TITLE

A pilot evaluation of a novel First Episode and Rapid Early Intervention service for Eating Disorders (FREED).

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Abstract

This pilot study assesses the impact of FREED [First Episode and Rapid Early Intervention for Eating Disorders (ED)], a novel transdiagnostic service for emerging adults with recent ED onset, on clinical outcomes. Data were collected from 56 patients and 19 carers for 12 months following enrolment. FREED patients showed significant improvements in ED and other symptoms across time. Carers also showed psychological improvements. For FREED anorexia nervosa (AN) patients, body mass index (BMI) at initial clinical assessment was similar to that of comparable patients (Audit cohort) seen in our service before (16.4 vs 16.1 kg/m^2). By start of treatment, because of their shorter wait, FREED-AN had gained weight whereas Audit patients' had lost (16.7 vs 15.8 kg/m^2). This difference continued throughout treatment and at 12 months nearly 60% FREED-AN returned to a BMI 18.5 or greater. FREED shows promise as a service model for emerging adults with EDs.

INTRODUCTION

Eating disorders (EDs) are common mental disorders, with the peak age of onset spanning adolescence and early adulthood (Micali, Hagberg, Petersen, & Treasure, 2013; Schmidt, Brown, McClelland, Glennon, & Mountford, 2016). In other psychiatric disorders, intervening during early stage, first episode illness, when symptoms are likely to be more malleable, is seen as critical in promoting favourable long-term outcomes. For example, in psychosis, systematic reviews and meta-analyses support the association between a shorter duration of untreated psychosis (DUP) and better clinical outcomes (Farooq, Large, Nielssen, & Waheed, 2009; Marshall et al., 2005; Penttila, Jaaskelainen, Hirvonen, Isohanni, & Miettunen, 2014). Analogous arguments support the need for early intervention (EI) in EDs (Currin & Schmidt, 2005). Firstly, it has long been known that in anorexia nervosa (AN) illness duration is a key predictor of outcome (Steinhausen, 2002). Secondly, growing evidence suggests that EDs are associated with significant structural and functional brain changes (Seitz, Herpertz-Dahlmann, & Konrad, 2016; Van den Eynde et al., 2012). As the typical age of ED onset is during a period, when prefrontal brain areas important in self-regulation are developing (Keverne, 2004), this has the potential to interfere with normal brain development. Thirdly, it has been recognised across different psychiatric disorders that with increasing duration, the illness becomes more entrenched and difficult to change. This is proposed to arise from 'neuroprogression', i.e. neurobiological changes that alter the trajectory of illness (Gama, Kunz, Magalhaes, & Kapczinski, 2013; Moylan, Maes, Wray, & Berk, 2013). In EDs, converging neuroimaging and cognitive neuroscience data support this idea (Berner & Marsh, 2014; O'Hara, Campbell, & Schmidt, 2015; Steinglass & Walsh, 2016). Finally, given the high physical, psychosocial and financial burden of EDs, treating symptoms early is valuable from both an ethical and economical perspective (Currin & Schmidt, 2005).

Stage-of-illness based ED models incorporate these ideas and findings and suggest that stage-appropriate EI may be able to halt illness progression (Currin & Schmidt, 2005; Treasure et al., 2015).In England, a Government-led EI initiative, has introduced specialist ED community teams together with waiting time standards for young people below the age of 18 (NHS, 2015). This initiative is grounded in concerns that across different countries hospitalisations of young people with AN are rising (Herpertz-Dahlmann et al., 2014). Studies of hospitalisation trends from the 1960s to the present, have shown large recent increases in hospitalisation rates in England, with the greatest rise in young women aged 15-19 (Holland, Hall, Yeates, & Goldacre, 2016). In contrast, admission rates for most other mental disorders have declined (Green & Griffiths, 2014). Pilot data suggest that in areas where specialist EDs adolescent outpatient services are available, rates of hospitalisations are significantly lower (House et al., 2012).

However, this initiative only covers part of the UK. Moreover, it does not cover emerging adults, who are aged 18 to 25, have a high incidence of AN, and like adolescents, face multiple developmental challenges (Arnett, Žukauskienė, & Sugimura, 2014).

Taken together, there is a strong rationale for EI for EDs but a lack of research. This led us to propose an EI service model for emerging adults with early stage EDs (Schmidt et al., 2016a). Our model is biopsychosocial, with a focus on optimising early care. A pilot evaluation of this First Episode Rapid Early Intervention service for ED (FREED) found significantly reduced waiting times and duration of untreated ED (Brown et al., 2016). The present study (1) assesses ED and other clinical outcomes in FREED patients and their carers, (2) compares FREED service utilisation to that of comparable patients seen previously in our service, and (3) compares BMI change in FREED anorexia nervosa (AN) patients and comparable AN patients seen previously.

MATERIALS AND METHODS

Ethical approval for the project was given on 4th August 2014 by the National Research Ethics Service Committee London – South East [ref: 14/LO/0873].

Participants

FREED cohort:

Participants were recruited during one year (September 2014 to August 2015) from consecutive referrals to the adult ED Outpatient Service at the South London and Maudsley NHS Foundation Trust (SLaM), London, UK, a large catchment area based specialist service covering a local population of approx. 2 million people. Inclusion criteria were: being aged 18-25, a primary DSM-5 ED diagnosis and an ED illness duration of ≤ 3 years (This criterion was chosen, based on illness staging models of AN, which suggest that after this time illness characteristics become more 'solidified' and treatment outcomes more muted (Treasure et al., 2015). Exclusion criteria were: need for immediate inpatient admission that was clear on referral (using NICE guidance (2017) to inform decision-making), factors that precluded completing questionnaires (severe learning disability, inability to speak English), not being available for the 12-month duration of the study, and/or the presence of a primary comorbid physical/mental disorder requiring priority treatment (e.g. substance dependence). All other comorbid patients were treated within the study.

Audit cohort

In order to have a comparison group, we carried out an audit of patients seen in our service during the two years prior to implementation of FREED. All patients referred during mid May 2012 - mid May 2014 who were aged 18-25 were identified from clinical records.

Information regarding ED onset was obtained from clinical assessment letters. Those with an illness duration ≤ 3 years were included.

