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RESEARCH ARTICLE

Early within-person weight gain and variability during inpatient treatment for anorexia nervosa: Age-dependent effects on treatment outcome

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Abstract

Objective: Early weight gain during inpatient treatment for anorexia nervosa (AN) is a dynamic process characterised by within-person variability that may be age-dependent. We examined whether age moderates the effect of within-person weight gain and variability on treatment outcome.

Method: Within-person level estimates of $N = 2881$ underweight adolescents and adults with AN for daily average weight gain (linear slope) and variability (root mean squared errors) were obtained using random-effects modelling. Between-person level regression analyses were calculated to assess effects on weight, eating disorder psychopathology and attaining normal body weight (body mass index [BMI]: 18.5–25 kg/m^2).

Results: Higher weight gain during first 2 weeks of inpatient treatment predicted higher weight, lower drive for thinness and lower body dissatisfaction at discharge, but not lower bulimic symptoms. Moreover, it predicted a higher probability of discharge weight within normal range. Younger age was associated with stronger effects of early weight gain on weight, drive for thinness and body dissatisfaction at discharge. Weight variability was not associated with any outcome.

Conclusions: Age moderated effects of early weight gain on treatment outcomes, with larger effects for younger patients. Weight variability alone did not influence treatment across age and should be of lesser clinical concern during early inpatient treatment.

KEYWORDS
anorexia nervosa, body weight, eating disorder, inpatient treatment, variability, weight gain

Abbreviations: AN, Anorexia Nervosa; BMI, Body Mass Index; BMI-SDS, Body Mass Index Standard Deviation Score; ED, Eating Disorder; EDI-2, Eating Disorder Inventory-2; RMSE, Root-Mean-Squared Error.

Highlights

- Higher weight gain during early inpatient treatment predicted higher weight, lower drive for thinness and lower body dissatisfaction at discharge.
- Younger age was associated with stronger effects of early weight gain on treatment outcome.
- Weight variability during early inpatient treatment was not associated with treatment outcome.

1 | INTRODUCTION

Anorexia nervosa (AN) is a serious eating disorder (ED) often associated with severe underweight (Attia, 2010). Hence, weight restoration is a primary goal for AN treatment, but rapid and continued weight gain is often only achievable with intensive inpatient treatment, especially when body weight is extremely low (e.g., Resmark et al., 2019). Still, a substantial proportion of adolescents and adults receiving inpatient treatment for AN do not achieve remission at end of treatment (Dalle Grave et al., 2020; Isserlin et al., 2020; Schlegl et al., 2014, 2016). Thus, it is necessary to identify potential early predictors of treatment outcome to increase treatment success and prevent prolonged inpatient treatment. In addition, differences in baseline conditions (e.g., duration of illness, symptom severity) and treatment trajectories between adolescents and adults with AN have been observed (Fisher, 2003; Fisher et al., 2001), underlining that age-dependent effects should be considered. The present study therefore aims to explore whether weight gain and weight variability during early treatment are age-dependent predictors of later treatment outcome in adolescent and adult inpatients with AN.

1.1 | Effects of early weight gain on treatment outcome

Early weight gain during inpatient treatment for AN has been repeatedly identified as an important and robust predictor of treatment success both at end of treatment and follow-up (Nazar et al., 2017; Vall & Wade, 2015). For example, there is evidence that clinical deterioration occurred less often at 1-year follow-up for adolescents and adults who gained ≥0.8 kg per week during inpatient treatment (Lund et al., 2009). Slower weight gain was associated with a higher risk of readmission after treatment in adolescents with AN (Castro et al., 2004). Studies investigating weight trajectories of both adolescents and adults with AN at an individual level identified that within-person weight gain in the first 2 weeks of inpatient treatment was strongly associated with optimal weight gain during remaining inpatient treatment, highlighting the importance of enabling initial weight gain (Chatelet et al., 2020). In addition, this study found a higher proportion of adults compared to adolescents in the inadequate weight gain group, indicating that younger age might be associated with higher early weight gain. However, age was treated as categorical in this study, and analysing age as continuous might further clarify this association. In addition, a similar study found that weight loss during the first 4 weeks of inpatient treatment was a strong predictor of treatment failure (Hartmann et al., 2007). Finally, patients with a fast weight gain trajectory during an inpatient refeeding protocol exhibit higher body mass index (BMI) at discharge and follow-up compared to patients following a slow or optimal weight gain trajectory (Makhzoumi et al., 2017), further underlining the importance of rapid weight gain in the treatment of AN.

1.2 | Effects of weight variability on treatment outcome

Only few patients show a steadily increasing weight trajectory in clinical practice. Consistently, Hart et al. (2011) noted that weight gain in underweight adolescent and adult patients with AN is highly variable, with some patients showing even no weight gain at all during inpatient treatment. A newer study identified subgroups of patients with AN based on their weight trajectories, indicating that some patients with AN continually gain weight, some reach a weight plateau, some appear treatment resistant with no weight gain or even weight loss, and a small group of patients shows substantial weight fluctuations throughout inpatient treatment (Jennings et al., 2018). However, these groups did not differ in overall change in body weight, further indicating that investigating weight gain and variability at an individual level is warranted.

From a clinical perspective, variability in weight *within* and not *between* individuals is of special interest,

as clinicians are often facing large weight fluctuations especially during the first 2 weeks of inpatient treatment (Chatelet et al., 2020; Hartmann et al., 2007). Thus, it can be challenging to predict whether early sudden weight gains or losses are reflective of overall weight gain during inpatient treatment or merely fluctuations around a weight gain trend, and how these fluctuations are related to treatment outcome. Within-person weight variability during early treatment might therefore be investigated as an additional predictor of treatment outcome in individuals with AN.

