CORE
Provided by Loughborough University Institutional Repository

Predictive factors of & early response to inpatient treatment

Predictors of positive treatment outcome in people with anorexia nervosa treated in a specialized inpatient unit: The role of early response to treatment

Authors:

Jackie Wales BA¹

Nicola Brewin BA¹

Rebecca Cashmore MBChB, M.Med Sci, MRCPsych¹

Emma Haycraft PhD²

Jonathan Baggott MBChB MRCPsych¹

Amy Cooper BSc^{1,2}

Jon Arcelus LMS, MSc, FRCPsych, PhD^{1,3}

Address:

¹Leicester Eating Disorder Service, Bennion Centre, Glenfield Hospital, Leicester, UK ²School of Sport, Exercise and Health Sciences, Loughborough University, UK ³Division of Psychiatry and Applied Psychology, Faculty of Medicine & Health Sciences, Nottingham University, Nottingham, UK

Correspondence:

Jackie Wales, Leicester Eating Disorder Service, Bennion Centre, Glenfield Hospital, Leicester LE3 9DZ

Jackie.Wales@leicspart.nhs.uk

+441162252583

Word count abstract: 150

Word count manuscript 4975 excluding abstract, tables & references

Abstract

OBJECTIVE: To investigate factors which predict positive treatment outcome in inpatients with anorexia nervosa (AN), particularly the role of early treatment response. **METHOD:** 102 patients entering specialist inpatient treatment were assessed for eating disorder history, psychopathology and motivation to change. Predictive factors assessed were: early treatment response defined as weight increase of at least 0.5-1 kg/week during the first six weeks of treatment; admission BMI; onset age; chronicity; motivation to change; diagnosis; and previous hospitalization for AN. Positive treatment outcome was defined as achieving BMI 17.5 kg/m² within an individual timeframe. **RESULTS:** Logistic regression indicated that patients were 18 times more likely to reach positive treatment outcome if they met NICE weight guidelines within the first six weeks of hospitalization. Higher entry BMI and early weight gain predict positive treatment outcome in individuals receiving specialist AN inpatient treatment.

KEYWORDS: early response, inpatient treatment, anorexia nervosa, BMI, weight gain, predictors

Predictors of positive treatment outcome in people with anorexia nervosa treated in a specialized inpatient unit: The role of early response to treatment

Introduction

The guideline from the National Institute for Health and Care Excellence (NICE) in the UK recommends that patients with anorexia nervosa (AN) should be treated as outpatients and that inpatient care should only be considered when the condition is severe or has not responded to initial outpatient treatment (NICE, 2004). Studies investigating factors which predict inpatient treatment outcome have found that chronicity, later age of AN onset, lower Body Mass Index (BMI) on admission, lower motivation to change, Binge Purge sub-type, symptom severity, and previous hospitalization are all factors which are more likely to be associated with a less positive outcome or a greater risk of relapse (Bewell & Carter 2008; Carter et al. 2012; Fichter, Quadflieg & Hedlund 2006; Hartmann, Wirth & Zeeck 2007; Kaplan et al 2009; Sly & Bamford 2011; Steinhausen 2002). These predictive factors are useful clinically. However, a recent multi-centre study of inpatient treatment for AN in the UK concluded that the overall response to treatment was modest (Goddard et al. 2013). The authors highlighted the need to further investigate how to improve treatment outcome for patients with AN treated as inpatients.

One of the factors that has received little attention in this specific population is early response to inpatient treatment, measured as early weight gain. This is surprising as early response to treatment has been demonstrated to predict treatment outcome in general psychiatric disorders, including those receiving outpatient treatment for eating disorders (e.g., Agras et al. 2000; Fairburn, Agras, Walsh, Wilson & Stice 2004; Grilo, Masheb & Wilson 2006; Zunker et al. 2010). The majority of these studies have only included patients with bulimia nervosa (BN) or binge eating disorder (BED) treated with Cognitive Behavioural Therapy (CBT) or Interpersonal Psychotherapy (IPT). The few studies investigating the predictive value of early treatment response in patients with AN, whether treated with family therapy (Doyle, Le Grange, Loeb, Doyle & Crosby 2010; Le Grange, Accurso, Lock, Agras &

Bryson 2014; Madden et al. 2015), adolescent supportive therapy (Le Grange et al. 2014), or CBT (Lockwood, Serpell & Waller 2012; Marcoulides & Waller 2012), have included only individuals treated as outpatients. A recent systematic review and meta-analysis of eating disorders concluded that the most robust predictor of outcome at both the end of treatment and at follow up was greater symptom change early during treatment (Vall & Wade 2015). These findings confirmed a previous study investigating predictive factors for inpatient treatment in adults with AN, which demonstrated that early weight increase, particularly in weeks 3 to 4 of admission, was highly predictive of discharge weight (Hartmann et al. 2007). The authors noted that their results needed to be replicated in other samples and settings. Hartmann et al.'s study was limited by a lack of information regarding refeeding oedema, which could affect weight increase, particularly in the first few weeks of inpatient treatment. Another study suggested that patients with AN can have a degree of water retention that peaks at week 4 of refeeding and is mostly resolved at week 6 (Rigaud, Boulier, Tallonneau, Brindisi & Rozen 2010). Therefore, using week 4 weights may mask weight gain secondary to oedema.

