3. establish whether a stepped-care approach is cost-effective compared to IP-TAU in terms of quality-adjusted life-years at 12 months post randomisation
4. investigate the experiences of and views on the treatment approaches from the perspective of patients, families and clinicians to provide insight into mechanisms of impact and how context and implementation inform outcomes.

While the trial was originally planned prior to the COVID-19 pandemic, adjustments were made to the protocol due to the profound impact of the pandemic on ED patients and on IP and DPT services in the UK. These changes will be explained in the relevant sections below.

Due to the poor recruitment and premature termination of the DAISIES trial, the original objectives could not be adequately investigated, excepting the qualitative work addressing objective 4. The priorities for the research team after trial closure became to present the available data from the trial, systematically investigate the difficulties encountered, and to consider what can be learnt for future research in this area.

Methods for data collection and analysis

Full details of the design, rationale, methodology and procedure are described in the study protocol;[1] here, they are described in brief. Following this, the methodology for qualitative research conducted after trial closure is presented.

Design

The DAISIES trial was a pragmatic two-arm multicentre open-label parallel-group non-inferiority RCT comparing two intensive treatment approaches for adult AN within a standard NHS setting: (1) IP-TAU and (2) a stepped-care DPT approach. An internal pilot trial was included in the study design to assess recruitment fidelity, aiming to include 62 patients over 4 months. If the full trial had proceeded after a successful internal pilot, the recruitment target would have been 386. Ethical approval was granted by Wales Research Ethics Committee 5 (Reference: 20/WA/0072; 14 April 2020).

Setting

The DAISIES trial was planned to be conducted at 12 specialist NHS ED services across the UK, each with both IP and DPT provision. Sites with only DPT services were included if they were members of provider collaboratives providing out-of-trust IP care pathways for their patients. Due to the impact of COVID-19 on intensive ED services, only 6 of the 12 sites opened for recruitment. A list of sites can be found in *Table 1*.

TABLE 1 Recruiting sites list

Site	Date site opened
South London and Maudsley NHS Foundation Trust	18 November 2020
Surrey and Borders Partnership NHS Foundation Trust	18 November 2020 (partial)[a]
South West London and St George's Mental Health NHS Trust	10 December 2020
Central North West London NHS Foundation Trust	3 March 2021
Dorset HealthCare University NHS Foundation Trust	20 September 2021
Birmingham and Solihull Mental Health NHS Foundation Trust	25 October 2021
Gloucestershire Health and Care NHS Foundation Trust	Not opened
Oxford Health NHS Foundation Trust	Not opened
Cambridgeshire and Peterborough NHS Foundation Trust	Not opened
NHS Grampian	Not opened
Leicestershire Partnership NHS Trust	Not opened
Orri	Not opened

a This trust has only outpatient and DP services; those patients requiring inpatient care are treated by South London and Maudsley NHS Foundation Trust or South West London St Georges NHS Foundation Trust.

Treatment approaches

Inpatient treatment-as-usual

The aim of the IP-TAU pathway was for patients to normalise their eating and reach a healthy weight or get as close to this as possible. Patients were treated by a multidisciplinary team (including psychiatrists, psychologists, dieticians, nurses and others) and received expert refeeding, therapeutic programmes and supervised meals and snacks. A proportion went on to DPT or were discharged to OPT, at the discretion of the treating team. However, every attempt was made to retain patients in the IP arm until they had completed their course of IP treatment.

Stepped-care day-patient treatment

The stepped-care DPT approach involved intensive DPT with the option of initial IP treatment for medical stabilisation. If the patient was admitted to IP, the aim was to step down patients to DPT within 1 month of being at an appropriate level of risk. Decisions around the step-up or -down of patients were guided by clinician discretion and a decision tool developed for the purposes of the trial (see below).

The stepped-care DP approach shared the same goal as IP-TAU: for patients to normalise their eating and reach a healthy weight or get to as close to this as possible. It involved a full-time programme covering 4–5 days a week with 2 or 3 meals per day, multi-disciplinary support (including psychiatrists, psychologists, dieticians, nurses and others) and high-quality evidence-based psychological interventions for patients and their carers. Patients returned home for weekends and evenings. Due to the COVID-19 pandemic, a study protocol change was made so that DPT could be delivered using a blended or hybrid approach, combining both remote and physical attendance at day service activities (e.g. supported meals, groups) and psychological therapies.

Participants and recruitment

Participants were adults with severe AN or avoidant-restrictive food intake disorder (ARFID) in need of intensive ED treatment and recruited from specialist IP and outpatient services. Our definition of severe AN was in accordance with the World Health Organisation's definition of severe thinness as a BMI ≤ 16 kg/m^2 and the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-V) definition of severe AN.[35]

Inclusion criteria were:

1. adults aged 17 years or above
2. DSM-V diagnosis of AN or ARFID
3. BMI of equal to or less than 16.0 kg/m^2
4. in need of intensive treatment because of either rapid weight loss and/or evidence of system/organ failure or medical instability and/or unsuccessful OPT, as defined by NHS England[36]
5. have mental capacity to give informed consent to participate in the study.

Exclusion criteria were:

1. individuals with insufficient knowledge of English to complete study assessments or understand treatment
2. individuals with severe learning disabilities
3. individuals with a severe medical or psychiatric (co) morbidity (e.g. psychosis, substance dependence) requiring treatment in its own right
4. those living too far away from DPT (and where no alternative arrangements for regular attendance at DPT can be made).

In total, 9 patients, 3 carers and 26 clinicians participated in the process evaluation component of the trial. Characteristics of participants who took part in interviews and/or focus groups can be found in *Report Supplementary Material 1*.

Procedure

A trial-specific Consolidated Standards of Reporting Trials (CONSORT) flow chart detailing the study procedure can be found in *Figure 1*. Details about the schedule of enrolment, allocation and assessments can be found in *Table 2*.

Written informed consent for participation was obtained from eligible patients and optionally from their carers. Thereafter, participants received a personal web link to access the self-report baseline questionnaires via Qualtrics, and structured clinical interviews were conducted by researchers via Microsoft Teams. ® (Microsoft Corporation, Redmond, WA, USA)

Upon completion of baseline assessments, randomisation was conducted by the trial coordinator through an online system provided by the King's Clinical Trials Unit and employed minimisation with stratifiers: (1) previous IP treatment (yes/no), (2) illness duration (≤ or > 3 years) and (3) recruitment centre. Participants were randomly allocated on a 1 : 1 ratio to either (1) IP-TAU or (2) stepped-care DPT arms. Neither participants (i.e. patients and carers) nor clinicians were blinded to treatment allocation. The trial coordinator was unblinded to treatment allocation and did not perform follow-up data collection; all other researchers were blinded.

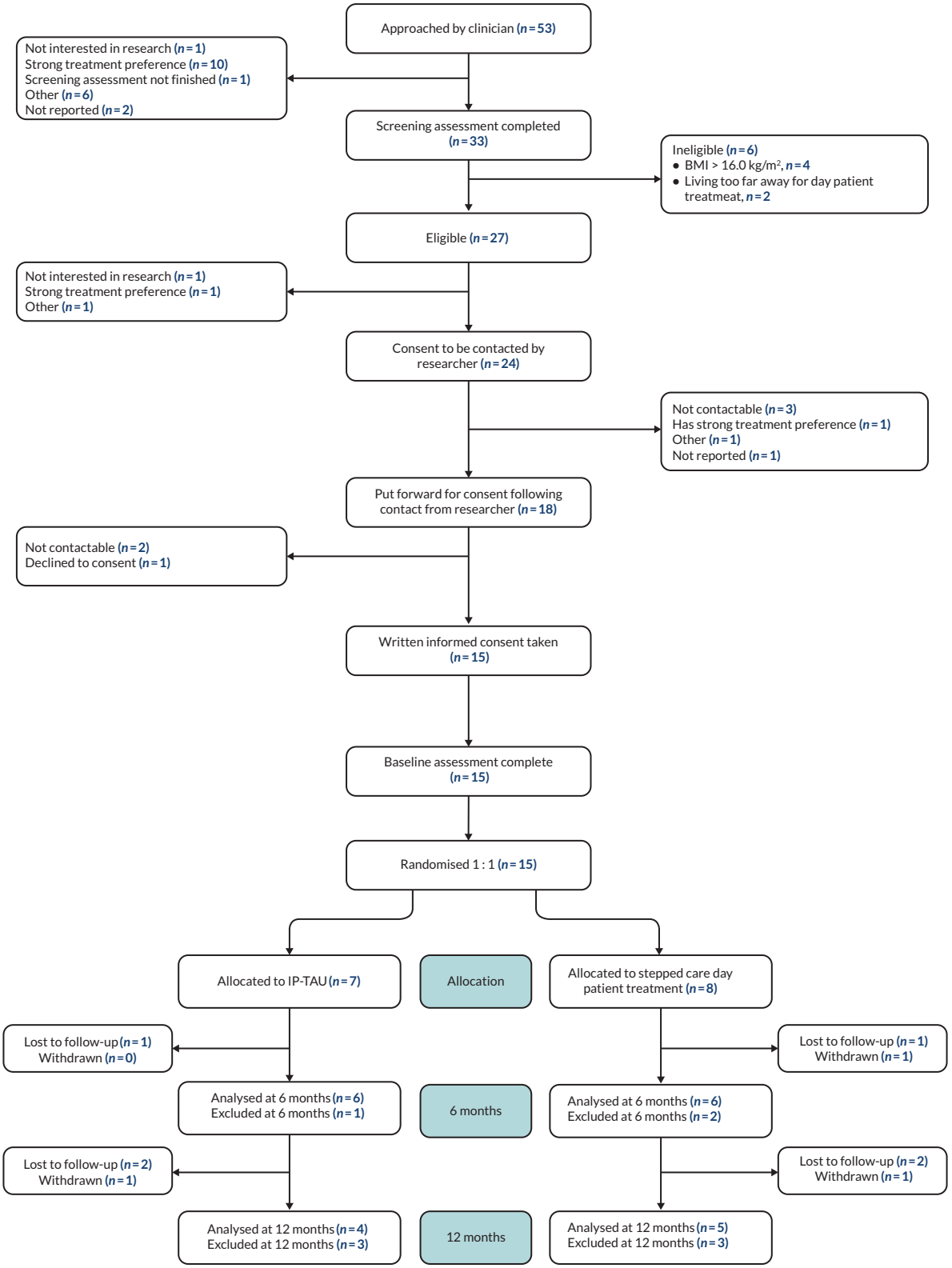

FIGURE 1 Study CONSORT diagram showing participant recruitment, allocation and assessments.