Examining associations of within-person variability on between-person outcomes requires complex statistical models, which is why only few studies so far investigated individual weight variability. For example, Hartmann et al. (2007) found a statistically significant negative association of within-person weight variability during week 3–4 of inpatient treatment on treatment success at discharge. Recently, a similar analysis in a treatment-seeking sample of individuals with bulimia nervosa found significant associations of within-person weight variability with core ED psychopathology at 6-month follow-up (Chen et al., 2021). Yet, it is unknown whether similar associations of weight variability with core ED pathology can be found in AN. Furthermore, both studies did not include age or treatment duration as covariates in their regression models, which are known predictors of treatment outcome, and possibly inflating the impact of their findings. Especially regarding age of individuals with AN, there is evidence that younger age is associated with faster weight gain (Zeeck et al., 2018) and a slightly better treatment outcome for adolescents compared to adults (Fisher, 2003). Therefore, it seems worthwhile to investigate moderating effects of age on weight gain and weight variability of patients with AN when analysing weight trajectories during inpatient treatment.

1.3 | Current study

Overall, early weight gain in inpatient treatment of adolescents and adults with AN has reliably been associated with treatment outcome. Less research investigated whether weight fluctuations around individual weight change during early treatment are also associated with treatment outcome, and no study so far examined age as a moderator of the association of individual weight trajectories in early inpatient treatment on outcome at discharge. In addition, most of these studies were based on small sample sizes, which might inflate effect sizes, warranting replication in larger datasets. Therefore, the current study examined the unique effects of individual weight gain and weight variability during early inpatient treatment on discharge weight, core ED psychopathology and attaining normal weight range at discharge. Finally, we explored whether age would be a moderator of the effects of weight gain and weight variability on treatment outcome in a very large sample of adolescents and adults with AN.

2 | METHOD

2.1 | Participants and procedure

The present analysis is based on data of $N = 3755$ adolescent and adult patients with AN that were consecutively admitted between July 2014 and July 2020 to the Schoen Clinic Roseneck, a large inpatient treatment centre in Southern Germany specialised in the treatment of EDs. All patients were diagnosed with either full-threshold or atypical AN according to the International Statistical Classification of Diseases, 10th revision (World Health Organization, 2004) by an experienced clinician at admission. Atypical was defined as one or more of the DSM-5 symptoms were only partially fulfilled but a clinical impression of AN emerged (e.g., less fear of weight gain than usual). Of note, all patients were underweight and patients with atypical AN did not differ from patients with full-threshold AN regarding average daily weight gain and weight variability estimates during early treatment (all $t\,(216) = 0.92$, $p > 0.361$). All patients received intensive cognitive behavioural therapy-oriented multimodal inpatient treatment, including individual psychotherapy and group therapy sessions twice per week, body image exposure, supervised meals, meal preparation courses, and exercise therapy (for a detailed treatment overview please cf. Meule et al., 2021). In addition, the treatment also included high-caloric oral refeeding to achieve a target weight gain of 700–1000 g per week (male patients: 800–1100 g). Enteral or parenteral refeeding was not administered on a regular basis, but in very few occasions nasogastric tube feeding was prescribed. All patients were admitted to the inpatient treatment by self-admission or referral by a clinician without a motivational threshold. Approximately 90% of admitted patients complete inpatient treatment. For the current study, patients were included when they were underweight (BMI ≤ 18.5 kg/m^2) to assure that weight restoration was a primary treatment target. Exclusion criteria were a) inpatient treatment for less than 14 days or b) more than 180 days, and c) missing weight data in the week prior to discharge. The final sample size consisted of $N = 2881$ patients. Baseline characteristics of the patients are provided in the results section.

2.2 | Measurements

Weight and height were recorded at admission using medical scales. Furthermore, patients were weighed at least twice a week to daily by nurses, depending on underweight severity at admission. Weights within 14 days after admission and at discharge were included. Furthermore, age, sex and treatment duration were recorded. BMI (kg/m^2) and age−adjusted standardized BMI (BMI-SDS) were calculated. Similar to Chatelet et al. (2020), we used a 2-week timeframe for our study as we were especially interested in very early weight gain and variability, as these estimates are most likely to be reflective of motivation to treatment and less influenced by therapeutic decisions. Furthermore, using a 2-week time frame allowed to include patients into the study that dropped out of treatment very early.

2.2.1 | Eating disorder inventory-2

The Eating Disorder Inventory-2 (EDI-2) (Garner, 1991) is a well-validated and widely used multidimensional assessment of the specific psychopathology of patients with EDs. Instead of using sum scores, we used item mean scores of the first three scales (drive for thinness, bulimia and body dissatisfaction) of the German version of the EDI-2 (Thiel et al., 1997) to assess three core ED symptoms at admission and discharge. This way, the scores on the three scales are comparable in size as the body dissatisfaction scale contains two more items than the drive for thinness and bulimia scale. The German EDI-2 is scored on a scale ranging from "1 – never" to "6 – always". Unlike the original version, the German version does not collapse the lowest three response categories into zero and counts the upper three categories from one to three, but rather maintains a scale ranging from one to six. Internal consistency was excellent both at admission ($0.85 < \alpha < 0.92$) and discharge ($0.81 < \alpha < 0.93$) in our sample.

2.3 | Statistical analyses

All analyses were carried out with *R* v4.0.3 (R Core Team, 2020) and RStudio v1.3.1093 (RStudio Team, 2020), using the packages nlme v3.1–152 (Pinheiro et al., 2020), tidyverse v1.3.0 (Grolemund et al., 2019) and interactions v1.1.0 (Long, 2019). All continuous predictors were centred at the grand-mean, with the exception of age, which was centred at 18 years to facilitate assessing differences between adults and adolescents.