A complication of undertaking research in eating disorder inpatient units is the lack of clear criteria to define treatment response and positive outcome. Most previous research studies have used some indicator of weight gain during the period of inpatient treatment as a measure of outcome (e.g., Davies & Jaffa 2005; Herzog, Zeeck, Hartmann & Nickel 2004; Lund et al. 2009; Sly & Bamford 2011). Schlegl, Quadflieg, Lowe, Cuntz and Voderholzen (2014) reported that despite considerable weight gain over the course of inpatient treatment (mean gain of 0.84kg/week), over half of their patients did not achieve a BMI of at least 17.5 kg/m² at discharge. This accords with results from a recent multi-centre study in the UK which also found that over half of those treated for AN did not reach a BMI ≥ 17.5 kg/m² by discharge (Goddard et al. 2013). Although many studies use the definition of achieving a BMI above 17.5 kg/m² they do not specify the amount of time required to achieve this. The study by Goddard et al. (2013) also reported that in 7 out of the 12 adult eating disorder specialist inpatient units included in their study, the mean rate of weight gain during

treatment was below the minimum of 0.5kg/week recommended by NICE. The conclusions of all the aforementioned studies indicate that the relationship between rate of weight gain and treatment outcome is in need of further investigation.

When treated as inpatients, NICE recommends that patients should gain between 0.5 to 1kg per week. Due to the lack of research in this area, this weight gain recommendation was made based on clinical experience. However, there has been little empirical research investigating optimal weight gain for this patient group. One study that compared the short-term impact of different weight gain targets on treatment outcome concluded that minimum weekly weight gain in the region of 0.5kg/week, rather than 0.75kg/week, was more effective at aiding patients to maintain or increase weight in the short-term during their inpatient stay (Herzog et al. 2004). A later study found that the rate of weight gain during inpatient treatment for AN was a significant predictor of short-term positive clinical outcome at follow up (Lund et al. 2009). Lund and colleagues found that clinical deterioration in the year post discharge occurred significantly less often among participants who gained ≥0.8kg/week during their inpatient stay. Evidence thus far concerning optimal weekly weight gain for recovery has not been clear.

The overall aim of this study was, therefore, to expand the existing evidence regarding predictors of inpatient treatment outcome for AN, with particular reference to early treatment response. The study had two specific aims. First, to investigate the role of rapid response to treatment by assessing whether there is a difference in treatment outcome between those who respond early to treatment, defined as gaining at least the NICE recommended weight gain of 0.5 to 1 kg/week during the first 6 weeks of treatment, and those who do not. This timeframe was selected as it extends the period studied by Hartmann et al. (2007) to allow for any excessive fluctuation in weight resulting from medical causes, for example refeeding oedema or abstinence from diuretic abuse (Rigaud et al. 2010). Second, to investigate the factors which predict positive treatment outcome in individuals with AN treated as inpatients. The study sought to replicate previous studies (Bewell & Carter 2008; Carter et al. 2012; Fichter et al. 2006; Hartmann et al. 2007; Sly & Bamford

2011) by assessing the role of: age of AN onset; chronicity; BMI on admission; motivation to change; sub-type of diagnosis (AN-Restricting and AN-Binge Purge sub-types); and previous hospitalization, on treatment outcome. The main outcome of interest was defined as achieving a target BMI of 17.5 kg/m² within the maximum amount of time that would be necessary to reach this with a weight increase at the lower end of the NICE guidelines (0.5kg per week). This BMI was chosen in line with other recent studies that have used a BMI of 17.5 kg/m² to define achieving a 'good outcome' (Hartmann et al. 2007; Sly & Bamford 2011). It was hypothesized that those reaching positive outcome (achieving a BMI of 17.5 kg/m² in the correct time) would be more likely to have had an early response to treatment (meeting NICE weight increase guidelines for the first 6 weeks of treatment), as per the outpatient literature. It was also hypothesized that the length of time taken to achieve a BMI of 17.5 kg/m² would be shorter for those achieving the NICE weight recommendation when compared to those who do not.

METHOD

Participants

Every patient, male or female, aged 18 years or over who fulfilled the diagnostic criteria for AN, as per the Diagnostic and Statistical Manual of Mental Disorders version IV (DSM-IV; American Psychiatric Association 1994), who was admitted to the weight restoration treatment programme at a regional eating disorders inpatient unit in the UK was invited to take part in this research. Participants were recruited during a 7 year period (1st January 2007 to 31st December 2013). DSM 5 (American Psychiatric Association 2013) was introduced during the studied period, however all patients who entered into the study fulfilled a diagnosis of AN as per DSM-IV. During the studied period, 127 patients were admitted into the treatment programme at the unit. Twenty five of these patients (20%) had a second admission during the time period studied. For these patients only data from the first admission were included. Therefore the final sample comprised a total of 102 unique individuals with AN.

The study received ethical approval from the Research and Development Department of the local Partnership NHS Trust, on behalf of the local ethics committee, in line with Health Research Authority guidance (HRA, 2013).

The setting

The Adult Eating Disorder Service offers inpatient treatment to individuals aged 18 years or over living in the region. It covers a population of approximately 5 million people. The unit has 14 beds and primarily accepts admissions for those diagnosed with AN. The majority of patients are admitted informally, although the unit also offers compulsory treatment under the Mental Health Act.

Every participant admitted to the treatment programme was invited to participate in this study. A small number of chronic patients are occasionally admitted to the unit, not with the aim of achieving a BMI of 17.5 kg/m² but to aid them in achieving a healthier weight, usually not more than a BMI of 15 kg/m², and to manage their physical consequences of the AN. These chronic patients were not invited into this study as they are not part of the treatment programme.

