Evaluation of Refeeding Outcomes Over 5-Years in A Specialist Adolescent Eating Disorder Center in The UK: A Retrospective Chart Review Study.

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Research article

Keywords: nutrition, refeeding management, adolescent anorexia nervosa

Posted Date: September 25th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-72123/v1

Abstract

Background and aims: Refeeding syndrome (RS) is a serious clinical syndrome, its early identification is key to safe management. The aim of this study was to evaluate existing practices in a highly specialist centre for eating disorders and compare refeeding management, nutritional, and clinical outcomes in cases admitted to secondary care with those managed in primary care.

Methods: Retrospective analysis of electronic case records of adolescent patients at moderate – high risk of developing refeeding syndrome and treated for anorexia nervosa by a specialist eating disorder centre in London over a 5-year period. Statistical analysis compared refeeding methods used in this population to establish if there were differences in refeeding methods used within the sample and if so, how they impacted on outcomes.

Results: Adolescents admitted to inpatient care had significantly lower energy intakes (374kcal/d ± 205 compared with 621kcal/d ± 348, $p = 0.001$) and higher rates of weight loss at assessment (0.86kg/week ± 0.7 compared with 0.38kg/week ± 0.7, $p = 0.003$), without significant differences in other markers of medical instability. Incidence of RS symptoms did not differ significantly between groups and, similarly, no statistically significant difference was found between groups in treatment outcomes, measured by discharge weight (kg) and percentage median BMI (41.5kg ± 8.3 compared with 43.7kg ± 7.7, $p = 0.322$ and 81.6% ± 8.5 compared with 82.3% ± 9.7, $p = 0.622$).

Conclusions: Findings from this study support the hypothesis that refeeding adolescents with AN, at high risk of developing RS, with higher energy feeds than that advised by national guidance, in the absence of prophylactic phosphate supplementation or incremental energy increases, does not increase the risk of developing refeeding complications. These findings support recent evidence that advocates a less conservative refeeding approach and a review of current national guidance.

Plain English Summary

Refeeding syndrome (RS) can cause ill health and even death. It can occur when nutrition is reintroduced to malnourished patients. This study aims to compare management of RS in two different settings: hospital and outpatient care, in terms of outcomes measures such as blood results and weight change over treatment. This was achieved by looking back over 5 years of patient records and by using statistical methods to compare patients who were treated in hospital with those who were treated solely as outpatients. The study found that, for most adolescents with anorexia nervosa, less conservative refeeding practices are safe and could be preferable. Results indicate that a review of current national guidance could be helpful.

Introduction

Refeeding syndrome (RS) is a serious and potentially fatal clinical condition that can occur when refeeding malnourished patients [1]. Cautious approaches to refeeding have historically been advocated in low weight adolescents with anorexia nervosa (AN) [2]. However, in more recent years, there has been a growing body of evidence supporting less conservative refeeding practices in this group [3,4]. Inconclusive evidence on how to safely refeed malnourished patients has resulted in widely variable and inconsistent refeeding practices [5,6]. This study focuses on children and young people with restrictive AN, at high risk of developing RS, and compares RS risk management and clinical outcomes between two treatment settings.

RS is defined as severe electrolyte and fluid shifts associated with metabolic abnormalities in malnourished patients undergoing refeeding, whether orally, enterally, or parenterally [1,7]. Its hallmark feature is hypophosphatemia. After prolonged fasting, as seen in AN, reserves of potassium, magnesium and phosphate are already depleted. Processes involved in moving from the fasted to fed state result in a further decrease of serum concentrations of these minerals [8]. Although prevalence of the syndrome in adolescents with AN is low, it is associated with high morbidity and mortality [2,9,10].

AN has the highest mortality rate amongst all psychiatric conditions [11]. Previous prevalence estimates, from 2009, of AN in young people ranged from 0.3 to 0.6%, with adolescent girls aged 10–19 having the highest incidence [12]. Incidence of the illness continues to increase in young people, with age of onset decreasing [12,13]. Junior MARSIPAN (management of really sick patients with anorexia nervosa), last updated in 2012, provides national guidance on the management of AN in adolescents in the UK [10].

This guidance originates from the MARSIPAN report, which identified a need amongst clinicians for guidance when managing adults with AN [14]. It sets out clear criteria and thresholds to allow clinicians to assess medical instability and risk of refeeding in patients with AN [10]. These criteria help to differentiate patients requiring admission to secondary care for medical stabilisation and refeeding from those that can be safely managed in an outpatient setting.

Disparities in refeeding recommendations worldwide have led to a lack of consensus on how to refeed these individuals safely [6]. Large variations in recommendations on starting energy intakes, prophylactic phosphate supplementation and the use of oral nutritional supplements exist in guidance documents across countries [15–19]. However, an association between the initial degree of malnutrition and development of hypophosphatemia, a predictor of RS, has been widely reported [8,20–22]. Emerging evidence also suggests that low starting energy intakes and incremental increases may be unimportant in reducing risk of RS in this group, whilst macro nutrient composition (carbohydrates in particular) may be the key [1,23].

