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## Inpatient target discharge weight for early-onset anorexia nervosa: Restoring premorbid BMI percentile to improve height prognosis

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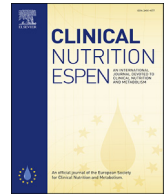
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Original article

## Inpatient target discharge weight for early-onset anorexia nervosa: Restoring premorbid BMI percentile to improve height prognosis



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### SUMMARY

**Objective:** Early-onset anorexia nervosa (EO-AN) is characterized by restricted food intake leading to low body weight, emerging before 14 years old. Most patients reaching a target body mass index (BMI) around the 25th percentile at hospitalization discharge display an incomplete prospective height catch-up. A better understanding of height prognosis determinants is required.

**Methods:** In 74 children with an EO-AN, we collected height and weight premorbidly, at hospitalization, and at discharge, 6 months, 12 months, and at longer-term follow-up of 36 months. We defined a height prognosis parameter (HPP) as the difference between the height percentile at follow-up times and the premorbid height percentile. We explored the relationship between weight parameters and height catch-up at follow-up with linear regression analyses.

**Results:** A higher weight suppression (WS) - *i.e.*, difference between premorbid and current BMI - at admission and discharge was associated with lower HPP - *i.e.*, a greater loss of height - at 12 months and 36 months follow-up. Similarly, a higher premorbid BMI percentile was associated with a lower HPP at 12 and 36 months.

**Conclusion:** Target discharge weight for EO-AN patients should be tailored and based on premorbid BMI trajectory to improve height prognosis.

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### Background

Anorexia nervosa (AN) is characterized by an intense fear of gaining weight or becoming fat and persistent restriction of energy intake relative to requirements, leading to significantly low body weight in the context of age, sex, and developmental trajectory [1]. Recent studies have reported an increasing prevalence of AN at an early stage of development (*i.e.*, before 14 years of age) [2]. Early-

onset AN (EO-AN) raises specific prognosis issues related to its onset at a critical period of physical growth and development. Significantly low body weight during childhood can lead to persistent growth retardation [3], cortical and subcortical brain atrophy [4], and abnormal mineralization associated with an over-risk of bone fractures [5,6]. Even after weight recovery before adolescence [7,8], EO-AN can impact upon height growth and result in a shorter stature at adult age than that predicted by theoretical height [9–11]. Most EO-AN patients display an incomplete growth catch-up, even when they accelerate their height growth following nutritional recovery [3,12].

The long-term effect of EO-AN on height growth raises the question of what should be the adequate weight restoration target

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Abbreviations	
AN	Anorexia nervosa
BMI	Body mass index
EO-AN	Early-onset anorexia nervosa
GH	Growth hormone
HPP	Height prognosis parameter
IGF-1	Insulin-like growth factor 1
WS	Weight suppression

in children, especially for the most severe circumstance where illness has necessitated inpatient admission. Restoring weight is an essential objective during inpatient treatment for AN [13–16] but the definition of target discharge weight remains unclear [17] and there are no consensual criteria to determine a threshold for weight restoration in terms of BMI or BMI percentile. In a previous study [18] on an EO-AN cohort hospitalized between 1998 and 2002 at our site, we reported on finding a persistent height deficit into adulthood for more than a third of patients with EO-AN, despite weight restoration and attainment of menarche after hospitalization discharge. This result combined with a publication by Golden et al. [19], led our team to redefine target discharge weight. In adolescents with AN, a mean body mass index (BMI kg/m<sup>2</sup>) percentile of 27 (range from 14 to 39 percentile) was suggested as treatment goal weight [19]. Based on this study, our clinical team defined the target discharge weight in EO-AN patients according to a theoretical BMI around the 25th percentile for the patient’s chronological age. Since 2010, all consecutively admitted EO-AN patients had this proposed as their target discharge weight.

The impact of target discharge weight in EO-AN is an important question, and has not been thoroughly investigated to date. This research aims to study the impact of a standardized target discharge weight at the 25th percentile of BMI on height prognosis in EO-AN. We will investigate height prognosis at 6, 12, and 36 months after discharge and determine the premorbid, hospitalization, and follow-up parameters associated with height prognosis.