TABLE 2 Study schedule of enrolment, allocation and assessments

	Enrolment	Baseline (pre randomisation)	Allocation	Monthly monitoring (randomisation – 12 months post randomisation)	6 months post randomisation	12 months post randomisation	24 months post randomisation[a]
Patient							
Enrolment							
Assessor checklist (eligibility screen)	X						
Intended treatment plan	X						
Informed consent	X						
Allocation			X				
Assessment							
Demographics		X					
BMI		X		X	X	X	X
Eating Disorder Examination – Interview (EDE)		X			X	X	
Eating Disorder Examination – Questionnaire (EDE-Q)							X
Eating Disorder Examination – Questionnaire Short (EDE-QS)		X		X	X	X	
Autism Spectrum Quotient (AQ-10)		X					
Depression, Anxiety and Stress Scales-Version 21 (DASS-21)		X			X	X	X
Obsessive Compulsive Inventory-Revised (OCI-R)		X			X	X	X
Clinical Impairment Assessment (CIA)		X			X	X	X
Multidimensional Perceived Social Support Scale (MSPSS)		X			X	X	X
Work and Social Adjustment Scale (WSAS)		X			X	X	X
UCLA Loneliness Scale (Version 3)		X			X	X	X

continued

TABLE 2 Study schedule of enrolment, allocation and assessments (*continued*)

	Enrolment	Baseline (pre randomisation)	Allocation	Monthly monitoring (randomisation – 12 months post randomisation)	6 months post randomisation	12 months post randomisation	24 months post randomisation[a]
Motivational rulers (willingness and readiness to change)		X			X	X	X
Visual analogue scale (VAS) assessing treatment acceptability		X			X	X	X
Visual analogue scale (VAS) assessing treatment expectations		X					
Perceived Coercion Scale – Adapted (PCS)		X			X		
Therapeutic Environment Scale (TESS)				X (at 3 months only)			
Health-related quality of life (EQ-5D-5L)		X			X	X	X
Adult Service Use Schedule (AD-SUS), designed for mental health populations and modified for AN		X			X	X	X
COVID-19 diagnosis and symptom checklist		X			X	X	X
Carer involvement (optional)							
Enrolment							
Informed consent	X						
Assessment							
Demographics		X					
Eating Disorder Symptom Impact Scale (EDSIS)		X			X	X	X
Depression, Anxiety and Stress Scales-Version 21 (DASS-21)		X			X	X	X

EQ-5D-5L, EuroQol-5 Dimensions, five-level version.
a The 24-month post-randomisation assessment was planned to be collected as part of a separate follow-up study.

Participants completed monthly symptom monitoring [self-reporting BMI and the Eating Disorder Examination – Questionnaire Short (EDE-QS)[37]] and follow-up assessments at 6 and 12 months post randomisation via Qualtrics (Qualtrics, Provo, UT, USA).

Optional semistructured process evaluation interviews were offered to all patients and carers following the 6-month follow-up and were conducted by researcher MP (blinded to treatment allocation at the outset of the interview). The topic guide (see *Report Supplementary Material 2*) focused on the participant's feelings, experience, and perceived benefits and challenges of each treatment setting, their overall treatment experience including transitions between settings, and if and how these changed over time. Clinicians working at planned DAISIES sites were also invited to participate in optional semistructured process evaluation interviews from May 2020 to June 2021. The topic guide (see *Report Supplementary Material 2*) concerned clinicians' views on and experiences of managing individuals with severe AN in intensive treatment settings, the impact of the COVID-19 on their services and how they support patients within them, and the implementation of the DAISIES trial in their sites.

After trial closure, further semistructured interviews and focus groups were held with clinicians between April and June 2022. The topic guide for these (see *Report Supplementary Material 2*) concerned participants' thoughts and feelings surrounding the closure of the DAISIES trial, experiences of its implementation within their services, and the perceived learning from the trial.

Assessments

Full details of the study schedule of assessments and time points can be found in *Table 2*.

Data analysis

Quantitative data analysis

Details of the original quantitative analysis plan can be found in the protocol.[1] Due to the small sample size, only descriptive statistics were calculated in the final analysis using Stata v17 (StataCorp LP, College Station, TX, USA). The mean, standard deviation (SD), median, 25th and 75th quartiles were calculated for each continuous outcome, and categorical outcomes were described using both numbers and proportions (percentages).

Economic evaluation

Details of the original economic evaluation plan can be found in the protocol.[1] Due to the small sample size, no statistical analyses of economic outcomes were conducted. Instead, resource use by participants is reported as the mean (SD) and median by treatment arm and as a percentage of the treatment arm who had at least one contact (% using).

Qualitative data analysis

All qualitative data were analysed in NVivo 12 (QSR International, Warrington, UK) following a reflexive thematic analysis approach.[38,39] For each analysis, multiple researchers were involved in coding and thematic development, continually meeting with a senior qualitative researcher throughout to discuss differing interpretations of the data and refine analysis. All researchers involved kept reflexive journals to reflect on how prior experiences of ED treatment may have influenced their interpretation of the data; this alongside multiple researcher coding helped enhance the rigour of analysis. Full details of the analyses can be found in İnce *et al.*[5] and Webb *et al.*[2,3]

The qualitative analysis regarding the implementation of the DAISIES trial followed the same process as above. The data corpus included clinician interview and focus-group transcripts, and the meeting minutes of all Trial Management Group (TMG) and TSC meetings held throughout the trial. An implementation science theory, the Non-Adoption, Abandonment, Scale-up, Spread, and Sustainability (NASSS) framework,[40] was applied to the interpretive themes in order to better understand the mechanisms underlying the implementation of the DAISIES trial. The NASSS framework consists of seven domains in implementation projects where complexity can lie: the condition, the technology itself, the value proposition, the adopters (e.g. patients and clinicians), the organisation, the wider sociopolitical context, and the evolution of each domain over time. Further details can be found in Phillips *et al.*[4]

Topic guides for each semistructured interview can be found in *Report Supplementary Material 2*. Dates for clinician interviews and focus groups can be found in *Report Supplementary Material 3*.

Summary of results

As the DAISIES trial was prematurely terminated in March 2022 by the funder due to poor recruitment, this section summarises the quantitative and qualitative data available from the trial, before moving to a discussion of the difficulties encountered.

Participant flow and sample characteristics

Fifty-three patients from 5 sites were approached about trial participation, 15 of whom (from 3 recruiting sites)

consented to participate and were randomly allocated to IP-TAU (n = 7) or stepped-care DPT (n = 8) arms. The CONSORT diagram, showing participant flow through the trial, can be found in *Figure 1*; demographic and clinical characteristics of the sample at baseline are summarised in *Table 3*. The mean (SD) BMI of participants was 14.4 (1.6) kg/m^2, and the majority (80%) had a diagnosis of AN restricting type, an illness duration > 3 years (60%) and had previous IP admission(s) (60%).

A total of six carers (IP-TAU, n = 4; stepped-care DP, n = 2) consented to participate. They had a mean (SD) age of 49.4 years (16.0). The majority were female (83.3%) and all identified as white. Most carers were parents (66.7%) and were living with the DAISIES participant (83.3%). Demographic characteristics of carers at baseline and descriptive data on carer burden assessments are provided in *Report Supplementary Material 4*.

TABLE 3 Baseline demographic and clinical characteristics of participants

	IP-TAU (n = 7)	Stepped-care DPT (n = 8)	Total (N = 15)
Demographics			
Age			
Mean (SD)	26.7 (9.0)	23.1 (9.4)	24.8 (9.1)
Median (interquartile range)	22.0 (20.0–32.0)	20.5 (18.0–22.0)	21.0 (18.0–31.0)
Ethnicity, n (%)			
White	6 (85.7)	7 (87.5)	13 (86.7)
Mixed/multiple ethnic groups	0 (0.0)	1 (12.5)	1 (6.7)
Asian/Asian British	1 (14.3)	0 (0.0)	1 (6.7)
Employment status, n (%)			
Paid full-time employment (35 or more hours per week)	1 (14.3)	0 (0.0)	1 (6.7)
Paid part-time employment (up to 34 hours per week)	1 (14.3)	0 (0.0)	1 (6.7)
Unemployed	2 (28.6)	2 (25.0)	4 (26.7)
Unable to work/sick leave	2 (28.6)	1 (12.5)	3 (20.0)
Student	1 (14.3)	5 (62.5)	6 (40.0)
Highest level of education, n (%)			
GCSEs or equivalent (e.g. O level, NVQ Level 2)	0 (0.0)	2 (25.0)	2 (13.3)
A levels or equivalent (e.g. NVQ Level 3)	2 (28.6)	4 (50.0)	6 (40.0)
Diploma or equivalent (e.g. BTEC, foundation degree)	2 (28.6)	0 (0.0)	2 (13.3)
Undergraduate degree	1 (14.3)	2 (25.0)	3 (20.0)
Postgraduate degree	2 (28.6)	0 (0.0)	2 (13.3)
Marital status, n (%)			
Single	5 (71.4)	6 (75.0)	11 (73.3)
In a relationship	1 (14.3)	1 (12.5)	2 (13.3)
Married or in a civil partnership	1 (14.3)	1 (12.5)	2 (13.3)
Current living situation, n (%)			
Live alone	0 (0.0)	1 (12.5)	1 (6.7)
Live with partner/spouse (with or without children)	1 (14.3)	1 (12.5)	2 (13.3)

TABLE 3 Baseline demographic and clinical characteristics of participants (*continued*)

	IP-TAU (*n* = 7)	Stepped-care DPT (*n* = 8)	Total (*N* = 15)
Live with parents and/or other family members	4 (57.1)	5 (62.5)	9 (60.0)
Live with housemates/lodgers/tenants (not friends)	2 (28.6)	1 (12.5)	3 (20.0)
Current accommodation status, n (%)			
Owned/family-owned property	3 (42.9)	6 (75.0)	9 (60.0)
Rented property	4 (57.1)	1 (12.5)	5 (33.3)
University halls of residence or university-owned accommodation	0 (0.0)	1 (12.5)	1 (6.7)
Clinical characteristics			
Diagnosis, n (%)			
AN (restricting type)	6 (85.7)	6 (75.0)	12 (80.0)
AN (binge-eating/purging type)	1 (14.3)	2 (25.0)	3 (20.0)
Illness duration, n (%)			
≤ 3 years	2 (28.6)	4 (50.0)	6 (40.0)
> 3 years	5 (71.4)	4 (50.0)	9 (60.0)
Treatment status prior to randomisation, n (%)			
Inpatient treatment	7 (100.0)	6 (75.0)	13 (86.7)
OPT	0 (0.0)	2 (25.0)	2 (13.3)
Previous inpatient treatment, n (%)			
Yes	4 (57.1)	5 (62.5)	9 (60.0)
No	3 (42.9)	3 (37.5)	6 (40.0)

BTEC, Business and Technology Education Council; GCSE, General Certificate of Secondary Education; NVQ, National Vocational Qualification.

Quantitative outcomes

At baseline, all participants felt that the stepped-care DPT approach would be more effective and acceptable in improving their condition than IP-TAU, with mean (SD) effectiveness scores of 8.4 (1.6) versus 5.6 (3.5) respectively and mean (SD) acceptability scores of 8.3 (1.5) versus 5.1 (3.3) respectively (where a score of 10 indicates the highest level of perceived effectiveness or acceptability). Scores on the Perceived Coercion Scale (PCS) indicated high levels of perceived coercion across both treatment settings at baseline and 12 months, while scores on the Therapeutic Environment Scale (TESS) were mixed [e.g. ratings of relationships with staff were appraised as less positive than relationships with those who were not staff in the service (see *Report Supplementary Material 5*)]. Overall, participants felt it important to change their ED behaviours [mean (SD) of 8.6 (1.5)] and to increase/adjust their daily food intake, to achieve/maintain a healthy weight [mean (SD) of 7.8 (2.7)]. However, they felt less able to change their ED behaviours [mean (SD) of 6.9 (2.6) overall], and to increase/adjust it [a mean (SD) of 6.7 (2.5)]. A similar pattern was observed for participants allocated to IP-TAU and stepped-care DPT approaches.

