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## Sex Differences in Refeeding Among Hospitalized Adolescents and Young Adults with Eating Disorders

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### Abstract

**Objective**—To determine sex differences in refeeding (i.e., short-term nutritional rehabilitation) outcomes among hospitalized adolescents and young adults with eating disorders.

**Methods**—We retrospectively reviewed electronic medical records of 601 patients aged 9–25 years admitted to the University of California, San Francisco Eating Disorders Program for medical and nutritional management between May 2012 and August 2020. Descriptive statistics, crude, and adjusted linear regression models were used to assess the association between sex and nutritional outcomes and predictors of length of stay.

**Results**—A total of 588 adolescents and young adults met eligibility criteria (16% male, mean [SD] age 15.96 [2.75], 71.6% anorexia nervosa, admission percent median body mass index [%mBMI]  $87.1 \pm 14.1$ ). In unadjusted comparisons, there were no significant sex differences in prescribed kilocalories (kcal) per day at admission (2013 vs. 1980,  $p = .188$ ); however, males had higher estimated energy requirements (EER, kcal) (3,694 vs. 2,925,  $p < .001$ ). In linear regression models adjusting for potential confounders, male sex was associated with higher prescribed kcals at discharge ( $B = 835$  kcal,  $p < .001$ ), greater weight change ( $B = 0.47$  kg,  $p = .021$ ), and longer length of stay ( $B = 1.94$  days,  $p = .001$ ) than females. Older age, lower admission weight, lower prescribed kcal at admission, higher EER, and lower heart rate at admission were factors associated with longer length of stay in a linear regression model.

**Discussion**—These findings support the development of individualized approaches for males with eating disorders to improve quality of care and healthcare efficiency among an underserved population.

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**Conflicts of interest statement:** The authors have no conflict to declare.

Availability of Data, Materials and Code

The data that support the findings of this study are available on request from the corresponding author, JN. The data are not publicly available due to confidentiality restrictions; e.g., they contain information that could compromise the privacy of research participants.

## Keywords

eating disorders; male health; sex differences; adolescent; nutrition; refeeding; young adult; anorexia nervosa; bulimia nervosa

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## 1. Introduction

It is well documented that eating disorders are underrecognized and undertreated in males (Button et al., 2008; Forrest et al., 2017; Murray et al., 2018; Nagata et al., 2020; Strother et al., 2012). Males with eating disorders may have delays in identification, diagnosis, referral to care, and present with a high severity of illness (Forrest et al., 2017). This problem is in part due to a lack of evidence to support sex-specific medical treatment guidance for health care professionals to utilize in clinical settings (Ganson et al., 2019, 2021). This gap has been increasingly recognized (Ganson et al., 2019, 2021); however, sex-specific care is not currently reflected in the treatment guidance from the Society for Adolescent Health and Medicine or the National Institute for Health and Care Excellence (Ganson et al., 2019, 2021; Hilbert et al., 2017; National Institute for Health and Care Excellence, 2017; Society for Adolescent Health and Medicine et al., 2015). The need to fill this gap is pressing given that males with eating disorders experience significant medical complications, have high mortality rates, and are requiring hospitalization at increasing rates (Ganson et al., 2021; Girz et al., 2014; Linville et al., 2010, 2012; Quadflieg et al., 2019; Vo et al., 2016). Numerous studies have examined the impact of various refeeding (i.e., short-term nutritional rehabilitation) approaches on key hospital outcomes, including rate of weight gain, resolution of vital sign instability, and length of stay (Garber et al., 2013, 2021; Golden, Keane-Miller, Sainani, & Kapphahn, 2013; Parker et al., 2016).

Patients with malnutrition and acute medical instability are admitted to the hospital for refeeding (Garber et al., 2021). Strong evidence now supports higher calorie refeeding as being more efficacious than the enduring standard of care, lower calorie refeeding, and higher calorie refeeding has not been associated with increased safety concerns when administered under close medical supervision (Garber et al., 2021). The largest randomized controlled trial to date of meal-based refeeding in hospitalized adolescents and young adults reported a three-day longer hospital stay in patients refed on lower calories, which incurred \$20,000 USD in additional healthcare costs and was attributable to slower restoration of medical stability (reversal of vital sign abnormalities) (Garber et al., 2021). However, these studies have primarily included females and used a standard caloric prescription regardless of sex. Because it is well established that males have higher energy needs than females (Institute of Medicine, 2005; Mifflin et al., 1990), starting males and females at similar initial caloric prescriptions may lead to underfeeding in males and extend their hospital stay. Characteristics that may impact refeeding, such as body weight and energy requirements, have not been described in males (Garber et al., 2013; Girz et al., 2014). Thus, current approaches do not reflect unique factors which may impact the course of treatment for males, including greater energy requirements due to greater body weights, metabolic response, and exercise (Whitelaw & Nagata, 2021).