**Methods**

*Participants*

We included participants under 14 years old consecutively hospitalized at the Child and Adolescent Psychiatry Department, Robert Debré University Hospital (Paris, France) from May 2010 to May 2018 with EO-AN (n = 74). All participants included had a formal diagnosis of AN based on the DSM IV-R criteria [20]: restrictive food intake, significantly low body weight in the context of age, sex, developmental trajectory, and physical health; and presence of abnormal weight cognitions, and were either prepubertal (Tanner stage 1) or at the early mid-pubertal stages (Tanner stage 2 or 3) at the time of hospitalization. All participants were hospitalized at inclusion since they presented with a BMI below the 3rd percentile, or lost two kilograms per week during the past month, or presented with a refusal to swallow [19]. Disease onset was defined retrospectively as the age of the first break in the growth curve [11]. Participants were excluded if they had a chronic medical disorder that may interfere with weight or height prognosis (such as Crohn’s disease or type I diabetes [20,21]), but none were excluded on this basis (Fig. 1). Inpatient care was based on a multidisciplinary approach with biological management, nutritional rehabilitation, and behavioral treatment. Diet was adjusted including tube-feeding if necessary. Initial caloric intake was

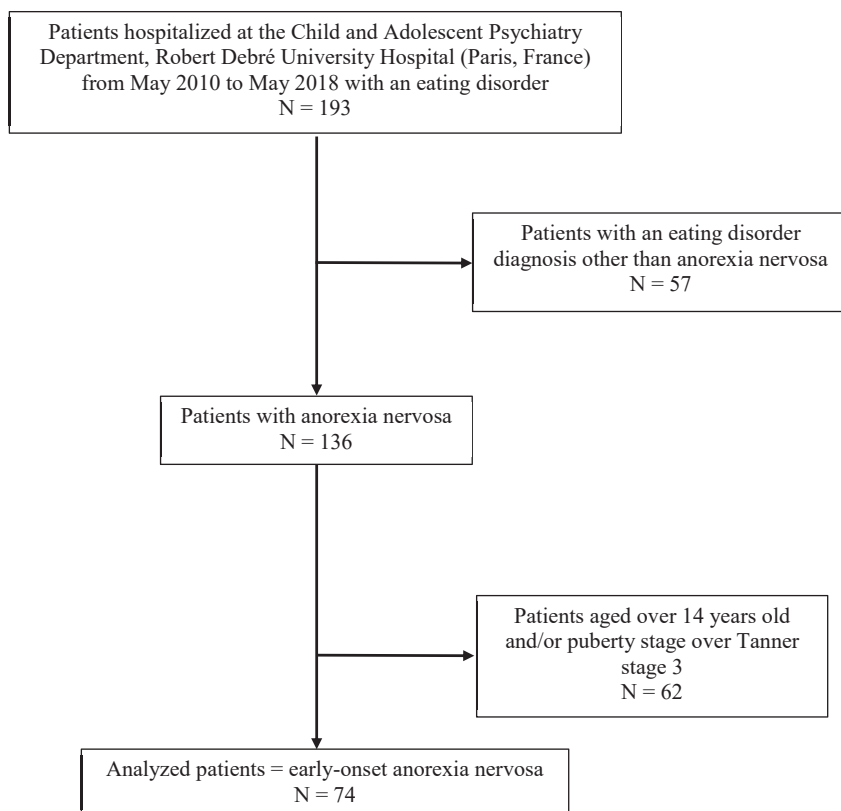


Fig. 1. Flowchart of the participants in the study.

comparable to that before hospital admission and was at least 250 kcal/day, then increased by 250 kcal/day until 1000 kcal/day and then gradually increased in 200 kcal steps to achieve a weight gain ranging from 500 to 1000 g per week according to French guidelines [22]. Discharge weight was set to a 25th percentile BMI for age and sex according to the literature before 2010 [19]. An outpatient follow-up with a psychiatrist who specialized in AN was conducted after discharge, associated with a follow-up by their general pediatrician. We retrospectively collected socio-demographic and clinical data from hospitalization reports including age at onset, disease duration before admission, age and Tanner stage at admission, length of hospitalization, bone age, insulin-like growth factor 1 (IGF-1), family history of AN and the occurrence of menstruation during follow-up.

### Study measures

For all participants included in the study, we retrospectively collected premorbid weight and height from their “carnet de santé” (a health care record that all children have in France since their birth, including their growth curves). We also retrospectively collected weight and height measurements that were collected at hospitalization admission, discharge and follow-up in patients' records. During hospitalization and follow-up, trained nurses or psychiatrists specialized in AN measured height and weight in underwear patients through the same digital scale for weight and stadiometer for height. Height was expressed as age- and sex-conditional percentile, referring to the World Health Organization growth charts for children [23]. We calculated the percentile BMI for each participant according to age and sex. In France, pediatricians and general practitioners regularly report height and weight measurements in a personal health care record in the context of the child's routine medical follow-up. We calculated the premorbid percentiles of BMI and height as the mean of the last three premorbid height/weight measurements prior to disease onset, defined as the point of first break in the growth curve, from longitudinal data reported in this personal health care record. We also calculated weight suppression (WS) as the difference between premorbid BMI percentile and BMI percentile at the time considered (e.g., at admission, discharge, or follow-up) (see supplementary for a worked example) [24]. Higher values of WS reflect incomplete weight restoration with reference to premorbid BMI. Similarly, we determined a height prognosis parameter (HPP) as the difference between the height percentile at follow-up times (e.g., at admission, discharge, or follow-up) and premorbid height percentile. Negative values of HPP reflect loss in height prognosis with reference to premorbid height.

