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Synopsis

Olanzapine for young people with anorexia nervosa: a synopsis of the main results from the OPEN open-label feasibility study

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Abstract

Background: In clinical practice, olanzapine is commonly used in young people with anorexia nervosa, although the underpinning evidence-base is limited. However, its efficacy, tolerability, acceptability and adherence rate, and the patients', carers' and clinicians' views of olanzapine treatment are unclear. This synopsis article summarises the methods and results of the OPEN feasibility study, overarching the findings and drawing comprehensive conclusions from a quantitative feasibility outcome paper and two qualitative research papers.

Methods: The OPEN study assessed the feasibility of a future randomised controlled trial on olanzapine in young people with anorexia nervosa in an open-label, one-armed feasibility study. In this study, we aimed to include 55

patients with anorexia nervosa or atypical anorexia nervosa aged 12–24 who gained < 2 kg within at least 1 month of treatment as usual. Time points for assessments were at baseline, 8 weeks, 16 weeks, and 6 or 12 months. We estimated recruitment, adherence and attrition rates and mean changes in body weight, body mass index and eating disorder psychopathology. In addition, we explored the views on and experiences with olanzapine treatment within a clinical trial setting using qualitative interviews with young people with anorexia nervosa, their families and clinicians.

Results: Fifty-two people were pre-screened, 35 were eligible and 20 participants were recruited and started olanzapine. Of these, 15 continued olanzapine for ≥ 16 weeks. Participants experienced, on average, a decrease in their eating disorder psychopathology, and body weight and body mass index increased during treatment with olanzapine as an adjunct to treatment as usual. Important themes derived from semi-structured qualitative interviews with young people and their parents were: moving away from the illness towards recovery, evaluating information on olanzapine, consent and trust in shared decision-making and the ambivalence around recovery. The main themes expressed by clinicians included: acknowledging the concerns of young people with anorexia nervosa and their families, prioritising person-centred care, the limited service capacity and strict study eligibility criteria.

Limitations: The study failed to meet the recruitment target and showed low adherence rates for treatment with olanzapine. Possible reasons for the recruitment difficulties and the low adherence rate include the high clinical workload of eating disorder services during and after the COVID-19 pandemic, the heterogeneity of eating disorder service setup across the country, and the reluctance of patients to agree to take olanzapine under the relatively restricted conditions of a clinical study.

Conclusions: A realistic time schedule for site-preparation, recruitment, treatment and follow-up, realistic recruitment targets and easy access to medical and laboratory examinations may improve the success of future feasibility studies and randomised controlled trials in this patient group.

Future work: The difficulties in conducting the OPEN study will inform the planning for future pharmacological and non-pharmacological studies in anorexia nervosa. Therefore, we developed a checklist with action points for the planning of pharmacological trials in eating disorders. Furthermore, novel pharmacological options such as typical and atypical psychedelic drugs (e.g. psilocybin and ketamine) might be more acceptable for people with anorexia nervosa as they do not have the side effect of immediate weight gain.

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Introduction

There is a need to improve treatment for patients with anorexia nervosa (AN), and antipsychotics may offer a useful adjunct to psychological and nutritional treatments. However, there are insufficient data available regarding the efficacy and safety of antipsychotics in this patient group to recommend the use of any antipsychotic for treatment of AN at present. Moreover, published studies regarding treatment with antipsychotics for AN do not cover changes in general psychopathology, health economic and quality of life-related aspects of such treatment.¹

Anorexia nervosa is a major health problem. Common comorbid conditions, such as depression and anxiety, add significantly to the burden and the high mortality,² and the impact on families is devastating. The course of AN is often chronic and this can lead to persistent disability.³ A longitudinal cohort study showed that only about 30% of patients with AN had recovered after 9 years.⁴ The dietary deficit is often accompanied by significant physical health issues, such as growth retardation, osteopenia, amenorrhoea and renal insufficiency, and also changes

in laboratory parameters, cardiac arrhythmia and disturbances of thyroid function.⁵ The most common causes of death in patients with AN are sudden cardiac death associated with ventricular arrhythmias and suicide.^{6–8} Mortality rates are nearly five times higher for people with AN than in the general population.⁹

Despite limited research evidence for the use of olanzapine in young people with AN, this is nonetheless widely used in clinical practice. A double-blind randomised placebo-controlled trial (RCT) by Attia *et al.* tested the effect of olanzapine in outpatients with AN aged 16 or over for 8 weeks.¹⁰ Even though the researchers had been in contact with 603 patients with AN, of whom 87 were eligible and agreed to a telephone screening interview, only 23 could be randomised. Seventeen patients completed the study revealing a significant drug effect on weight gain but not on psychological symptoms. These findings were replicated in a larger RCT in adult outpatients with AN.¹¹ One hundred and fifty-two participants were randomised to receive placebo or olanzapine. The completion rate of the study was 55%. There was a significantly greater body mass index (BMI) increase in the olanzapine group, but no

group differences for the psychological symptoms of AN. Brambilla *et al.* conducted an RCT with olanzapine in 30 adult outpatients with AN.¹² There was no significant difference in weight gain between olanzapine and placebo, but some drug benefits in eating disorder (ED) psychopathology. In another RCT, Bissada *et al.* randomised 34 adult patients with AN to olanzapine or placebo over 10 weeks in a day-care treatment program.¹³ The olanzapine group gained significantly more weight and showed a significant reduction of obsessive symptoms. Kafantaris *et al.* conducted a small RCT in 20 adolescents with AN up to the age of 21 to test olanzapine versus placebo.¹⁴ Both groups had similar weight gain and no differences in psychological symptoms. For a more detailed summary of these studies, see Himmerich *et al.*¹

Thus, there is evidence for olanzapine from five RCTs in adult patients with AN. Four of these RCTs show significant weight gain.^{10–13} However, the evidence for olanzapine in adolescents with AN is very limited. Furthermore, its effect on ED psychopathology, its efficacy and tolerability, its acceptability and adherence rate, and the way patients, carers and clinicians view olanzapine treatment for this population are unclear.