The treatment programme is split into two phases:

Initial Phase. Patients begin with significant restrictions. They are initially not allowed time off the ward and have supervised access to the bathroom. All meals are supervised with a starting diet of 1500 calories per day which increases to 2500 calories per day over a few weeks. Patients work closely with their named/key nurse who oversees their nursing care on the ward and meets regularly with them in order to review progress. The aim of this phase is to gain a minimum of 0.5kg/week (as per NICE (2004) guidelines). After 6 weeks there is a review meeting to decide whether moving on to the next phase is appropriate and advisable. Patients are still able to move to the treatment phase if they have not met the minimum NICE guidelines for the first 6 weeks of stay.

• Treatment Phase. Patients will have progressed to a 2500/day calorie diet and be able to eat on a supervised dining table with other patients with AN. The aim of this phase is to continue, or start, to gain a minimum of 0.5kg/week (as per NICE guidelines) and to try to reach a target weight above 17.5 kg/m². Patients will attend the ward group therapy programme and will be allocated a weekly appointment with an individual psychotherapist who will work using a psycho-dynamically informed model. The group therapy programme includes courses such as CBT, addressing abnormal exercise (Taranis, Meyer, Touyz, Arcelus & Puma 2011), mindfulness, psycho-education, Pilates, and self-esteem. Food handling, preparation, and portioning are taught in sandwich making and meal cookery groups conducted in the therapeutic kitchen. Attendance at a minority of groups, e.g. Pilates, depends on BMI. This is the phase of treatment that prepares patients for discharge It is expected that patients continue to gain weight after discharge. Some patients who live locally are invited to attend the day programme that will help transferring the progress they have made as an inpatient to that of their home environment.

Measures and procedure

Participants were invited to complete a series of pre-treatment questionnaires by a member of the research staff on admission into the treatment programme; those that are relevant to this study are outlined below.

Socio-demographic information

Socio-demographic information was collected from patients including gender, employment status, ethnicity and information regarding the eating disorder history including age of onset, diagnosis, previous hospitalizations, and BMI at admission.

<u>Clinical Eating Disorders Rating Instrument (CEDRI; Palmer, Christie, Cordle, Davies, &</u> <u>Kenrick 1987; Palmer, Robertson, Cain & Black 1996</u>

The CEDRI is a semi-structured investigator based interview that measures eatingrelated behaviours and attitudes. All patients were assessed by experienced clinicians on admission to the inpatient programme using this tool which allowed them to reach an eating disorder diagnosis in accordance with the DSM-IV criteria. The tool has been shown to have good reliability and validity.

Eating Disorders Examination Questionnaire (EDE-Q; Fairburn & Beglin 1994)

The EDE-Q is a widely used self-report measure of eating disorder symptoms experienced over the previous 28 days. It has good reliability and validity in clinical samples. Items are rated on a 0-6 Likert scale with higher scores indicating a greater level of eating disorder psychopathology. The EDE-Q yields a global score and four subscales (Restraint, Eating Concern, Weight Concern and Shape Concern), all of which are used in this study.

The Anorexia Nervosa Stage of Change Questionnaire (ANSOCQ; Reiger et al. 2000)

The ANSOCQ is a 20 item self-report questionnaire which measures a person's motivation to change a range of shape and weight issues, eating behaviours, weight control strategies and emotional and interpersonal difficulties. For each item individuals are asked to select which of 5 statements best represents their current attitude or behaviour. The statements cover the motivational stages of pre-contemplation, contemplation, preparation, action and maintenance. Questions are scored 1-5 with higher ratings indicating a greater motivation to change. The ANSOCQ gives an overall score which corresponds to the various stages of change and also gives three subscales: Weight Gain; Eating, Shape and Weight Concerns and Ego-Alien Aspects, these are all examined in this study.

Weight measurement

Inpatients were weighed twice a week on Tuesday and Saturday mornings after going to the toilet, before breakfast and wearing nightwear. A digital scale was used which is calibrated annually.

Statistical Analyses

Primary outcome was defined, as per the Hartmann et al. study (2007), as achieving a BMI of 17.5 kg/m² within the maximum amount of time that would be necessary to reach this BMI with a weight increase at the lower end (0.5kg/week) of the NICE guidelines. For example, a patient who was admitted at a BMI of 12.5 kg/m² (weight 32kg; height 1.60m) would have to restore their weight to 44.8kg to obtain a BMI of 17.5 kg/m². To achieve the 12.8kg required, she/he would need to attain this weight gain in a maximum of 25.6 weeks (12.8kg x 0.5 kg per week, 180 days) to be defined as having achieved a positive outcome. Thus participants who achieved a BMI of 17.5 kg/m² within their individual timescale were deemed to have a positive outcome.

Additionally, we examined which patients achieved a minimum weight gain of at least 3kg over the first 6 weeks of admission to determine whether this early weight gain and adherence to NICE guidelines was linked to positive outcome. Comparisons between those who had a positive outcome and those who did not were conducted, as appropriate, using *t* tests or chi-square tests.

Age of AN onset; chronicity; BMI on admission; motivation to change; sub-type of diagnosis (AN-Restricting and AN-Binge Purge sub-types); previous hospitalization for AN and gaining weight according to NICE guidelines for the first 6 weeks of stay were analyzed as predictors of outcome using binary logistic regression.

All statistical analyses were conducted using SPSS 20 (IBM 2011) and the level of significance was set at p<.05.