Procedures

Clinical procedures

Details of the FREED service model and care pathway are described elsewhere (Brown et al., 2016; Schmidt et al., 2016). Briefly, all referrals for individuals aged between 18-25 years, are screened by telephone (within 48 hours of referral). All telephone screenings were carried out by an ED clinician working in the outpatient service with the role of 'FREED champion'. Patients deemed eligible for FREED (and where there are no gate-keeping arrangements restricting access to care), are immediately booked in to the next available assessment (aiming for < 2 weeks from date referral received). Each screening call took approximately 15 minutes to complete. The standard ED assessment protocol used in the service was adapted for FREED clinical assessments, i.e. it consists of a biopsychosocial, person-centred assessment which considers the young person within their family and social context, focusing on their needs, priorities and strengths. Where possible, family members and close others join part of the assessment. Attention is paid to the young person's use of social media and health-related apps, given ubiquitous use of these amongst young people and their known role in maintaining ED symptoms (Holland & Tiggemann, 2016). Assessing clinicians offer psycho-educational information about the effects of the illness on all aspects of the young person's life. A care plan is formulated collaboratively. Individuals eligible for the FREED service are rapidly allocated to a therapist (aiming for < 2 weeks from assessment) to start an evidence-based, stage-appropriate psychological treatment. For young people with BN and BED, treatment is cognitive behavioural therapy (CBT), delivered online, individually or in a

group, with typically up to 24 sessions. For young people with AN, individual outpatient therapy using the Maudsley Model of Anorexia Nervosa Treatment, a formulation-based treatment with a patient workbook, is typically used. Treatment duration typically is 24 to 34 sessions (Schmidt et al., 2015; Schmidt et al., 2016b). Sessions with family members/carers are an integral part of treatment. Pharmacotherapy (e.g. antidepressants) is added as appropriate. Early involvement of the team dietician is emphasised to provide an appropriate meal plan, particularly for young people with complex nutritional needs. All treating clinicians were employees of the South London and Maudsley NHS Foundation Trust.

Research procedures

FREED cohort:

Patients (and where appropriate, their carers) entered into the FREED service were invited to participate in the FREED service evaluation study at assessment and were required to give their written, informed consent. Following this, patients and, where possible, their carers completed the first of four questionnaire packs. This time point is referred to as 'baseline'. Participants and carers were asked to complete similar questionnaires packs at 3, 6 and 12 months following the initial assessment. Patients were followed up irrespective of whether they completed treatment.

Audit cohort:

For patients in the audit cohort, their referral, assessment and service usage data (number of outpatient sessions attended; additional in-patient or day-care treatment during the year following assessment) were extracted from their clinical notes. For AN patients, BMI data were also extracted from the notes (where possible) within 1 month of each of the four time points used in FREED. Questionnaire data were not available for the audit cohort at FREED-comparable time points.

Outcomes

Process outcomes

The waiting time for treatment was defined as the time period (in weeks) from the date the referral was made (e.g. by the GP) to the date patients attended their first treatment session. The waiting time (in weeks) between assessment and treatment was also calculated. Treatment uptake was defined as attending a minimum of one treatment session after assessment. Service utilisation was also assessed in terms of total number of treatment sessions attended, and the need for additional intensive treatment (i.e. day-care or inpatient treatment) during the year following assessment.

Clinical outcomes

Psychological measures

Eating Disorder Examination Questionnaire (EDE-Q). Version 6 of the EDE-Q (Fairburn & Beglin, 2008) was completed by patients. Questions relate to the past 28 days and are measured on a 7-point Likert scale ranging from zero (no days) to six (every day). Four subscale-scores (restraint, eating concern, shape concern and weight concern) are calculated and based on these a global score. High global scores indicate greater ED psychopathology, with a proposed clinical cut-off score of ≥ 2.8 (Mond et al., 2008).

Clinical Outcomes in Routine Evaluation (CORE-10). A short, 10 item version of the CORE-OM was completed by both patients and carers (Barkham et al., 2013). The CORE-10 is a measure of global distress and functioning. Each item is rated on a 5-point Likert scale from ‘not at all’ (0/4) to ‘most or all of the time’ (4/0). The clinical score is calculated by adding the values of all 10 items. Scores below 10 are deemed non-clinical, whilst scores of 11 or above are within the following clinical ranges: 11-15 mild, 15-20 moderate, 20-25 moderate/severe and >25 severe.

Depression, Anxiety and Stress Scale (DASS-21). The DASS-21, completed by both patients and carers, is a short version of a 42 item self-report measure that assesses mood state over the past seven days (Lovibond & Lovibond, 1995). It is comprised of 21 items measured on a 4-point Likert scale ranging from 0 (did not apply to me at all) to 3 (applied to me very much, or most of the time). Each item loads on to one of three subscales, depression, anxiety and stress, which when added together provide a total score indicative of general psychopathology. A normative baseline cut-off of 13 for the total DASS-21 score has been proposed (Crawford & Henry, 2003), and high scores indicate worse symptomatology.

Work and Social Adjustment Scale (WSAS). The WSAS was completed by both patients and carers. It is a 5-item self-report scale designed to measure functional impairment attributable to an identified problem, in this case an ED (Marks, 1986). Each item is rated on a 9-point Likert scale ranging from 'no impairment' (0) to 'very severe impairment' (8). The maximum total score is 40. Scores above 20 suggest moderate-severe psychopathology, scores 10-20 indicate less severe clinical impairment and scores below 10 are deemed subclinical.

Clinical Impairment Assessment (CIA). The 22-item CIA was completed by patients. It is a self-report measure of the severity of psychosocial impairment due to ED features (Bohn et al., 2008). The CIA focuses on the past 28 days and the 22 items cover impairment in domains of life typically affected by ED psychopathology, e.g. mood, self-perception, cognitive functioning, interpersonal functioning and work performance. Each item is rated on a 4-point Likert scale ranging from 'not at all' (0) to 'a lot' (3). A global CIA impairment score is calculated by adding all items together and dividing by the total number of items completed. Global CIA scores range from 0 to 3, with a higher score indicative of greater secondary psychosocial impairment.

Level of Expressed Emotion Scale (LEE). Patient and carer versions of the LEE were completed in the current study. The LEE aims to measure the perception of expressed emotion in a person's influential relationships. Both versions of the LEE include 60 items with the option of a 'true' or 'false' response (Cole & Kazarian, 1988). An overall score is generated by summing the 38 items, with a higher score indicative of greater perceived expressed emotion.

Accommodation and Enabling Scale for Eating Disorders (AESED). The AESED is a 33-item self-report measure that aims to assess accommodating and enabling behaviours of ED carers (Sepulveda, Kyriacou, & Treasure, 2009). Each item is rated on a 5-point Likert scale from 'never/no' (0) to 'everyday/extreme' (4), with the exception of item 24 which is transformed into a 5-point Likert scale. A total score is calculated by summing the score on all items. A higher score is associated with higher accommodation of ED symptoms.

Weight and Body Mass Index (BMI)

Patients' weight and height was measured and their body mass index (BMI; kg/m^2) was calculated. These data were taken from clinical notes nearest to the date of the four time points (approximately 1 month from the baseline, 3-, 6- and 12-months measurement points) that questionnaires were completed. In addition, BMI at the start of treatment was also taken.

Statistical Analyses

Overall, our analyses followed the recommendations of the Child Outcome Research Consortium (CORC) for service data (http://www.corc.uk.net/media/1533/fupsleaflet.pdf). The CORC suggestion is to provide accessible descriptive analyses first and foremost, and only undertake statistical tests where there is a clear reason to do so.