For additional relevant literature that informed the Olanzapine for young PEople with aNorexia nervosa (OPEN) study, see the research papers which are synthesised in this synopsis^{15–17} and the protocol paper.¹⁸

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Methods

Study design

We performed an open-label feasibility study in adolescents (12–17 years old) or young adults (18–24 years old) with AN.¹⁵ The aim was to include 55 young people with AN who received inpatient, day-care or outpatient treatment, were diagnosed with AN or atypical AN according to the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, had gained < 2 kg within at least 1 month of treatment as usual and were able to read and write in

English.^{15,18} Study participants were treated with olanzapine and followed up for up to 12 months.¹⁵ Outcomes were assessed at baseline, 8 weeks, 16 weeks, 6 months and 12 months after starting olanzapine.¹⁵ For the specific inclusion and exclusion criteria, see the published protocol article.¹⁸

Olanzapine was prescribed off-label for AN in the form of tablets or dispersible tablets of 2.5, 5, 7.5 or 10 mg. Olanzapine was initiated at 1.25 or 2.5 mg/day in adolescents. In adults, the starting dose was 2.5 mg/day. Patients were maintained at this dose if it was deemed sufficient clinically.¹⁵ A slow titration schedule was followed, comprising weekly increments of 1.25 or 2.5 mg/day for adolescents and 2.5 mg/day for adults, up to a maximum of 10 mg/day for both.¹⁵

The primary feasibility parameters to assess the feasibility of a future definitive RCT included recruitment, adherence and completion of the assessments. Secondary feasibility parameters were the feasibility of recording the following measures at baseline, 8 weeks, 16 weeks, 6 months and 12 months: demographics, the alcohol, smoking and substance involvement screening test, height, weight and BMI, ED psychopathology questionnaires, general psychopathology questionnaires, health economic and quality of life assessments, olanzapine plasma level, physical examination measures, electrocardiogram (ECG), laboratory parameters and a measure of sleepiness.¹⁵ We also asked about participants' willingness to participate in a future blinded, placebo-controlled RCT at baseline and at the end of the study.¹⁵

The mean change in BMI and the mean change in ED psychopathology as measured by the Eating Disorder Examination Questionnaire (EDE-Q) Global score over time were explored in the sample to inform future sample size calculations. For a description of all specific measures and questionnaires, see Said *et al.*¹⁸ To assess medication safety, we used physical examination, ECG, measurement of routine laboratory parameters and the UKU-Side Effect Rating Scale.¹⁵ Feasibility thresholds were chosen based on the needs of a future phase 3 trial that would aim to demonstrate effectiveness (and safety) of olanzapine in this population. An approximate preliminary sample size estimation for this future trial was carried out at grant application stage, with a difference of 1 kg/m² in mean BMI as the minimal clinically important difference, as this is associated with improvements in quality of life.¹⁹ Based on Attia *et al.*,¹¹ we estimated the within-group standard deviations (SDs) of BMI change to be 2.39 kg/m². This translates into a standardised effect size of Cohen's *d* = 0.42. To detect such an effect size

with 90% power using a 2-sided independent samples *t*-test at the 5% significance level, 121 patients per trial arm would be required. Allowing for 25% attrition, this would involve randomisation of 322 patients (161 per trial arm). The sample size for this feasibility trial of 55 (the feasibility threshold for recruitment) was chosen as to the minimum viable number of study participants (between 30 and over 50) that could be recruited in order to up-scale to a future phase 3 trial (with a corresponding increase in resources).

Statistical analyses

Means and SDs are reported for descriptives of continuous variables and frequencies or proportions used to describe categorical variables. Published guidance was used to handle missing items in scales where present; otherwise scales were pro-rated if fewer than 20% of items were missing.

The main feasibility outcome of recruitment is presented as a proportion of the required sample size. Completion rates of individual measures are presented as numbers with percentages; some measures only applied to certain subgroups of the sample (e.g. the age-dependent measures) and completion rates are presented out of the number who should have completed the measure.¹⁵

Adherence to treatment was pre-defined in the statistical analysis plan as taking at least 16 weeks (112 days) of olanzapine calculated from the total number of daily doses taken according to pill returns.¹⁵

Exploratory analyses: EDE-Q Global score, weight (kg), and BMI (kg/m²) were explored for changes over time. The EDE-Q Global score was calculated by summing the four subscales and dividing the resulting total by the number of subscales (i.e. four).¹⁵

Linear mixed models were used to model change over time in these measures, with time as the independent variable and with a random intercept for participant. Models using both categorical time (per the expected assessment time visit) and linear time (actual timing of assessment) were considered, with the latter used to calculate change in time per week [with 95% confidence intervals (CI)]. Other time parameters were not considered due to the low sample size. These were constructed for the whole sample and in only the sample who 'adhered' to olanzapine. Baseline observations were included in the model as the reference group to estimate mean differences from baseline.¹⁵

No *p*-values were presented for any analyses, and all analyses were treated as underpowered and not to be used to make inferential conclusions.

Qualitative research

Participants' experience of recruitment and treatment, acceptability, reluctance to take olanzapine and reasons for adherence and non-adherence were examined in qualitative interviews. Clinicians from recruiting sites were also interviewed to understand their views and experiences of using olanzapine in AN and examine barriers and facilitators to recruitment and implementation of a clinical trial assessing olanzapine for AN in young people. Additionally, a web-based semi-structured Qualtrics survey was administered to ED clinicians across the UK to corroborate and expand on the information derived from qualitative interviews.^{16,17}

Reporting

The reporting of the study followed the Consolidated Standards of Reporting Trials (CONSORT) 2010 checklist of information for feasibility trials. The checklist can be downloaded from the section 'Electronic supplementary material' of the original article of the feasibility results¹⁵ (supplementary material 1, Consort Checklist).