2.3.1 | Modelling intraindividual weight gain and variability estimates

As patients were required to gain weight during inpatient treatment, we computed two estimates to disentangle linear weight gain and weight variability at the individual level (Level-1). To do so, we computed a random-effects model using maximum likelihood with intercept, slope of day (ranging from day 0 to day 13, with day 0 reflecting admission day) and residuals. Root-mean-squared errors (RMSE) were calculated of the individual residuals. Thus, the intercept can be interpreted as an estimate for weight at admission and the slope of day as the average daily weight gain of a patient, whereas the RMSE is an estimate of the detrended weight variability of each patient around the regression line (for an illustration see Figure 1). Root-mean-squared errors and average daily weight gain were then winsorized at the 5% and 95% percentiles to manage the impact of extreme outliers and to meet assumptions for the level-2 models. A similar winsorisation procedure was used to estimate weight variability in individuals with obesity and bulimia nervosa (Benson et al., 2020; Chen et al., 2021).

2.3.2 | Estimating the age-dependent effects of weight gain and variability on treatment outcome

We then used the Level-1 estimates in multiple linear and logistic regression models to investigate whether early individual weight gain and intraindividual weight variability predicted treatment outcome. In a set of multiple linear regression models, we disentangled linear growth and weight variability by including average daily weight gain, RMSE and their interactions with age simultaneously. In all models, sex, age, admission weight estimate (i.e., the individual Level-1 intercept), and treatment duration were included as covariates. Outcome variables were discharge weight and ED core psychopathology (drive for thinness, bulimia, and body dissatisfaction) as measured with the EDI-2 subscales. The respective admission score of the outcome variable was also included as a covariate. To estimate the influence of average daily weight gain and intraindividual weight variability during early inpatient treatment on attaining a weight within the normal weight range at discharge, we computed a logistic regression model with the same set of predictors and covariates. Attaining normal weight was operationalised as whether an individual patient reached BMI $\geq$ 18.5 kg/m^2 at discharge, which reflects normal weight according to the World Health Organization (2000). Moderating effects of predictor by age interactions were investigated using

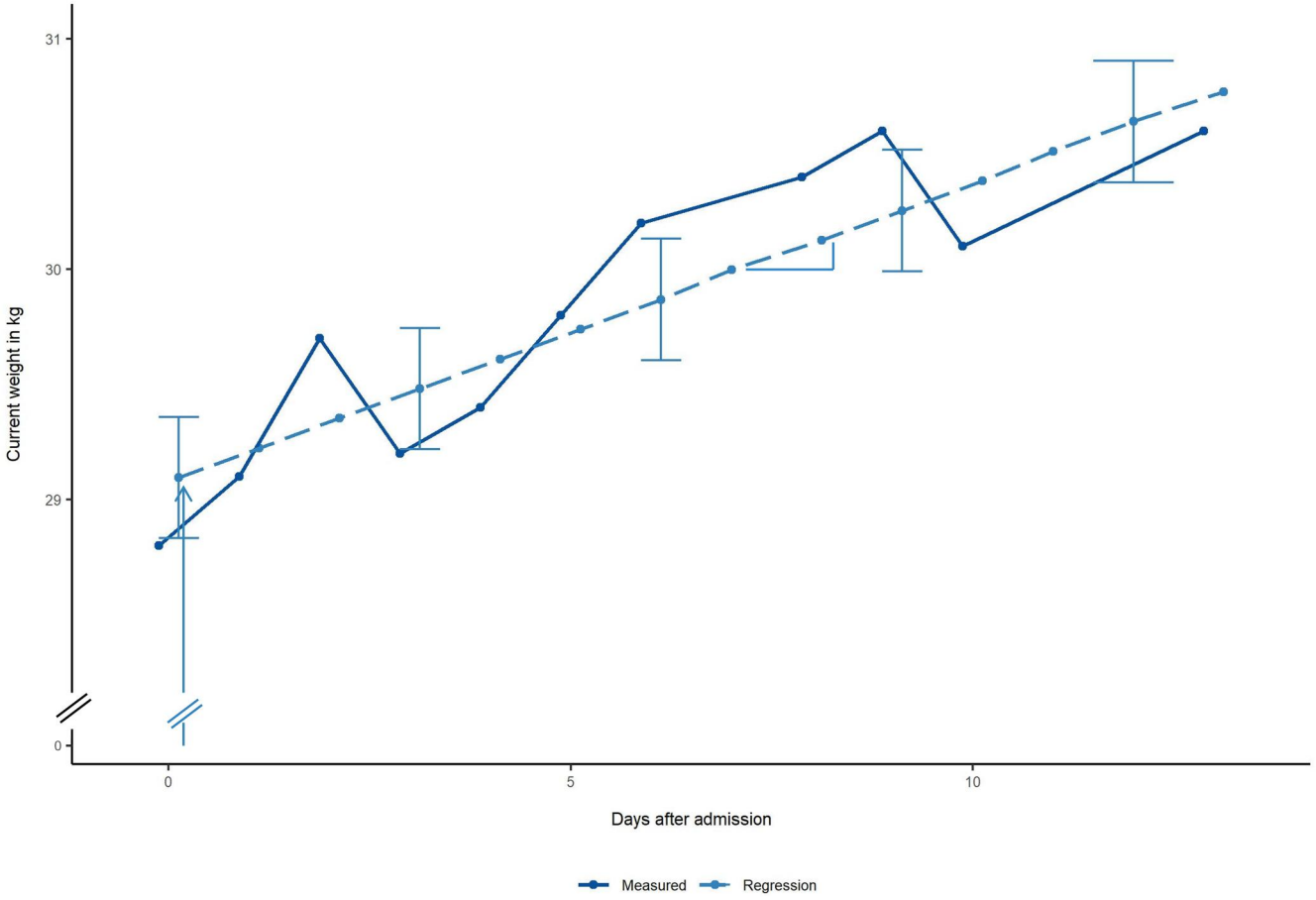

FIGURE 1 Comparison of measured weights of a patient with anorexia nervosa (AN) with the Level-1 linear regression coefficients during 2 weeks after admission to inpatient treatment. Measured body weight (straight line) and body weight regressed on measurement day (dashed line) of an exemplary patient during the first 2 weeks after admission to inpatient treatment. The arrow indicates the intercept of the regression. The error bars indicate the weight variability estimates of the regression model (root-mean-squared error based on individual residuals). The snapped line indicates the average weight gain between to measurement days (slope of day) [Colour figure can be viewed at wileyonlinelibrary.com]