Participants' raw mean monthly BMIs and mean monthly EDE-QS scores and 95% confidence intervals (CIs) per treatment arm over the trial period are presented in *Figures 2–3* respectively.

Data on adherence to allocated treatment showed that all seven participants randomised to IP-TAU received this. Of those randomised to stepped-care DPT, six received this, while one patient self-discharged from initial IP admission and one disengaged from initial IP treatment. For the IP-TAU arm, the median number of weeks spent in allocated treatment was 11.6 [interquartile range (IQR) = 5.7–15.7], and in DPT after discharge, 9.1 (IQR = 7.1–16.8). For the stepped-care DP arm, the median number of weeks spent in allocated treatment was 9.0 (IQR = 2.7–17.8), and in IP treatment prior to step-down, 5.2 (IQR = 2.9–10.2).

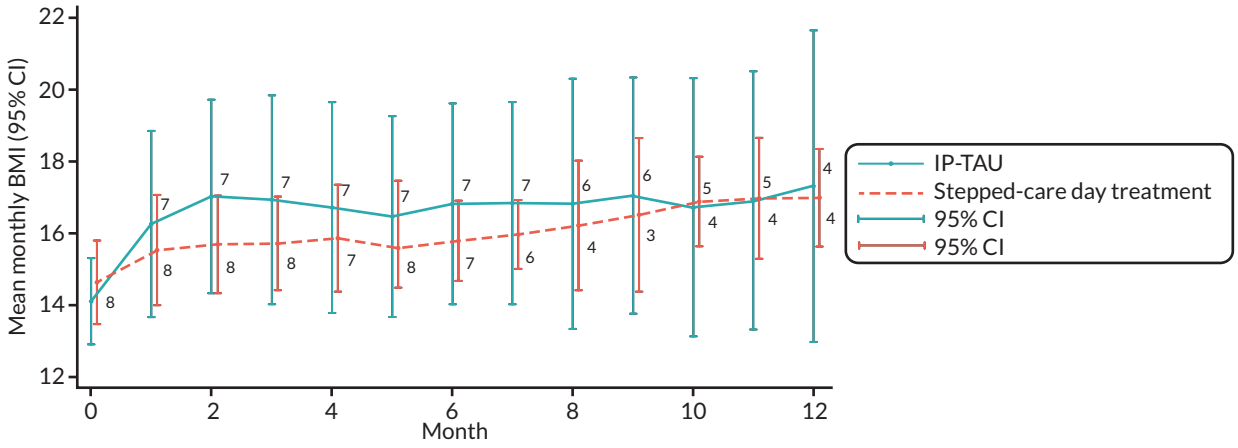

FIGURE 2 Mean monthly BMI and 95% CIs per treatment arm.

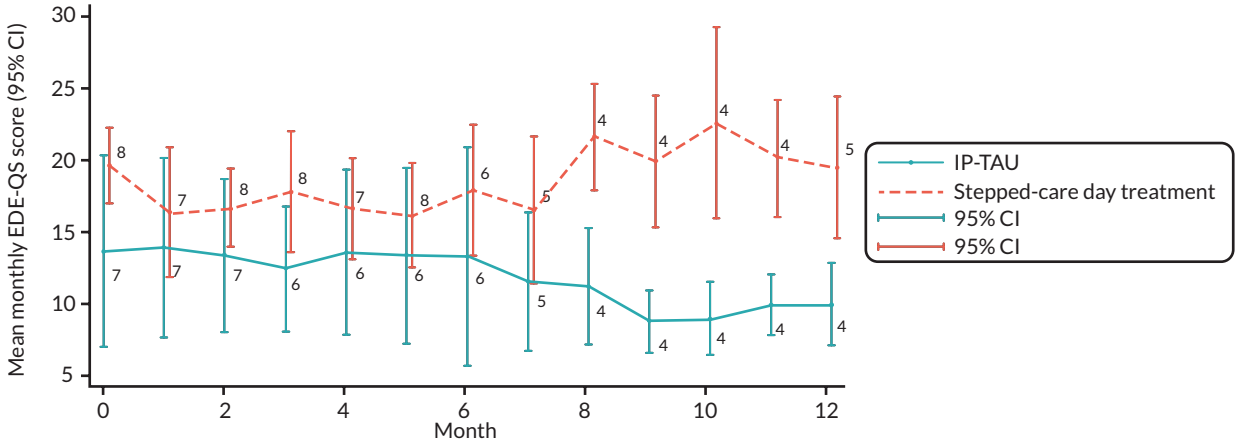

FIGURE 3 Mean monthly EDE-QS and 95% CIs per treatment arm.

Patient clinical outcomes, carer outcomes and health economic data (hospital and community-based service and medication use data) are presented in *Report Supplementary Material 4–6*.

Qualitative results

For brevity, only theme and subtheme titles are presented here, with a brief summary of each. Tables with indicative quotes included can be found in *Report Supplementary Material 1*. For the full write-up of the results of each qualitative analysis, see İnce *et al.*,[5] Webb *et al.*[2,3] and Phillips *et al.*,[4] in that order.

Patients and carers

Six patients and three carers participated in the process evaluation (*Table 4*).

Clinicians: experiences of intensive treatment before and during the COVID-19 pandemic

Twenty-one clinicians participated in the semistructured interviews. The results of the analysis are here presented in two tables: the first (*Table 5*) concerning clinicians' perspectives on supporting those with severe AN in intensive services, and the second (*Table 6*) concerning their perspectives on providing this support during the COVID-19 pandemic.

Stakeholders: experiences of implementing the DAISIES trial

Participants were 47 professionals all involved in the DAISIES trial; 26 were clinicians and 21 were members of the TMG and TSC (see *Report Supplementary Material 1*).

The NASSS framework[40] was applied to the interpretive themes after analysis was completed to classify barriers and facilitators to implementation of the DAISIES trial (see *Report Supplementary Material 7* for the full application). Applying the NASSS suggested that all domains aside from the technology and the value proposition were characterised by barriers to implementation and complexity. Of these complex domains, the adopters, organisation and wider system domains had the greatest

TABLE 4 Results of the thematic analysis of patient and carer interviews

	Description
Theme 1: valued aspects of care	
Degrees of collaboration between staff and patient	Collaboration was valued across both treatment settings, seen to enhance autonomy and communication, though was often observed to be absent, particularly in IP settings.
The importance of supportive others	The support of both staff and patients was felt to be beneficial for the treatment experience and recovery where present.
Perceived staff over-focus on eating and weight	A dislike for the stringent focus on eating and weight was expressed, meaning that treatment did not take into account emotional and social aspects of recovery. This was particularly noted for IP settings.
Theme 2: challenging experiences across treatment settings	
More positive appraisals of DPT experience	Many expressed an explicit preference for DPT, and all who had experienced IP treatment reported negative experiences, particularly in terms of emotions.
Negative impact of external factors on treatment	The negative impact of COVID-19 on both settings was commonly mentioned, in terms of visitation and social-distancing restrictions, and staff shortages influencing a decreased standard of care.
Theme 3: experiences of transitions across treatment settings	
Day patient helping transition after inpatient	Transitioning to DP after IP admission was felt to assist the transition from hospital to home.
Desire for better communication around transition	Several participants commented on the common lack of information around transitions; where transitions were reported positively, communication and clear goal-setting were present.

TABLE 5 Results of the thematic analysis of clinician interviews concerning perspectives and experiences of supporting those with severe AN in intensive services

	Description
Theme 1: intensive support	
Comprehensive package of care	Clinicians valued the multidisciplinary approach and variety of support options available in intensive settings, though some challenges over the medical orientation and nasogastric feeding were noted.
Intensity of treatment	Across both settings clinicians valued that treatment intensity allowed them to really get to know patients. IP was described as the highest level of support, aiding a recovery focus, though some worried about the risk of institutionalisation. For DP, emphasis was placed on the individualised approach and offering practical support.
Treatment boundaries	Boundary-setting in DP (e.g. asking patients to take a week off if they have not met a target) was commonly mentioned as a difficult but necessary aspect of treatment.
A different environment	The separation of the patient from the home environment in IP was described as both beneficial and challenging. In contrast, DP was seen as more applicable and supportive of the skill transfer across settings.
Theme 2: illness severity	
Complex or risky patients	Challenges relating to the complexity of AN were described, including establishing trusting relationships, long-standing illness, and, for DP clinicians, managing risk within their services.
Patients' ambivalence to change	Across both settings, concerns over patient engagement in treatment and perceived resistance to change were raised. Treatment engagement was a particular worry in DPT due to the increased autonomy entailed.
Patients' tendencies to compare	Concerns over perceived patient tendencies to compare and negatively influence one another were raised, particularly in regard to IP settings. The IP environment was described as potentially triggering and distressing, particularly for new patients.

continued

TABLE 5 Results of the thematic analysis of clinician interviews concerning perspectives and experiences of supporting those with severe anorexia nervosa in intensive services (*continued*)

	Description
Theme 3: hope and recovery	
Sustaining hope	Sustaining hope that recovery is possible was seen to be highly important but challenging, especially where patients had experienced multiple treatments.
Change is both possible and rewarding	Clinicians valued supporting and witnessing patients making changes and recovering.
Theme 4: which treatment when	
Tricky treatment decisions	Decisions as to which intensive treatment approach was most appropriate were described as challenging, particularly with new patients or where there were risk concerns. Some clinicians mentioned that they did not have any tools or protocols to facilitate decision-making.
Ensuring a seamless flow	Patient movement between OP, DP and IP services was described as difficult due to substantial differences in level of care, especially from IP to OP. Different ED services were described as separated and better communication between them was desired.
Collaborative decisions	Almost half of clinicians raised the importance of collaborative decision-making between themselves, patients and carers in intensive treatment.
Theme 5: carer burden	
Relief/respite	Clinicians in both settings suggested that intensive treatments are helpful for carers, offering periods of relief. It was noted that carer burden was increased in DP settings.
Carer involvement	Intensive treatment was felt to provide greater opportunities for family involvement, particularly in DP. However, some described inadequate carer support or communication in their services.
Theme 6: limited service resources	
	Concerns over limited resources underpinned most clinicians' narratives. A lack of specialist staff support was mentioned, as well as the challenges of limited service capacity and lengthy waiting lists within both settings. For IP, changes to discharge aims were often mentioned as a concern, and, for DP, equity of access in the face of tight admission criteria.

number of barriers, indicating the greatest challenges to implementation. Several subthemes, such as 'Increasing risk, increasing anxiety' were present across multiple domains (*Table 7*).

Narrative summary of recruitment difficulties

Part of one of the resulting papers, İnce *et al.*,[5] provides a researcher-led description of the difficulties encountered during recruitment.