Results

Feasibility results and exploratory outcomes

Participants were recruited across 10 sites in England from June 2022 to May 2023. For the CONSORT diagram, see Said *et al.*¹⁵ Fifty-two people were assessed at pre-screening for initial eligibility, of which 13 were excluded. Thirty-nine people were therefore approached, of which 10 declined, 4 were found to be ineligible or became ineligible following being approached and 5 were excluded for an unknown reason as data were missing.¹⁵ Twenty participants were consented, all of whom had a baseline assessment and started olanzapine.¹⁵

Baseline demographics and clinical characteristics for the 20 consented participants are presented in [Table 1](#).

Baseline scores and baseline subscores of the EDE-Q, the Beliefs About Voices Questionnaire (BAVQ-R), the Self-Regulation of Eating Behavior Questionnaire (SREBQ), the Depression Anxiety Stress Scales (DASS), the Revised Children's Anxiety and Depression Scale (RCADS), the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) or the Children's Obsessive-Compulsive Scale (CY-BOCS), the Epworth Sleepiness Scale (ESS) or the Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD) and the Eating Disorders Symptom Impact Scale (EDSIS) are presented in [Table 2](#). The last column of the table informs about the theoretically lowest and highest possible scoring range of the particular questionnaire or

TABLE 1 Baseline demographics and clinical characteristics for the 20 consented participants¹⁵

Baseline demographics and clinical characteristics	Available data	n (%) / mean (SD)
Self-reported gender	20 (100%)	
Male		0 (0%)
Female		19 (95%)
Non-binary		1 (5%)
Ethnicity	20 (100%)	
Black		0 (0%)
White		15 (75%)
Asian/Asian British		2 (10%)
Mixed/Multiple ethnic groups		3 (15%)
Other		0 (0%)
Primary diagnosis	20 (100%)	
AN		18 (90%)
Atypical AN		2 (10%)
Setting at time of recruitment	20 (100%)	
Outpatient		18 (90%)
Inpatient		1 (5%)
Day care		1 (5%)
Age	20 (100%)	16.3 (3.1)
Adolescents (12–17)		15 (75%)
Adults (18–24)		5 (25%)
Height (m)	20 (100%)	1.6 (0.082)
Weight (Kg)	20 (100%)	46 (7.2)
Systolic blood pressure (mmHg)	18 (90%)	106 (11)
Diastolic blood pressure (mmHg)	18 (90%)	72 (9.7)
Pulse rate (bpm)	17 (85%)	83 (17)
Body temperature (°C)	10 (50%)	37 (0.52)
BMI (kg/m ²)	20 (100%)	17 (1.8)

Source

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its subscore. For most interviews, greater scores indicate a higher level of illness severity. However, a high SREBQ score indicates an individual's greater ability to regulate their eating. The protocol article by Said *et al.*¹⁸ provides further information on the interviews and the specific versions used.

The main feasibility parameter was recruitment; 20 participants out of the 55 required per the sample size calculation were recruited and 20 participants were recruited out of the 35 who were approached and identified as eligible (57%, 95% CI 39 to 74). Fifteen out of 20 (75%, 95% CI 50 to 91) participants were prescribed olanzapine for

TABLE 2 Baseline questionnaire scores for the 20 consented participants and the lowest and highest possible scoring range of the respective questionnaire¹⁵

Questionnaire scores	Available data (%)	Mean (SD)	Scoring range
EDE-Q Restraint subscore	19 (95)	4.8 (0.92)	0–6
EDE-Q Eating subscore	20 (100)	3.9 (0.94)	0–6
EDE-Q Shape subscore	20 (100)	5.4 (0.77)	0–6
EDE-Q Weight subscore	20 (100)	5 (0.88)	0–6
EDE-Q Global score	20 (100)	4.8 (0.68)	0–6
BAVQ-R Malevolence ^a	14 (100)	14 (4.0)	0–18
BAVQ-R Benevolence ^a	14 (100)	13 (4.0)	0–18
BAVQ-R Omnipotence ¹	14 (100)	16 (3.8)	0–18
BAVQ-R Resistance – Emotion ^a	14 (100)	11 (3.8)	0–18
BAVQ-R Resistance – Behaviour ^a	14 (100)	11 (4.3)	0–18
BAVQ-R Engagement – Emotion ^a	14 (100)	8.4 (3.0)	0–18
BAVQ-R Engagement – Behaviour ^a	14 (100)	8.8 (3.1)	0–18
SREBQ – Total mean score	20 (100)	2.9 (0.5)	1–5
DASS – Depression score ^b	17 (100)	29 (11)	0–42
DASS – Anxiety score ^b	17 (100)	21 (9.4)	0–42
DASS – Stress score ^b	17 (100)	31 (7.3)	0–42
RCADS – Social phobia score ^c	3 (100)	22 (2.9)	0–27
RCADS – Panic disorder score ^c	3 (100)	20 (0)	0–27
RCADS – Major depression score ^c	3 (100)	27 (5.5)	0–30
RCADS – Separation anxiety score ^c	3 (100)	16 (1.7)	0–27
RCADS – Generalised anxiety score ^c	3 (100)	17 (2.3)	0–18
RCADS – Obsessive compulsive score ^c	3 (100)	13 (2.6)	0–18
Y-BOCS/CY-BOCS Total score	16 (80)	20 (8.1)	0–40
ESS/ESS-CHAD Total Score	20 (100)	5.5 (4.2)	0–24
EDSIS Social Isolation score ^d	11 (85)	8.1 (3)	0–16
EDSIS Guilt score ^d	11 (85)	14 (5.1)	0–20
EDSIS Nutrition score ^d	10 (77)	24 (5.6)	0–32
EDSIS Dysregulation score ^d	10 (77)	4.8 (5.1)	0–28

a Only required for those age 15 years or over, $n = 14$. Any extraneous data completed by those under 15 years was removed.

b Only required for those age 14 years or over, $n = 17$. Any extraneous data completed by those under 14 years was removed.

c Only required for those under 14 years, $n = 3$. Any extraneous data completed by those 14 years or over was removed.

d Completed by a parent/caregiver only if they agreed to have data collected about themselves, $n = 13$.