simple slope analyses (Aiken & West, 1991), and Johnson-Neyman plots (Johnson & Neyman, 1936) were computed to visualise regions of significance. *p*-values of the Johnson-Neyman plots were adjusted using the procedure of Esarey and Sumner (2017).

As our hypotheses have not been preregistered, we consider our analyses exploratory. Still, we applied a familywise Bonferroni-Holm correction (Holm, 1979) to each multiple regression model to account for multiple comparisons of predictors of interest ($\alpha = 0.05/4$). Thus, the lowest critical significance threshold was set at $p < 0.0125$.

3 | RESULTS

3.1 | Study demographics

Data of $N = 2881$ patients (1186 adolescents aged 12–17 years and 1695 adults) were analysed. Table 1 depicts admission and discharge characteristics of key measures. Body mass index at admission (overall range: 8.96–18.50 kg/m^2) was significantly higher in adolescents compared to adults (t (2846.5) = 3.63, $p < 0.001$). Regarding EDI-2 admission scores, no differences between adults and adolescents were found for the drive for thinness subscale (t (2000.2) = 0.70, $p = 0.487$). However, adults showed higher bulimia scores compared to adolescents (t (2319.9) = −9.45, $p < 0.001$), whereas adolescents showed higher body dissatisfaction scores compared to adults at admission (t (2051.1) = 2.58, $p = 0.010$). In addition, more adults ($N = 664$, 39.2%) had missing values in their EDI-2 scores compared to adolescents ($N = 342$, 28.8%; total sample: $N = 1006$, 34.9%, $\chi^2 = 32.81$, $p < 0.001$). Patients were treated on average for 87.94 days ($SD = 40.61$), with a statistically significant difference (t (2608.3) = 5.23, $p < 0.001$) between adolescents ($M = 92.61$; $SD = 39.54$ days) and adults ($M = 84.67$; $SD = 41.04$ days).

TABLE 1 Sample characteristics at admission and discharge for the total, adolescent and adult samples

	Adolescents		Adults		Total sample	
	N = 1186		*N* = 1695		*N* = 2881	
	M	*SD*	*M*	*SD*	*M*	*SD*
Age (years)	15.5	1.26	27.1	10.1	22.31	9.65
Length of inpatient treatment (days)	92.61	39.54	84.67	41.04	87.94	40.61
	N	%	*N*	%	*N*	%
Discharge BMI ≥ 18.5 kg/m^2	357	30.1	715	42.18	1072	37.21

	Admission		Discharge			Admission		Discharge			Admission		Discharge		
	M	*SD*	*M*	*SD*	*d*[a]	*M*	*SD*	*M*	*SD*	*d*[a]	*M*	*SD*	*M*	*SD*	*d*[a]
BMI (kg/m^2)	15.2	1.58	17.67	1.56	1.58	14.9	2.03	17.78	2.15	1.67	15.05	1.86	17.74	1.93	1.6
BMI-SDS	−2.75	1.20	−1.24	0.92	1.39	−4.52	2.08	−2.42	1.59	1.30	−3.79	1.97	−1.94	1.48	1.3
EDI-2 drive for thinness[b]	4.20 (29.4)	1.43 (10.01)	3.25 (22.75)	1.40 (9.80)	−0.77	4.16 (29.12)	1.33 (9.31)	3.20 (22.40)	1.32 (9.24)	−0.82	4.18 (29.26)	1.37 (9.59)	3.22 (22.54)	1.36 (9.52)	−0.8
EDI-2 bulimia[b]	1.79 (12.53)	0.99 (6.93)	1.37 (9.59)	0.56 (3.92)	−0.45	2.25 (15.75)	1.34 (9.38)	1.41 (9.87)	0.67 (4.69)	−0.63	2.06 (14.42)	1.34 (9.38)	1.39 (9.73)	0.62 (4.34)	−0.51
EDI-2 body dissatisfaction[b]	4.37 (39.33)	1.12 (10.08)	3.94 (35.46)	1.25 (11.25)	−0.45	4.25 (38.25)	1.08 (9.72)	3.92 (35.28)	1.18 (10.62)	−0.36	4.30 (38.7)	1.10 (9.90)	3.93 (35.37)	1.21 (10.89)	−0.4

Note: EDI-2 subscale outcomes are item mean scores with sum scores in parenthesis. BMI-SDS: Body Mass Index Standard Deviation Score, a z-score transformed measure of BMI adjusted for age and sex. We used Kromeyer-Hauschild et al. (2001) as reference, therefore BMI-SDS of adults might be slightly overestimated.

[a]Cohen's *d* effect sizes were corrected for the correlation between pre- and post-inpatient treatment scores and based on the standard deviation of the pre-test, according to Morris and DeShon (2002). All pre-post scores were statistically significant at $p < 0.001$.

[b]EDI-2: Eating Disorder Inventory-2. The German EDI-2 is scored on a scale ranging from "1 – never" to "6 – always".