With this in mind, statistical analyses followed from the three study aims. Firstly, there was a within-group evaluation of the clinical outcomes for the FREED group. To estimate

within-group changes in the whole FREED cohort over the course of treatment linear mixed models were used. Change was estimated using time as a fixed categorical factor (baseline, 3, 6 and 12 months) with correlations within patient repeated measures accounted for by inclusion of a random intercept for participant and slope to allow change over time to vary by person. Changes from baseline to 3, 6 and 12 months and 6 to 12 months were calculated with *p* values and confidence intervals Bonferroni adjusted for multiple comparisons. Using mixed models for the analysis fit with maximum likelihood (ML) allows missing data to be included in model estimates under the assumption that the data were missing at random. Predictors of missingness such as diagnosis, age of onset, treatment completion, gender, ethnicity and BMI at assessment were examined. Only diagnosis was found to be a predictor of missingness and was therefore included in the mixed model as a covariate.

Secondly, the relative impact of FREED on process outcomes was evaluated by comparing the FREED cohort with the Audit cohort, constructed from eligible patient notes from the period May 2012 –May 2014 inclusive. Between-group demographic and clinical baseline features were compared with t-tests, chi-Square tests or Fisher's exact tests as appropriate. Group differences in process outcomes and in particular waiting-times and total number of sessions attended were analysed using a generalized linear model with negative binomial errors. Proportions were also calculated to compare intensive treatment usage for FREED and the Audit group and carer involvement within the FREED group.

As indicated above, the only clinical information available for the Audit group was BMI which was collected from patient records. Thus, in the third and final part of the analysis we compared change in BMI for FREED and Audit patients with an AN diagnosis. To do this we fitted a linear mixed model with measurement time-point (baseline, 3, 6 and 12 months) and group (FREED vs Audit) as main effects and a group by time-point interaction. As for the within group analysis, predictors of missing data were sought but none were identified.

Statistical analyses were performed using IBM® SPSS® software (Version 23) and Stata version 14.1 IC.

RESULTS

Participant flow

Figure 1 shows the participant flow through the study. Nine 'FREED pilot cases' were referred before the study period (i.e. prior to September 2014) but treated under the FREED service model. These nine cases were not included in the process outcomes we previously reported (Brown et al., 2016). However, as they received clinical care within the FREED service, we have included them in all outcomes reported here. This left a total of 56 patients in the current FREED sample. Nineteen carers (relating to 19 patients) provided longitudinal data. In the audit sample (N=86), 22/86 patients only attended an initial assessment and did not take up the offer of further treatment within the outpatient service. Therefore the number of audit patients with outcomes after initial assessment are N=64.

Baseline characteristics

Table 1 presents demographic and clinical characteristics for FREED and (audit) patients. There were no differences in the FREED and Audit groups in regards to age at referral, age of ED onset, sex, or ED diagnoses (p-values between 0.647 and 0.93).

Clinical outcomes in FREED cohort

Eating disorder symptoms:

Figure 2A shows EDE-Q estimated means for the whole FREED cohort across time. Raw data for all patient and carer clinical outcomes are shown in Table 2. In the patient data, internal consistency assessed with Cronbach's alpha at baseline was excellent (i.e. $0.9 \leq \alpha$) for the EDE-Q ($\alpha = 0.916$), DASS ($\alpha = 0.935$), LEE ($\alpha = 0.95$) and CIA ($\alpha = 0.936$) and good (i.e. $0.8 \leq$ alpha < 0.9) for CORE ($\alpha = 0.844$) and WASA ($\alpha = 0.844$). In the carer data, internal consistency assessed was excellent (i.e. $0.9 \leq$ alpha) for the DASS ($\alpha = 0.925$), WASA ($\alpha = 0.949$) and AESED ($\alpha = 0.904$), good (i.e. $0.8 \leq$ alpha < 0.9) for the CORE ($\alpha = 0.809$) and acceptable (i.e. $0.7 \leq$ alpha < 0.9) for the LEE ($\alpha = 0.759$). Table 3 shows estimated changes between baseline and follow-up assessment points. From this it can be seen that all EDE-Q follow-up time points differ significantly from baseline (T1) and that significant improvements occur between baseline (T1) and 3 months (T2) and 3 months (T2) and 6 months (T3) assessments. Between 6 and 12 months assessments a smaller improvement occurs. Proportions of patients with an EDE-Q score below the clinical cut-off (i.e. < 2.8; (Mond et al., 2008) were as follows: T1: 18% (10/56) T2: 33% (13/39), T3: 53% (18/34) and T4:70% (19/27).

Other patient and carer outcomes:

Table 3 also shows estimated changes from baseline for all other patient and carer questionnaire outcomes and for patient BMI collected within the whole FREED cohort at baseline, 3, 6 and 12 months.

Patient scores were generally improved from 3, 6 and 12 months compared to the start of treatment. Change between 6 and 12 months (when people had mainly finished treatment) was generally small showing slight benefit or loss. This indicates improvement of general psychopathology, secondary psychosocial impairment and expressed emotion, respectively.

Nineteen carers provided questionnaires. Interestingly, carer scores showed strong improvements at 12 months but with the majority of the change in scores occurring between 6 and 12 months. There was improved general psychopathology, expressed emotion and less accommodation of ED symptoms in carers of patients in the FREED service.

Process outcomes

Wait times

Patients in the FREED cohort waited 19.5 days less than those in the Audit cohort from the time their GP made their referral to their initial assessment [FREED median wait 42.5 days (IQR 23,66) vs Audit cohort 62 days (41,98)], but this difference was not significant (Rate Ratio = 0.74, 95% CI:0.53,1.05; χ^2 =2.98; p=0.084). However, the waiting time was 14 days shorter from assessment to starting treatment for the FREED cohort versus Audit (20 days (IQR 11,31) vs 34 (IQR 16, 125), Rate Ratio = 0.34, 95% CI: 0.23, 0.49) (χ^2 =34.1; $p < 0.001$).

Treatment usage

A greater proportion of individuals in FREED, compared to those in the Audit cohort, took up treatment after their assessment [FREED: 56 (100%) vs Audit 64/86 (74%); Fisher's exact $p < 0.001$]. There were no differences between the FREED and Audit cohorts in the median number of total sessions attended [FREED: 21.5 (IQR 9,29.5) vs Audit: 16 (IQR 8, 24); Rate ratio = 1.16, 95% CI: 0.80, 1.70)]. Treatment completion was comparable in both groups [FREED 40/56 (71%) and Audit 45/64 (71%)]. The proportions of patients who required additional intensive treatment (specialist in-patient care, day-care treatment) for their

ED during the 12 months study period were also examined. In the FREED cohort, 8.9% (5/56) of patients required additional in-patient or day-care treatment, whereas 14.1% (9/64) of the Audit cohort needed such treatment (Fisher's exact test; p=0.999).

Carer involvement

Nearly 61% (60.7%; 33/56) of carers had some type of involvement in the treatment. This included attending either the assessment, inclusion in some treatment or group sessions.