Source

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112 days or longer during the study.¹⁵ Thirteen out of 20 (65%, 95% CI 41 to 85) participants completed follow up (either 6 or 12 months).¹⁵

Fourteen out of 18 participants (77%) at baseline said they would have participated in an RCT of olanzapine versus placebo (3 participants, 17% responded as 'don't know' and data were missing for 2 other participants). The percentage of people who would have agreed to take part in an RCT went down from 77% at baseline to 45% (5/11 participants) at month 6, and was 100% (2/2 participants) at 12 months.¹⁵

Thirteen adverse events were recorded affecting 7 (35%) participants. There were two adverse reactions reported: diarrhoea/incontinence (assessed as possibly related to olanzapine) and elevated alanine transferase (assessed as definitely related). Two events of hospitalisation for AN were reported, but neither were considered related to the intervention by trial investigators and these events were not considered serious adverse events for this trial as outlined in the protocol.¹⁸

There was a mean decrease of 0.07 (95% CI 0.04 to 0.09) in EDE-Q Global score per week in the whole sample of 20 participants and a mean BMI increase of 0.08 kg/m² (95% CI 0.06 to 0.10) per week. These values did not change when analyses used only the subsample of 15 participants who had olanzapine prescribed over 112 days. [Table 3](#) depicts the changes in EDE-Q, body weight and BMI over time. For further quantitative results, see.¹⁵

Results of qualitative interviews with patients and their families

Four main themes emerged from the qualitative interviews with patients and their families: (1) Moving away from illness and moving towards recovery: some hoped olanzapine would help move away from suffering, including broad quality-of-life issues; some had longer-term goals such as returning to education. (2) Evaluating information on olanzapine and its purpose: participants integrated information from clinicians, peers and independent research. (3) Consent and trust versus coercion and trauma in decision-making around olanzapine: it was important to be able to withdraw from research and medication at any

TABLE 3 Changes in EDE-Q, body weight and BMI over time¹⁵

Measure/visit	N	Mean (SD)	Estimated mean (SE) change from baseline	95% CI for mean change from baseline
EDE-Q Global score				
Baseline	20	4.8 (0.68)	–	–
Week 8	11	3.8 (1.1)	–0.95 (0.27)	(–1.47 to –0.42)
Week 16	9	3.9 (1.3)	–0.96 (0.34)	(–1.61 to –0.29)
Month 6	7	2.9 (1.4)	–1.87 (0.52)	(–2.90 to –0.85)
Weight (kg)				
Baseline	20	46.0 (7.2)	–	–
Week 8	10	50.7 (8.6)	2.7 (1.1)	(0.5 to 4.9)
Week 16	10	50.0 (7.2)	3.8 (1.0)	(1.8 to 5.8)
Month 6	11	52.3 (7.4)	6.2 (1.2)	(3.8 to 8.5)
BMI (kg/m²)				
Baseline	20	16.9 (1.8)	–	–
Week 8	10	18.2 (2.5)	0.9 (0.4)	(0.1 to 1.6)
Week 16	10	18.1 (2.1)	1.3 (0.4)	(0.5 to 2.0)
Month 6	11	19.1 (2.2)	2.2 (0.4)	(1.4 to 3.0)

SE, standard error.

Source

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time; this could be complicated in context. (4) Ambivalence around recovery: recovery could be frightening, particularly if rapidly pharmacologically induced.¹⁶

Results of qualitative interviews with clinicians

Four main themes were identified from the qualitative interviews with clinicians: (1) acknowledging service user's and their family's concerns; (2) prioritising person-centred care; (3) limited service capacity and (4) study eligibility criteria. Findings suggest the greatest barriers to recruitment to be an overburdened healthcare system and concerns regarding olanzapine on both clinicians' and service users' sides, while the greatest facilitators consist of a positive rapport with service user and their families, and olanzapine as an appropriate adjunct treatment.¹⁷ Survey findings underlined confidence in prescribing and informing on olanzapine, the various possible benefits of olanzapine besides weight gain, and the importance of therapeutic alliances and informed consent. Both data sets highlighted the need for further evidence on long-term safety, side effects and efficacy of olanzapine use for AN. Where clinical service capacity is impaired, research implementation is not prioritised.¹⁷

Discussion

In summary, only 20 of the 55 potential participants could be included into the study; only 13 of these 20 participants (65%) completed the trial up to 6 or 12 months. Thus, the study failed to meet the recruitment target and showed low adherence rates for treatment with olanzapine.

There are several potential reasons why this feasibility study did not recruit the envisaged number of patients.

- The study was conducted around the COVID-19 pandemic when inpatient and day-care services had reduced numbers of therapy places and outpatient services worked mainly remotely. This situation led to fewer patients who could be approached in person and recruited for the study. Another consequence of the pandemic was that clinical services for people with EDs were overwhelmed because many staff members were on sick leave or deployed (e.g. to vaccination hubs or specialised COVID-19 services), with some ED services having half their positions vacant. The current study included laborious baseline measurements (e.g. physical examinations, ECG, blood tests and questionnaires) which, taken together, meant a significantly bigger effort

than the usual clinical prescription of olanzapine. Therefore, staff may have prioritised clinical needs over research.¹⁵

- Furthermore, heterogeneity of ED service setup across the country possibly meant that some clinicians refrained from offering olanzapine, despite clinical appropriateness, due to their inability to regularly review and monitor its use.
- The exclusion criteria of this feasibility study may have been too strict. Clinicians identified multiple young people in their services that were already on, or were being started on, olanzapine but would not have been eligible due to rather strict criteria and procedures. These included providing ample time for informed consent, undertaking screening and baseline assessments, self-harm and suicidality being common in AN yet exclusion criteria, the amount and time period for lack of weight gain, having to request regular pregnancy tests in a population not subject to this in routine clinical practice, and more severe initial presentations in current setting generating clinical urgency and motivation to start olanzapine promptly.
- Olanzapine is known to lead to weight gain, and patients with AN fear this particular side effect of medication as it relates to their core psychopathology. Offering a balanced view on possible effects of olanzapine on potential therapeutic targets for patients with AN, for example, anxiety, concentration, sleep, and anorexic thoughts, might be valued by young people with AN and their families.