A contrast exists between current guidance and emerging evidence on refeeding in AN. The latter encourages a more aggressive strategy for increased remission rates, whilst the former advocates a conservative approach to ensure safety [10,22]. Garber and colleagues concluded, in their 2018 systematic review, that initial higher calorie feeding is feasible in moderately malnourished patients with AN, and that although higher calorie approaches to refeeding appear safe in combination with close medical monitoring, there is insufficient evidence to support changes in current standards in severely malnourished patients [3].

Although a lack of intervention studies has previously hindered advancements in refeeding practices in this group, a recent study has become the first randomised controlled trial (RCT) in this area. O'Connor and colleagues, found in 2016 that higher energy starting rates were associated with greater weight initial gain, without increased incidence of RS, suggesting that higher calorie feeding may be safe and preferable [4]. Similar conclusions have been drawn from multiple other recent studies in this area.

Further studies are needed to define risk factors related to the development of the refeeding syndrome specific to this group of chronically malnourished and underweight individuals. Whilst the evidence base supporting higher energy initial feeding continues to grow, national guidance remains the same. Recent literature has identified that greater weight during initial treatment predicts full remission after one year [24], which emphasises the importance of findings that suggest safety in higher energy feeding. Further research on refeeding practices in adolescent AN is essential to support a review of current guidance and to optimise RS management and treatment outcomes in this group.

The current study was based on patients treated at the Maudsley centre for child and adolescent eating disorders (MCCAED) in London, England. MCCAED is large regional national and specialist service treating over 500 young people with diagnosed eating disorders every year. On presentation to the service patients are assessed for their risk of medical instability including risk of developing RS. Patients who are deemed to be medically unstable and at high risk of RS are admitted initially to King's College Hospital, London, until medically fit to commence outpatient treatment.

Most patients assessed by MCCAED are treated solely as outpatients. Inpatient refeeding protocols include low energy starting rates, prophylactic phosphate supplementation and incremental energy increases. Outpatient refeeding practices are less cautious, starting at higher energy rates, without stepped increases or prophylactic phosphate supplementation.

The overall aim of this piece of work was to compare refeeding management, nutritional and clinical outcomes in young people with AN admitted to secondary care with those managed in primary care. The hypothesis that higher calorie initial feeding (1500 kcal/d), in the absence of prophylactic phosphate supplementation or incremental increases, does not increase incidence of RS complications, compared with lower energy intakes (1200 kcal) with phosphate supplementation and stepped increases, was tested.

Methods

Data Collection

Ethical approval was sought from the Audit Project Manager for the CAMHS CAG in the South London and Maudsley Trust. Ethical approval was also granted by London Metropolitan University ethics committee.

MCCAED research group were consulted to gain access to the electronic data base containing information on patients referred to the service over the past 5 years. The research group compiled data on all patients referred to MCCAED from local boroughs, served by the South London and Maudsley NHS Trust, that were diagnosed with anorexia nervosa, treated, and discharged between January 2015 and December 2019. The Junior MARSIPAN checklist, a tool used to measure medical instability in patients with anorexia nervosa, alongside consultation with a consultant paediatrician specialising in eating disorders, was used to create a data capture tool.

Baseline, time 1 (initiation of feeding) and time 2 (discharge from hospital for those in secondary care, or 1-week post food re-introduction for cases in primary care) data collected included age, gender, weight, height, percentage median body mass index, actual body mass index, weight loss per week for 1 month prior to assessment, temperature, heart rate, QT interval, blood glucose, phosphate, magnesium, potassium, corrected calcium, white blood cell, neutrophil, aspartate aminotransferase (AST) and gamma-glutamyl transpeptidase levels (GGT), as well as initial treatment setting, in primary or secondary care and reason for admission to secondary care for relevant cases.

Only cases at high risk of physical deterioration and of developing refeeding syndrome were included in the study. The junior MARSIPAN checklist was used by all clinicians within MCCAED to assign a risk factor to each case to identify those cases that are most medically unstable and at highest risk of developing the refeeding syndrome. Cases treated solely in primary care and documented as high risk of physical deterioration and developing refeeding syndrome by the assessing clinician were included in the study. All local cases admitted to secondary care at Kings College Hospital, London, for medical stabilisation and management of refeeding risk were also included.

Data was collected on outcomes at the end of the refeeding period as well as at discharge for both groups. Overall treatment outcome was measured by percentage median body mass index at discharge and change in actual weight from assessment to discharge. Percentage median body mass index was used as an objective marker of weight status in adolescent patients with anorexia nervosa. Actual weight gain (kg) has been shown to be a highly variable outcome measure and may not be comparable between groups due to wide variation between cases but was included to identify change in weight over the course of treatment.