RESULTS

Descriptive results

During the studied period 102 patients were admitted to the programme. Six week weight data were available for 87 participants (85%), as 15 did not complete the early stages of treatment. When comparing those participants who completed the early stages of

treatment (n=87) with those who did not (n=15), significant differences were found in occupation (p=.001), where there were more students in the group that completed a minimum of six weeks and conversely more unemployed in the group that did not complete the early stages of treatment. The two groups also differed on readmission to hospital after this episode (p=.034) where those who completed the first 6 weeks of treatment were more likely to have a further admission to hospital after this episode. The remainder of the study's analyses are conducted on those patients who completed at least 6 weeks of inpatient treatment (n=87). An intention to treat analysis showed no differences in outcome.

The socio-demographic characteristics of the participants in this study (n=87) are shown in Table 1. The cohort was divided into two groups; one that was defined as having a positive outcome (i.e. achieved a BMI of 17.5 kg/m² within their individual time frame) and one that did not. No differences in socio-demographics were noted between the two groups (Table 1).

Insert table 1 around here

Comparison of 'positive outcome' patient group and 'non-positive outcome' patient group (Table 1)

Just over half (51.7%, n=45) of all patients treated during the studied period were categorized as having a positive treatment outcome by achieving a BMI of 17.5 kg/m² within their individual time frame. There were no statistically significant differences between the two groups for any of the variables on the self-report questionnaires examined. For motivation, both groups had a very similar mean score on the ANSOCQ indicating that patients in both groups were at the 'preparation to change' stage at admission. The only statistically significant differences noted between the groups related to admission BMI and early weight restoration. The positive outcome group had a higher admission BMI (p=<.011) and were more likely to achieve early weight restoration (p=<.001) than the non-positive outcome group. Interestingly one third of those in the non-positive outcome group had achieved the

early weight gain target yet did not go on to be part of the positive outcome group, indicating that this initial weight gain was not sustained to achieve a BMI of 17.5 kg/m². Those who achieved a BMI of 17.5 kg/m² and made early weight gain in line with NICE recommendations did so in a significantly shorter length of time than those who did not make this early weight gain (p=0.019). For everyone who achieved a BMI of 17.5 kg/m², weight gain was an average of 0.49kg/week. This was lower for those whose length of stay was sufficiently long enough to achieve a BMI of 17.5 kg/m² but did not attain this with a mean weight gain of 0.44kg/week, less than that recommended by NICE.

Predictors of good outcome

A logistic regression analysis (see Table 2) was performed using only those variables found to significantly differ between the positive outcome and non-positive outcome groups, i.e. entry BMI and early response to weight gain. A full model significantly predicted outcome (Chi-square=34.49, df(2), p<.001). The model explained between 33% (Cox & Snell R^2) and 44% (Nagelkerke R^2) of the variance in achieving a BMI of 17.5 kg/m² and the model correctly classified 78.2% of cases. A Hosmer and Lemeshow test returned a non-significant result (p=.739) implying the model adequately fits the data. The values of the coefficients revealed that for those who achieved the NICE weight restoration guideline in the first 6 weeks of treatment, the odds of achieving a positive treatment outcome were 18 times higher than for those who did not meet this early weight gain target. Additionally, for every extra BMI point at entry, the odds of achieving a BMI of 17.5 kg/m², in the appropriate time, increase by a factor of 2.

Insert Table 2 about here

DISCUSSION

The first aim of this study was to investigate the role of rapid response to treatment by assessing whether there was a difference in treatment outcome between those who respond early to treatment, defined as gaining at least the NICE recommended weight gain of 0.5 to 1 kg/week during the first 6 weeks of treatment, and those who did not. To our knowledge this is the first study that evaluates the possible advantages of adhering to the NICE guidelines. The study shows that in spite of having a comprehensive and intense treatment programme, just over half of the patients admitted into the unit achieved a BMI of 17.5 kg/m² within a fixed period of time. Some additional patients (n=6) did achieve a BMI of 17.5 kg/m² but initially increased their weight at a lower rate than advised by NICE (2004). Others did not achieve this BMI at all, usually as they discharged themselves or, in a small number of cases, were discharged due to non-adherence to the treatment programme prior to achieving this weight; however everyone who completed a minimum of 6 weeks of treatment was included in the analyses. Those in the positive outcome group had an average weekly weight gain of 0.49kg/week on reaching a BMI 17.5 kg/m², and we note that this is lower than that found in the study by Schlegl et al. (2014).

The second study aim was to investigate the predictors of positive treatment outcome in individuals with AN treated as inpatients. Based on previous literature, this study considered age of AN onset; chronicity; BMI on admission; motivation to change; sub-type of diagnosis; and previous hospitalization, as potential predictors. The study found that individuals who were admitted to inpatient treatment at a higher BMI were more likely to have a positive outcome; a finding in accordance with research conducted by SIy and Bamford (2011). Although this could be explained by the fact that the length of stay required by those patients is shorter, it could also be a result of a higher degree of cognitive impairment in those with lower weight at entry. Making early engagement with treatment in patients with cognitive difficulties may be more difficult as recent studies have demonstrated an association between cognitive function and low BMI (Chan et al. 2014; Weider, Indredavik, Lydersen & Hestad 2014). However the relationship between BMI and cognitive functioning is complex and our clinical impression is that some patients at low BMI still perform astonishingly well for example, by continuing with their studies and work even at very low weights. Future studies could explore this association further. As the average entry

BMI in the positive outcome group was 13.4 kg/m², our findings may suggest that a BMI at admission of around 13.4 could be a useful starting point for achieving a BMI of 17.5 kg/m² adhering to NICE weight gain guidelines. However as the range of BMI's in both the positive and non-positive outcome groups was very similar, it is difficult to give clear guidelines regarding entry BMI.