However, most alternative medications in AN have been used and tested in the past because of their ability to help with weight recovery. As there are novel biological treatment options under investigation in AN, such as psilocybin and ketamine, as well as non-invasive brain stimulation treatments on the horizon,²⁰ olanzapine may not be the preferred medication for people with AN and their clinicians. However, these treatments are currently labour- and cost-intensive because patients either have to be observed for long periods of time in a clinical setting for safety reasons or they receive psychedelic-assisted therapy for several hours per dosing session. Thus, olanzapine may still be considered by clinicians as a treatment option for AN.¹⁵

Our sample size calculation took the future sample size, the number of prospective sites and the potential number of participants in the target population at each site into the consideration. Thus, we chose a number at the upper end of this scale. Regardless of this, we did not reach even the lower end of this suggested potential

range. Rates of retention and adherence were additional feasibility measures, with thresholds set in order to show that we would be able to collect sufficient data for both the intention to treat (effectiveness) and per protocol (efficacy) estimands of a future phase 3 trial. However, given the low recruitment, the estimates of these rates for a future trial could not be made with sufficient precision.

The exploratory measures of changes in EDE-Q, body weight and BMI over time, which we aimed to use inform future sample size calculations, need also to be interpreted very cautiously in respect to the low sample size.

Public and patient involvement

People with lived experience [public and patient involvement (PPI)] made significant contributions to the ideas, decisions and drawing up of this study and the publication of the results. Our trial team included two PPIs with lived experience of AN from the start. They helped review the literature, design the study, conduct a chart review on olanzapine-treated inpatients, develop questionnaires assessing patient and carer views on medication for AN, and facilitate a workshop at the National Carers Conference 2017. A PPI and HH facilitated a workshop with patients, carers and professionals at the Eating Disorders International Conference 2018 to discuss the topic of the study. Two PPIs from the Research Design Service gave feedback for this application.

Public and patient involvement input led to the following decisions to measure symptoms of depression, anxiety and side-effects (sleepiness, cardiac and metabolic problems) as outcomes and to include inpatients and outpatients. The PPI coapplicant ensures continuous PPI involvement and PPI contribution to data evaluation and coauthoring of publications. The scientific evaluation of the qualitative interviews was led by PPIs. Two PPIs were members in our Trial Steering Committee (TSC). One of the PPIs has become an official PPI representative for EDs with the Royal College of Psychiatrists.

Two qualitative researchers have lived experience of AN and/or off-label use of antipsychotics. Nine of the clinicians that responded to our web-based survey also disclosed lived experience of an ED either as a service user, a carer or both. The presence of lived experience in the study at various roles enhanced the strength of our understanding of patient and carer views.

Equality, diversity and inclusion

Although the population recruited into OPEN was somewhat limited in terms of gender and ethnic diversity, we included several participants from an ethnic minority background into the study (see [Table 1](#)). The main shortcomings were that no male and no participant from a Black ethnic background were recruited. As the participant information and the consent forms were available only in English, that may have prevented access among non-English-speaking migrant populations or those with English as a second language.

Impact and learning

The experienced difficulties in conducting the study which were the shortage of time to set up and conduct the study, the ambitious recruitment target and the limited access to medical and laboratory examinations in clinical practice have already informed and will inform the planning of current and future pharmacological and non-pharmacological studies in AN.

These insights have already informed the planning of the study 'Efficacy and Safety of COMP360 Psilocybin Therapy in Anorexia Nervosa: a Proof-of-concept Study'. This is a COMPASS Pathways-funded and -sponsored proof-of-concept study testing psilocybin in AN. AHY, JT and HH have been advisers for COMPASS Pathways in the planning stage, and HH is the principal investigator for this study. Moreover, the experiences in OPEN have informed a successful application to the Medical Research Council for a double-blinded randomised controlled feasibility trial to test oral ketamine in people with AN and depression; the trial will start in 2025. As the process of opening additional trial sites was very slow in the OPEN study, our next trial to test oral ketamine in people with AN and depression was planned as a single-centre study.

The quantitative and the qualitative part of the study protocol were presented as two different posters at the Royal College of Psychiatrists Faculty of Eating Disorders Spring Conference on the 24 May 2023. The posters won the first and the second poster prizes.

The study results were presented by ESF at a main symposium during the 16th World Congress of Biological Psychiatry in Istanbul on the 8 June 2024. The title of her presentation was 'Olanzapine for young people with AN: Results from a feasibility study'.

Thus, the study, its design and results have been well received at the national and international level; and the identified shortcomings have informed the planning of future studies.

Both qualitative papers^{16,17} emphasised the importance of shared information regarding the medication to facilitate shared decision-making. From the qualitative research perspective, the ambivalence regarding recovery¹⁶ may be a significant obstacle on the way to recovery. Thus, information around this ambivalence may also be helpful.

Research recommendations

A realistic time schedule for site-preparation, recruitment, treatment and follow up, realistic recruitment targets and

unrestricted access to medical and laboratory examinations may improve the success of future clinical studies (e.g. feasibility studies, RCTs) in people with AN. Additionally, the trial team should be adequately resourced to provide the increased medical and psychological monitoring that is necessary to conduct all measurements and document the result and avoid missing data.