Study Design

This study was a retrospective case note review of electronic patient records that was undertaken to explore characteristics of patients treated under the MCCAED team over the past 5 years and compare refeeding protocols used as well as treatment outcomes within the sample. The study included young people between the ages of 10-18 years of age, in treatment with MCCAED for anorexia nervosa according to the DSM5 diagnostic criteria. Cases were assigned to 2 independent groups, inpatient and outpatient, based on their initial treatment setting during the refeeding phase. These groups were compared using statistical analysis to explore differences and similarities in their characteristics and their outcome measures.

Selection of Participants

Children and adolescents diagnosed with anorexia nervosa and accepted for treatment by MCCAED between January 2015 and December 2019 were included in the study. To ensure that groups were comparable in terms of risk of developing refeeding syndrome, only cases admitted to secondary care for medical stabilisation and cases treated in primary care documented as at high physical risk of deterioration were included.

Statistical analysis

Data collected at baseline (initial assessment), time 1 (initiation of feeding, usually day 1) and time 2 (discharge from hospital or transition to weight restoration meal plan, usually day 7-10) was compiled, screened for missing variables and added to the IBM SPSS 26 software program for statistical analysis. Descriptive statistics were used to explore mean characteristics of each group for baseline, time 1 and time 2 data.

Data were tested for normality of distribution using the Shapiro – Wilk test, due to small sample size. Levene's test for homogeneity of variance was used to identify if normally distributed variables had equal variance across groups. Independent samples t-tests were used to compare mean differences between groups for those normally distributed variables, whilst the Mann Whitney U test compared variables that did not follow normal distribution. Paired sample t-test and the Wilcoxon signed-rank test were used to compare differences within groups. Significance was determined by a *p* value, corrected for all ties, of less than 0.05 for all tests.

Results

Case Selection

Selection of participants for inclusion in the study is displayed in Fig. 1. Cases were excluded based on missing key data, lacking a diagnosis of AN, not being accepted for treatment or not attending treatment, not residing in the local are or moving during treatment to another service and having a physical health comorbidity that affected treatment. Remaining cases were assessed on physical risk, and those identified as being at high risk of deterioration and of developing refeeding syndrome were included. Two groups were created and included in final analysis: an inpatient and outpatient group.

Characteristics of Groups

Descriptive statistics, shown in Table 1, carried out on inpatient and outpatient groups revealed that baseline mean age, weight, BMI and percentage median BMI and intake were all lower amongst the inpatient group. Mean temperature was the same across both groups and mean weight loss was higher in the inpatient group. Mean QTc interval was shorter for the inpatient group, whilst heart rate was higher on average.

Descriptive statistics carried out on baseline blood results for both groups, shown in Table 1, showed that mean baseline blood results for all markers except neutrophils were lower in inpatients group compared to those of outpatients.

Out of all cases, only one inpatient (1.7%) had hypophosphatemia at baseline (0.11 mmol/L). This same case was the only one to have hypophosphatemia at time 1 (0.63 mmol/L). Despite having a low phosphate at baseline and time 1, phosphate did not drop further on refeeding and had increased to within the reference range by time 2 (1.46 mmol/L). No cases had hypophosphatemia at time 2, the end of the refeeding period.

Comparison of characteristics between groups before refeeding.

Baseline characteristics of inpatients and outpatients were compared to determine if any significant differences existed between groups on initial assessment (see Table 1).

Baseline blood results; magnesium, potassium and calcium in the inpatient group were found to be significantly lower those of the outpatient group (magnesium: $t(56) = -3.39$, $p < 0.001$, potassium: $t(57) = -2.12$, $p = 0.04$ and calcium: $t(56) = -2.31$, $p = 0.02$), with a difference of 0.06, 0.2 and 0.04 mmol/L. However, none of these markers were below reference ranges in either group (see Table 1 and Table 2).

Mean age, weight loss, intake, phosphate and GGT also differed significantly between groups. Mean age, intake, phosphate and GGT were lower in the inpatient group, whilst weight loss was higher when compared with outpatients, shown in Table 1 and Table 2.

Comparison of characteristics between groups during refeeding.

Mean characteristics of the two groups were again compared at time 1, after initiation of feeding, to determine if any significant differences existed between inpatient and outpatient groups, that may be related to the refeeding protocol used in either treatment setting. Results are displayed in Table 1 and Table 2.

Significant differences were found between various mean blood markers (potassium, phosphate, magnesium and white cell count) and mean daily intakes between groups, with all variables being significantly lower amongst the inpatient group when

compared with outpatients, (potassium: t (52) = -4.59, p < 0.001, phosphate: t (53) = -2.52, p = 0.015, magnesium: t (52) = -3.32, p = 0.002, white cell count: U = 169.5, p = 0.044, daily intake: U = 120, p < 0.001).