BMI comparison in FREED AN versus audit AN patients

Twenty-two FREED patients and 28 Audit patients who entered treatment had an AN diagnosis. Figure 2.B shows estimated mean BMI by group (FREED-AN and Audit AN) and estimated outcome differences between treatment arms at different time points from start of treatment to the follow-up 12 months later. There was no group by time interaction ($\chi^2(3) = 0.20$, $p = 0.978$). Over time, the marginal BMI was lower in the 28 Audit-AN patients than FREED-AN patients, although this difference was not significant ($\chi^2(1) = 2.70$, $p = 0.100$). At initial clinical assessment, the mean BMI of the FREED-AN group was 16.4 and Audit-AN group was 16.1. (This data point is not included in the figure due to variable waiting times from assessment to treatment in the two groups). Between initial assessment and the start of treatment, BMI increased for the FREED-AN group to 16.7 but decreased for the Audit-AN group to 15.8 (for those entering treatment). This difference of 0.9 BMI-points at the start of treatment was maintained across the 6 months (Figure 3). By 12 months, estimated mean BMI in the FREED group had risen further to 18.9, a mean difference of 2.26 (95% CI 1.54, 2.98) BMI points compared to the start of treatment. Given missing data it is not clear how representative BMI at 12 months in the Audit group is.

We also calculated proportions of patients who were weight recovered (defined as BMI > 18.5 kg/m^2) at each time point. For the FREED cohort these figures were T1: 3/22 (13.6%), T2: 2/21 (9.5%); T3: 5/19 (26.3%); T4: 10/17 (58.8%). For the Audit cohort figures were T1: 1/29 (3.4%), T2: 3/24 (12.5%); T3 3/21 (14.3%); T4: 1/6 (16.7%).

DISCUSSION

This study investigated the impact of a novel early intervention service on the clinical outcomes of patients with ED and their carers, and also examined the impact of the service on treatment usage.

Within the whole transdiagnostic FREED cohort, there were significant and large reductions in ED psychopathology over time, as measured by the EDE-Q. Moreover, the percentage of individuals with scores below the clinical cut off of the EDE-Q (< 2.8) increased from 18% at the start of treatment to 70% at 12 months after starting of treatment. These findings are comparable to those found under optimal conditions in recent research cohorts and large scale clinical trials, such as the UK-Italy study of CBT-E in AN (Fairburn et al., 2013) and the MOSAIC trial (Schmidt et al., 2015; Schmidt et al., 2016b). Similar improvements in the FREED cohort were observed across all other clinical outcomes including depression, anxiety and stress, CORE-10, work and social adjustment and expressed emotion. In parallel, there were improvements on psychological outcomes for FREED carers. Given the significant burden and high levels of distress for carers and families (Rhind et al., 2016; Treasure & Nazar, 2016) these improvements are encouraging.

Within the FREED AN group, BMI increase over time was excellent and broadly comparable to outcomes from a recent large scale clinical trial of family therapy in adolescents with AN (Eisler et al., 2016), A high proportion of FREED AN patients (60%) returned to a normal BMI (> 18.5kgs/m^2) at 12 months. A comparison of BMI change between FREED and

Audit patients found non-significant differences in BMI between the groups at several time points and a significant difference at 12 months. Of note whilst the BMI of FREED-AN patients increased between initial assessment and start of treatment, there was a decrease in the BMI of the Audit cohort. This observation is important for two reasons. Firstly, the Audit cohort waited significantly longer to start treatment compared with the FREED cohort. The decrease in BMI seen in the Audit cohort supports the idea that waiting for treatment is detrimental for patients. Secondly, the slight increase in BMI observed in the FREED cohort could be due to the positive impact of certain core components of the FREED assessment, such as the motivational and engaging style, use of psycho-education and emphasis on illness malleability. These are key elements to the FREED model and they are likely to increase patient motivation in this targeted age group and led to improved engagement and outcomes.

In both the FREED and the Audit cohort few patients needed additional intensive treatment (FREED 8.9% and Audit 14.06%), i.e. slightly favouring FREED. Against a background of national and international trends of rising numbers of hospitalisations in young people with AN, this is promising. It is also important as intensive treatments, such as in-patient or day-care treatment, are a significant financial burden to health services and far more costly than outpatient treatment (Byford et al., 2007; Herpertz-Dahlmann et al., 2014). Reducing the likelihood of the need for intensive treatments may also impact on downstream costs, as previous inpatient or intensive treatments are a strong predictor of relapse in EDs (Carter, Blackmore, Sutandar-Pinnock, & Woodside, 2004). If the FREED service is able to target emerging adults in their first illness episode, it may be able to disrupt the course of illness, preventing the need for future costly treatment.

A significant proportion of potentially eligible patients (n=50) could not be included into the study for a variety of reasons, such as not being available for treatment due to moving away or travelling or simply not responding to our efforts to contact them after referral. This

highlights the transient nature, high mobility, limited treatment motivation and thus vulnerability of the emerging adult population for whom the FREED service was designed. This suggests that additional alternative avenues for engaging with these young people, e.g. via electronic and mobile health tools may be necessary.

This study has several limitations that should be noted. Firstly, as the audit comparison group was collected retrospectively it was only possible to report BMI data as an outcome. Secondly, there was a high proportion of missing self-report data at the follow-up stages in the FREED cohort. Although this is disappointing, it is still important to report this information. The UK Child Outcomes Research Consortium (CORC) acknowledges the difficulties with collecting service data, and comment that although such data are often Flawed, Uncertain, Proximate and Sparse (FUPS), they should still be shared as this is likely to prompt dialogue between key stakeholders and improves care (http://www.corc.uk.net/media/1533/fupsleaflet.pdf).

Furthermore, due to the limited number of participants in the study it was not possible to analyse the data for each of the ED diagnoses separately, or in relation to different treatments received. We hope that we will be able to provide this information in our future studies.

This study is the first report of clinical outcomes of an early intervention service within the ED field. One other study has recently reported on the impact of early intervention in 1st episode AN (Gumz, Weigel, Wegscheider, Romer & Löwe., 2017). The intervention comprised a comprehensive public health intervention implemented across the Hamburg metropolitan area. Patients recruited before and after introduction of the intervention were compared on (a) mean duration of untreated illness until specialist treatment and (b) mean duration of illness until first contact with the health service. Mean duration of untreated illness was 36.5 months before the implementation of the intervention and remained unchanged thereafter (40.1

months). Mean duration until first contact with the health service was 25.0 months before introduction of the intervention and 32.8 months thereafter, suggesting that help-seeking patients face very considerable delays in the German health care system, until they reach specialist care. Clinical outcomes are not reported in the German sample. In this study, baseline demographic and clinical features were very similar to those in our sample, but a much higher proportion of patients in the German sample (55.9 % pre-intervention and 83.3% post-intervention) were treated as in-patients (Gumz, et al., 2017). In our study, duration of untreated illness for adult patients was 19.1 months and for FREED patients was 16.4 months. Duration of illness till first contact with health services was 16.2 months for audit patients and 15.7 months for FREED patients (Brown et al., 2016).