Based on our experience, aspects pertaining to the stakeholders, the funder, the sponsor, the approval agencies, the study sites, the pharmacy and the investigators should be considered from the planning and application stage. These aspects include the consulting with patients, their carers and clinicians, the application itself, contracts with all involved parties, the costing for personnel, space, facilities and consumables, the support from a trials unit and a trials office, the medicines regulatory agency and the

TABLE 4 Checklist for investigators with action points structured according to the involved parties for planning pharmacological trials in EDs

Involved parties	Action points
Stakeholders	PPI: • People with EDs • Carers and families • Clinicians
Funder	Application: • Pilot data • Statistical analysis plan • Utilisation of a research design service (e.g. NIHR Research Design Service) Contracts for/with all parties involved: • Funder • Sponsor • Industry partners • Study sites • Copyright and patent holders Costing: • Researchers working time • Consumables • Space • Facilities • Publication costs • Overhead
Sponsor	Support from a clinical trials unit regarding: • Study design • Study protocol • Rights to use questionnaires • Statistical support • Database (including development and testing) Support from a clinical trials office: • Financial management of commercial trials Internal risk assessment committee approval Sponsor and cosponsor approval: • University sponsor • Clinical trust sponsor

TABLE 4 Checklist for investigators with action points structured according to the involved parties for planning pharmacological trials in EDs (*continued*)

Involved parties	Action points
Approval agencies	The Medicines and Healthcare products Regulatory Agency (MHRA): • Decision about Clinical Trial Investigation of Medicinal Product (CTIMP) vs. non-CTIMP classification • Safety advice Research Ethics Committee (REC): • Information sheets • Consent forms • Measures for risk reduction and management
Study site(s)	Utilisation of a clinical research network (e.g. the NIHR Research Delivery Networks) Cooperation with GPs and clinical EDs services R&D approval including capacity assessment regarding: • Personnel (e.g. trial manager, trial doctor, senior EDs specialist with experience in clinical risk assessment) • Space (e.g. for research, food and fluid intake, area for carers) • Facilities (e.g. laboratory, ECG) • Research costs
Pharmacy	Agreement to costings prior to grant application Capacity check: • Facilities • Equipment • Staffing Sourcing and/or importing medication Review of the pharmacy manual - Prescribing and dispensing procedures for the study medication - Randomisation - Emergency code break - Emergency medication Pharmacy site file
Research team	Recruitment strategy: • Involvement and support from stakeholders • Study website with contact details • Advertisements in newsletters and newspapers • Presentation at conferences and meetings of professional societies • Recruitment videos • Waiting list for study participants Investigator's brochure (e.g. reporting side effects) Trial files including: • Trial Master File • Case report forms • Delegation log Monitoring (e.g. clinical research associate, clinical trial assistant) and emergency procedures (e.g. rescue medication and procedures) Delegation log, emergency unblinding Study setup (e.g. site initiation visits) Archiving Guidance from trial committees: • Trial management group • TSC • Data monitoring and ethics committee

ethics committee, the utilisation of a clinical research networks and the cooperation with clinical services, general practitioners and research and development (R&D) departments, all aspects of sourcing, importing and handling medication as well as aspects of conducting, documenting and archiving the study charts. In particular, a study should have a clear recruitment strategy that might include the involvement and support from stakeholders, a study website with contact details, advertisements in newsletter and newspapers, presentations at conferences and meetings of professional societies, recruitment videos, and a waiting list for potential study participants even before the study is fully approved. [Table 4](#) provides a checklist that covers the most important action points.

Finally, the value of sharing information about a research study, the treatment that is tested by this study, and the ambivalence towards recovery in AN should be further evaluated. This may motivate a person with AN to accept treatment, to stay in a trial and to work towards recovery.

Future pharmacological studies in eating disorders

In AN, several classes of medications have been tested including antidepressants, antipsychotics, antiepileptics and mood stabilisers, appetite modulators, opioid antagonists, gastroprokinetic agents and nutritional supplements.¹ However, up until now, there is no approved pharmacological treatment for AN. Promising novel developments seem to be human recombinant leptin (metreleptin),²¹ the typical psychedelic medication psilocybin,²² and the atypical psychedelic drug ketamine.^{23,24} As these medications do not lead immediately to weight gain like olanzapine^{21–25} and might lead to a relief from symptoms often associated with AN such as anxiety, depression and the urge to exercise,^{21–24} they might be more acceptable for people with AN.

To our knowledge, there have been very few pharmacological RCTs in patients with bulimia nervosa (BN) in recent years. The last RCT in BN was published 10 years ago. It tested oxytocin with a negative result.²⁶ Fluoxetine was successfully tested by RCTs in the 1990s and is approved in most countries for the treatment of BN.¹ In binge ED (BED), four RCTs examined the stimulant lisdexamfetamine (LDX) with positive results which is why LDX has been approved by the US Food and Drug Administration (FDA).^{1,27} Promising novel medications for BED seem to be the glucagon-like peptide-1 (GLP-1) receptor agonists.²⁷

Therefore, hormone analogues like metreleptin and GLP-1 receptor agonists, medications that modulate wakefulness

like LDX or psychedelics such as psilocybin might be future pharmacological approaches to the treatment of EDs.

Conclusions

Our OPEN feasibility study to test olanzapine in young people with AN failed to recruit enough patients, and the adherence rate was lower than expected. Possible reasons include the high clinical workload during the COVID-19 pandemic and the relatively restricted conditions of a clinical study. More realistic planning and more information sharing may improve the success of future feasibility studies and RCTs in this patient group. Future pharmacological approaches might include hormone analogues, medications that modulate wakefulness and psychedelics.

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OPEN has a separate sister study planned in Australia, which aims to recruit 15 participants. The study was planned in two countries to allow for differences in healthcare systems and care processes to be explored. The study protocols are largely similar, with separate ethics approval, funding and sponsorship. The Australian part of the study was approved by the Sydney Children Hospitals Network Human Research Ethics Committee (HREC reference 2021/ETH01321) on 20 September 2021 and has been funded by the National Health and Medical Research Council (NHMRC). The sponsor is the

University of Sydney. The current article refers exclusively to the OPEN study performed in the UK.