Only 5% ($N = 141$) of the patients were males. $N = 2690$ (93.4%) had a full-threshold AN diagnosis, whereas $N = 191$ (6.6%) of the patients were diagnosed with atypical AN. Patients with atypical AN were comparable to patients with full-threshold AN on EDI-2 bulimia scores at admission and average daily weight gain and RMSE during early inpatient treatment (all ts < 0.91, ps > 0.361). However, patients with atypical AN showed lower EDI-2 drive for thinness ($M_{full\text{-}threshold} = 4.25$, $M_{atypical} = 3.03$; $t(155.51) = 8.42$, $p < 0.001$) and body dissatisfaction scores ($M_{full\text{-}threshold} = 4.33$, $M_{atypical} = 3.77$; $t(161.87) = 5.74$, $p < 0.001$) at admission. They also showed a higher admission BMI ($M_{full\text{-}threshold} = 14.97$ kg/m^2, $M_{atypical} = 16.12$ kg/m^2; $t(214.59) = -7.92$, $p < 0.001$) compared to patients with full-threshold AN. Of patients with full-threshold AN, AN subtypes were only recorded for 38.2% ($N = 1028$) of the patients[1]: $N = 731$ (27.2%) were diagnosed with AN restrictive type, $N = 297$ (11.0%) with AN binge-purge subtype, and $N = 1657$ (61.6%) were recorded without a specified subtype.

Regarding the effectiveness of the inpatient treatment, statistically significant differences between admission and discharge scores were found for BMI, BMI-SDS, and psychological outcomes (i.e., drive for thinness, bulimia and body dissatisfaction) on average and for both age groups (see Table 1 for effect sizes). The observed treatment effects were larger than in recent studies on inpatient treatment for AN in adolescents and adults (Mairhofer et al., 2021; Marzola et al., 2018).

3.1.1 | Effects of individual daily weight gain and weight variability on discharge weight

First, we regressed discharge weight on average daily weight gain, RMSE, their interactions by age, with sex, age, admission weight (i.e., Level-1 intercept) and treatment duration as covariates. The multiple $R^2 = 0.810$ was statistically significant ($F(8, 2872) = 1534$, $p < 0.001$). Table 2 presents unstandardised regression coefficients of all predictors and covariates. We found significant effects of average daily weight gain ($b = 18.87$, $t(2872) = 19.08$, $p < 0.001$) and its interaction by age on discharge weight ($b = -0.22$, $t(2872) = -2.56$, $p = 0.010$), but no conditional ($b = -0.42$, $t(2872) = -1.22$, $p = 0.222$) or interaction effect of RMSE by age ($b = -0.01$, $t(2872) = -0.35$, $p = 0.730$) on discharge weight was found. This suggests that a 1 *SD* (0.092 kg) increase in daily weight gain during early inpatient treatment is statistically significantly associated with a 1.74 kg higher discharge weight ($b = 18.87$, $t(2872) = 19.08$, $p < 0.001$) for the 18-years-old patient with average admission weight and treatment duration. The Johnson-Neyman plot (Figure 2a) indicates that the slope of the interaction is statistically significant for patients aged up to 68.45 years. A simple

TABLE 2 Regression coefficients for the level-2 models of individual early weight gain and variability on outcome after inpatient treatment

	Discharge weight			Drive for thinness at discharge			Bulimia at discharge			Body dissatisfaction at discharge		
Predictors	***b***	***SE***	***p***	***b***	***SE***	***p***	***b***	***SE***	***p***	***b***	***SE***	***p***
Intercept	48.931	0.064	<0.001	3.207	0.028	<0.001	1.401	0.014	<0.001	3.923	0.025	<0.001
Sex (0 = female; 1 = male)	1.486	0.308	<0.001	−0.537	0.146	<0.001	0.060	0.073	0.412	−0.463	0.128	<0.001
Age	0.024	0.006	<0.001	0.002	0.003	0.441	−0.001	0.001	0.350	0.005	0.002	0.052
Admission weight estimate[a]	0.908	0.009	<0.001	0.012	0.004	0.003	−0.002	0.002	0.337	0.006	0.006	0.103
Treatment duration[b]	0.074	0.001	<0.001	0.001	0.001	0.276	−0.000	0.000	0.449	0.002	0.001	0.001
Score at admission	—	—	—	0.594	0.019	<0.001	0.271	0.011	<0.001	0.692	0.020	<0.001
Average daily weight gain	18.866	0.989	<0.001	−1.167	0.422	0.006	−0.257	0.214	0.229	−1.226	0.371	<0.001
RMSE	−0.421	0.345	0.222	−0.178	0.149	0.234	0.003	0.076	0.970	0.028	0.131	0.832
Average daily weight gain × Age	−0.219	0.085	0.010	0.133	0.040	0.001	−0.021	0.020	0.311	0.086	0.035	0.014
RMSE × Age	−0.009	0.027	0.728	<0.001	0.012	0.994	0.003	0.006	0.593	−0.021	0.011	0.055

Note: RMSE: Root-mean squared error based on individual level-1 residuals. Outcomes for weight are in kg. EDI-2: Eating Disorder Inventory-2. EDI-2 subscale outcomes are item mean scores. The German EDI-2 is scored on a scale ranging from "1 – never" to "6 – always". All continuous predictors were centred at the grand-mean and winsorized at the 5th and 95th percentile, except age and score at admission, which were not winsorized. Age was centred at 18 years.

[a]We used the intercept of the respective level-1 model as an estimate of admission weight.

[b]Treatment duration in days from admission to discharge (range: 14–180 days).

