

Nutrition Therapy during Initiation of Refeeding in Underweight Children and Adolescent Inpatients with Anorexia Nervosa: A Systematic Review of the Evidence

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ABSTRACT

Restoration of weight and nutritional rehabilitation are recognized as fundamental steps in the therapeutic treatment of children and adolescent inpatients with anorexia nervosa (AN). However, current recommendations on initial energy requirements for this population are inconsistent, with a clear lack of empirical evidence. Thus, the aim of our study was to systematically review, assess, and summarize the available evidence on the effect of differing nutrition therapies prescribed during refeeding on weight restoration in hospitalized children and adolescents (aged 19 years and younger) with diagnosed AN. Searches were conducted in Scopus, Web of Science, Global Health (CABI), PubMed, and the Cochrane database for articles published in English up to May 2012, and complemented by a search of the reference lists of key publications. Seven observational studies investigating a total of 403 inpatients satisfied the inclusion criteria. The range of prescribed energy intakes varied from 1,000 kcal to >1,900 kcal/day with a progressive increase during the course of hospitalization. It appeared that additional tube feeding increased the maximum energy intake and led to greater interim or discharge weight; however, this was also associated with a higher incidence of adverse effects. Overall, the level of available evidence was poor, and therefore consensus on the most effective and safe treatment for weight restoration in inpatient children and adolescents with AN is not currently feasible. Further research on refeeding methods is crucial to establish the best practice approach to treatment of this population.

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ANOREXIA NERVOSA (AN) IS AN EATING DISORDER with a high morbidity and mortality rate.¹ AN is characterized by a significantly lower-than-expected body weight, intense fear of becoming overweight, and a distorted body image.² The disorder primarily affects adolescent girls aged 15 to 19 years³; however, incidences of early onset AN in children aged 5 to 13 years has been reported.⁴ Although the overall prognosis for recovery from AN is better in younger patients than in adults,^{5,6} the treatment for AN is a complex and protracted process, involving a multidisciplinary approach across a range of health care settings.^{7,8} Life-threatening consequences of malnutrition as a result of AN may lead to one or more admissions for inpatient treatment.^{1,9,10}

Weight restoration through continuous increases in energy intake is one of the priorities in the initial stages of inpatient care and is an essential step for overall rehabilitation and recovery.¹¹⁻¹³ Regaining weight during hospitalization has been shown to be one of the major factors predicting favorable short-¹⁴ and long-term outcomes,¹⁵ and has been associated with improvement in a number of psychological and

medical complications.¹⁶⁻¹⁸ In adolescents, weight restoration has been shown to significantly improve cognitive impairment compared with pretreatment, thus facilitating psychological or psychiatric therapy.¹⁹ Restoring weight in young patients can also reverse growth retardation, developmental delay, and compromised bone density.^{7,20} Conversely, failure to gain weight before discharge can increase the likelihood of the symptomatic progression of the disorder and the chance for consecutive readmissions.^{10,18,21} Thus, timely and effective nutrition treatment for weight restoration is crucial to ameliorate the debilitating consequences of AN.^{6,22}

Currently there is no consistent approach in recommendations for optimal refeeding practices or nutrition-related treatment of patients with AN.^{6,8,13} Most guidelines^{8,23-25} for young patients advocate for conservative energy intake at the initiation of treatment (800 to 1,000 kcal/day)²⁴ due to the risk of refeeding syndrome (RS),²⁶ a potentially life-threatening disturbance of electrolytes that can occur in severely malnourished individuals following the reintroduction of food.^{11,27,28} Although RS is a relatively rare condition (previously reported in <6% of hospitalized

adolescents²⁹), it can affect the cardiovascular, pulmonary, renal, hepatic, and neuromuscular systems, potentially leading to multiple organ failure and death.²⁷ Severely malnourished patients (those with <70% of expected body weight), are at most danger of developing the syndrome, particularly during the first week of nutrition treatment.¹¹ Therefore, energy recommendations for the initiation of refeeding are commonly set lower than the estimated energy requirements of the individual.³⁰ However, there is an opposing view that this approach could potentially postpone weight recovery, thus delaying the therapeutic process^{9,30} and initiation of refeeding should commence at around 2,000 kcal whilst closely monitoring vital signs.³⁰ Research on the current practice of refeeding reflects the lack of consistent recommendations on treatment for weight restoration in this population. A 2008 survey of North American physicians treating adolescents with AN suggested a “tremendous variation in care”³¹ with refeeding regimens at initiation of treatment ranging from 100 to 1,500 kcal/day.³¹ Similarly, a recent study of Australian dietitians revealed discrepancies in estimation of the initial energy requirements for children and adolescent inpatients with AN.³²