King's College London is the lead sponsor and South London and Maudsley NHS Foundation Trust (SLaM) is the cosponsor for this study. The sponsors act as data controllers.

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Patient data statement

This study did not collect any clinical patient data that are routinely collected by the NHS. However, the study used routinely measured laboratory parameters to ensure patients' safety during the treatment with olanzapine (e.g. electrolytes, full blood count, kidney and liver function tests).¹⁸ These parameters were measured as part of their clinical NHS treatment.

Data-sharing statement

Ethical approval and the obtained consent from study participants did not include public availability of the data. However, the data are available from the corresponding author upon reasonable request.

Ethics statement

OPEN received a favourable REC opinion from the Research Ethics Committees Northern Ireland (ORECNI) on 10 March 2022; REC reference: 22/NI/0010; IRAS project ID: 295297.

Before inclusion into the study, informed consent was obtained from each participant who was 16 years old or older. Children and adolescents who were younger than 16 years were asked to give their informed assent before inclusion into the study, and additional informed consent was obtained from their parents.

Information governance statement

King's College London 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. Under data protection legislation, KCL is the data processor; KCL is the data controller, and we process personal data in accordance with their instructions. You can find out more about how we

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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/GJHH0812>.

Primary conflicts of interest: Hubertus Himmerich was the Principal Investigator and Katie Rowlands was the study manager of 'Efficacy and Safety of COMP360 Psilocybin Therapy in Anorexia Nervosa: a Proof-of-concept Study', a COMPASS Pathways-funded and -sponsored proof-of-concept study testing psilocybin in AN.

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Ben Carter is a member of the HTA General Committee (1 November 2016–31 July 2028) and the HTA Post Funding (CET and GB) Programme Oversight Committee (1 November 2017–31 July 2027).

All other authors declare no competing interests.

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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.

Trial registration

This trial is registered as ISRCTN80075010. Registration date: 27 April 2022.

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Award publications

This synopsis provided an overview of the research award *Olanzapine for young PEOple with aNorexia nervosa: An open-label feasibility study to test recruitment, treatment acceptance, adherence, safety, outcome measures and patients' experience to prepare for a randomised placebo-controlled trial (OPEN)*.

Other articles published as part of this thread are:

Said O, Stringer D, Sengun Filiz E, Mutwalli H, Bektas S, Akkese MN, et al. Olanzapine for young PEOple with aNorexia nervosa (OPEN): results of a feasibility study. *BMC Psychiatry* 2024;**24**:779. <https://doi.org/10.1186/s12888-024-06215-y>

Kellermann V, Sengun Filiz E, Said O, Bentley J, Khor JWT, Simic M, et al. Clinicians' perspectives on the acceptability and feasibility of a clinical trial of olanzapine for young people with anorexia nervosa. *J Eat Disord* 2024;**12**:146. <https://doi.org/10.1186/s40337-024-01106-9>

Olive RR, Kellermann V, Said O, Sengun Filiz E, Treasure J, Schmidt U, et al. What does taking olanzapine mean to young people with anorexia nervosa and their families? Findings from the OPEN feasibility trial. *J Eat Disord* 2025;**13**(228). <https://doi.org/10.1186/s40337-025-01401-z>

For more information about this research please view the award page (www.fundingawards.nihr.ac.uk/award/NIHR130780).

Additional outputs

Said O, Sengun Filiz E, Stringer D, Applewhite B, Kellermann V, Mutwalli H, et al. Olanzapine for young PEOple with aNorexia nervosa (OPEN): a protocol for an open-label feasibility study. *Eur Eat Disord Rev* 2024;**32**:532–46. <https://doi.org/10.1002/erv.3060>

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List of abbreviations

AN	anorexia nervosa
ARC	Applied Research Collaboration
BAVQ-R	Beliefs About Voices Questionnaire
BED	binge eating disorder
BMI	body mass index
BN	bulimia nervosa
BRC	Biomedical Research Centre
CONSORT	Consolidated Standards of Reporting Trials

CY-BOCS	Children's Yale-Brown Obsessive Compulsive Scale
COVID-19	coronavirus disease 2019
DASS	Depression Anxiety Stress Scales
ECG	electrocardiogram
ED	eating disorder
EDE-Q	Eating Disorder Examination Questionnaire
EDSIS	Eating Disorders Symptom Impact Scale
ESS	Epworth Sleepiness Scale
ESS-CHAD	Epworth Sleepiness Scale for Children and Adolescents
GLP-1	glucagon-like peptide-1
KCL	King's College London
LDX	lisdexamfetamine
OPEN	Olanzapine for young PEople with aNorexia nervosa
PPI	public and patient involvement
RCT	randomised controlled trial
R&D	research and development
REC	Research Ethics Committee
SLaM	South London and Maudsley NHS Foundation Trust
SREBQ	Self-Regulation of Eating Behavior Questionnaire
TSC	Trial Steering Committee
Y-BOCS	Yale-Brown Obsessive-Compulsive Scale