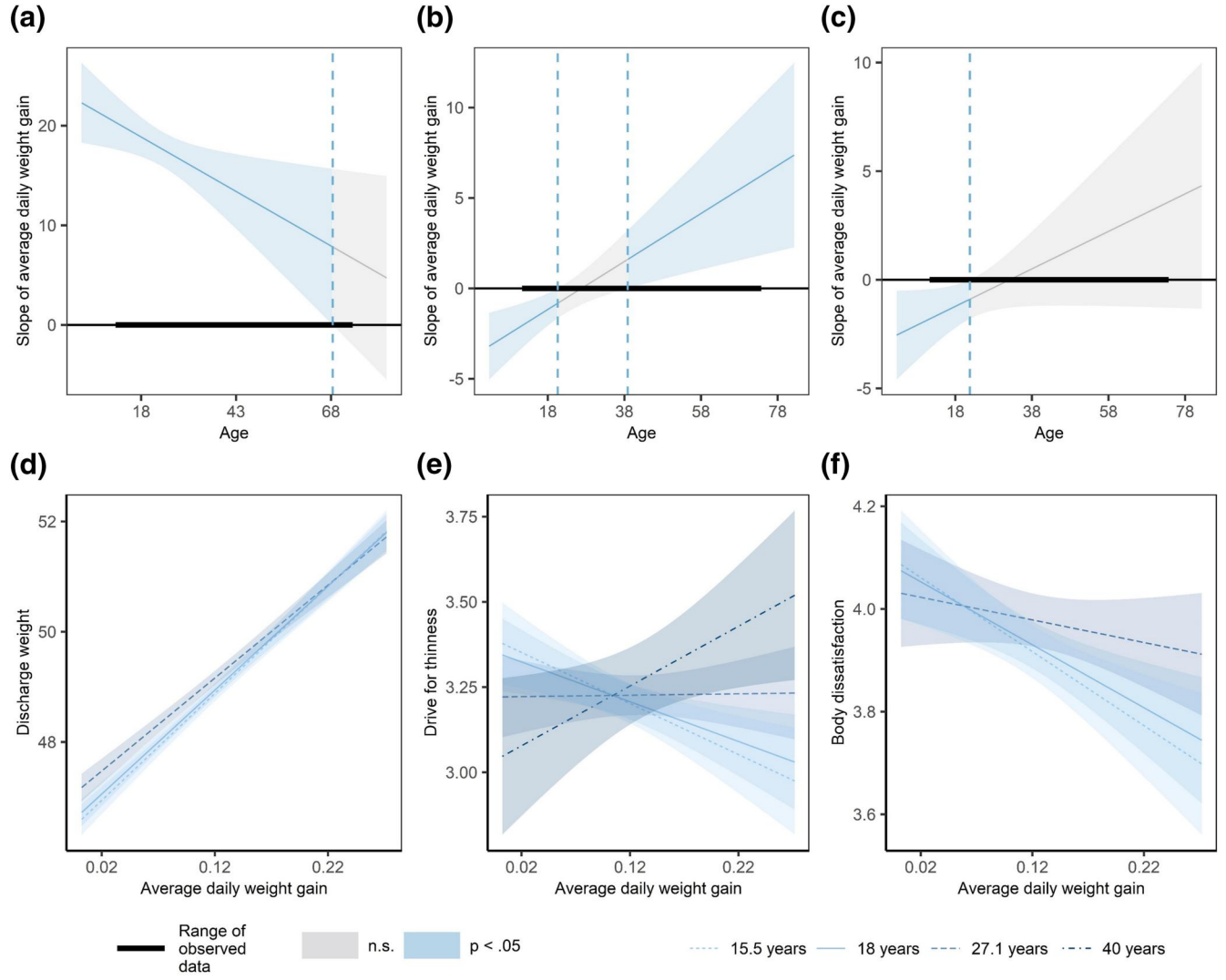

FIGURE 2 Johnson–Neyman plots and simple slopes plots that both visualise the interaction effect between individual average daily weight gain and age when predicting weight, drive for thinness, and body dissatisfaction at discharge. Panels (a, b and c) display Johnson–Neyman plots representing the interaction effect of individual average daily weight gain and age on (a) weight, (b) drive for thinness and (c) body dissatisfaction at discharge. The plot illustrates the conditional effect of average weight gain on discharge weight, drive for thinness at discharge and body dissatisfaction at discharge. Vertical dashed lines represent points of transition between a statistically significant and nonsignificant association between average daily weight gain and the outcome variable. Panels (d, e and f) are interaction plots depicting simple slopes of average daily weight gain on (d) weight, (e) drive for thinness and (f) body dissatisfaction at discharge separately for mean age of adolescents (15.5 years), age 18 years, mean age of adults (27.1 years), and, in (e) also for age 40 years to illustrate the reversed simple slope for older adults. Discharge weight is measured in kg, drive for thinness and body dissatisfaction are the item mean scores of these Eating Disorder Inventory-2 (EDI-2) subscales. The German EDI-2 is scored on a scale ranging from "1 – never" to "6 – always" [Colour figure can be viewed at wileyonlinelibrary.com]

slope analysis (Figure 2d) of the moderating effect of age on average daily weight gain revealed that the positive effect of higher daily weight gain during early inpatient treatment is somewhat smaller the older a patient is. For example, an adolescent aged exactly the mean age of the adolescent sample (15.5 years) benefits from a 1 *SD* increase in daily weight gain with a 1.79 kg higher discharge weight ($b = 19.41$, $t\ (2878) = 17.54$, $p < 0.001$) compared to an increase of only 1.56 kg of a 27.1 years old adult ($b = 16.88$, $t\ (2878) = 18.34$, $p < 0.001$).