The DAISIES trial was originally designed prior to COVID-19, so adjustments were made to the initial protocol. The study set-up phase started in December 2019 and participant recruitment was anticipated to commence in April 2020. Due to the first wave of COVID-19 in the UK and related infection-control restrictions, the start of recruitment was delayed to November 2020 and the start of the internal pilot was postponed to September 2021. DPT services remained closed or operated at reduced capacity across the majority of sites throughout the recruitment period. Of the 12 sites that had initially agreed to take part, only 6 opened to recruitment, and 2 did not open for recruitment until September 2021. The spread of the Omicron variant across the UK towards the end of 2021 led to additional negative impacts on NHS staffing capacity due to sick leave and unfilled vacancies. Since the beginning of the pandemic, services had dramatically reduced bed capacities (i.e. IP capacity reducing from 97 to 61 beds and DPT capacity reducing from 140 to 58 across all recruitment sites during the pandemic; see *Table 8*). In parallel, increased patient acuity and illness severity necessitated more emergency and longer admissions than pre-pandemic. These factors jointly hindered patient turnover, which in turn dramatically reduced our participant pool and ability to recruit (see *Case study* section below for a more detailed account of service provision change at one recruiting site). Therefore, we had only approached 53 participants at the point of the trial closure decision in March 2022. Approximately one-third of those approached agreed to participate over this 16-month period. Among those who did not show

TABLE 6 Results of the thematic analysis of clinician interviews concerning perspectives and experiences of supporting those with severe AN in intensive services during COVID-19

	Description
Theme 1: negotiating disruptions to routine treatment	
Facing abrupt closures	Sudden changes to services were described and viewed as uncomfortable, including service closure, patient discharge and closing to new referrals.
Running with restrictions	Clinicians in both settings described challenges and frustrations around COVID-19 restrictions. For IP, clinicians described leave and visitation restrictions, and changes to meal support (e.g. being unable to eat with patients). DP services had to transition to hybrid models of care, and clinicians worried about patient engagement, reduced physical monitoring and lack of practical support.
Theme 2: reach of virtual treatments	
Adjusting to virtual treatment	In DP services, virtual provision became the norm, with services working to adapt their full schedule of support (e.g. meal support, therapeutic modalities) to an online format. IP services also made some virtual adaptations, such as virtual meals with carers. Generally, it was felt that patients and families adjusted well to these changes.
New opportunities	DP clinicians commonly mentioned that virtual provision brought increased access to treatment for staff, carers and patients, and aided more individualised treatment and a focus on personal recovery. New provision was also evident, including troubleshooting and creative groups, and there was a desire to see these continue post pandemic.
Limitations	DP clinicians described challenges monitoring physical health, providing effective meal support, and ensuring that patients had private spaces to engage in virtual treatment. Clinicians across both settings described difficulties adjusting to the new format, particularly with new patients, and the presence of technical difficulties.
Theme 3: separation from treatment, others, and the world	
Shift of responsibility	Responsibility for patient support was described to increasingly shift in both settings towards carers, due to faster IP discharge and virtual DP provision, which provoked unease for some carers. DP clinicians also described how the pandemic entailed increased responsibility for patients over their own recovery, due to decreased provision.
Absence of social connection	Patients in IP settings were described as isolated from friends and family due to restrictions, and DP clinicians also shared concerns over their patients' social isolation, though some felt certain patients were more comfortable in their own environments.
Bubble from the outside world	Two IP clinicians suggested that some patients had become disconnected from the outside world and resistant to discussing the reality of the pandemic.
Theme 4: uncertainty around recovery	
Continued recovery	Some DP clinicians described how some patients had adjusted well to remote treatment, were engaged and continued to gain weight.
Maintenance or a 'pausing' of recovery	Some DP clinicians described how they felt that the change in DP expectations (e.g. weight-gain requirements) had led to a 'pausing' of treatment that impeded many patients from improving clinically.
Deterioration	Some clinicians also described how some patients had deteriorated in intensive treatment during the pandemic.
Theme 5: accumulative burden on staff	
Managing uncertainty, frustration and burnout	Clinicians in both settings described challenges around managing the ongoing uncertainty and frequent changes, seen by some as a bonding experience, but causing continued anxiety for others, particularly around navigating COVID-19 changes where there was no guidance, as well as the risk of burnout.
Increased workload	Several DP clinicians suggested virtual working increased their workload, including increased therapeutic provision and greater e-mail communication.
Managing risk	Several DP clinicians suggested that they now had to manage greater risk due partly to the speed with which patients were discharged from IP and patients in the community having nowhere to go. This brought increased pressure on clinicians.
Theme 6: pressure on referral pathways	
	Clinicians in both settings described increasing referrals, lengthy waiting lists, closing to new referrals, and reduced OP/DP support during the pandemic.

TABLE 7 Results of the thematic analysis of stakeholder's views and experiences of implementing the DAISIES trial

	Description
Theme 1: incompatible participation interests	
The perceived appeal of DAISIES to participants	Many clinicians felt that the DAISIES trial would be appealing to patients, though some reflected on some aspects that may be less appealing, such as treatment being decided via randomisation.
Difficulty pitching the trial to patients	Pitching the trial was seen as difficult, in terms of presenting it as something non-restrictive to treatment options, and difficulty engaging with patients presenting with high ambivalence and anxiety around treatment.
Strong preference for day treatment	The stepped-care DP arm was seen as more desirable to patients than IP, which was appraised as both a help and a hindrance towards recruitment.
Theme 2: changing standard practice	
The appeal of changing standard practice	Clinicians commonly identified DAISIES as an important trial addressing necessary questions about intensive treatment practice. Several clinicians noted that being a part of the trial had facilitated discussions among their team about their practice.
Changes in workloads and roles	Many wondered about how their work may change when implementing the trial, with some suggesting an extra burden on staff, in terms of both clinical work with non-traditional patients in their services and also for completing trial tasks (e.g. data collection). Clearly defining staff roles helped to reduce burden.
The importance of communication between clinical and research teams	The clear channels of communication between the DAISIES research team and clinicians were mostly praised, easing anxiety, though some clinicians felt confused as to what was expected of them. Trial learning events were noted as being helpful for information-sharing and enhancing motivation.
Theme 3: concerns around the clinical management of participants	
Worries of appropriateness for level of acuity	Clinicians worried about the appropriateness of trial treatment pathways for the severity of patient presentations, particularly for those stepping down from IP to DP in terms of their engagement. However, the stepped-care arm was seen as beneficial for patient care in principle, aiding the transition back to the community from IP care and enhancing motivation.
Increasing risk, increasing anxiety	DP clinicians often reported anxiety and some resistance to working with more risky patients in their services. Several reported a dislike of over-riding day services' typical admission criteria, reflecting a wider concern of research over-riding clinical practice.
Perceived impact on patient dynamics in services	While some DP clinicians felt that being around higher-weight patients may be beneficial for DAISIES participants, others worried about the negative impact on current patients. Worries of emergent dynamics of envy and perceived injustice between participants were reported, as well as how best to manage these dynamics.
Theme 4: systemic capacity and capability issues	
National bed-availability concerns	Concerns over the availability of spaces in intensive treatment settings were commonly raised, particularly for IP settings. This, among other resource scarcity concerns (e.g. low staffing), led to some questioning how viable it was for a fluid stepped-care model to be implemented.
Difficulty implementing the DAISIES trial in pathway logistics	Resource scarcity concerns, particularly around bed availability, made implementation of the DAISIES trial into treatment pathways challenging. Continuity of care between services was described as an issue, and it was hoped that the DAISIES trial may improve inter-service communication. Provider collaboratives were felt to further complicate implementation of the stepped-care pathway as eligible patients came from a wide geographic area.
Theme 5: COVID-19 disrupting implementation	
COVID-19 reducing the recruitment pool	Recruitment from IP services was described as becoming more challenging due to the mounting demand, which, coupled with increasing pressure to discharge patients early, meant that new patients had more severe presentations than before and were either difficult to engage or not suitable for the DAISIES trial due to risk. This service burden also negatively impacted the stepped-care pathway.
COVID-19 changing the format of service provision	The standard and intensity of care across both treatment settings were seen to change as a result of the pandemic. Clinicians often felt that virtual DP provision was less intense than in-person, and changes to provision were unequal across trusts. This led many question whether DAISIES was applicable to this new normal.
DAISIES no longer a priority for clinicians	The pressures brought by COVID-19 were reported to have led to changes in mind-set around implementing the trial. Clinical responsibilities became more pressing, and staff became increasingly burnt-out, leading to less focus on research responsibilities for staff at recruiting sites.

TABLE 8 Service capacities of recruitment sites throughout the study period

	IP units			DP units		
	1 January 2020 (pre-pandemic)	Lowest bed/capacity availability (between November 2020 and February 2022)	March 2022 (pre-trial termination)	1 January 2020 (pre-pandemic)	Lowest bed/capacity availability (between November 2020 and February 2022)	March 2022 (pre-trial termination)
Site 1	18	0	13	21	10	15
Site 2	18	9	19	8	3	6
Site 3	–	–	–	12	0	6
Site 4	–	–	–	12	12	12
Site 5	6	4	6	4	2	3
Site 6	15	15	15	20	0	0
Site 7	6	5	5	4	0	0
Site 8	10	10	10	6	0	3
Site 9	14	8	14	12	6	10
Site 10	10	10	10	4	4	4
Site 11	–	–	–	21	21	30
Site 12	NI	NI	NI	NI	NI	NI
Total	97	61	92	140	58	89

NI, no information.

Notes
Site names are anonymised for the purpose of confidentiality.
Sites 4 and 10 moved from in-person to virtual day-treatment during the pandemic, and thereafter their provision moved to hybrid delivery.
Site 11 is a private DP provider taking NHS patients and was able to respond flexibly to increasing demand.

interest or declined to take part, the most common reason given was a strong treatment preference for one of the trial treatment arms (see *Figure 1*).

Throughout the study period, we employed several strategies to aid successful recruitment and data collection. The research team remained in close contact with recruiting sites throughout the study: sending regular reminder e-mails for recruitment and data collection, offering 'refresher' sessions on study procedures, attending clinical team meetings to aid identification of potential participants, and circulating monthly newsletters. We held several 'Learning Events' with site clinicians where we disseminated detailed descriptions of the study, recruitment materials and strategies and relevant resources (e.g. flyers, information sheet, risk-assessment tools). Later in the recruitment period, these learning events also provided forums for clinicians to share recruitment difficulties that were collectively problem-solved. We also established a network of DAISIES recruitment champions from members of the allied specialist ED teams. These champions helped to promote DAISIES in teams and identify eligible patients, completed the clinical data tracker and acted as contacts between the clinical and research teams. Additionally, we produced study merchandise with the DAISIES trial logo (e.g. t-shirts, notebooks, pen) to help patients and clinicians keep the study and recruitment in mind. Nevertheless, recruitment remained challenging.