To our knowledge, no studies have examined sex differences in inpatient nutritional rehabilitation of adolescents and young adults with eating disorders. Therefore, the objective of this study was to determine sex differences in nutritional management including nutrition prescriptions at admission and discharge, weight change, and length of stay among a sample of adolescents and young adults hospitalized for eating disorders. We hypothesized that males would have similar admission nutrition prescriptions but require greater nutrition prescriptions at discharge (which are more reflective of actual metabolic needs), leading to prolonged vital sign instability and longer lengths of stay. As a secondary objective, we aimed to determine nutritional factors associated with greater lengths of stay. These investigations can inform a more individualized approach for inpatient nutritional management of adolescent and young adults, particularly males, with eating disorders.

## 2. Methods

### 2.1 Study population

We retrospectively reviewed the electronic medical record (EMR) of 601 patients, who were aged 9–25 years, presenting for an evaluation to the Eating Disorders Program at the University of California, San Francisco (UCSF), between May 2012 and August 2020. Although some patients were initially diagnosed using DSM-IV criteria (prior to 2013), we reviewed their clinical and psychosocial characteristics and recategorized them using DSM-5 criteria.

We used the following inclusion criteria to determine the sample: patients aged 9–25 years with an initial hospitalization for the medical management and nutritional refeeding of an eating disorder between May 22, 2012 and August 31, 2020. A total of 13 patients were excluded from the study because they left against medical advice or were transferred to an inpatient psychiatric hospital, were diagnosed with a medical comorbidity that required ending the refeeding protocol and/or transferring to a hospital medicine team, did not see a dietitian, or were not admitted for an eating disorder. Patients who were assigned a lower intake of kilocalories (kcal) as part of the Study of Refeeding to Optimize iNpatient Gains (StRONG), a prospective randomized controlled trial examining two different diets for nutritional rehabilitation during hospitalization, were excluded; most others received a fixed starting caloric prescription (Garber et al., 2021; Golden et al., 2021). Details on treatment center protocols and study design can be found in Appendix 1. The final sample was 588 patients.

### 2.2 Study design

Clinical and hospital staff, including registered dietitians with the UCSF Eating Disorders Program, completed assessments for the purposes of medical care. We then retrospectively reviewed their clinical assessments in the EMR and entered them into the UCSF Eating Disorder Program Medical Database. We collected demographics, anthropometric measures, disease characteristics, and nutrition data documented in the EMR. Length of stay was calculated using admission and discharge dates. Weight change was calculated using admission and discharge weight measurements. Body mass index (BMI, kg/m<sup>2</sup>) was calculated using initial weight and height measurements measured at admission. Percent

median BMI (%mBMI) was calculated using calculated BMI and median BMI for age and sex. Prescribed intake of kcals at admission and discharge, estimated energy requirements (EER), and treatment goal weights were extracted from diet orders placed in the EMR and registered dietitian notes. Heart rate at admission was extracted from the EMR. This retrospective study was approved by the UCSF Institutional Review Board (IRB).

### 2.3 Statistical analysis

Data cleaning was completed using R (R Foundation for Statistical Computing, Vienna, Austria) and data analysis was conducted using Stata 15.1 (StataCorp LP, College Station, TX). Unadjusted differences between males and females in demographic characteristics, BMI, weight change, diagnosis, length of stay, kcals at admission and discharge, treatment goal weights, and EER were calculated using independent sample t-tests or Fisher's exact tests. Although data were not normally distributed, the sample size was sufficiently large to conduct linear regression (Lumley et al., 2002). Multiple linear regression analyses were used to examine the association between dependent study variables (admission kcals, discharge kcals, weight change, and length of stay) and sex as the independent variable, adjusted for age (adolescent vs. young adult), race/ethnicity (White vs. non-White), and diagnosis (anorexia nervosa vs. non-anorexia nervosa). A linear regression model with length of stay as the dependent variable and sex, age, admission weight, kcals at admission, EER, and heart rate at admission as the independent variables was conducted. We conducted a separate subgroup analysis for individuals diagnosed with anorexia nervosa (supplemental Table 1).