When seen in the context of the German data, our process outcomes and clinical outcomes are encouraging and support further evaluation and wider implementation of FREED. The scalability of the FREED service is now being evaluated across several specialist ED services within the UK National Health Service, with the aim of assessing whether FREED is a suitable national model of service delivery.

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REFERENCES

Arnett, J. J., Žukauskienė, R., & Sugimura, K. (2014). The new life stage of emerging adulthood at ages 18–29 years: implications for mental health. *The Lancet Psychiatry, 1*(7), 569-576.

Barkham, M., Bewick, B., Mullin, T., Gilbody, S., Connell, J., Cahill, J., . . . Evans, C. (2013). The CORE-10: A short measure of psychological distress for routine use in the psychological therapies. *Counselling and Psychotherapy Research, 13*(1), 3-13.

Berner, L. A., & Marsh, R. (2014). Frontostriatal circuits and the development of bulimia nervosa. *Frontiers in Behavioral Neuroscience, 8*, 395.

Bohn, K., Doll, H. A., Cooper, Z., O'Connor, M., Palmer, R. L., & Fairburn, C. G. (2008). The measurement of impairment due to eating disorder psychopathology. *Behaviour Research and Therapy, 46*(10), 1105-1110. doi:10.1016/j.brat.2008.06.012

Brown, A., McClelland, J., Boysen, E., Mountford, V., Glennon, D., & Schmidt, U. (2016a). The FREED Project (first episode and rapid early intervention in eating disorders): service model, feasibility and acceptability. *Early Intervention in Psychiatry*. DOI: 10.1111/eip.12382.

Byford, S., Barrett, B., Roberts, C., Clark, A., Edwards, V., Smethurst, N., & Gowers, S. G. (2007). Economic evaluation of a randomised controlled trial for anorexia nervosa in adolescents. *The British Journal of Psychiatry, 191*(5), 436-440.

Carter, J., Blackmore, E., Sutandar-Pinnock, K., & Woodside, D. (2004). Relapse in anorexia nervosa: a survival analysis. *Psychological Medicine, 34*(04), 671-679.

Child Outcomes Research Consortium. (2016). Flawed, Uncertain, Proximate and Sparse Data (FUPS). Retrieved from: http://www.corc.uk.net/media/1533/fupsleaflet.pdf

Cole, J. D., & Kazarian, S. S. (1988). The Level of Expressed Emotion Scale: a new measure of expressed emotion. *Journal of Clinical Psychology, 44*(3), 392-397.

Crawford, J. R., & Henry, J. D. (2003). The Depression Anxiety Stress Scales (DASS): Normative data and latent structure in a large non‐clinical sample. *British Journal of Clinical Psychology, 42*(2), 111-131.

Currin, L., & Schmidt, U. (2005). A critical analysis of the utility of an early intervention approach in the eating disorders. *Journal of Mental Health, 14*(6), 611-624.

Eisler, I., Simic, M., Hodsoll, J., Asen, E., Berelowitz, M., Connan, F., . . . Treasure, J. (2016). A pragmatic randomised multi-centre trial of multifamily and single family therapy for adolescent anorexia nervosa. *BMC Psychiatry, 16*(1), 422.

Fairburn, C., & Beglin, S. (2008). Eating Disorder Examination Questionnaire (EDE-Q 6.0) *Cognitive Behaviour Therapy and Eating Disorders*. New York, USA: Guilford Press.

Fairburn, C. G., Cooper, Z., Doll, H. A., O'Connor, M. E., Palmer, R. L., & Dalle Grave, R. (2013). Enhanced cognitive behaviour therapy for adults with anorexia nervosa: A UK–Italy study. *Behaviour Research and Therapy*, *51*(1), R2-R8.

Gama, C. S., Kunz, M., Magalhaes, P. V., & Kapczinski, F. (2013). Staging and neuroprogression in bipolar disorder: a systematic review of the literature. *Revista Brasileira de Psiquiatria, 35*(1), 70-74.

Green, B., & Griffiths, E. (2014). Hospital admission and community treatment of mental disorders in England from 1998 to 2012. *General Hospital Psychiatry, 36*(4), 442-448.

Gumz A, Weigel A, Wegscheider K, Romer G, Löwe B. The psychenet public health intervention for anorexia nervosa: a pre-post-evaluation study in a female patient sample. *Prim Health Care Res Dev*. 2017 Aug 22:1-11 [Epub ahead of print].

Larry V. Hedges & Ingram Olkin (1985). Statistical Methods for Meta-Analysis. Orlando: Academic Press. ISBN 0-12-336380-2.

Herpertz-Dahlmann, B., Schwarte, R., Krei, M., Egberts, K., Warnke, A., Wewetzer, C., . . . Holtkamp, K. (2014). Day-patient treatment after short inpatient care versus continued inpatient treatment in adolescents with anorexia nervosa (ANDI): a multicentre, randomised, open-label, non-inferiority trial. *The Lancet, 383*(9924), 1222-1229.

Holland, G., & Tiggemann, M. (2016). A systematic review of the impact of the use of social networking sites on body image and disordered eating outcomes. *Body Image, 17*, 100-110.

Holland, J., Hall, N., Yeates, D. G., & Goldacre, M. (2016). Trends in hospital admission rates for anorexia nervosa in Oxford (1968–2011) and England (1990–2011): database studies. *Journal of the Royal Society of Medicine, 109*(2), 59-66.

House, J., Schmidt, U., Craig, M., Landau, S., Simic, M., Nicholls, D., . . . Eisler, I. (2012). Comparison of specialist and nonspecialist care pathways for adolescents with anorexia nervosa and related eating disorders. *International Journal of Eating Disorders, 45*(8), 949-956.

Keverne, E. B. (2004). Understanding well-being in the evolutionary context of brain development. *Philosophical Transactions -Royal Society of London Series B Biological Sciences*, 1349-1358.

Lovibond, P. F., & Lovibond, S. H. (1995). The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy, 33*(3), 335-343.

Marks, I. (1986). *Behavioural Psychotherapy*. Bristol.

Marshall, M., Lewis, S., Lockwood, A., Drake, R., Jones, P., & Croudace, T. (2005). Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: a systematic review. *Archives General Psychiatry, 62*(9), 975-983. doi: 10.1001/archpsyc.62.9.975

Micali, N., Hagberg, K. W., Petersen, I., & Treasure, J. L. (2013). The incidence of eating disorders in the UK in 2000–2009: findings from the General Practice Research Database. *BMJ open, 3*(5), e002646.

Mond, J. M., Myers, T. C., Crosby, R. D., Hay, P. J., Rodgers, B., Morgan, J. F., . . . Mitchell, J. E. (2008). Screening for eating disorders in primary care: EDE-Q versus SCOFF. *Behaviour Research and Therapy, 46*(5), 612-622.