Case study

To illustrate the capacity and consequent recruitment challenges experienced by the recruiting sites of the trial we present the trajectory of bed/service capacity changes and significant events leading up to them in the IP and DPT services from the South London and Maudsley NHS Foundation Trust (SLaM) during the trial (i.e. January 2020–March 2022). The SLaM site was the first to open and the lead site for the trial. It covers a local catchment area population of approximately 2 million people. It operates two intensive DPT service streams, one (Daycare) which aims to help people achieve full recovery, and the other (Step-up) which is designed for patients with more long-standing illness who may need to work at a slower pace to improve quality of life and improve their health.

Inpatient service Before the COVID-19 pandemic, the IP service (Tyson House West 2; TW2) in SLaM had 18 beds available. Following the announcement of the first lockdown in the UK on 23 March 2020, the TW2 unit was closed, as part of the Trust's contingency plans for creating more 'COVID-19 beds'. Almost all TW2 patients were abruptly discharged to the outpatient team, which was operating mainly remotely at the time. A small number of patients were transferred to a specialist unit at a neighbouring Trust [where two ED wards (child and adult) had already been condensed into one]. In June 2020, TW2 re-opened with reduced bed capacity (eight beds). Bed capacity then increased gradually throughout 2020 and 2021 (e.g. 10 beds in October 2020, 14 beds in October 2021), yet did not reach the pre-pandemic level at any stage. The maximum number of available beds during the pandemic consistently varied due to the outbreak status of the ward, changes in COVID-related rules and staffing issues. In January 2022, the bed capacity reduced from 14 to 13 because of staffing issues. After the closure of the DAISIES trial in March 2022 to the present bed capacity fell further due to persistent staff shortages. At the time of writing, TW2 has eight patients and is closed to any new admissions. As an alternative to admissions, a new Enhanced Treatment Team (offering intensive community-based treatment) has been established with a capacity of working with four patients at a time.

Day-care service In January 2020, the in-person day-care capacity was 11 patients. In March 2020, the service moved from in-person to virtual treatment delivery, with capacity for only six patients. Virtual provision lasted throughout the DAISIES trial. During a 2-week transition to virtual working, the service paused new admissions to allow patients and staff to settle and acclimatise to virtual treatment before introducing new patients. The intensity (contact) of the programme reduced during virtual treatment, removing more collaborative aspects of the programme, such as face-to-face supported meals and practical groups. Virtual treatment included two groups a day, a weekly one-to-one check-in phone call for patients to review progress and goals, and occupational therapy, nursing and dietetics sessions as usual. From the summer of 2020 onwards, the unit began admitting new patients again but limited the capacity to 7–9 per day. At the time of the trial termination in March 2022, the capacity was seven patients. In June 2022, the service transitioned back to in-person provision, with a cohort of five patients making this transition. Again, admissions were paused for a brief period to allow for adjustment and settling in to in-person treatment.

Step-up service The step-up service had capacity for 10 patients in January 2020. After the lockdown decision in March 2020, step-up transitioned to virtual working only, with a capacity of four patients. The programme had previously run from 8 a.m. to 8 p.m. Monday to Friday, but during the pandemic hours were reduced to 8 a.m.–4 p.m. or 9 a.m.–5 p.m. By June 2020, capacity had returned to 9 or 10 patients in the virtual service and remained at this level until April 2021 when the programme returned to an in-person format. Due to social-distancing measures, only 6–8 patients could attend in person at any one time. This capacity remained unchanged until June 2022 when the step-up and day-care services moved to the same site and social-distancing rules were eased.

Discussion/interpretation

Due to insufficient recruitment and the consequent premature termination of the trial, many of the original objectives of the trial best investigated through a quantitative methodology could not be adequately examined. However, the extensive qualitative work conducted during the DAISIES trial does provide an understanding of the two intensive treatment approaches and the implementation of the trial from varying perspectives. Additionally, the failure of the DAISIES trial provides a useful example of the challenges of conducting an intensive treatment trial within the context of highly stretched, over-burdened NHS services that has implications for future research in this area.

Here, we discuss the available findings within the context of previous research, before moving on to a consideration of the challenges faced during the DAISIES trial, the strengths and limitations of our approach, and finally concluding with the lessons learnt for future research into intensive treatments for adult AN.

Interpretation of quantitative findings

The interpretation of quantitative data and their comparison to existing research are greatly limited due to the low sample size of the DAISIES trial. Nevertheless, we highlight findings of interest here.

Baseline demographic data indicated that our participants were severely ill (mean BMI at baseline = 14.4 kg/m^2) and all had an initial IP stay for medical stabilisation regardless of their allocated treatment. For both the IP-TAU and the stepped-care DPT arm, participants' BMIs increased to a similar level at 12-month follow-up. However, the rate of BMI increase was faster in the IP-TAU arm as compared to the stepped-care DPT arm. Regarding self-reported ED symptomatology, baseline self-reported mean EDE-QS scores, especially for the IP-TAU arm, appeared to be lower than previously found in community populations with AN.[41] The low EDE-QS scores may reflect the high proportion of restricting AN patients in our sample and their well-known tendency to downplay severity of concerns. While mean EDE-QS scores decreased over the 12-month trial period for those in the IP-TAU arm, scores in the stepped-care DPT arm increased during this period. Visual analogue scale scores across baseline, 6- and 12-month follow-up consistently suggested that participants in both treatment arms perceived the importance of changing their ED behaviours as greater than their ability to do so. These findings might be explained by common features of AN which are likely to remain consistent over time, such as poor insight, underestimation of or unwillingness to accept symptom severity, and low self-efficacy for change.[42,43]

Inpatient and DPT approaches have the same treatment objectives in principle (i.e. normalisation of eating and weight recovery and wider improvements in mental health), yet the acceptability of the IP-TAU approach at baseline was considerably lower than for the stepped-care DPT approach in our sample, suggestive of a pronounced preference for DPT even within the subset of patients who chose to participate and agreed to be allocated to either treatment arm. However, scores on the PCS and the TESS were similar for participants across both treatment settings. TESS scores have previously been reported for an inpatient affective and personality disorders unit,[44] and were similar to those found in the DAISIES study. However, in that study, in-patient scores were on average lower (i.e. the environment was perceived more negatively) across the scale as compared to a residential anxiety disorder setting and a therapeutic community for personality disorders.[44] Regarding the PCS, the average scores across settings found in the DAISIES trial appeared to be higher than those reported for other adult and adolescent IP AN samples;[45,46] however, it should be noted that PCS scores in the DAISIES trial are presented as total scores rather than subscale scores. These findings regarding the acceptability of treatment arms require interpretation alongside the qualitative findings given below.

Interpretation of qualitative findings

This section concerns a discussion of the qualitative findings presented in *Tables 4–6*, covering patient, carer, and clinician views and experiences of intensive treatment for adult AN in specialist ED services. For a discussion of stakeholder views and experiences of the implementation of the DAISIES trial, see the section *Interpretation of recruitment and implementation challenges*.

The themes and subthemes identified in qualitative analyses of both clinicians' and patients'/carers' accounts convey several perceived beneficial and challenging aspects of intensive treatment. Patients and carers emphasised the importance of intensive treatment incorporating aspects of recovery other than weight and eating, of collaboration around treatment goals and transitions between settings, and of supportive relationships with both staff and patients. The presence of these aspects was perceived to facilitate more positive treatment experiences, and these were more commonly discussed regarding DP treatment. In contrast, participants' emotional experiences were often expressed very negatively for IP. These findings echo previous qualitative research on ED service users' concerns surrounding the perceived over-focus on weight restoration and food intake in intensive treatment, the difficulty of not being seen as a whole person past their ED, the neglect or minimisation of psychological difficulties, as well as a desire for enhanced psychotherapeutic and transition support.[47–51]

The views expressed by patients and carers are similar to those of clinicians, who valued the intense, comprehensive and multidisciplinary provision of care across both settings. Generally, this is recognised as crucial for individuals with AN requiring medical stabilisation.[35,52] Clinicians highlighted the importance of consistent nutritional support and medical monitoring (particularly within IP settings), offering various types of family and psychological support, and the provision of frequent and graded practical (food-related) exposure tasks. However, some concerns were expressed by IP clinicians about an emphasis on physical over mental recovery, as well as the risk of institutionalisation or loss of personal autonomy over recovery. In contrast, clinicians felt that DPT facilitates greater links to patients' home environments (and consequently, increased opportunities to work/volunteer, and maintain social relationships), greater autonomy/responsibility in recovery, and potentially

smoother transitions out of intensive treatment. Yet, DP clinicians also raised concerns over patients' engagement in ED behaviours outside of treatment hours, patients being unable to sufficiently focus on recovery, and (lesser) concerns over negative peer comparisons and influences. These juxtapositions of supportive, yet potentially harmful/problematic, intensive environments concur with previous research,[15,53–55] including that into IPs' perspectives.[56–58] Taken together, our qualitative findings suggest that both settings have valued aspects, but both clinicians and patients/carers recognise undesirable aspects which are experienced by patients as particularly difficult (e.g. stringent focus on eating and weight). These findings highlight the importance of an individualised, holistic and collaborative approach within intensive treatment and transition management.

There is growing evidence that involving carers in treatment is valuable, including for adults with AN, in preventing relapse and sustaining recovery.[59,60] While clinicians recognised the importance of this, they identified a contradiction in the impact of intensive treatment on carers. IP and DPT were seen to offer carer relief and respite for some carers and, for others, increased opportunities for involvement (as compared to OP settings), both of which may decrease carer burden and distress.[61] However, as noted by carers, DPT can increase carer burden due to its nature (i.e. patients are home at evenings/weekends). Clinicians highlighted a lack of service resources (particularly communication and carer support provision) as a contributing factor to carers feeling isolated or overburdened within intensive treatment, and feeling unprepared for transitions back to the home/community.[62] This was also reflected in carers' accounts, as was the opinion that DPT may facilitate an easier transition back to the home environment for both patients and carers. Taken together, these findings indicate the need to continue and enhance provisions for carers at all stages of intensive treatment.[61,63]

Clinicians spoke of COVID-19-related disruptions to the usual standard of care across both treatment settings, which evoked challenges and frustrations. The provision of key components of intensive treatment, including meal support/nutritional rehabilitation[35,52] and the opportunity for skill transfer outside of intensive treatment settings,[64] had to change in response to the pandemic, and clinicians expressed differing opinions as to the impact of these changes on patients. For instance, DP clinicians here and elsewhere have suggested that virtual meal support provision is less beneficial for patients,[65] but our sample also noted increased opportunities to better facilitate the transfer of skills to real life, due to patients' increased presence within their home environments. Clinicians also expressed concerns over the increased social isolation of their patients due to social-distancing restrictions, both in IP and in DP settings. For patients, IP settings during the pandemic were particularly highlighted as solitary experiences, and indeed related reduced patient engagement and autonomy over treatment may exacerbate IP institutionalisation.[2,54] Generally, social difficulties are a risk and maintaining factor in AN, rendering individuals with AN especially vulnerable to COVID-19 restrictions and the associated isolation;[66,67] these findings therefore highlight the importance of encouraging social connections during intensive treatment, as well as greater consideration of how to foster virtual social connections and positive therapeutic relationships.[66,68]

Clinicians also reported several opportunities that arose from the changes to intensive treatment brought by COVID-19. Clinicians in both settings suggested virtual treatment increased access, consistent with other research into virtual ED OPT or DPT.[65,69–71] For patients, it was perceived to reduce geography- (e.g. travel time/expenses, locality limits) and comorbidity-related (e.g. for individuals with autism or social anxiety) barriers to treatment. Concurring with previous research, virtual treatment was also perceived to enable easier access to and greater provision of carer involvement and support (in both settings),[65,72] encouraged wider multidisciplinary team attendance (e.g. at patient reviews),[73] increased the frequency of one-to-one encounters with patients, and in DP settings it also facilitated a more individualised approach that was less bound to a specific therapeutic environment. Additionally, DP and IP clinicians described innovation and creativity; many wished for the newly created virtual groups in their services (e.g. trouble-shooting groups) to continue. Taken together, these findings suggest that the pandemic instigated a necessary re-consideration of treatment-as-usual[65] and afforded greater accessibility in ways that might have otherwise not been tried.