3.1.2 | Effects of individual daily weight gain and weight variability on discharge eating disorder psychopathology

Next, we regressed core ED psychopathology (ED-2 drive for thinness, bulimia, and body dissatisfaction scores) at discharge on the same predictors and covariates in three separate linear regression models to assess the effect of weight gain and variability during early treatment on these outcome measures. We furthermore included the

respective EDI-2 scale scores at admission as covariates. The goodness-of-fit of all three models was statistically significant ($0.269 \leq R^2 \leq 0.420$; F (9, 1865) ≥ 77.6, $p < 0.001$). Again, weight variability (RMSE, and its interaction with age) was not statistically significantly associated with the outcome measures. Weight gain during early treatment, and its interaction with age, were only statistically significantly associated with drive for thinness and body dissatisfaction at discharge, but not with bulimia (see Table 2 for details). Negative main effect coefficients of average daily weight gain (drive for thinness: $b = -1.17$, t (1865) $= -2.77$, $p = 0.006$, body dissatisfaction: $b = -1.23$, t (1865) $= -3.30$, $p < 0.001$) and positive interaction coefficients of the weight gain by age interaction (drive for thinness: $b = 0.13$, t (1865) $= 3.34$, $p < 0.001$; body dissatisfaction: $b = 0.09$, t (1865) $= 2.46$, $p = 0.014$) emerged. This indicates that higher average daily weight gain during early inpatient treatment is associated with higher improvements in core ED psychopathology at discharge, but to a lesser degree in adults compared to adolescents.

To probe interactions, we again computed Johnson-Neyman plots and conducted simple slope analyses: For drive for thinness as outcome, the Johnson-Neyman plot (Figure 2b) suggests that simple slopes are statistically significant for patients younger than 20.58 years and older than 38.86 years. A simple slope analysis thus revealed that for an adolescent patient aged 15.5 years (mean age of adolescents) a 1 *SD* (0.092 kg) increase in daily weight gain is associated with a 0.138 points reduction of drive for thinness at discharge ($b = -1.50$, t (1871) $= -3.18$, $p < 0.002$). This effect is reversed and statistically significant for adults older than 39 years: For example, an adult patient aged 40 years has an increase of 0.161 points in drive for thinness for a 1 *SD* increase in daily weight gain ($b = 1.75$, t (1871) $= 2.19$, $p = 0.030$, Figure 2e). Regarding body dissatisfaction at discharge, the Johnson-Neyman plot (Figure 2c) indicates that the simple slopes are only significant for patients younger than 21.81 years. For example, Figure 2f shows that for an adolescent patient aged 15.5 years, a statistically association of a 1 *SD* increase in daily weight gain is associated with a reduction of 0.132 points in body dissatisfaction at discharge ($b = -1.44$, t (1871) $= -3.47$, $p < 0.001$).

3.1.3 | Effects of individual daily weight gain and weight variability on attaining normal weight range at discharge

Finally, we were interested in whether daily weight gain and weight variability during early inpatient treatment were associated with attaining a body weight within the normal weight range (18.5 kg/m^2 $\leq$ BMI $<$ 25) at discharge. $N = 1072$ patients were discharged with a BMI $\geq$ 18.5 kg/m^2 (37.21% of all patients), and no one with a BMI $\geq$25 kg/m^2. Of those, $n = 1050$ had a weight gain of more than 2 kg, and $n = 911$ of more than 5 kg. A logistic regression model (Table 3) with the same predictors and covariates as above showed a good fit with a McFadden's $R^2 = 0.261$ (McFadden, 1973). Of the weight gain and variability predictors and their interactions with age, only a statistically significant main effect of average daily weight gain emerged ($b = 6.45$, $z = 7.70$, $p < 0.001$). This indicates that by an increase of 1 *SD* in daily weight gain during early inpatient treatment, the probability of a body weight within the normal weight range at the end of treatment increases by 59% for an 18-years-old adult patient with average admission weight and treatment duration.

4 | DISCUSSION

In this study, we examined the effect of weight gain and weight variability during early inpatient treatment on treatment outcome and its moderation by age. Higher

TABLE 3 Regression coefficients of the level-2 logistic regression model of individual early weight gain and variability on attaining a body weight within the normal body weight range at discharge

	Body weight within normal BMI range at discharge (18.5 kg/m^2 $\leq$ BMI $<$ 25 kg/m^2)		
Predictors	***b***	***SE***	***p***
Intercept	−0.806	0.055	<0.001
Sex (1 = male)	−1.122	0.259	<0.001
Age	0.020	0.005	<0.001
Admission weight estimate[a]	0.218	0.010	<0.001
Treatment duration[b]	0.027	0.001	<0.001
Average daily weight gain	6.451	0.837	<0.001
RMSE	−0.253	0.283	0.370
Average daily weight gain × age	−0.049	0.071	0.487
RMSE × age	<0.001	0.023	0.995

Note: RMSE: Root-mean squared error based on individual level-1 residuals. All continuous predictors were centred at the grand-mean and winsorized at the 5th and 95th percentile, except age and score at admission, which were not winsorized. Age was centred at 18 years.

[a]The intercept of the level-1 model was used as an estimate for admission weight.

[b]Treatment duration in days from admission to discharge (range: 14–180 days).

individual daily weight gain during early inpatient treatment predicted higher discharge weight, lower drive for thinness, and body dissatisfaction at discharge. These effects were moderated by age, indicating stronger effects of daily weight gain on treatment outcome in adolescents. Higher individual daily weight gain during early treatment was also associated with a higher probability for attaining a BMI $\geq$ 18.5 kg/m^2 at discharge. Contrary to our expectations, we did not find any effect of weight variability on treatment outcomes when simultaneously estimating effects for daily weight gain.