Moylan, S., Maes, M., Wray, N. R., & Berk, M. (2013). The neuroprogressive nature of major depressive disorder: pathways to disease evolution and resistance, and therapeutic implications. *Molecular Psychiatry, 18*(5), 595-606. doi: 10.1038/mp.2012.33

NHS. (2015). Access and Waiting Time Standard for Children and Young People with an Eating Disorder. Retrieved Accessed 11th April 2017, from https://www.england.nhs.uk/wp-content/uploads/2015/07/cyp-eating-disorders-access-waiting-time-standard-comm-guid.pdf

NICE. (2017). *Eating Disorders: Recognition and Treatment.* London: National Institute for Health and Care Excellence.

NICE. (2014). *Psychosis and schizophrenia in adults: prevention and management*. London: National Institute for Health and Care Excellence.

O'Hara, C. B., Campbell, I. C., & Schmidt, U. (2015). A reward-centred model of anorexia nervosa: a focussed narrative review of the neurological and psychophysiological literature. *Neuroscience Biobehavioural Reviews, 52*, 131-152. doi: 10.1016/j.neubiorev.2015.02.012

Penttila, M., Jaaskelainen, E., Hirvonen, N., Isohanni, M., & Miettunen, J. (2014). Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. *British Journal of Psychiatry, 205*(2), 88-94. doi: 10.1192/bjp.bp.113.127753

Rhind, C., Salerno, L., Hibbs, R., Micali, N., Schmidt, U., Gowers, S., . . . Tchanturia, K. (2016). The Objective and Subjective Caregiving Burden and Caregiving Behaviours of Parents of Adolescents with Anorexia Nervosa. *European Eating Disorders Review*.

Schmidt, U., Brown, A., McClelland, J., Glennon, D., & Mountford, V. (2016a). Will a comprehensive, person-centred, team-based early intervention approach to first episode illness improve outcomes in eating disorders? *International Journal of Eating Disorders, 49*(4), 374-377.

Schmidt, U., Magill, N., Renwick, B., Keyes, A., Kenyon, M., Dejong, H., . . . Yasin, H. (2015). The Maudsley Outpatient Study of Treatments for Anorexia Nervosa and Related Conditions (MOSAIC): Comparison of the Maudsley Model of Anorexia Nervosa Treatment for Adults (MANTRA) with specialist supportive clinical management (SSCM) in outpatients with broadly defined anorexia nervosa: A randomized controlled trial. *Journal of Consulting and Clinical Psychology, 83*(4), 796.

Schmidt, U., Ryan, E. G., Bartholdy, S., Renwick, B., Keyes, A., O'Hara, C., . . . Dejong, H. (2016b). Two‐year follow‐up of the MOSAIC trial: A multicenter randomised controlled trial comparing two psychological treatments in adult outpatients with broadly defined anorexia nervosa. *International Journal of Eating Disorders*. doi: 10.1002/eat.22523

Seitz, J., Herpertz-Dahlmann, B., & Konrad, K. (2016). Brain morphological changes in adolescent and adult patients with anorexia nervosa. *Journal of Neural Transmission, 123*(8), 949-959.

Sepulveda, A. R., Kyriacou, O., & Treasure, J. (2009). Development and validation of the Accommodation and Enabling Scale for Eating Disorders (AESED) for caregivers in eating disorders. *BMC Health Services Research, 9*(1), 1.

Steinglass, J. E., & Walsh, B. T. (2016). Neurobiological model of the persistence of anorexia nervosa. *Journal of Eating Disorders, 4*, 19. doi: 10.1186/s40337-016-0106-2

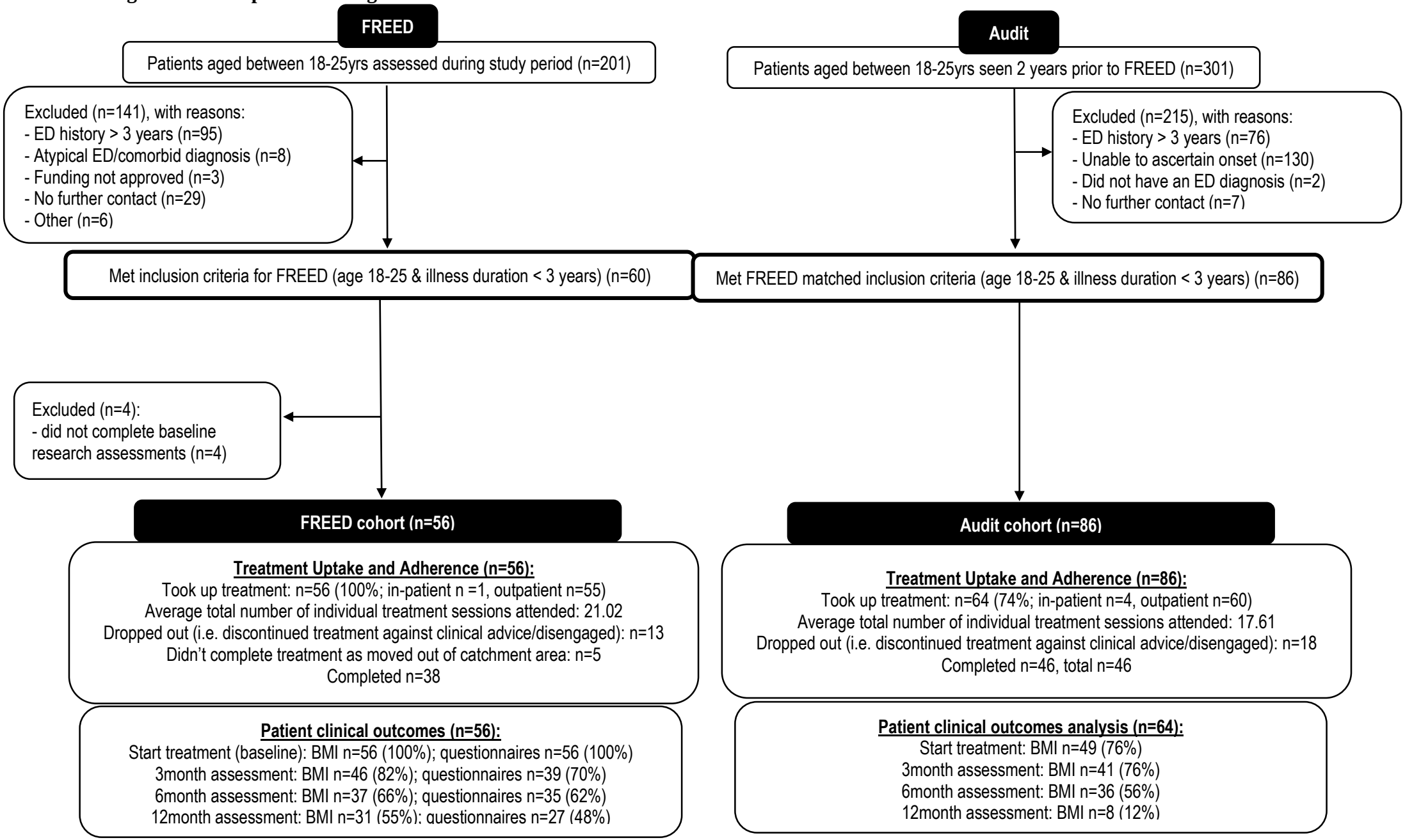
Steinhausen, H.-C. (2002). The outcome of anorexia nervosa in the 20th century. *American Journal of Psychiatry, 159*(8), 1284-1293.