Pervasive across both qualitative analyses with clinicians were accounts of uncertainty. Clinicians described a lack of guidance and protocols for decision-making around intensive treatment, which is a longstanding area of uncertainty,[74] including what setting works best for whom and transitions between settings. The pandemic was seen to further this and create new ambiguity, including how best to manage risk remotely,[71,72] and know which patients may benefit from virtual provision. The lack of resourcing of intensive ED services relative to their demand[27,75,76] also underlay many of the themes and subthemes of the analyses. Within resource-limited contexts, managing the severity, complexity and diversity of patients' illnesses

arose as a clear challenge, echoing previous research into clinicians' perspectives.[77,78] The accounts of our sample of patients interviewed during the DAISIES trial convey the potential after-effects of these systemic issues on patient care, such as subpar communication and short staffing. Taken together, these findings highlight the need for research and investment into intensive ED services in the UK, existent at the point of funding for the DAISIES trial and persistent to the present moment.[79]

Interpretation of recruitment and implementation challenges

As mentioned in the introduction, it is not uncommon for clinical trials to be prematurely terminated. Conducting large-scale RCTs in patients with AN in particular is well-recognised to be especially challenging due to the nature of the illness (e.g. low motivation to change, high medical risk, low illness prevalence).[80,81] Accordingly, recruitment periods may be lengthy or meeting the recruitment target may not be possible, even after extending the study period or altering the design.[82,83] For example, recruiting a target sample (n = 242) from 10 sites for the Anorexia Nervosa Treatment of OutPatients study took 4 years.[84] Recruitment to studies involving hospital admission might bring additional obstacles, especially in the case of anxious or ambivalent patient attitudes towards recovery.[85]

Despite the difficulties of conducting large-scale RCTs in intensive treatment settings for patients with AN, several have successfully recruited. It is therefore prudent to consider the differences between the DAISIES trial and these other RCTs, to elucidate where DAISIES-specific difficulties may lie. The TRIANGLE study, an RCT of added online support to ease transitions back to the community after intensive treatment for AN,[86] successfully recruited 371 adult patients and their carers in the UK (Cardi, personal communication). However, the majority of the recruitment for the TRIANGLE study took place prior to the COVID-19 pandemic, meaning that the service capacity-related issues present in the DAISIES trial were mostly absent. The nature of the randomised treatment in either study also deserves consideration. TRIANGLE presented patients with the possibility of receiving either TAU (i.e. the participant's present setting, either IP or DP care) or TAU plus added online support. Where the randomisation of the DAISIES trial presented a possible significant change in treatment setting for the participant (e.g. being randomly allocated to IP or DP treatment), the randomisation of the TRIANGLE study presented no major change to current standard of care, only a possible addition to it, which may have been experienced as more acceptable than the treatment randomisation of the DAISIES trial.

Another notable RCT comparing intensive treatments for AN that successfully recruited is the ANDI trial,[19] comparing inpatient treatment with stepped-care DPT in adolescents. The design of the DAISIES trial was broadly based upon that of the ANDI trial. While the treatment arms of the ANDI trial are very similar to those of the DAISIES trial, the population (adolescents), healthcare setting (Germany) and timing (pre-COVID-19) are different. These factors influence a different recruitment context. Intensive treatments are better-resourced and more populous in Germany as compared with the UK,[87] and IP admission thresholds are consequently more liberal; this, combined with a pre-pandemic service environment, would have greatly increased the recruitment pool in the ANDI trial compared with the DAISIES trial.

Although the DAISIES trial is not the first RCT on EDs to be prematurely terminated due to poor recruitment (e.g. ClinicalTrials.gov Identifier: NCT02792153; NCT00584688) or affected by COVID-19 (e.g. ClinicalTrials.gov Identifier: NCT03647943; NCT04028635), the research team felt that systematically investigating the implementation of the DAISIES trial through qualitative research involving clinicians related to the trial would help illuminate some of the challenges faced. We here present a discussion of the findings from our qualitative investigation of the experiences of implementing the DAISIES trial. The themes and subthemes identified in the analysis span from the individual level (e.g. patient preference factors) to the systemic level (e.g. service capacity), and suggest that the greatest challenges in implementation existed with the adopters, organisational systems and the wider socio-political context.

The barriers identified in the adopter system domain chiefly concern patients and clinicians. Patient-related barriers primarily surrounded the acceptability of treatment arms, which was further complicated by aspects of ED symptomatology, such as high ambivalence. This is consistent with previous literature suggesting patient treatment preference as a key recruitment barrier in RCTs.[88–90] A potential solution may be to better accommodate patient preferences in the conduct of trials, either during the recruitment 'pitch'[91] or in research design.[92]

Clinician-related barriers involved changes to staff modes of working and concerns over patient appropriateness for trial interventions. Both have been previously identified as common barriers to recruitment in trials,[89,93–96] and represent a larger tension between clinical and researcher roles for recruiting clinicians.[97] This tension was commonly expressed around decision-making for stepping-down patients from IP to DP services. It has previously been

suggested that trial research processes should be well-integrated into the existing working patterns of clinicians,[98] especially within IP services,[99] since clinical responsibilities will always take priority over those of research.[89] These previously disseminated challenges were, however, known to the DAISIES team, being composed of a group of applicants with extensive experience in clinical trials, and several facilitating strategies were implemented,[5] including assigning research champion roles to clinicians, previously shown to improve recruitment within mental health service contexts.[100]

In parallel to the implementation barriers identified above, clinicians positively appraised the rationale of the DAISIES trial. There were several facilitators in the value proposition domain, including staff belief in the importance of the trial, and a perception that patient altruism would motivate participation, consistent with literature on patient-centred enablers of recruitment.[101] Previous research has identified positive opinions of a trial among recruiting staff, good communication, and supportive relationships between research and clinical teams as facilitators of trial success.[97–99,102] All were present in the DAISIES trial; however, their utility appears to have been overshadowed by other implementation barriers.

Both the organisation and wider system domains were characterised by complexity and barriers to implementation. Barriers in the organisation domain primarily concerned low service capacity and difficulty implementing the stepped-care DP pathway in existing service structures. Barriers in the wider system domain concerned the impact of COVID-19 on the intensive ED healthcare system. Regarding service demand, hospital admissions for EDs were increasing prior to COVID-19 without an appropriate rise in funding for adult ED intensive services.[12,27] During the pandemic, specialist ED services experienced further increases in admissions, referrals and symptom severity, concurrent with service closure and capacity reductions, both in the UK and internationally.[12,27–29] As shown in *Table 8*, reductions in service capacity among recruiting DAISIES sites were substantial. In the context of the implementation of the DAISIES trial, this systemic pressure diminished the recruitment pool and services' abilities to implement timely stepped-care. The introduction of provider collaboratives, partnerships between healthcare providers that aim to improve access to specialist services within their catchment areas,[103] additionally may have hindered implementation due to inequitable access to DP care post discharge. This reflects broader concerns of geographical inequality in ED care across provider collaboratives.[104] Finally, the impact of COVID-19-related infection-control restrictions created a unique challenge for the DAISIES trial, facilitating an unpredicted pivot to virtual DP provision. Aside from some promising preliminary data,[70,105] the efficacy and effectiveness of virtual DP provision are largely unknown and should be investigated in future research.

Organisational factors have ramifications for individual-level areas of implementation. Primarily, systemic overburden contributes to increased clinical workloads and decreased available time for research, both of which have been previously identified as barriers to recruitment and research implementation in clinical services[97,106,107] and as contributors to the tension between clinical and researcher roles.[89,98] The negative impacts of under-resourcing and overburden on ED patient safety and clinician experiences have been previously reported,[2,75,104] but the DAISIES trial is the first time these negative impacts on research implementation in a UK healthcare context have been qualitatively explored. The results suggest that while organisational barriers to implementing the DAISIES trial existed prior to COVID-19, the impact of the pandemic strengthened these barriers while creating unique challenges. As suggested by both the qualitative results and quantitative data on service capacities of DAISIES recruiting sites (see *Table 8*), these barriers remained even after the acute phase of the pandemic in the UK. More generally, the results indicate that systemic overburden and underfunding limited the capacity for research and innovation in intensive ED services at a time when they were most needed.

Patient and public involvement

This section follows the Guidance for Reporting Involvement of Patients and the Public.

Pre-funding preparation

Early patient and public involvement (PPI) work prior to funding aimed to explore experiences of DPT and/or IP treatment from the perspective of people who had received intensive treatment for severe AN, to ascertain their views on the trial design and any suggestions they might have for its improvement. Two focus groups were conducted with a total of 12 patients with severe AN with the experience of either IP treatment, DPT or both. At the start of the interview the NIHR's call for research comparing DP with IP treatment in adults with severe AN was briefly introduced. Then, patients were asked about their experiences of these treatment settings and their views on the design of the study (e.g. randomisation,

clinical outcomes, impact on families, cost-outcomes, safety) and the proposed stepped-care approach (and potential alternatives).

Patients agreed that both settings played an important role in the treatment of severe AN and that they might be appropriate for people at different stages of their illness. Nevertheless, while some patients preferred DPT and highlighted that it allowed one to stay in touch with family and friends and had a greater focus on practising skills outside the hospital setting, others felt that when they had been very unwell, having someone else take over responsibility and being in an IP setting had made treatment easier. Patients strongly endorsed the trial design, in particular the stepped-care aspect, as this was felt to offer individually tailored care. There was a consensus among the group that they would have been happy to participate, as they felt both treatment options were credible and equivalent, and would not have minded which they were offered when very unwell. Based on patients' perceived pros and cons of the treatment approaches in the study arms we decided to add measures of motivation for treatment, social supports and measures of therapeutic environment and perceived coerciveness of different treatment settings to the protocol.

Two patients and a carer who agreed to be PPI representatives for the DAISIES trial were asked to review and comment on the full proposal and study materials (e.g. information sheet, consent form, advertising materials), and their suggestions were incorporated by the research team. These PPI representatives also became members of the TSC.