Comparison of characteristics between groups at the end of refeeding.

Mean characteristics were, once again, compared between the two groups at time 2, to identify if any significant differences existed by the end of the refeeding period in either treatment setting, results are shown in Table 1 and Table 2.

Mean heart rate was significantly lower amongst the outpatient group compared to the inpatient group, (t (24) = 2.22, p = 0.036). Mean potassium and magnesium were shown to be significantly lower in inpatients compared with outpatients, (potassium: t (39) = -3.29, p = 0.002 and magnesium: t (37) = -3.75, p = 0.001).

Table 1
Comparison between inpatient and outpatient groups for cardiovascular, anthropometric and nutrition variables at baseline, time 1 and time 2 of refeeding.

	Baseline			**Time 1**			**Time 2**		
Characteristic	Inpatients (n = 19)	Outpatients (n = 40)	*P* Value	Inpatients (n = 19)	Outpatients (n = 40)	*P* Value	Inpatients (n = 19)	Outpatients (n = 40)	*P* Value
Age, years	13.6 ± 1.5	14.7 ± 1.8	**0.033**	-	-	-	-	-	-
Weight, kg	39.4 ± 7.8	42.5 ± 7.9	0.170	39.4 ± 7.8	42.7 ± 7.9	0.152	41.5 ± 8.3	43.7 ± 7.7	0.322
Height, cm	161.2 ± 9.6	162.9 ± 8.4	0.489	-	-	-	-	-	-
BMI, kg/m^2	15.1 ± 1.8	15.9 ± 2.2	0.180	15.1 ± 1.8	15.9 ± 2.2	0.176	15.9 ± 1.6	16.5 ± 2.1	0.368
mBMI, %	78.1 ± 9.1	79.9 ± 10.3	0.533	78 ± 9.1	81 ± 11	0.303	81.6 ± 8.5	82.3 ± 9.7	0.622
Weight loss, kg	0.86 ± 0.7	0.38 ± 0.7	**0.003**	-	-	-	-	-	-
Intake, kcal/d	374 ± 205	621 ± 348	**0.001**	1331 ± 309	1500 ± 0	**< 0.001**	2321 ± 322	2437 ± 202	0.094
Temperature, ˚C	36.5 ± 0.7	36.5 ± 0.5	0.559	36.4 ± 0.2	36.5 ± 0.2	0.936	36.5 ± 0.1	36.4 ± 0.4	0.231
QTc, ms	396 ± 25	397 ± 20	0.198	407 ± 9	405 ± 30	0.885	400 ± 0	389 ± 3	0.333
Heart rate, bpm	66 ± 24	60 ± 18	0.172	57 ± 12	59 ± 12	0.628	66 ± 14	55 ± 12	**0.036**
Glucose, mmol/L	4.4 ± 1.1	4.6 ± 1.2	0.573	4.6 ± 1.2	3.3 ± 0.7	0.054	4.2 ± 0.4	3.2 ± 1.7	0.271
Phosphate, mmol/L	1.1 ± 0.3	1.2 ± 0.2	**0.011**	1.2 ± 0.2	1.3 ± 0.1	**0.015**	1.4 ± 0.2	1.3 ± 0.2	0.140
Magnesium, mmol/L	0.87 ± 0.1	0.93 ± 0.1	**0.001**	0.82 -± 0.1	0.89 ± 0.1	**0.002**	0.82 ± 0.1	0.9 ± 0.1	**0.001**
Potassium, mmol/L	3.9 ± 0.4	4.2 ± 0.3	**0.035**	3.8 ± 0.5	4.3 ± 0.4	**< 0.001**	4.1 ± 0.4	4.4 ± 0.4	**0.002**
Calcium, mmol/l	2.2 ± 0.1	2.2 ± 0.1	**0.024**	2.2 ± 0.1	2.2 ± 0.1	0.264	2.2 ± 0.1	2.2 ± 0.1	0.521
WCC, $10^9/L$	4.9 ± 1.5	5 ± 1.1	0.816	4.3 ± 1.6	5.2 ± 1.4	**0.022**	4.7 ± 1.3	5.2 ± 1.4	0.344
Neutrophils, $10^9/L$	2.7 ± 1.4	2.7 ± 0.9	0.328	2.1 ± 1	2.5 ± 1	0.086	2.4 ± 0.8	2.6 ± 1.1	0.496
AST, units/L	22 ± 4	27 ± 8	**0.035**	26 ± 18	25 ± 9	0.300	23 ± 12	26 ± 7	0.421
GGT, units/L	9 ± 4	14 ± 7	**0.004**	9 ± 3	13 ± 7	0.056	9 ± 5	13 ± 7	0.060

Data are mean ± SD. *P* values represent comparisons between inpatient and outpatient groups obtained from independent-sample *t* test and Mann-Whitney *u* test. Time 1 represents data from days 2–5 of refeeding and Time 2 represents data from days 7–10 of refeeding. BMI, body mass index; mBMI, median BMI for height and gender; WCC, white cell count; AST, aspartate aminotransferase; GGT, gamma-glutamyl transpeptidase. P **< 0.05** indicates significance.