Currently there is no evidence for the best approach to weight restoration in this population, because most recommendations are based solely on clinical experience and expert opinion.^{22,24,33} Empirical evidence to support best practice in this field is lacking.^{13,34} A systematic review of randomized controlled trials (RCTs) by Bulik and colleagues in 2007³⁵ found that no clinical trials on weight restoration in AN had been conducted, with the authors concluding that the literature “...has failed to address the optimal approach to renutrition...” in AN across the age groups. Therefore, due to the lack of empirical research on this topic, the aim of our study was to systematically review, assess, and summarize the available evidence on the effect of energy prescriptions during refeeding on weight restoration in hospitalized children and adolescents aged 19 years and younger with diagnosed AN.

METHODS

Methodology

This study was guided, where applicable, by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.³⁶ One key question and one subquestion were developed using the Patient, Intervention, Comparators, Outcome, Study Design criteria³⁷ as follows:

1. What is the strength of the evidence for the effect of the starting energy intake prescribed during refeeding on weight gain in inpatient underweight children and adolescents aged 19 years and younger with AN?
 - 1.1 What is the evidence of any adverse effects of refeeding conducted in an inpatient setting in an attempt to restore weight in underweight children and adolescents aged 19 years and younger with AN?

Inclusion and Exclusion Criteria

RCTs and observational studies published in English up to June 2012 were included in our review. RCTs are regarded as

the best evidence for treatment; however, based on a preliminary review of the literature and consultations with the experts, a lack of RCTs was expected; thus, observational studies were included per the inclusion/exclusion criteria listed in [Figure 1](#).

Literature Search

References were identified by an online search conducted between March and May 2012. Three electronic databases were searched: Scopus, Web of Science, and Global Health (CABI) for articles published up to May 2012 with a combination of broad key terms *anorexia nervosa*, *children or adolescent**, *inpatient*, *nutrition therapy*, and *hospital** (modified as required) to maximize article retrieval. The PubMed database and Cochrane Collaboration libraries were searched using Medical Subject Heading terms *anorexia nervosa* and *dietary therapy*, and *anorexia nervosa*, respectively. A citation search of the identified key studies was performed in the Web of Science database. Individual authors were contacted for further information where required.

The titles and abstracts of the retrieved articles were imported into a commercial reference management software package (EndNote version X4.0.2, 2010, Thomson Reuters) and all duplicates were excluded. One author reviewed the references to identify potentially eligible studies, with full articles obtained for the latter. The full articles were examined using a priori exclusion and inclusion criteria ([Figure 1](#)) by two authors using a previously developed form with any disagreement resolved through discussion. The categories for the data extraction were based on Patient, Intervention, Comparators, Outcome, Study Design criteria³⁷ ([Figure 1](#)). The primary measures sought were: energy intake at initiation of refeeding, maximum energy intake during hospitalization, methods of delivery, weight gain, and reported adverse effects. A meta-analysis could not be conducted due to the small number of studies that met the inclusion criteria as well as the lack of heterogeneity in their study designs, energy intake prescribed, feeding methods used, and duration of the follow-up. Rather, our systematic review focused on the description of the intervention and outcome measures, including weight changes during treatment and presence or absence of reported adverse events. A qualitative synthesis of the strength of available evidence was also conducted.

Quality Assessment

There is currently no agreed upon gold-standard tool for the quality assessment of observational studies.⁴¹⁻⁴⁴ Furthermore, the variety in design and methodology of studies included in our review introduced a propensity to bias; thus, a single tool was not applied. Instead, the quality assessment of the included studies was guided by the Cochrane risk of bias tools.⁴⁵ The risk of bias was rated in two areas that were applicable to all of the selected studies: study design and study reporting.

RESULTS

Results of the Literature Search

Overall, 593 nonduplicated publications were identified during the initial search, with nine additional articles identified through snowball sampling. A total of seven studies⁴⁶⁻⁵²

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