Towards the end of the trial

Pandemic-related restrictions and factors (e.g. social distancing, visiting restrictions, staff shortages) are likely to have profoundly altered the patient experience of intensive ED treatment settings and also participant recruitment for the DAISIES trial. Thus, we aimed to obtain a clearer view of the recruitment challenges from a patient perspective and to discuss whether potential adaptations to the trial design would influence their decision to participate. Adaptations to the trial design included three options: a partially randomised design including patient preference arms, a design comparing DP to any other TAU (e.g. OP treatment), and comparing IP-TAU with a stepped-care arm offering other forms of intensive treatment, such as intensive community treatment (see the *Research recommendations* section for more detail). Three focus groups were held in January 2022 with patients in two DP and one IP services from two of the DAISIES recruiting sites. In total, 17 patients attended these meetings, all of whom would likely have met eligibility criteria for the trial (i.e. all were above the age of 17, all required intensive treatment for their ED). The majority of patients felt that research comparing IP and DP treatments for AN is necessary, and research like the DAISIES trial could help improve the number and variety of ED services offered around the country (e.g. more day-service options), which was seen as highly important. Nonetheless, a strong dislike for the randomisation component of the trial was commonly expressed and cited as the key reason why participating in the DAISIES trial would not be appealing. The reasons expressed for the dislike of randomisation were a desire for greater control over one's own treatment, the uncertainty and associated stress of random allocation, and, for day patients specifically, a desire to avoid IP treatment, especially in the context of COVID-19 restrictions. Regarding the proposed adaptations to the trial, patients reported that these adaptations would make the study more attractive. They also expressed that investigating alternatives to IP-TAU for severe AN would be valuable. However, concerns about the randomisation component remained irrespective of trial design.

Equality, diversity and inclusion

Participant representation

To ensure the equality, inclusivity and diversity of our sample, we aimed to offer study participation to all adult patients with AN qualifying for intensive treatment under current NHS practice. However, while the study was open to people across all demographic backgrounds, we did not assess gender identity and sexual orientation as part of the demographic questionnaire. As the carers of patients with AN are likely to experience burden, anxiety and low mood, and the interpersonal relationship between patient and carers can play a significant role in the maintenance of the illness,[108] we included an optional carer assessment component within the study. Regarding the optional carer component, we took a flexible, inclusive and person-centred approach, and patients were asked for consent to involve their carer within the research.

All UK-based specialist ED services were informed about the study, and those with DPT services were invited to participate, via the listservs of the Royal College of Psychiatrists' Eating Disorders Faculty and the British Eating Disorders Society. Twelve services from different regions across the UK agreed to participate in the trial, including sites in London and the South East, the South West, the Midlands, and Scotland. These services covered a wide variety of catchment areas, including metropolitan, urban, suburban and rural.

Notwithstanding all efforts, all 15 participants were female, were recruited from London-based sites among those which were fully or partially opened for recruitment across the UK (*n* = 3/6), and 13/15 (86.7%) of them were white. Considering higher level of barriers accessing health care among under-represented groups (e.g. ambivalence, stigma, under-recognition),[109–111] we had a fair representation of demographic characteristics of patients admitted to intensive treatment settings within the UK (e.g. 94.6% of patients were white in the TRIANGLE study; Cardi, personal communication).

Reflections on the research team and wider involvement

The co-applicants of the DAISIES trial consisted of a multidisciplinary team with expertise in EDs, clinical trials, statistics, health economics and qualitative methodologies, and had previously successfully collaborated on several large-scale multicentre clinical trials in intensive treatment settings. Additionally, postdoctoral research associates (i.e. the trial coordinator) and research assistants with a range of clinical and research experience and lived experience of ED were involved in the study. The junior members of the team were given the opportunity to contribute to study presentations and publications, and received training for the eating disorder examination interview and supervision for qualitative analysis.

The Data Monitoring Committee included senior researchers with expertise in ED, trials and statistics from the UK and Europe. The TSC included ED professionals with psychiatry, psychology and nutrition backgrounds, as well as personal or caring experience with EDs to ensure all design decisions, study procedures and materials and dissemination outputs maintained an element of co-production.

Impact and learning

As noted in prior sections, a significant number of RCTs discontinue due to recruitment difficulties. Also, conducting research on patients with AN, particularly in IP treatment settings, is well-recognised to be challenging. Nonetheless, in-depth investigations and discussions around the barriers encountered and the strategies used to overcome these in the terminated studies are almost non-existent. To our knowledge, the DAISIES trial is the first study to provide in-depth insight concerning challenges of participant recruitment and mitigation strategies used to overcome these. In this regard, the DAISIES trial has made a unique contribution to the literature by providing researcher-led and clinician-led description of difficulties on implementing an RCT in intensive ED services in the UK.[4,5] Furthermore, the accounts of patients, carers and clinicians involved in the DAISIES trial provide in-depth insight into valued and disliked aspects of care across both intensive treatment settings, particularly regarding patient and carer difficulties with the experience of IP care. These accounts provide substantial information that can inform the improvement of intensive ED service provision.

The pre-planned dissemination regarding the main study objectives could not be achieved as the DAISIES trial failed to recruit enough participants to conduct the original analyses. Nonetheless, the dissemination of findings concerning clinicians' and patients' experiences and views of intensive treatments as well as the in-depth investigations of factors contributing to the premature termination of the DAISIES trial has been performed through international peer-reviewed publications and conference presentations. We have therefore shared valuable insights and directions for both future research and for healthcare professionals treating patients with AN and their carers.

In line with previous research, our findings have demonstrated that patients with severe AN and their carers share negative perceptions and experiences towards IP treatment settings, which may have been heightened within our sample due to the restrictions brought to IP treatment by the COVID-19 pandemic. Patients and carers further expressed a strong desire for alternative intensive treatment options that are more flexible, holistic and empowering. Therefore, we have started working on a scoping review of intensive community treatments for EDs that are designed as an alternative to IP treatment (e.g. home treatment, intensive OPT) (published protocol:[112]). This review will provide an overview of the clinical outcomes and cost-effectiveness of community-based intensive treatments for EDs, potentially informing the design of new services or enhancing existing ones.

Lessons learnt for future research

Conducting an RCT of the scope and magnitude of the DAISIES trial may not be possible within intensive adult ED services in the UK within the current funding and governance context.

- Adult patients with severe AN demonstrated a marked dislike of the random allocation to treatments offered in the DAISIES trial. This dislike of randomisation was not apparent during the PPI work conducted during the planning of the study, and may have been due to the potential to be randomised to a more restrictive treatment setting within the context of

the COVID-19 pandemic. It is worth noting that other RCTs in similar populations and settings (e.g. TRIANGLE[86]) or with similar designs albeit conducted in a different healthcare system (e.g. ANDI[19]) have successfully recruited. Better incorporating patient preferences in the design of future trials in this area, or providing randomisation as an option for those who are comfortable with it, may improve acceptability and recruitment in future trials. Designing treatment arms that are less disruptive to a patient's current standard of care may also improve acceptability.

A more holistic (i.e. a more balanced focus on weight restoration, food intake and psychological aspects of recovery) and collaborative approach within intensive treatment settings as well as during transition management may have the potential to increase service users' satisfaction with treatment, adherence and sustained recovery.

- The results of the qualitative process evaluation highlight a desire among patients for an approach better aligned with that given above, further supported by the high PCS scores (see *Report Supplementary Material 5*) across both IP and DP settings within our sample. Future research which includes treatments aligned with a more holistic approach may be more acceptable to potential participants.

  Ensuring that recruitment sites have the resources to balance clinicians' clinical and research workloads would facilitate their involvement in the research process and thus participant recruitment and data collection.
- Protecting research time for clinicians, maintaining open communication between clinical and research teams, and clearly demarcating trial-related roles and responsibilities within clinical teams may aid implementation efforts.

Implications for decision-makers

Randomised controlled trials are considered to be the gold standard in research, generating high-quality evidence to inform and improve clinical applications and healthcare policies. RCTs are time-consuming and costly, so the premature termination of one represents an undesirable return on research resource investment, particularly within the context of limited funding for ED research in the UK.[113] However, there remain important key implications of the DAISIES trial for decision-makers.

Our qualitative research on patients', carers' and clinicians' experiences of specialist ED services provides valuable insights into several aspects of intensive treatment settings that can facilitate positive treatment experiences. In particular, the presence of supportive and collaborative staff that offer a holistic approach to care alongside enhanced psychotherapeutic and transition support appears to be appreciated and associated with more positive experiences. Consistent with past research,[47,114,115] our findings indicated that patients hold a sceptical view regarding the efficacy of IP treatment for recovery, and this negative evaluation may result from the perceived over-focus on weight and eating and insufficient consideration of psychological aspects within IP settings. Clinical practices and policies better integrating these suggested valued aspects and more responsive to patients' needs have the potential to improve service users' experiences and consequently treatment adherence and acceptability.

There is no previous RCT conducted on the comparative effectiveness of a stepped-care DPT approach to IP-TAU for treating adults with severe AN, and the DAISIES trial failed to recruit participants. Previously demonstrated successful recruitment strategies for RCTs may not be feasible and acceptable for this patient population within the confines of the treatment arms offered within the DAISIES trial, and within the resource-strained UK healthcare system. To ensure that funded clinical research is more likely to produce conclusive empirical data that can inform clinical practice and health policies, investments should be made towards alternative study designs (see *Research recommendations*) that will provide more comprehensive insights into the clinical and cost-effectiveness of intensive treatments for AN.

Clinical staff play a key role in the success of clinical trials. Our qualitative study investigating stakeholders' views and experiences of implementing the DAISIES trial within intensive ED services has demonstrated several clinician-related barriers to participant recruitment.[4] Although clinicians broadly supported the investigation of alternatives to IP care for severe AN, understandably clinical responsibilities and decisions took priority when it came to implementing the DAISIES trial within their services in the context of the COVID-19 pandemic. Furthermore, clinicians may have experienced difficulty 'pitching' the trial to patients when they are in their most acute state and worry about the appropriateness of research participation for those severely unwell.[4,94,95] In this regard, investment in the development of strategies to balance clinical responsibilities and involvement in research processes for under-resourced and overburdened ED clinicians is critical for the implementation of future research.

Research recommendations

The numerous challenges faced during the DAISIES trial may suggest that alternative trial designs should be explored when considering future research surrounding intensive treatments for adult AN in the UK. When considering how to best adapt the study in the face of the extensive recruitment challenges outlined above, the research team conceptualised three alternative research design options in February of 2022.

Option 1: partially randomised design

This option involves randomising those who agree to be randomised and running two patient preference arms alongside this, that is, patients in need of intensive treatment who have a strong preference for either (1) IP or (2) DPT. This would allow an assessment of what proportion of these patients would agree to participate in a longitudinal study of this kind and what proportion of those who are eligible would allow themselves to be randomly allocated to either option. Additionally, qualitative interviews could be conducted in tandem to understand key patient-related and service-related factors that drive patient and carer preferences and impede recruitment to an RCT. The advantage of this option is that it would allow a thorough and generalisable exploration of these patient preference factors in this acute population. In addition, the feasibility of conducting a full large-scale RCT in this area would also be explored. This design (which is more accommodating of patient choices) would allow meaningful questions about the characteristics and outcomes of patients in the four different arms (two randomised, two non-randomised) to be addressed.