Table 2

Comparison between inpatient and outpatient groups for cardiovascular, anthropometric and nutrition variables at baseline, time 1 and time 2 of refeeding; test statistics, confidence intervals and significance values.

	Baseline			Time 1			Time 2		
Characteristic	*t*/Z* value	95% CI	*P* Value	*t/Z** value	95% CI	*P* Value	*t/Z** value	95% CI	*P* Value
Age, years	-2.124*	-	0.033	-	-	-	-	-	-
Weight, kg	-1.139	-7.46, 1.34	0.170	-1.456	-7.86, 1.26	0.152	-1.000	-6.69, 2.24	0.322
Height, cm	-0.696	-6.61, 3.2	0.489	-	-	-	-	-	-
BMI, kg/m^2	-1.357	-1.92, 0.37	0.180	-1.373	-2.03, 0.38	0.176	-0.900*	-	0.368
mBMI, %	-0.626	-7.25, 3.79	0.533	-1.041	-9.1, 2.89	0.303	-0.502*	-	0.622
Weight loss, kg	-2.921*	-	**0.003**	-	-	-	-	-	-
Intake, kcal/d	-2.921*	-	**0.001**	-5.577*	-	**< 0.001**	-1.674*	-	0.094
Temperature, ˚C	-0.595*	-	0.559	-0.068*	-	0.936	-1.522*	-	0.231
QTc, ms	-0.858*	-	0.198	0.149	-27.7, 31.5	0.885	-1.633*	-	0.333
Heart rate, bpm	-0.958*	-	0.172	-0.489	-9.64, 5.89	0.628	2.224	0.83, 22.2	**0.036**
Glucose, mmol/L	-0.568	-1.09, 0.61	0.573	-4.887*	-	0.054	1.140	-0.83, 2.78	0.271
Phosphate, mmol/L	-2.262*	-	**0.011**	-2.524	-0.23,-0.03	**0.015**	1.507	-0.03, 0.20	0.140
Magnesium, mmol/L	-3.387	-0.09,-0.03	**0.001**	-3.326	-0.1, -0.03	**0.002**	-3.754	-0.12, -0.04	**0.001**
Potassium, mmol/L	-2.166	-0.39, -0.02	**0.035**	-4.589	-0.75,-0.29	**< 0.001**	-3.285	-0.60, -0.14	**0.002**
Calcium, mmol/l	-2.312	-0.08, -0.01	**0.024**	-1.129	-0.05, 0.01	0.264	0.648	-0.03, 0.05	0.521
WCC, 10^9/L	-0.234	-0.78, 0.62	0.816	-2.015*	-	**0.022**	-0.960	-1.36, 0.49	0.344
Neutrophils, 10^9/L	-0.455*	-	0.328	-1.375*	-	0.086	-0.689	-0.86, 0.43	0.496
AST, units/L	-1.818*	-	**0.035**	-0.534*	-	0.300	-0.815	-8.52, 3.64	0.421
GGT, units/L	-2.637*	-	**0.004**	-1.595*	-	0.056	-1.899*	-	0.060

P* values represent significance of comparisons between inpatient and outpatient groups obtained from independent-sample *t* test and Mann-Whitney *u* test. Time 1 represents data from days 2–5 of refeeding and Time 2 represents data from days 7–10 of refeeding. CI, confidence interval. BMI, body mass index; mBMI, median BMI for height and gender; WCC, white cell count; AST, aspartate aminotransferase; GGT, gamma-glutamyl transpeptidase. P **< 0.05 indicates significance

Exploration of Treatment Outcomes of Inpatients and Outpatients

Weight change over treatment.

Descriptive statistics were used to explore mean discharge weight and discharge percentage median BMI (%mBMI) for each group. All inpatients and all but one outpatient had both measures reported at discharge. Mean discharge weight was higher for the outpatient group compared to the inpatient group. Mean percentage median BMI was similar in the outpatient group compared to the inpatient group.

Results relating to outcomes of both groups are displayed in Table 5 and Table 6. Differences between discharge weight and percentage median BMI were not statistically significant between groups, (weight: t (56) = -0.86, p = 0.39, %mBMI: t (56) = 0.109, p = 0.914).

Changes in BMI and weight between baseline and discharge were explored. Mean change in weight was marginally higher in the inpatient group compared to the outpatient group. Mean change in percentage median BMI was also higher for inpatients compared to outpatients, although, neither if these differences were statistically significant (see Table 6).