Our findings are in line with previous research that highlighted the importance of early weight gain for successful inpatient treatment (Chatelet et al., 2020; Hartmann et al., 2007; Jennings et al., 2018; Makhzoumi et al., 2017). Several explanations for our finding that younger patients benefit to a greater extent from early weight gain during inpatient treatment compared to adults are conceivable. Psychological and biological changes coming with duration of illness might prevent the maintenance of early weight gain throughout inpatient treatment. For example, as on average older patients show longer duration of illness compared to younger patients, their body image and self-concept might be more strongly attached to being underweight. Thus, older patients might have more difficulties to adjust to or react more fearfully to weight gain, especially if it occurs rapidly, and therefore tend to control weight gain more strongly throughout the rest of the treatment ultimately resulting in a lower discharge weight. In addition, older patients are more likely to have received previous treatments. Failure to respond to previous treatment might also partially explain age differences in the effect of early weight gain on treatment outcome. Furthermore, younger patients might receive more parental support during inpatient treatment. This could result in higher daily weight gain continually throughout inpatient treatment, especially when internal motivation of patients is low or difficulties emerge. These considerations are also supported by other studies as a potential causal explanation to the effect of early weight gain on treatment outcome, as weight gain is merely a proxy variable for other treatment responses (Crisp et al., 1986; Hart et al., 2011).

An alternative interpretation would be that a higher proportion of binge-purge AN subtype in adults is accountable for the dampening moderator effect of age on the association of early weight gain with treatment outcome. Patients with binge-purge subtype might show reduced compensatory behaviours during early treatment but react even more strongly to rapid weight gain once their weight increased. In fact, there is some evidence that patients with binge-purge AN were older compared to patients with restrictive AN in our sample, but subtype was not recorded reliably for all patients. This is a clear limitation of our study that warrants further investigation in a future study.

It is notable that weight variability was not associated with any treatment outcome when simultaneously accounting for average daily weight gain, especially as recent research highlighted the predictive value of weight variability on core ED pathology in individuals with bulimia nervosa (Chen et al., 2021). This is also in contrast to Hartmann et al. (2007), where weight variability was associated with treatment failure. However, this discrepancy might be partially explained by differences in the setting and methodology of our study. First, our patients were required to increase body weight during treatment and weight was monitored closely especially for severe cases. This might have reduced variance in weight variability in our sample compared to individuals with bulimia nervosa. Second, Chen et al. (2021) used a slightly different level-1 model that included fixed effect estimates for weight change, and only included BMI and weight variability into their level-2 analyses, but not linear weight gain. Thus, their weight variability estimate might be confounded by weight gain for patients that increased weight during the study. In contrast to Hartmann et al. (2007), we used a substantially larger sample, mainly used dimensional outcome measures and included several covariates such as treatment duration. Altogether, these methodological issues might explain differences in results. Finally, it is thinkable that weight fluctuations have a higher impact on psychopathology in bulimia nervosa than in AN due to differences in compulsivity and impulsivity between patients with these disorders. The rigid, compulsive and controlling features often associated with AN might facilitate reducing variability (by rapid regression to baseline) whereas impulsive behaviours such as binge-eating or purging might further exacerbate and prolong out-of-control weight fluctuations in patients with bulimia nervosa. If so, differences between restrictive and binge-purge AN might also emerge regarding the impact of weight variability on treatment outcomes, and future studies should address potential differences between restrictive and binge-purge AN when investigating weight gain and weight variability.

Our sample, although being very large, is comprised of patients that on average were highly motivated for treatment, although most likely comparable to other inpatient treatment centres. Thus, it is questionable whether our findings generalise to other treatment setting such as involuntary treatment, outpatient treatment or even untreated individuals with AN. In the light of increasing day treatment approaches for eating disorders (Madden et al., 2015), it might also be worthwhile to investigate early weight gain and weight variability in day

treatment compared to inpatient treatment. It is conceivable that weight variability might be larger in a less restrictive setting, but it is unclear whether this would impact treatment outcome. Finding a similar pattern of effects of early weight gain and weight variability on treatment outcome would further strengthen the evidence for day treatment. Another limitation is that the diagnoses in this study were based on clinical assessment only. Thus, subtype and atypical diagnoses might not be as reliable as in other studies that, for example, used structured interviews for diagnostic assessment. Although both adults and adolescents were included, we did not differentiate between them when assessing whether they reached a body weight within the normal weight range. In clinical practice, normal body weight for adults is mostly defined as having a BMI within 18.5–25 kg/m^2, whereas age- and sex-adjusted BMI percentiles are often used for adolescents and differ sometimes from the adult criterion. For the sake of comparability, we used the adult criterion for adolescents in our study as well. This is in contrast to an earlier study by Hartmann et al. (2007), which used a somewhat more liberal treatment success criterion of BMI $\geq$ 17.5 kg/m^2 or $\geq$ 2 kg weight gain at discharge which could explain why fewer patients reached the more conservative criterion in our study. We also decided to use kg instead of kg/m^2 as measurement units and thus discharge weight and daily weight gain instead of discharge BMI and daily BMI gain to facilitate interpretability of our findings, as for example, daily weight gain in kg is directly translatable to clinical practice instead of very small increases in BMI points measured in kg/m^2.

Notwithstanding these limitations, our findings provide insights into the role of early weight gain and variability during inpatient treatment on treatment outcome, suggesting new avenues for future research and being of direct importance for clinical practice. For example, high weight variability early after admission should be of lesser concern if the patient is on average continuing to gain weight. Future research might want to further investigate the role of weight variability in AN in a community sample that is not currently in treatment. Weight variability might be associated with current levels of ED psychopathology, and a closer look on AN stage and age dependencies might further advance our understanding of weight variability in AN.

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CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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ENDNOTE

[1] In Germany, the fourth digit of the ICD-10 codes specifies AN subtype. However, entering a fourth digit was not enforced in the electronic clinical database that collected routine data during inpatient treatment.

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