Option 2: stepped-care day-patient treatment versus any other treatment-as-usual

This option involves changing the existing DAISIES trial design to a two-armed trial comparing the stepped-care DPT option with any TAU (i.e. not just IP treatment but also OPT). This option keeps questions about the role of day services in the treatment of patients with AN at the centre of the study and retains the randomisation component, while also allowing recruitment from a broader number of patients. This also allows for sites who only have a day service to become recruiting sites. However, this option has several limitations, including that it is unlikely to be informative on health economic questions. This design also assumes that day treatment is relatively similar across services, while in a post-COVID-19 environment variability in day service design and provision is probably greater than ever.

Option 3: inpatient treatment-as-usual versus broadened stepped-care

This option involves a comparison (with randomisation) of an IP treatment arm with a broadened stepped-care arm that provides either DPT or any other intensive community treatment provided as an alternative to IP admission (e.g. intensive OPT, home treatment). This design would broaden the number of sites available to recruit to the trial, and allow all suitable patients to participate irrespective of travel time to their nearest ED service. This option focuses on questions as to whether a broad range of community alternatives are as effective, acceptable and cost-effective as IP-TAU. These alternative intensive treatment options are being more commonly provided for those with severe AN post pandemic.

For all potential redesign options, we highly recommend that a feasibility trial is first commissioned prior to a full-scale version. This would provide insight into the scientific merit, feasibility and acceptability of conducting a larger-scale trial while providing information concerning the quality of trial outcome measures and implementation strategies. Furthermore, a feasibility trial would facilitate more cost-savvy use of resources within the ED field. In the DAISIES trial an internal pilot study was included as part of the design instead of a feasibility trial. However, this meant that from the beginning the costly 'machinery' of a large effectiveness trial had to be put into place.

We have further identified several priority areas for future research to focus on, without any predefined priority order:

1. Evaluating the efficacy and effectiveness of forms of intensive treatment delivery that emerged or grew in popularity after the COVID-19 for adults with AN, including virtual/hybrid DPT provision and community-based intensive treatments. The latter are particularly popular as alternatives to day services with the recently developed provider collaboratives that usually span large geographical areas where often only part of the catchment area population can travel to a day service that is situated in an urban centre.

    - Since the original funding of the DAISIES trial, the intensive ED treatment service landscape within the UK has changed due to the impact of the COVID-19. Research into emerging forms of intensive treatment (such as home treatment or intensive OPT) will be more timely and future-proof.

2. Evaluating the long-term effectiveness and cost-effectiveness of routinely delivered intensive treatments for AN.

    - This can be investigated through the research designs highlighted above.

3. Further investigating patient experiences of intensive treatment settings, and the adjustments to the current standard of care (reflective of patient desires) that could be made to improve acceptability (e.g. added provision of psychological interventions within intensive treatment settings).

    - The results of the qualitative interviews with patients and carers convey dissatisfaction with aspects of current intensive treatment settings (e.g. perceived over-focus on weight gain for recovery). Scores on the TESS further indicate this, for instance the less positive ratings of relationships with staff as compared with patients, as well as the high scores on the PCS as previously reported for patients admitted to IP and DP settings.[45] Further investigating patient experiences can help an understanding of the transferability of these results outside of a time of acute COVID-19 impacts on care, both through a qualitative methodology as well as through routine assessment of experiences using the TESS and PCS, as these aspects of experience have the potential to impact on treatment satisfaction and clinical outcome.[45,116] Investigating adaptations to intensive settings will inform the acceptability and feasibility of adjustments that aim to improve the patient experience.

4. Investigating workforce-related issues within intensive treatment settings.

    - The qualitative results, alongside the case study given in the introduction section, highlight workforce-related challenges within intensive treatment settings, including short staffing and a reliance on agency staff, both of which have a strong negative impact on team morale and quality of care. Research seeking to investigate the reasons behind and solutions to these challenges may help improve staff satisfaction and the standard of care in intensive treatment.

Conclusions

This synopsis provides in-depth insight into the views and experiences of patients, carers and clinicians regarding the intensive treatments for adults with severe AN and the challenges faced in implementing the DAISIES trial within UK-based intensive ED services. Although both intensive treatment settings are valued, the stepped-care DPT approach is perceived more positively than IP-TAU by service users. Overall, patient- and service-related factors, alongside wider systemic factors, seem to have contributed to the premature termination of the DAISIES trial. As no inferential analysis could be conducted, clear questions remain over the clinical effectiveness and cost-effectiveness of IP-TAU and DPT for adult patients with severe AN. Even though research into alternatives to IP-TAU for adult EDs remains necessary, conducting an RCT of the scope and magnitude of the DAISIES trial may not be possible within intensive adult ED services in the UK. Thus, alternative research designs and treatment options should be explored.

Additional information

Acknowledgements

We thank the independent Trial Steering Committee (Jess Griffiths, Professor Beate Herpertz-Dahlmann, Isa Robinson, Dr Lucy Gallop) and the independent Data Monitoring and Ethics Committee (Dr Jacinta Tan, Dr Jane Morris, Dr Dennis Görlich).

This study was funded by the National Institute for Health and Care Research (NIHR) Evaluation, Trials and Studies Coordinating Centre (NETSCC) (Reference: 17/123/03). This research was also supported by the NIHR Biomedical Research Centre (BRC) for Mental Health at the South London and Maudsley NHS Foundation Trust (SLaM) and Institute of Psychiatry, Psychology and Neuroscience (IoPPN), King's College London (KCL).

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Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/FTJP6744.

Primary conflicts of interest: Ulrike Schmidt, Janet Treasure, Sabine Landau and Sarah Byford receive salary support from the NIHR BRC for Mental Health at SLaM and KCL. Sabine Landau also receives salary support from the NIHR Applied Research Collaboration (ARC) – South London. Catherine McCombie is funded by an Economic and Social Research Council London Interdisciplinary Social Science Doctoral Training Partnership Studentship.

All other authors declare they have no competing interests.

Data-sharing statement

Anonymised data requests should be submitted to the corresponding author for consideration.

Ethics statement

Ethical approval was granted by Wales Research Ethics Committee 5 (Reference: 20/WA/0072; 14 April 2020) and approvals from Research and Development departments of recruiting sites were obtained.

Information governance statement

King's College London (sponsor) is committed to handling all personal information in line with the UK Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679. The Research Governance office manages the King's Data Protection Register (KDPR).

Department of Health and Social Care disclaimer

This publication presents independent research commissioned by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, MRC, NIHR Coordinating Centre, the Health Technology Assessment programme or the Department of Health and Social Care.

This synopsis was published based on current knowledge at the time and date of publication. NIHR is committed to being inclusive and will continually monitor best practice and guidance in relation to terminology and language to ensure that we remain relevant to our stakeholders.

Publications

İnce B, Phillips MD, Zenasni Z, Shearer J, Dalton B, Irish M, *et al*. Autopsy of a failed trial part 2: outcomes, challenges, and lessons learnt from the DAISIES trial. *Eur Eat Disord Rev* 2023;1–14. https://doi.org/10.1002/erv.3058

İnce B, Phillips M, Arcelus J, Byford S, Himmerich H, Landau S, *et al*. *Lessons Learned from a Failed Multi-Centre Clinical Trial: The DAISIES Study*. Conference poster, London International Eating Disorders Conference, London, UK, 16 -17 March 2023.

Irish M, Dalton B, Potts L, McCombie C, Shearer J, Au K, *et al*. The clinical effectiveness and cost-effectiveness of a 'stepping into day treatment' approach versus inpatient treatment as usual for anorexia nervosa in adult specialist eating disorder services (DAISIES trial): a study protocol of a randomised controlled multi-centre open-label parallel group non-inferiority trial. *Trials* 2022;**23**:500. https://doi.org/10.1186/s13063-022-06386-7

Webb H, Dalton B, Irish M, Mercado D, McCombie C, Peachey G, *et al*. Clinicians' perspectives on supporting individuals with severe anorexia nervosa in specialist eating disorder intensive treatment settings during the COVID-19 pandemic. *J Eat Disord* 2022;**10**:30. https://doi.org/10.1186/s40337-022-00555-4

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Phillips M, İnce B, Webb H, Dalton B, McCombie C, Irish M, *et al*. Autopsy of a failed trial part 1: a qualitative investigation of clinician's views on and experiences of the implementation of the DAISIES trial in UK-based intensive eating disorder services. *Eur Eat Disord Rev* 2023;**31**:489–504. https://doi.org/10.1002/erv.2975

Phillips M, İnce B, McCombie C, Irish M, Dalton B, Peachey G, *et al*. *Lessons from a Failed Trial: A Qualitative Analysis of Stakeholders' Experiences of Implementing the DAISIES Trial in UK Intensive Eating Disorder Services*. Conference presentation, London International Eating Disorders Conference, London, UK, 16 -17 March 2023.

Study registration

This study is registered as ISRCTN10166784.

Funding

This synopsis presents independent research funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme as award number HTA 17/123/03.

This synopsis provides an overview of the research award A Randomised Controlled Multi-Centre Open-Label Parallel Group Non-Inferiority Trial of the Clinical Effectiveness, Acceptability and Cost-Effectiveness of a 'Stepping into Day Treatment' Approach versus Inpatient Treatment as Usual for Anorexia Nervosa in Adult Specialist Eating Disorder Services. For more information about this research please view the award page (www.fundingawards.nihr.ac.uk/award/17/123/03).

About this synopsis

The contractual start date for this research was in December 2019. This article began editorial review in August 2023 and was accepted for publication in June 2024. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The Health and Social Care Delivery Research editors and publisher have tried to ensure the accuracy of the authors' article and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this article.

List of abbreviations

AN	anorexia nervosa
ARFID	avoidant restrictive food intake disorder
BMI	body mass index
CONSORT	Consolidated Standards of Reporting Trials
DPT	day-patient treatment
DSM-V	*Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition
ED	eating disorder
EDE-QS	Eating Disorder Examination Questionnaire Short
IP-TAU	inpatient treatment as usual
NASSS	Non-Adoption, Abandonment, Scale-up, Spread, and Sustainability
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
OPT	outpatient treatment
PCS	Perceived Coercion Scale
PPI	patient and public involvement
RCT	randomised controlled trial
SLAM	South London and Maudsley NHS Foundation Trust
TESS	Therapeutic Environment Scale
TMG	Trial Management Group
TSC	Trial Steering Committee
TW2	Tyson House West 2

List of supplementary materials

Report Supplementary Material 1
Participant data and indicative quotes in thematic analysis of semistructured interviews and focus groups with clinicians, patients and carers

Report Supplementary Material 2
Semistructured interviews and focus groups topic guides

Report Supplementary Material 3 Dates of semistructured interviews and focus groups

Report Supplementary Material 4
Demographic information of carers and their outcomes at baseline, 6 and 12 months

Report Supplementary Material 5
Patient clinical outcome summaries by treatment arm and time points

Report Supplementary Material 6
Health economic data

Report Supplementary Material 7
Application of NASSS framework to identify implementation barriers and facilitators in the DAISIES trial

Supplementary material can be found on the NIHR Journals Library report page (https://doi.org/10.3310/FTJP6744).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

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