Treasure, J., & Nazar, B. P. (2016). Interventions for the Carers of Patients With Eating Disorders. *Current Psychiatry Reports, 18*(2), 1-7.

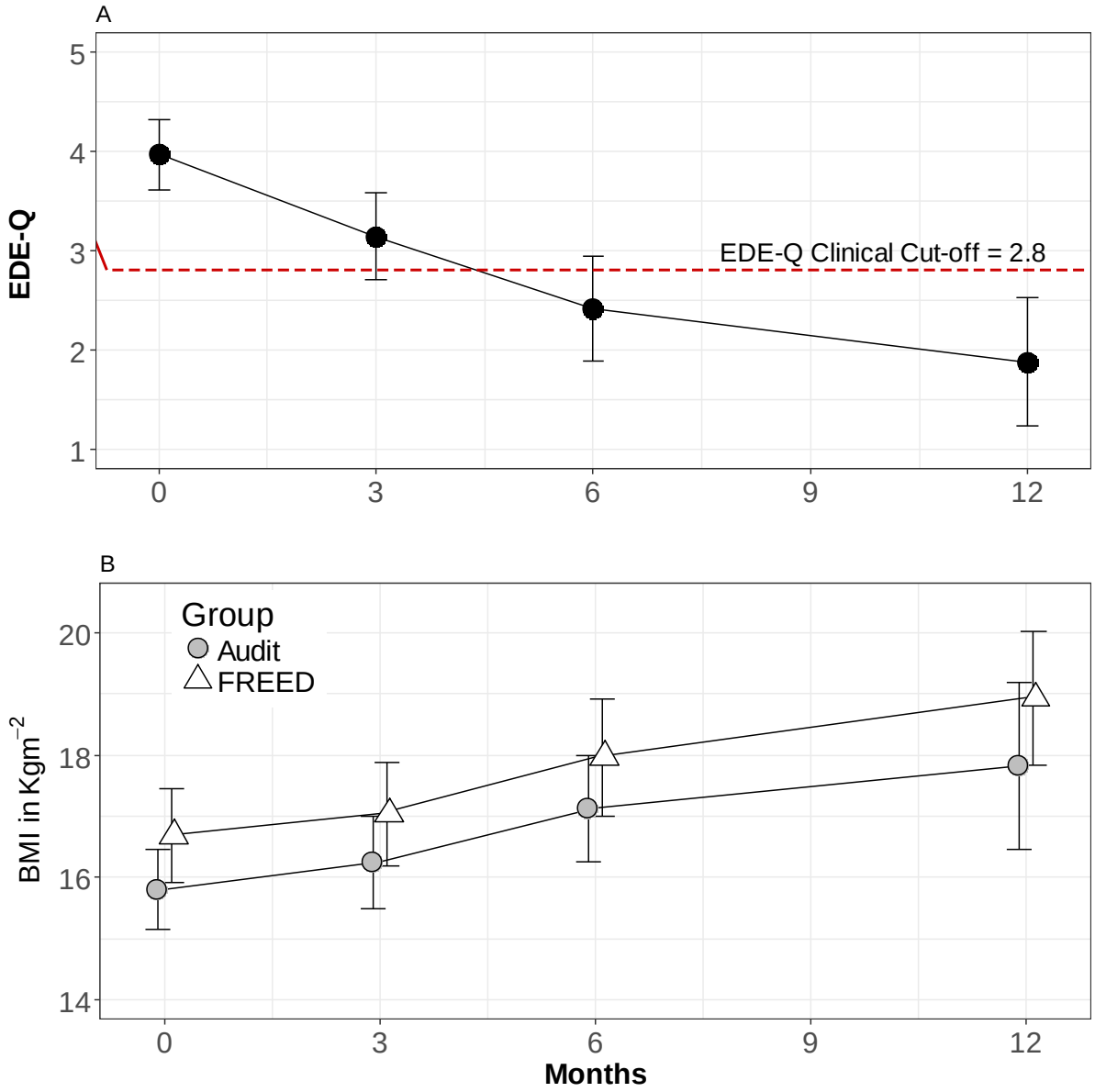
Treasure, J., Stein, D., & Maguire, S. (2015). Has the time come for a staging model to map the course of eating disorders from high risk to severe enduring illness? An examination of the evidence. *Early Intervention in Psychiatry, 9*(3), 173-184.

Van den Eynde, F., Suda, M., Broadbent, H., Guillaume, S., Van den Eynde, M., Steiger, H., . . . Schmidt, U. (2012). Structural magnetic resonance imaging in eating disorders: a systematic review of voxel-based morphometry studies. *European Eating Disorder Review, 20*(2), 94-105. doi: 10.1002/erv.1163

Figure 1. Participant flow diagram



Figures 2A and 2B. Estimated means (and 95% CI) for (A) EDE-Q for all FREED patients (n=53) and (B) BMI from start of treatment (T 0 months) to 12 months assessment for FREED (n=22, n=17) versus Audit (n=28, n=6) anorexia nervosa patients.


A
EDE-Q
5
4
3
2
1
0
3
6
9
12
EDE-Q Clinical Cut-off = 2.8
B
Group
Audit
FREED
BMI in Kgm^{-2}
20
18
16
14
0
3
6
9
12
Months

TABLES

Table 1. Demographic and clinical baseline characteristics.

	FREED cohort (N=56)	Audit cohort (N=86)
Age on GP referral (years): mean (SD)	20.4 (2.4)	20.4 (2.0)
Gender (Female): n (%)	54 (96%)	85 (98%)
Clinical Baseline		
Age of onset (years): mean (SD)	19.3 (2.6)	19.3 (2.1)
Diagnosis		
AN: n (%)	22 (35%)	35 (40%)
BN: n (%)	18 (32%)	24 (28%)
BED: n (%)	1 (2%)	4 (5%)
OSFED: n (%)	15 (27%)	23 (27%)

AN = anorexia nervosa; BN = bulimia nervosa; BED = binge eating disorder; OSFED = other specified feeding or eating disorder