One surprising finding of our study was that levels of motivation did not significantly differ between the positive and non-positive outcome groups. This could be explained by the fact that the majority of patients (n=86, 98.9%) were admitted voluntarily which indicates a level of motivation to treatment. It has been noted that patients can often feel motivated to make changes until faced with food at which point their motivation ebbs away only to return when they are no longer in the anxiety provoking situation of being expected to eat (Nordbø et al. 2012; Waller 2010). Interestingly, having a previous history of inpatient care, which could reflect the disorder's chronicity, their eating disorder severity, and/or levels of patients' motivation did not differentiate between those in the positive outcome and non-positive outcome groups.

The study's first hypothesis, that those achieving a positive outcome would have had an early response to treatment in terms of weight gain, was supported by the findings. The study found that patients with AN treated at the specialized unit who adhered to the NICE weight restoration guideline during the first 6 weeks of stay were eighteen times more likely to achieve a positive outcome (measured as achieving a BMI 17.5 kg/m²). However those whose weight gain rate was slower either never achieved the required weight gain or took on average 44% more bed days to achieve the same BMI, which supports the second hypothesis. This suggests that clinically not achieving the early rate of weight gain may be a useful indicator of poor treatment outcome. This may indicate the need for intensive work during the first phases of treatment in order to achieve early response. While it may seem obvious that those who made early weight gain in accordance with the NICE weight restoration guide were more likely to have a positive outcome, this is the first study that has actually shown this to be the case. However, how best to promote early response is not

clear given that there was no difference in the levels of motivation on admission between the two groups suggesting that interventions aimed at increasing motivation (Dean, Touyz, Reiger & Thornton 2008) may not be advantageous.

As inpatient care is seen as expensive it is frequently only used for the more severe group of patients; however, this study clearly indicates that an earlier admission may save the health service providers a considerable amount of money and time for the patient. For every extra BMI point at entry, the odds of achieving a BMI of 17.5 kg/m², in the appropriate time, increase by a factor of two. Our study suggests that professionals should be encouraged to consider admissions earlier and to intensify the work with patients particularly in the first few weeks of admission in order to achieve a rapid weight gain, as this will more likely predict a positive treatment outcome.

This study includes a large sample from a single centre, which could be seen as strength as it eliminates treatment bias, but also as a limitation, as it may make it more difficult to generalize. There are also limitations in using early weight gain as a possible predictor of outcome. Sudden weight increases in the early stages of treatment can be an indication of oedema and complications of refeeding although, as weight gain was examined for a 6 week period, it is thought that any early problems with these issues would have been minimized (Rigaud et al. 2010). Patients may also have been involved in covert manipulation e.g. using weights or water loading. Weight gain is only one parameter and needs to be viewed within the context of the individual patient.

The study is also limited by the use of the same variable to describe rapid response (weight gain as per NICE guidelines) and treatment outcome based on BMI. It could be argued that those who gain weight early on in treatment would be more likely to reach a higher BMI, however the converse is also true, that early weight gain could alarm patients and thus prevent them from achieving a BMI of 17.5 kg/m². Given that one-third of the patients in the non-positive outcome group actually achieved early weight gain, this supports the notion that early weight gain does not always result in achieving a positive outcome. The

association found between early weight gain and positive outcome may actually be due to another factor not studied here e.g. co-morbidity.

The study is also limited by the lack of follow up data, so there is no evidence as to whether the NICE guidelines are useful in the longer term. However, the study is a clear indication of the difficulties patients have in achieving a healthier BMI even when treated in specialized units. The report on the Management of Really Sick Patients with Anorexia Nervosa (Royal College of Psychiatrists, 2014) cautions against the underfeeding syndrome which can result from overly cautious re-feeding rates. A recent study by Redgrave et al. (2015) suggests that with higher calorie regimes, refeeding can safely be achieved at much faster levels than those suggested by NICE, with rates of weight gain close to 2kg/week, although it would have been interesting to see if this weight restoration was maintained after discharge. However the speed of weight gain is not the only consideration in recovery and there are many factors which influence long term outcome. Goddard et al. (2013) concluded that response to inpatient treatment was modest for those who had a severe enduring form of AN. For some patients a longer admission with a slower rate of weight gain to restore them to a BMI of at least 17.5kg/m² may be more clinically useful and cost efficient than a brief admission, especially if this would lead to fewer admissions and lower risk of relapse in the longer term. This suggestion would need further analysis and the potential increased costs would need to be considered alongside an economic analysis of wider inpatient service outcomes.

In spite of these limitations this study is one of the few that includes a large number of patients with AN treated at a specialized unit. Generally there is a lack of studies looking at the long term outcome of inpatient treatment for AN due to the low prevalence of the disorder. Data collection for the present study has taken 7 years to achieve a sufficient sample size for the analyses suggesting the need for multi-centre outcome studies in the future although these are potentially limited by differences in treatment models.

Specialist inpatient units should consider the study findings both in terms of their refeeding regimens and the timing of admissions. Although only a small proportion of

patients require inpatient hospital treatment in the UK such treatment is expensive, costing the UK's National Health Service (NHS) £434/day, per patient (BEAT, 2015). This equates to a cost of approximately £50,000 for a patient in the positive outcome group to reach a BMI of 17.5 kg/m². Understandably inpatient care may be seen as such an expensive and scarce resource that it should be reserved for the most severe patients but delaying admission risks further deterioration and may impair chances of recovery. An earlier admission, which is more likely to be successful, may be in the patient's best interests and be more cost effective for the health service provider.