Table 5
Comparison of weight and percentage median BMI change after 7–10 days of refeeding and upon discharge between inpatients and outpatients.

	Time 2			**Discharge**		
Marker	Inpatients (n = 19)	Outpatients (n = 37)	*P* Value	Inpatients (n = 19)	Outpatients (n = 39)	*P* Value
Weight change, kg	11.6 ± 8.2	10.4 ± 7.5	0.598	51.1 ± 9.7	53 ± 7.2	0.392
mBMI change, %	16.5 ± 13.5	15 ± 10	0.590	94.8 ± 10.5	94.5 ± 10	0.914

Data are mean ± SD. *P* value represent comparisons made between groups obtained from independent *t* test and Mann-Whitney *u* test. mBMI, median body mass index for height and age. Time 2 represents the end of the refeeding period, day 7–10. Discharge represents the end of eating disorder treatment for both groups. P **< 0.05** indicated significance.

Table 6
Comparison of weight and percentage median BMI change after 7–10 days of refeeding and upon discharge between inpatients and outpatients; test statistics and significance values.

	Time 2			**Discharge**		
Marker	*t/Z**	95% CI	*P* Value	*t/Z**	95% CI	*P* Value
Weight change, kg	0.530	-3.19, 5.49	0.598	-0.862	-6.49, 2.58	0.392
mBMI change, %	-0.547*	-	0.590	0.109	-5.40, 6.02	0.914

P value represent comparisons made between groups obtained from *t*, independent *t* test and *Z**, Mann-Whitney *u* test. mBMI, median body mass index for height and age. Time 2 represents the end of the refeeding period, day 7–10. Discharge represents the end of eating disorder treatment for both groups. P **< 0.05** indicated significance.

Weight change over the refeeding period.

Mean weight and percentage median BMI increased from initial assessment to the end of the refeeding period in both inpatient and outpatient groups, see Table 7 and Table 8. Increase in both weight and percentage median BMI over the refeeding period was statistically significant for both groups (inpatients: Z = -3.507, p < 0.001 and Z = -3.201, p = 0.001), (outpatients: Z = -3.85, p = 0.000 and Z = -3.598, p < 0.001).

Mean weight gain and increase in percentage median BMI were both higher amongst the inpatient group when compared with the outpatient group, however these differences were not statistically significant (U = 303.5, p = 0.411 and U = 314, p = 0.520).

Table 7
Comparison of weight and percentage median BMI between baseline and time 2 in inpatients and outpatients.

	Inpatients			**Outpatients**		
	Baseline (n = 19)	Time 2 (n = 19)	*P* Value	Baseline (n = 40)	Time 2 (n = 37)	*P* Value
Weight, kg	39.4 ± 7.8	41.5 ± 8.3	**< 0.001**	42.5 ± 7.9	43.7 ± 7.7	**< 0.001**
mBMI, %	78.1 ± 9	81.6 ± 8.5	**0.001**	79.9 ± 10.3	82.3 ± 9.7	**< 0.001**

Data are mean ± SD. *P* value represent comparisons made between groups obtained from independent *t* test and Mann-Whitney *u* test. mBMI, median body mass index for height and age. Time 2 represents the end of the refeeding period, day 7–10. P **< 0.05** indicated significance.

Table 8
Comparison of weight and percentage median BMI between baseline and time 2 in inpatients and outpatients; test statistics and significance values.

	Inpatients			**Outpatients**		
	*t/Z***	95%CI	*P* Value	*t/Z***	95%CI	*P* Value
Weight, kg	-3.507**	-	**< 0.001**	-3.850**	-	**< 0.001**
mBMI, %	-3.201**	-	**0.001**	-3.598**	-	**< 0.001**

P value represent comparisons made between groups obtained from *t*, independent *t* test and *Z***, Wilcoxon signed rank test. mBMI, median body mass index for height and age. Time 2 represents the end of the refeeding period, day 7–10. P **< 0.05** indicated significance.

Discussion

Summary of Results

This study also identified that protocols used in the management of refeeding risk in either setting were safe, and evidence based. Clinical experience and judgement were often used in combination with the current guidance in refeeding risk management.

Differences in Characteristics of Groups

Physical health assessments were used as an objective measure of medical instability in this study. National guidance, as well as local guidance, advises that admissions to secondary care may be required for medical stabilisation and refeeding for those at highest risk [10,25]. However, admission to hospital in this study was not based on immediate medical risk but rather the rate of physical deterioration. Those admitted to inpatient care had significantly lower energy intakes and significantly higher rates of weight loss when compared with cases who remained in outpatient care.

These findings are consistent with recent literature on the medical management of AN, attributing high physical risk predominantly to rapid weight loss and malnutrition [26,27]. Although sample size of cases included in final analysis was small, this was representative of the number of high risk adolescents treated by a large specialist centre for eating disorders over a five year period, and may be indicative of the proportion of this population that are at highest physical risk.