References

- Himmerich H, Lewis YD, Conti C, Mutwalli H, Karwautz A, Sjögren JM, *et al.* World Federation of Societies of Biological Psychiatry (WFSBP) guidelines update 2023 on the pharmacological treatment of eating disorders. *World J Biol Psychiatry* 2023;**24**:643–706.
- Søeby M, Gribsholt SB, Clausen L, Richelsen B. Overall and cause-specific mortality in anorexia nervosa; impact of psychiatric comorbidity and sex in a 40-year follow-up study. *Int J Eat Disord* 2024;**57**:1842–53. <https://doi.org/10.1002/eat.24223>
- Russell J, Mulvey B, Bennett H, Donnelly B, Frig E. Harm minimization in severe and enduring anorexia nervosa. *Int Rev Psychiatry* 2019;**31**:391–402.
- Eddy KT, Tabri N, Thomas JJ, Murray HB, Keshaviah A, Hastings E, *et al.* Recovery from anorexia nervosa and bulimia nervosa at 22-year follow-up. *J Clin Psychiatry* 2017;**78**:184–9.
- Himmerich H, Treasure J. Anorexia nervosa: diagnostic, therapeutic, and risk biomarkers in clinical practice. *Trends Mol Med* 2024;**30**:350–60.
- Sachs KV, Harnke B, Mehler PS, Krantz MJ. Cardiovascular complications of anorexia nervosa: a systematic review. *Int J Eat Disord* 2016;**49**:238–48.
- Zerwas S, Larsen JT, Petersen L, Thornton LM, Mortensen PB, Bulik CM. The incidence of eating disorders in a Danish register study: associations with suicide risk and mortality. *J Psychiatr Res* 2015;**65**:16–22.
- Steinhausen HC. The outcome of anorexia nervosa in the 20th century. *Am J Psychiatry* 2002;**159**:1284–93.
- Himmerich H, Hotopf M, Shetty H, Schmidt U, Treasure J, Hayes RD, *et al.* Psychiatric comorbidity as a risk factor for mortality in people with anorexia nervosa. *Eur Arch Psychiatry Clin Neurosci* 2019;**269**:351–9.
- Attia E, Kaplan AS, Walsh BT, Gershkovich M, Yilmaz Z, Musante D, Wang Y. Olanzapine versus placebo for outpatients with anorexia nervosa. *Psychol Med* 2011;**41**:2177–82.
- Attia E, Steinglass JE, Walsh BT, Wang Y, Wu P, Schreyer C, *et al.* Olanzapine versus placebo in adult outpatients with anorexia nervosa: a randomized clinical trial. *Am J Psychiatry* 2019;**176**:449–56.
- Brambilla F, Garcia CS, Fassino S, Daga GA, Favaro A, Santonastaso P, *et al.* Olanzapine therapy in anorexia nervosa: psychobiological effects. *Int Clin Psychopharmacol* 2007;**22**:197–204.
- Bissada H, Tasca GA, Barber AM, Bradwejn J. Olanzapine in the treatment of low body weight and obsessive thinking in women with anorexia nervosa: a randomized, double-blind, placebo-controlled trial. *Am J Psychiatry* 2008;**165**:1281–8.
- Kafantaris V, Leigh E, Hertz S, Berest A, Schebendach J, Sterling WM, *et al.* A placebo-controlled pilot study of adjunctive olanzapine for adolescents with anorexia nervosa. *J Child Adolesc Psychopharmacol* 2011;**21**:207–12.
- Said O, Stringer D, Sengun Filiz E, Mutwalli H, Bektas S, Akkese MN, *et al.* Olanzapine for young PEople with aNorexia nervosa (OPEN): results of a feasibility study. *BMC Psychiatry* 2024;**24**:779.
- Olive RR, Kellermann V, Said O, Sengun Filiz E, Treasure J, Schmidt U, *et al.* What does taking olanzapine mean to young people with anorexia nervosa and their families? Findings from the OPEN feasibility trial. *J*

- Eat Disord* 2025;13:228. <https://doi.org/10.1186/s40337-025-01401-z>
17. Kellermann V, Sengun Filiz E, Said O, Bentley J, Khor JWT, Simic M, et al. Clinicians' perspectives on the acceptability and feasibility of a clinical trial of olanzapine for young people with anorexia nervosa. *J Eat Disord* 2024;12:146.
 18. Said O, Sengun Filiz E, Stringer D, Applewhite B, Kellermann V, Mutwalli H, et al. Olanzapine for young PEople with aNorexia nervosa (OPEN): a protocol for an open-label feasibility study. *Eur Eat Disord Rev* 2024;32:532–46.
 19. Bamford BH. Assessing quality of life in the eating disorders: the HeRQoLED-S. *Expert Rev Pharmacoecon Outcomes Res* 2010;10:513–6.
 20. Himmerich H, Keeler JL, Davies HL, Tessema SA, Treasure J. The evolving profile of eating disorders and their treatment in a changing and globalised world. *Lancet* 2024;403:2671–5.
 21. Gradl-Dietsch G, Milos G, Wabitsch M, Bell R, Tschöpe F, Antel J, Hebebrand J. Rapid emergence of appetite and hunger resulting in weight gain and improvement of eating disorder symptomatology during and after short-term off-label metreleptin treatment of a patient with anorexia nervosa. *Obes Facts* 2023;16:99–107.
 22. Peck SK, Shao S, Gruen T, Yang K, Babakanian A, Trim J, et al. Psilocybin therapy for females with anorexia nervosa: a phase 1, open-label feasibility study. *Nat Med* 2023;29:1947–53.
 23. Keeler JL, Treasure J, Himmerich H, Brendle M, Moore C, Robison R. Case report: intramuscular ketamine or intranasal esketamine as a treatment in four patients with major depressive disorder and comorbid anorexia nervosa. *Front Psychiatry* 2023;14:1181447.
 24. Keeler JL, Treasure J, Juruena MF, Kan C, Himmerich H. Ketamine as a treatment for anorexia nervosa: a narrative review. *Nutrients* 2021;13:4158.
 25. Himmerich H, Minkwitz J, Kirkby KC. Weight gain and metabolic changes during treatment with antipsychotics and antidepressants. *Endocr Metab Immune Disord Drug Targets* 2015;15:252–60.
 26. Kim YR, Eom JS, Yang JW, Kang J, Treasure J. The impact of oxytocin on food intake and emotion recognition in patients with eating disorders: a double blind single dose within-subject cross-over design. *PLOS ONE* 2015;10:e0137514.
 27. Himmerich H, Bentley J, McElroy SL. Pharmacological treatment of binge eating disorder and frequent comorbid diseases. *CNS Drugs* 2024;38:697–718.