Table 2. Raw data of psychological outcomes in FREED cohort: patients and carers

	Baseline		3 months		6 months		12 months	
	n	Score	n	Score	n	Score	n	Score
PATIENTS								
Eating Disorders Examination (EDE)	53	4.0 (1.3)	37	3.2 (1.4)	32	2.5 (1.4)	25	2.2 (1.6)
Body Mass Index (BMI)	50	19.8 (3.7)	45	19.7 (3.3)	35	19.9 (2.9)	30	20.7 (3.2)
Clinical Outcomes in Routine Evaluation (CORE-10)	53	19.8 (8.2)	37	16.1 (7.0)	32	14.2 (7.8)	25	15.4 (8.3)
Depression Anxiety and Stress Scale (DASS)	51	32.7 (13.7)	37	24.3 (15.5)	33	21.1 (14.6)	26	23.0 (14.0)
Work and Social Adjustment Scale (WSAS)	51	21.0 (9.7)	36	18.1 (9.7)	32	14.5 (10.5)	26	11.8 (10.3)
Levels of Expressed Emotion Scale (LEE)	51	17.3 (11.0)	37	14.9 (9.9)	31	12.0 (7.4)	26	12.2 (12.3)
Clinical Impairment Assessment (CIA)	52	1.8 (0.62)	32	1.67 (0.66)	33	1.20 (0.69)	26	1.0 (0.71)
CARERS								
Clinical Outcomes in Routine Evaluation (CORE-10)	16	10.4 (5.9)	17	9.6 (7.2)	14	10.0 (4.5)	13	4.9 (3.5)
Depression Anxiety and Stress Scale (DASS)	16	10.3 (8.9)	17	10.1 (9.2)	13	10.6 (8.7)	13	3.1 (4.3)

Work and Social Adjustment Scale (WSAS)	16	8.9 (10.0)	17	10.1 (8.3)	14	9.4 (9.3)	14	4.1 (4.3)
Levels of Expressed Emotion Scale (LEE)	18	8.7 (4.6)	18	8.6 (6.3)	14	8.8 (5.1)	14	6.4 (4.3)
Accomodation and Enabling Scale (AESED)	15	37.7 (18.2)	18	35.7 (19.6)	11	35.3 (22.0)	13	22.2 (11.2)

Cut-off scores: 10 item Clinical Outcomes in Routine Evaluation (CORE-10): scores of 11-15 mild, 15-20 moderate, 20-25 moderate/severe and >25 severe; 21 item Depression, Anxiety and Stress Scale (DASS-21): total score of 13 is normative baseline; Work and Social Adjustment Scale (WSAS): >20 moderate-severe, 10-20 moderate, <10 subclinical; higher scores on the Level of Expressed Emotion (LEE) indicative of greater perceived expressed emotion (no severity score ranges available). higher scores on the Clinical Impairment Assessment (CIA) indicative of worse secondary psychosocial impairment (no severity score ranges available); and higher scores on the Accommodation and Enabling Scale for Eating Disorders (AESED) indicative of higher accommodation to ED symptoms (no severity score ranges available).

Table 3: Estimated mean change on clinical outcomes from baseline for patients and carers at 3, 6 and 12 months and from 6 to 12 months, with standardised regression coefficients. and p-values and 95% CI Bonferroni adjusted for multiple comparisons (4 comparisons per outcome). SES (standardised effect size) here are regression coefficients standardised by dividing by the baseline standard deviation (Hedges & Olkin, 1985).

	0 - 3 months			**0 - 6 months**			**0 - 12 months**			**6 – 12 months**		
	β, 95%CI	**z p**	**SES**	**β, 95%CI**	**z p**	**SES**	**β, 95%CI**	**z p**	**SES**	**β, 95%CI**	**z p**	**SES**
Patients												
Eating Disorders Examination (EDE)	-0.82 -1.21, -0.43	-5.27 0.001	-0.63	-1.55 -2.06, -1.05	-7.70 0.001	-1.19	-2.08 -2.76, -1.41	-7.76 0.001	-1.60	-0.53 -1.02, -0.03	-2.67 0.030	-0.28
BMI	0.16 -0.40, 0.71	0.71 1.00	0.04	0.69 -0.02, 1.41	2.41 0.064	0.19	1.20 0.29, 2.12	3.28 0.004	0.9	0.51 -0.16, 1.18	1.90 0.229	0.14
Clinical Outcomes in Routine Evaluation (CORE-10)	-3.61 -6.81, -0.42	-2.82 0.019	-0.44	-5.57 -9.00, -2.13	-4.05 0.001	-0.68	-5.43 -9.33, -1.54	-3.48 0.002	-0.66	0.13 -3.83, 4.09	0.08 1.00	0.02
Depression Anxiety and Stress Scale (DASS)	-9.09 -14.94, -3.25	-3.89 0.001	-0.66	-12.21 -18.24, -6.17	-5.05 0.001	-0.89	-12.33 -18.92 -5.74	-4.67 0.001	-0.90	-0.12 -5.49, 5.27	-0.04 1.00	-0.01
Work and Social Adjustment Scale (WSAS)	-2.87 -7.07, 1.34	-1.70 0.354	-0.30	-7.16 -11.74, -2.58	-3.91 0.001	-0.74	-10.21 -15.50, -2.58	-4.81 0.001	-1.05	-3.04 -8.13, 2.05	-1.49 0.541	-0.31
Levels of Expressed	-1.45 -4.96, 2.06	-1.03 1.00	-0.13	-3.52 -7.35, 0.32	-2.29 0.088	-0.32	-3.86 -8.17, 0.46	-2.23 0.102	-0.35	-0.34 -4.66, 3.98	-0.20 1.00	-0.03

Emotion Scale (LEE)												
Clinical Impairment Assessment (CIA)	-0.18 -0.47, 0.10	-1.64 0.102	-0.29	-0.66 -0.95, -0.36	-5.52 0.001	-1.06	-0.98 -1.33, -0.63	-7.03 0.001	-1.58	-0.33 -0.66, 0.00	-2.48 0.053	-0.53
Carers												
Clinical Outcomes in Routine Evaluation (CORE-10)	-1.39 -5.07, 2.29	-0.94 1.00	-0.24	-1.67 -5.56, 2.22	-1.07 1.00	-0.28	-6.92 -10.91, -2.93	-4.33 0.001	-1.17	-5.25 -9.14, -1.36	-3.37 0.003	-0.89
Depression Anxiety and Stress Scale (DASS)	-0.51 -6.44, 5.43	-0.21 1.00	-0.06	-0.26 -6.74, 6.22	-0.10 1.00	-0.03	-7.28 -13.70, -0.86	-2.83 0.019	-0.82	-7.02 -13.41, -0.63	-2.74 0.024	-0.79
Work and Social Adjustment Scale (WSAS)	-0.94 -6.98, 5.11	-0.39 1.00	-0.09	-2.99 -9.43, 3.45	-1.16 0.984	-0.30	-8.16 -14.54, -1.78	-3.20 0.006	-0.82	-5.17 -11.30, 0.96	-2.11 0.141	-0.52
Levels of Expressed Emotion Scale (LEE)	-0.39 -3.06, 3.83	0.28 1.00	-0.08	0.09 -3.62, 3.80	0.06 1.00	0.02	-2.25 -5.93, 1.42	-1.59 0.503	-0.49	-2.35 -6.09, 1.39	-1.57 0.468	-0.51
Accomodation and Enabling Scale (AESED)	-3.63 -14.58, 7.33	-0.83 1.00	-0.20	-5.75 -18.46, 6.96	-1.13 1.00	-0.32	-18.5 -30.5, -6.56	-3.87 0.001	-1.02	-12.78 -24.84, -0.72	-2.65 0.032	-0.70