Recent literature shows that thresholds for medical indicators of admission, such as those advised in Junior MARSIPAN, are based on expert opinion without clear evidence and that a review of these indicators is warranted [28,29]. There is also evidence to suggest that objective physical risks are modest in even the most severe cases on AN and that a high medical risk should not be assumed in most cases but based on objective assessments [9].

Impact of Refeeding Method on Outcomes

A concern reported widely in the literature is that of the 'underfeeding-syndrome', whereby the 'start low and advance slow' approach to refeeding postpones weight recovery and worsens treatment outcomes in adolescent with AN [8,23,26]. There is increasing evidence supporting the benefits of higher energy feeding in terms of reducing length of hospital stay and initiating early weight gain without increasing refeeding complications [4,30]. Despite the potential benefits of more rapid refeeding, there is a lack of high quality evidence to support the hypothesis that detrimental effects may be caused by slow refeeding [3].

The current study found that overall outcome, measured by change in percentage median BMI, was not related to initial refeeding method or setting. Weight gain was possible during the refeeding period for both inpatient and outpatient groups.

These results support the hypothesis that higher calorie feeding may be safe and preferable over the more cautious approach advised by current guidance and that incremental energy increases, as well as prophylactic phosphate supplementation, may be falsely reassuring in protecting against RS. The findings of this study do not, however, suggest that lower calorie feeding worsens treatment outcomes or delays weight restoration. Garber and colleges concluded similar findings in their 2018 systematic review. This review, which included 22 papers on refeeding in adolescent AN, found that the impact of differing approaches to refeeding on treatment outcomes remains unclear [3].

Strengths, Limitations, and Areas for Improvement

A key strength of this study was a representative sample of adolescent participants with AN over five years from a large specialist centre for child and adolescent eating disorders.

The main weakness of the study, like most retrospective reports, was the large volume of missing data, resulting in many cases being excluded. Others limitation were the small sample size and difference in group sizes. Although the inpatient cohort was representative of admission rates in the MCCAED service, the outpatient cohort was significantly reduced by exclusions from missing data. Specific statistical methods were chosen based on these limitations to ensure that results were still valid. Further testing could be carried out to include previously excluded cases to determine if results differ.

A confounding factor of this study was the prophylactic supplementation of phosphate within the inpatient group. All inpatient cases received oral phosphate supplementation. Although cases remaining as outpatients were prescribed a phosphate rich diet, they did not receive supplementation. Serum phosphate levels in the inpatient group may have been influenced by this supplementation and limited the number of cases that developed hypophosphatemia. However, both groups were shown to be comparable in terms of medical instability and at similar risk of developing refeeding hypophosphatemia. The fact that no patients in the outpatient group developed hypophosphatemia supports the theory that phosphate supplementation is not required to prevent this complication.

Conclusions

In conclusion, results from this five year retrospective case note review support the hypothesis that refeeding adolescents with AN, at high risk of developing RS, with higher energy feeds than that advised by national guidance, in the absence of prophylactic phosphate supplementation or incremental energy increases, does not increase the risk of developing refeeding complications. These findings support recent evidence that advocates a less conservative refeeding approach and a review of current national guidance.

Recommendations

Findings from this study, similar to those of other recent literature in this area, support a move towards less conservative refeeding in adolescent AN [4,23]. These results provide additional evidence to suggest that medical instability should not be assumed in all low weight, malnourished adolescents, but should be objectively assessed and managed on a case by case basis [9]. A greater understanding of the physiological response to refeeding of adolescents with AN is essential to improve and update current guidance [1].

Conclusions drawn from the results of this study supported five recommendations:

1. All adolescents diagnosed with AN require a full physical health assessment at baseline that can be used as an objective measure of medical instability. Medical instability should not be assumed based on anthropometric or nutritional measures alone.
2. Higher calorie initial feeds of 1500 kcal/d should be considered for all cases, regardless of treatment setting. Regular review and monitoring of biochemistry and physical observations should be carried out to ensure safety of higher calorie feeding.
3. Phosphate should be prescribed when medically indicated for certain cases, rather than universally administered as a prophylactic intervention in inpatient care. A diet rich in phosphate should be advised on during the refeeding period for all cases.
4. National guidance on refeeding management in adolescent AN should be reviewed and updated to include current evidence to advance practice in this area, with rapid weight loss likely being a better indicator of admission than other markers.

Abbreviations

RS: refeeding syndrome, AN: anorexia nervosa, MARSIPAN: management of really sick patients with anorexia nervosa, MCCAED: Maudsley centre for child and adolescent eating disorders, CAMHS: child and adolescent mental health service, BMI: body mass index.

Declarations

Ethics approval:

Ethical approval was sought from the Audit Project Manager for the CAMHS CAG in the South London and Maudsley Trust. Ethical approval was also granted by London Metropolitan University ethics committee.