## 3. Results

### 3.1 Unadjusted demographic and nutrition hospitalization characteristics

The retrospective chart review included 95 male and 493 female adolescents and young adults. Demographic and nutrition hospitalization characteristics by sex are shown in Table 1. The average age, BMI, %mBMI, weight change, length of stay, and initial intake of kcals was 15.96 years, 17.57 kg/m<sup>2</sup>, 87.1%, 2.47 kg, 9.64 days, and 1985 kcals, respectively. There were no significant sex differences in age, BMI, %mBMI, or weight change. There were no significant sex differences in percent of treatment goal weight at admission, discharge or change from admission to discharge. There were no sex differences in prescribed kcal at admission, but males had a higher prescribed kcal at discharge (3796 ± 647 kcal vs 3002 ± 437 kcal, Cohen's d=1.66, p < .001). Males had a longer length of stay (11.01 ± 4.86 vs 9.38 ± 5.02 days, Cohen's d=0.33, p = .004) and higher EER (3694 ± 529 kcal vs 2925 ± 254 kcal, Cohen's d=2.44, p < .001) than females. Notably, males were prescribed a lower percentage of their EER at admission compared to females (55.49% ± 10.86% vs 68.03% ± 8.56%, Cohen's d=1.40, p < .001) but there were no significant differences at discharge. Findings were similar in a subgroup analysis limited to those with anorexia nervosa (supplemental Table 1).

### 3.2 Correlates of nutrition status

The linear regression models examining sex differences adjusted for covariates are summarized in Table 2. Male sex was significantly associated with higher discharge kcals (B

= 835.82 higher calories than females,  $p < .001$ ), greater weight change ( $B = 0.47$  kg more than females,  $p = .021$ ), and greater length of stay ( $B = 1.94$  days longer stay than females,  $p < .001$ ) when adjusting for age, race/ethnicity, and diagnosis. Beginning kcals were not significantly associated with sex when adjusting for age, race/ethnicity, and eating disorder diagnosis.

### 3.3 Factors associated with length of stay

In a linear regression model (Table 3), older age, lower admission weight, lower prescribed kcal at admission per 1000 kcal, higher EER per 1000 kcal, and lower heart rate at admission were associated with longer length of stay. Every 1000 lower kcal prescribed at admission was associated with a 3.99 day longer length of stay. Every 1000 greater kcal in the EER was associated with a 1.61 day longer length of stay.

## 4. Discussion

In this retrospective chart review of adolescents and young adults hospitalized at a tertiary care hospital for medical stabilization and nutritional refeeding for an eating disorder, we found that males required a longer length of stay than females, though most male and female patients were prescribed a standard diet around 2000 kcals at admission. Extended stay was related to higher energy requirements, which are calculated based on goal weight and height and known to differ by sex (Institute of Medicine, 2005; Mifflin et al., 1990). Although the finding that males have greater kcal requirements is not unexpected, this study is among the first to document the association of sex with increased length of stay, suggesting that current treatment guidelines may be inadequate for males. Because discharge was based on medical stability (e.g., vital signs), we suspect that the underfeeding of males contributed to increased hospitalization time.

We found that male adolescents and young adults hospitalized for eating disorders were prescribed greater kcals at discharge than females. This is consistent with prior literature (Whitelaw & Nagata, 2021). Overall, adolescent and young adult males have greater EER than females, in part due to body weight and height, physical activity, and metabolic demands. Adolescent males with eating disorders report over 8 hr of exercise per week, and half of adolescent males with eating disorders report engaging in team sports (Nagata et al., 2017; Whitelaw & Nagata, 2021). Although most studies of refeeding in eating disorders are based on predominantly female samples, the seminal study of starvation, the Minnesota Starvation Experiment, was based on young men (Keys, 1950). After a 24-week period of semi-starvation, when average daily intake was reduced to 1,570 kcals per day, participants were refeed on a controlled diet and required approximately 4,000 kcal per day to promote weight gain. This was similar to our finding of 3,800 kcals at discharge in males and may reflect a hypermetabolic state associated with refeeding. Different age groups may account for some differences given that our study included adolescents.

### 4.1 Clinical protocols are not sex specific

Although there are wide variations in clinical practice for inpatient nutritional refeeding, current guidance does not address sex differences and many current refeeding protocols

across the US, including our own, are not sex-specific (Garber et al., 2021; Golden et al., 2021; Maginot et al., 2017; Peebles et al., 2017; Smith et al., 2016). However, our finding that hospitalized males with eating disorders generally have greater prescribed kcal/day at discharge and have increased length of stay based on medical instability criteria emphasizes the need for further research on sex-specific treatment approaches. Protocols could be individualized to improve care for males by starting males at a higher kcal/day diet to account for their greater energy requirements. Protocols could consider current weight, goal weight, %mBMI, and calories ingested prior to admission. Other potential options include advancing kcal/day more rapidly in males; there are already published protocols that advance by 400 kcal/day (Peebles et al., 2017). These adaptations could lead to improved care and avoid prolonged hospitalizations for males; however, future research is needed to determine their efficacy and safety. Clinical guidance such as the Society for Adolescent Health and Medicine Position Paper on the Medical Management of Restrictive Eating Disorders could also provide further sex-specific guidance for inpatient refeeding (Society for Adolescent Health and Medicine et al., 2015).