References

- Agras, W., Crow, S., Halmi, K., Mitchell, J., Wilson, G. & Kraemer, H. (2000). Outcome predictors for the cognitive-behavioral treatment of bulimia nervosa: data from a multisite study. *American Journal of Psychiatry* 157:1302-1308. DOI/10.1176/appi.ajp.157.8.1302
- American Psychiatric Association. Diagnostic & statistical manual of mental disorders (4th ed). Washington DC: 1994.
- American Psychiatric Association. Diagnostic & statistical manual of mental disorders (5th ed). Washington DC: 2013.
- BEAT (beating eating disorders). The Costs of Eating Disorders. Social Health & Economic Impacts. Prepared by PricewaterhouseCoopers (PwC), 2015

www.b-eat.co.uk/assets/000/000/302/The_costs_of_eating_disorders_Final_original.pdf.

- Bewell, C.V. & Carter, J.C. (2008). Readiness to change mediates the impact of eating disorder symptomatology on treatment outcome in anorexia nervosa. *International Journal of Eating Disorders* 41:368-371. DOI: 10.1002/eat.20513
- Carter, J.C., Mercer-Lynn. K. B., Norwood, S.J., Bewell-Weiss, C.V., Crosby, R.D.,
 Woodside, D.B. & Olmsted, M.P. (2012). A prospective study of predictors of relapse in anorexia nervosa: Implications for relapse prevention. *Psychiatry Research*, 200(2):518-523. DOI:10.1016/j.psychres.2012.04.037
- Chan, T.W.S., Ahn, W.Y., Bates, J.E., Busemeyer. J.R., Guillaume. S., Redgrave, G.W.,
 Danner, U.N. & Courtet, P. (2014). Differential impairments underlying decision making
 in anorexia nervosa and bulimia nervosa: a cognitive modeling analysis. *International Journal of Eating Disorders* 47:157-167. DOI: 10.1002/eat22223
- Davies, S. & Jaffa, T. (2005). Patterns of weekly weight gain during inpatient treatment for adolescents with anorexia nervosa. *European Eating Disorders Review* 13:273-277.
 DOI:10.1002/erv.652

- Dean, H.Y., Touyz, S.W., Reiger, E. & Thornton, C.E. (2008) Group motivational enhancement therapy as an adjunct to inpatient treatment for eating disorders: a preliminary study. *European Eating Disorders Review* 16: 256-267. DOI: 10.1002/erv.851
- Doyle, P.M., Le Grange, D., Loeb, K., Doyle, A.C. & Crosby, R.D. (2010). Early response to family-based treatment for adolescent anorexia nervosa. *International Journal of Eating Disorders* 43:659-662. DOI: 10.1002/eat.20764
- Fairburn, C.G. & Beglin, S.J. (1994). Assessment of eating disorders: Interview or selfreport questionnaire? International Journal of Eating Disorders 16:363-370. DOI: 10.1002/1098-108X(199412)16:4
- Fairburn, C.G., Agras, W.S., Walsh, B.T., Wilson, G.T. & Stice, E. (2004). Prediction of outcome in bulimia nervosa by early change in treatment. *American Journal of Psychiatry* 161:2322-2324 DOI:10.1176/appi.ajp.161.12.2322
- Fichter, M.M., Quadflieg, N. & Hedlund, S. (2006). Twelve-year course and outcome predictors of anorexia nervosa. *International Journal of Eating Disorders* 39: 87-100 DOI: 10.1002/eat.20215.
- Goddard, E., Hibbs, R., Raenker, S., Salerno, L., Arcelus, J., Boughton, N., Connan, F.,
 Goss, K., Laszlo, B., Morgan, J.F., Moore, K., Robertson, D., Saeidi, S., SchreiberKounine, C., Sharma, S., Whitehead, L., Schmidt, U. & Treasure, J. (2013). A multicentre cohort study of short term outcomes of hospital treatment for anorexia nervosa
 in the UK. *BMC Psychiatry* 13:287. DOI:10.1186/1471-244X-13-287
- Grilo, C.M., Masheb, R.M., Wilson, G.T. (2006) Rapid response to treatment for binge eating disorder. *Journal of Consulting & Clinical Psychology* 74:602–613 DOI:10.1037/0022-006X.74.3.602
- Hartmann, A., Wirth, C., Zeeck, A. (2007). Prediction of failure of inpatient treatment of anorexia nervosa from early weight gain. *Psychotherapy Research* 12(2):218-229.
 DOI: 10.1080/10503300600702315

Health Research Authority. Guidance for NHS research studies 2013 www.hra.nhs.uk.

Herzog, T., Zeeck, A., Hartmann, A. & Nickel, T. (2004). Lower targets for weekly weight gain lead to better results in inpatient treatment of anorexia nervosa: A pilot study. *European Eating Disorders Review* 12:164-168 DOI: 10.1002/erv.424

IBM SPSS Statistics for Windows, 20th ed. Amonk, NY: IBM Corp 2011.