Consent for publication:

Not applicable

Availability of data and materials:

The datasets supporting the conclusions of this article are available in the 'Google Drive' repository, https://drive.google.com/drive/u/1/folders/1Zv_zMh3a1llQY2AfYzH8xQ6MqGd9Fc4R.

Competing Interests

The authors declare that they have no competing interests.

Funding:

There are no funding sources to declare.

Author Contributions

CB was responsible for study design, data collection and interpretation of results as well as drawing of conclusions. SC was involved in study design, advising on medical aspects of study and creation of data collection tool.SI was responsible for providing supervision for all elements of the project.

Acknowledgements

Thank you to Mima Simic, Catherine Stewart, Anna Konstantellou and James Davis for their support and advice in carrying out this piece of work.

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Figures

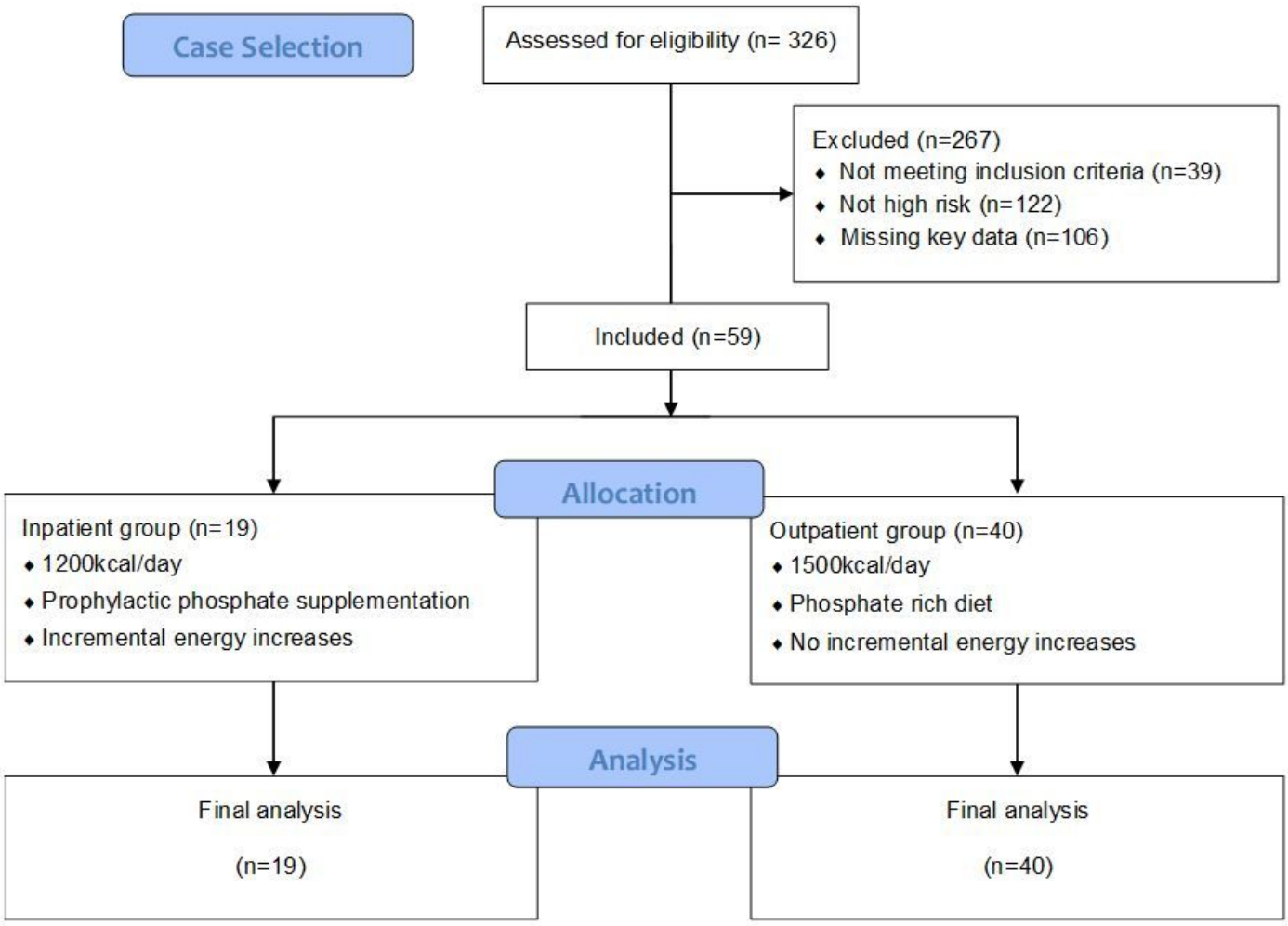

Figure 1

Flow chart of participants included in the current study.