## 4.2 Predictors of length of stay

We found that in general, males had greater lengths of stay than females hospitalized for eating disorders. Factors associated with a longer length of stay included older age, a lower admission weight, a lower prescribed kcal at admission, a higher EER, and a lower heart rate. Males have higher EER and are prescribed a lower percentage of their EER at admission under many protocols, suggesting that the underfeeding of males with eating disorders could contribute to their longer lengths of stay, which is based on achievement of medical stability at this institution (National Institute for Health and Care Excellence, 2017; Robinson & Rhys Jones, 2018). Length of stay is an important clinical outcome in terms of healthcare costs, efficacy of treatments, and patient satisfaction (Owens et al., 2019). Males may present for treatment in poorer health (e.g., in our anorexia nervosa subgroup analysis, males presented with lower heart rate [Table S1]), due to diagnosis and treatment delays, thus requiring more time in care. These findings emphasize the need for more training for clinical professionals to identify, diagnose, and treat eating disorders among males to ensure positive prognosis.

## 4.3 Limitations/Strengths

Several limitations of the study should be noted, including its retrospective and observational nature, which preclude causal inferences. Findings are from a single tertiary care hospital in Northern California and may not be generalizable to other populations. Practice guidelines, including treatment protocols and discharge criteria, vary across institutions and internationally. Although the treatment protocol at this institution is supported by national guidelines (Society for Adolescent Health and Medicine et al., 2015) and is similar to other institutions across the United States (Golden et al., 2021; Maginot et al., 2017; Peebles et al., 2017; Smith et al., 2016), the clinical implications of this study may be less generalizable outside of the United States. Certain racial groups were under-represented in our sample but reflect the patient demographics hospitalized in our program. Although there were no significant differences in demographic or anthropometric data between those included in the study and those excluded, selection bias may arise as a result of the study being conducted

at a single institution. Finally, pubertal status of the participants was not adjusted for in the analysis. Also, given that EER is based partially on physical activity and we generally used a fixed activity factor in the calculations, EER values may be less accurate. Strengths of the study include over eight years of clinical data evaluated by a specialized eating disorder team including registered dietitians. It is noteworthy that over 16% (n=95) of the sample was male and this represents the first study, to our knowledge, to examine sex differences related to inpatient nutritional refeeding for eating disorders.

## 5. Conclusions

We report for the first time that males hospitalized for eating disorders require higher kcal/day at discharge than females and have an increased length of stay. Although male patients have higher energy requirements, most clinical protocols and national (United States) guidelines standardize the beginning kcal/day regardless of sex, which may lead to inferior care for males with eating disorders—an already understudied and underserved population. Clinical protocols and guidelines may consider incorporating sex-specific guidance for inpatient nutritional management, such as starting males at higher prescribed kcal/day at admission, taking weight into account when prescribing starting kcal/day, or advancing kcal/day more rapidly in males to avoid prolonged and costly hospitalizations. Future research can inform other aspects of eating disorder treatment to be more inclusive of and improve care for male populations. There is also a need to explore how other sociodemographic factors, such as age and race/ethnicity, influence treatment practices and outcomes.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1.**

Demographic characteristics and nutritional status of adolescents and young adults hospitalized for eating disorders by sex <sup>a</sup>