- Kaplan, A.S, Walsh, B. T., Olmsted, M., Attia, E., Carter, J. C., Devlin M. J., Pike K. M.,
 Woodside B., Rockert, W., Roberto, C. A. & Parides, M. (2009). The slippery slope:
 prediction of successful weight maintenance in anorexia nervosa. *Psychological Medicine* 39(06) 1037-1045 DOI: 10.1017/S003329170800442X
- Le Grange, D., Accurso, E.C., Lock, J., Agras, S. & Bryson, S. (2014). Early weight gain predicts outcome in two treatments for adolescent anorexia nervosa. *International Journal of Eating Disorders* 2014;47:124-129 DOI: 10.1002/eat.22221.
- Lockwood, R., Serpell, L., Waller, G. (2012). Moderators of weight gain in the early stages of outpatient cognitive behavior therapy for adults with anorexia nervosa. *International Journal of Eating Disorders* 45:51-56 DOI: 10.1002/eat.20885
- Lund, B., Hernandez, E., Yates, W., Mitchell, J., McKee, P. & Johnson, C. (2009) Rate of inpatient weight restoration predicts outcome in anorexia nervosa. *International Journal of Eating Disorders* 42:301-305 DOI: 10.1002/eat.20634.
- Madden, S., Miskovic-Wheatley, J., Wallis, A., Kohn, M., Hay, P. & Touyz, S. (2015). Early weight gain in family-based treatment predicts greater weight gain and remission at the end of treatment and remission at 12-month follow-up in for adolescent anorexia nervosa. *International Journal of Eating Disorders* 48(7):919-22. DOI:

10.1002/eat.22414

- Marcoulides, O.K. & Waller, G. (2012). Nonspecific predictors of weight gain in the early stages of outpatient cognitive behavioural therapy for adults with anorexia nervosa: replication and extension. *International Journal of Eating Disorders* 45:746-750 DOI: 10.1002/eat.22014
- National Institute for Health and Care Excellence (NICE). Guidelines for eating disorders: Core interventions in the treatment and management of anorexia nervosa, bulimia

nervosa and related eating disorders. Clinical guideline 9, 1.2 Anorexia Nervosa, managing weight gain 1.2.4.1 London 2004: National Collaborating Centre for Mental Health.

- Nordbø, R.H.S., Espeset, E.M.S., Gulliksen, K.S., Skårderud, F., Geller, J. & Holte, A. (2012). Reluctance to recover in anorexia nervosa. *European Eating Disorders Review* 20:60-67. DOI:10.1002/erv.1097
- Palmer, R., Robertson, D., Cain, M. & Black, S. (1996). The clinical eating disorders rating instrument (CEDRI); a validation study. *European Eating Disorders Review* 4:149-156.
 DOI: 10.1002/(SICI)1099-0968(1996096)4:3<149
- Palmer, R.L., Christie, M., Cordle, C., Davies, D. & Kenrick, J. (1987). The clinical eating disorders rating instrument (CEDRI); a preliminary description. *International Journal of Eating Disorders* 6: 9-16. DOI: 10.1002/1098-108X(198701)6:1<9</p>
- Redgrave, G. W., Coughlin, J.W., Schreyer, C.C., Martin, L. M., Leonpacher, A.K., Seide,
 M., Verdi, A. M., Pletch, A. & Guarda, A.S. (2015). Refeeding and weight restoration
 outcomes in anorexia nervosa: Challenging current guidelines. *International Journal of Eating Disorders* DOI: 10.1002/eat22390
- Reiger, E., Touyz, S., Schotte, D., Beumont, P., Russell, J., Clarke, S., Kohn, M. & Griffiths,
 R. (2000). Development of an instrument to assess readiness to recover in anorexia
 nervosa. *International Journal of Eating Disorders* 28:387-396. DOI:10.1002/1098-108X(200012)28:4<387
- Rigaud, D., Boulier, A., Tallonneau, I., Brindisi, M.C. & Rozen, R. (2010). Body fluid retention and body weight change in anorexia nervosa patients during refeeding. *Clinical Nutrition* 29:749-755. DOI:10.10.16/jclun.2010.05.007
- Royal College of Psychiatrists. MARSIPAN: Management of Really Sick Patients with Anorexia Nervosa. College report: CR189, 2014.

www.rcp.ac.uk/files/pdfversion/CR189.pdf

Schlegl, S., Quadflieg, N., Lowe, U., Cuntz, U. & Voderholzen, U. (2014). Specialized inpatient treatment of adult anorexia nervosa: effectiveness and clinical significance of

changes. BMC Psychiatry 14:258 DOI:10.1186/s12888-014-0258-z

- Sly, R. & Bamford, B. Why are we waiting? (2011). The relationship between low admission weight and end of treatment weight outcomes. *European Eating Disorders Review* 19:407-410 DOI: 10.1002/erv.1061
- Steinhausen, H. C. (2002). The outcome of anorexia nervosa in the 20th century. *American Journal Psychiatry* 159:1284-1293 DOI:10.1176/appi.ajp.159.8.1284
- Taranis, L., Meyer, C., Touyz, S., Arcelus, J. & La Puma, M. (2011). *Loughborough Eating Disorders Activity Programme*, Loughborough University, Loughborough UK.
- Waller, G. (2010). The myths of motivation: Time for a fresh look at some received wisdom in the eating disorders? *International Journal of Eating Disorders* 45:1-16. DOI: 10.1002/eat20900
- Vall, E. & Wade, T. D. (2015). Predictors of treatment outcome in individuals with eating disorders: a systematic review & meta-analysis. *International Journal of Eating Disorders* 48:7 946-971 DOI:10.1002/eat.22411
- Weider, S., Indredavik, M.S., Lydersen, S. & Hestad, K. (2104). Intellectual function in patients with anorexia nervosa and bulimia nervosa. *European Eating Disorders* Review 22:15-24. DOI: 10.1002/erv.2260
- Zunker, C., Peterson, C.B., Cao, L., Mitchell, J.E., Wonderlich, S.A., Crow, S. & Crosby, R.
 (2010). A receiver operator characteristics analysis of treatment outcome in binge eating disorder to identify patterns of rapid response. *Behavior Research & Therapy* 48: 1227-1231. DOI:10.1016/j.brat.2010.08.007

Table 1 Demographic, clinical characteristics & eating disorders symptomatology of the total sample, those with a positive treatment outcome & a non-

positive treatment outcome (n=87)

	Positive outcome Non-positive			
	(BMI 17.5 within	outcome		
	individual time	(BMI <17.5 within		
	frame) ¹	individual time		
		frame) ¹		
	n=45	n=42	-	
	Mean (SD)	Mean (SD)	Group difference	p
Gender				
• Female	91.1% n=41	97.6% n=41	<i>x</i> ² (1, n=87)=1.699	<i>p</i> =.362 ²
Male	8.9% n=4	2.4% n=1		
Civil status				
Single/separated	82.2% n=40	83.3% n=35	<i>x</i> ²(1, n=87)=.564	<i>p</i> =.453
Married/cohabiting	11.1% n=5	16.7% n=7		
Occupation				
Employed full/part-time	26.7% n=12	28.6% n=12	<i>x</i> ²(2, n=87)=2.158	<i>p</i> =.340
Unemployed	37.7% n=17	23.8% n=10		

• Student	35.6% n=16	7.6% n=20		
Ethnicity				
White British/White Other	97.8% n=44	92.9% n=39	<i>x</i> ²(1, n=87)=1.199,	<i>p</i> =.349 ²
Asian/Black/Other	2.2% n=1	7.1% n=3		
Age on admission (years)	27.62 (10.04)	25.50 (7.86)	<i>t</i> =1.092; df 85	p=.278
Duration of illness (months)	93.40 (96.53)	80.50 (75.59)	<i>t</i> =0.680; df 83	p=.498
Age of onset (years)	19.83 (7.62)	18.47 (5.78)	<i>t</i> =0.923; df 83	<i>p</i> =.359
Previous hospitalization for treatment of AN	28.9% n=13	47.6% n=20	<i>x</i> ² (1, n=87)=3.237	<i>p</i> =.072
BMI on admission	13.47 (1.29)	12.67 (1.55)	+-2 612. df 95	p=<.010*
	range 10.97-15.94	range 10.16-15.30	(-2.042, ul 85	
AN Restrictive	77.8% n=35	71.4% n=30	x ² (1,n=87)= 464	n= 496
AN Binge Purging	22.2% n=10	28.6% n=12	- x (1) 077 1101	μ.130
Mean weight gain (kg) weeks 0-6	4.40 (1.83)	2.38 (2.21) t=4.668 df 8		p =<.001**
Achieved NICE weight restoration guide (6 weeks)	82.2% n=37	35.7% n=15	<i>x</i> ² (1,n=87)=19.54	p =<.001**
Time to BMI 17.5 kg/m ² (weeks)	16.54 (6.96)	23.74 (5.79)		~~ < 010*
	n=45	n=6	<i>t</i> =2.410; df 49	μ-<.019

Hospitalization for AN after this episode		33.3% n=15	35.7% n=15	<i>x</i> ² (1,n=87)=0.550	<i>p</i> =.815
EDE-Q		n =43	n =36		
Global	score	4.26 (1.37)	4.39 (1.26)	<i>t</i> =0.439; df 77	<i>p</i> =.662
0	Restraint	4.20 (1.76)	4.34 (1.65)	<i>t</i> =0.374; df 77	<i>p</i> =.710
0	Weight concerns	4.37 (1.52)	4.25 (1.55)	<i>t</i> =0.333; df 77	<i>p</i> =.740
0	Eating concerns	3.74 (1.62)	4.03 (1.49)	<i>t</i> =0.821; df 77	<i>p</i> =.414
0	Shape concerns	4.72 (1.20)	4.92 (1.19)	<i>t</i> =0.759; df 77	<i>p</i> =.450
ANSOCQ		n =26	n =26		
• Total		2.65 (0.63)	2.67 (0.74)	<i>t</i> =0.122; df 50	<i>p</i> =.903
0	Weight gain	2.53 (0.78)	2.46 (0.79)	<i>t</i> =0.308; df 50	<i>p</i> =.759
0	Shape & weight	2.73 (0.69)	2.75 (0.79)	<i>t</i> =0.115; df 50	<i>p</i> =.909
0	Ego alien	2.68 (0.64)	2.74 (0.80)	<i>t</i> =0.298; df 50	<i>p</i> =.767

¹individual time frame calculation = maximum number of days to achieve a BMI of 17.5 kg/m² based on entry weight and a minimum weekly

weight gain of 0.5kg

²an exact significance test was used for Pearson's chi-square as some cells had expected count <5

*significant at 0.05 level **significant at 0.01 level

Table 2 Logistic Regression predicting likelihoo	d of achieving a BMI of 17.5 kg/m ²	(n=87)
--	--	--------

	В	S.E.	Wald	df	р	Odds Ratio	95% C.I. for Odds Ratio	
							Lower	Upper
Entry BMI	.742	.226	10.736	1	.001	2.100	1.347	3.273
Met NICE guidelines 0-6 weeks (coding no=0, yes=1)	2.895	.657	19.401	1	.001	18.080	4.986	65.558
Constant	-11.374	3.202	12.621	1	.000	.000		

Acknowledgements

With thanks to inpatient staff & patients and to Dr Carolyn Plateau for assistance with interpreting the logistic regression.