Characteristic	Total (N=588) <sup>b</sup>	Sex		P-value <sup>d</sup>
		Male (N = 95) <sup>c</sup>	Female (N = 493) <sup>c</sup>	
Age, years	15.96 ± 2.75	16.23 ± 2.64	15.90 ± 2.77)	0.280
Race/ethnicity, N (%)				<b>0.014</b>
Non-Hispanic white	348 (59.18)	46 (48.42)	302 (61.26)	
Hispanic	101 (17.18)	27 (28.42)	74 (15.01)	
Asian or Native Hawaiian and Other Pacific Islanders	47 (7.99)	6 (6.32)	41 (8.32)	
Multiracial	32 (5.44)	5 (5.26)	27 (5.48)	
Other	30 (5.10)	3 (3.16)	27 (5.48)	
Unknown/Declined	17 (2.89)	3 (3.16)	14 (2.84)	
Non-Hispanic Black or African American	13 (2.21)	5 (5.26)	8 (1.62)	
BMI, kg/m <sup>2</sup>	17.57 ± 2.96	17.97 ± 3.78	17.49 ± 2.77	0.142
% median BMI	87.09 ± 14.10	87.63 ± 17.39	86.99 ± 13.4	0.685
Weight change, kg	2.47 ± 1.82	2.73 ± 2.00	2.42 ± 1.78	0.118
% TGW <sup>f</sup>				
Admission	81.24 ± 9.28	81.09 ± 10.60	81.27 ± 9.02	0.860
Discharge	85.73 ± 8.72	85.49 ± 9.94	85.77 ± 8.47	0.777
Change	4.56 ± 3.23	4.58 ± 2.92	4.55 ± 3.28	0.947
Diagnosis, N (%)				<b>0.012</b>
Anorexia Nervosa	421 (71.60)	58 (61.05)	363 (73.63)	
Unspecified Feeding and Eating Disorder (UFED)	58 (9.86)	9 (9.47)	49 (9.94)	
Other	44 (7.48)	12 (12.63)	32 (6.49)	
Avoidant Restrictive Food Intake Disorder (ARFID)	36 (6.12)	13 (13.68)	23 (4.67)	
Other Specified Feeding and Eating Disorder (OSFED)	19 (3.23)	2 (2.11)	17 (3.45)	
Bulimia Nervosa	9 (1.53)	1 (1.05)	8 (1.62)	
Binge-eating Disorder	1 (0.17)	0	1 (0.20)	
Heart rate at admission, beats per minute	62.02 ± 17.74	61.17 ± 19.30	62.18 ± 17.44	0.612
Length of stay, days	9.64 ± 5.03	11.01 ± 4.86	9.38 ± 5.02	<b>0.004</b>
Prescribed kcal				
Admission	1985 ± 223	2013 ± 311	1980 ± 202	0.188
Discharge	3130 ± 559	3796 ± 647	3002 ± 437	<b>&lt;0.001</b>
EER <sup>g</sup> , kcal	3049 ± 423	3694 ± 529	2925 ± 254	<b>&lt;0.001</b>
% of EER <sup>g</sup>				
Admission	66.01 ± 10.08	55.49 ± 10.86	68.03 ± 8.56	<b>&lt;0.001</b>
Discharge	102.91 ± 13.44	103.51 ± 14.94	102.80 ± 13.14	0.638

<sup>a</sup>Table values are mean ± SD for continuous variables and n (column %) for categorical variables.

<sup>b</sup>Due to missing data, sample sizes for % TGW were 582 and 584 for EER and % EER.

<sup>c</sup>Percentages may not sum to 100% due to rounding.

<sup>d</sup>P-value is for t-test or Fisher's Exact test as appropriate for continuous and categorical variables, respectively.

<sup>f</sup>TGW = Treatment Goal Weight

<sup>g</sup>EER= Estimated Energy Requirements

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**Table 2.**

Associations between male sex and eating disorder hospitalization outcomes in adjusted multiple linear regression analyses <sup>a</sup>

Outcome	Male sex, B (95% CI) <sup>b</sup>	p
Prescribed kcal at admission	29.32 (-20.74, 79.39)	0.250
Prescribed kcal at discharge	835.82 (730.13, 941.51)	< <b>0.001</b>
Weight change, kg	0.47 (0.07, 0.87)	<b>0.021</b>
Length of stay, days	1.94 (0.83, 3.05)	<b>0.001</b>

<sup>a</sup>The table represents the abbreviated output from four linear regression models, each adjusted for age (adolescent vs. young adult), race/ethnicity (white vs non-white), and eating disorder diagnosis (anorexia nervosa vs. non-anorexia nervosa).

<sup>b</sup>Females are the reference category in all models.

**Table 3.**Factors associated with length of stay, adjusted linear regression analysis<sup>a</sup>

Predictors	B (95% CI) <sup>b</sup>	p
Male sex	1.20 (-0.21, 2.62)	0.094
Age, years	0.18 (0.04, 0.33)	<b>0.016</b>
Weight at admission, kg	-0.10 (-0.14, -0.06)	<b>&lt;0.001</b>
Prescribed kcal at admission (per 1000 kcal)	-3.99 (-5.79, -2.18)	<b>&lt;0.001</b>
EER (per 1000 kcal) <sup>b</sup>	1.61 (0.28, 2.94)	<b>0.018</b>
Heart rate at admission	-0.05 (-0.07, -0.03)	<b>&lt;0.001</b>

<sup>a</sup>The table represents outputs from a single linear regression model including all six listed predictor variables. Due to missing data, the sample size is 584

<sup>b</sup>EER = Estimated Energy Requirements