### Statistical analysis

Descriptive data for the sample including demographic and clinical characteristics were calculated. We investigated the relationship between the participants' premorbid, admission, discharge, and follow-up parameters and height prognosis at the three follow-up occasions. We included concepts identified in prior literature as being associated with height prognosis in adults and adolescents with AN, including premorbid BMI and height percentiles, age at admission, length of disease [25,26], hospitalization WS [24], and the occurrence of menstruation [8,25]. We examined variables in separate linear regression models. We reported nominal p-values corrected for multiple comparisons with the false discovery rate procedure [27]. At our sample size, we had 100% and 90% power in the separate regressions to detect large ( $f^2 = 0.35$ ) and medium ( $f^2 = 0.15$ ) effect sizes, respectively, at an alpha of 0.05.

We also performed a quartile subgroup analysis to study BMI and height percentile trajectories over the follow-up period according to the quartiles of premorbid BMI. We thus compared the number of patients in each subgroup with the expected normal distribution. We evaluated the assumption of normality using the Shapiro-Wilk test. For BMI and height, we defined the baseline for each quartile subgroup as the mean of participants' premorbid percentile in each subgroup and calculated the mean difference from baseline at each time measurement (i.e., 6 months, 12 months, and the last visit at follow-up).

Referring to height and weight measurement, we observed approximately 10% missing values in premorbid, 30% missing values at 6 and 12 months follow-up, and 20% missing values at longer-term follow-up. We performed multiple imputations using the Multivariate Imputation by Chained Equations (MICE) method to create five imputed data sets, and we combined the results using Rubin's method [28]. We performed statistical analysis with RStudio version 1.1.456.

### Ethics statement

This study was carried out under the recommendations of the local ethics committee (Comité de l'Evaluation de l'Ethique des Projets de Recherche de Robert Debré, number 2021-538bis).

## Results

### Clinical characteristics

The sample was predominantly females (86%), with a mean age of 11.40 (SD = 1.16) years at admission. Table 1 presents the demographic and clinical characteristics, including the distributions of height and weight throughout the study. The mean length of the 6-month and 12-month follow-up visits were 6 months and 4 days (SD = 1 month and 4 days) and 12 months and 3 days (SD = 1 month and 5 days) after discharge, respectively. The longer-term follow-up mean length was 36 months since discharge (SD = 18) (min: 13 months, max: 78 months, with normal distribution).

**Table 1**

Clinical and demographic characteristics of consecutively hospitalized EO-AN patients enrolled in the study (n = 74).

Variables	Participants enrolled in the study
Male/female ratio % (n)	14 (n = 10)/86 (n = 64)
Age at admission, years	11.40 (1.16)
Age at onset of AN, years	9.69 (1.50)
Bone age at admission, years	11.32 (1.34)
IGF-1 z score at admission	-2.09 (1.13)
Tanner stage, % (n)	
1	30 (n = 22)
2	22 (n = 16)
3	16 (n = 12)
Missing data	32 (n = 24)
Length of hospitalization, days	96.58 (44.82)
Premorbid BMI percentile	49 (23)
Premorbid height percentile	61 (28)
Weight suppression at admission	45 (25)
Weight suppression at discharge	21 (24)
Occurrence of menarche during follow-up, % (n)	56.25 (n = 36)
Family history of AN in first-degree relatives, % 20 (n = 15) (n)	

Note: For continuous variables, values are mean (SD); AN = Anorexia Nervosa; BMI = Body Mass Index; IGF-1 = insulin-like growth factor 1; Weight suppression: defined as the difference between premorbid BMI percentile and BMI percentile at the time considered.

**Table 2**  
Body mass index and height percentile of the EO-AN sample over time (n = 74).

	Premorbid	At admission	At discharge	6 months follow-up	12 months follow-up	Longer-term follow-up
BMI (percentile)	49.35	4.28	28.96	25.03	26.22	27.54
	±23.01	±10.44	±12.78	±19.37	±18.07	±21.40
Height (percentile)	60.56	42.72	38.37	34.74	36.84	42.32
	±28.48	±32.49	±31.37	±30.04	±29.70	±30.82

Note: For continuous variables, values are mean ± SD; BMI = Body Mass Index.

**Table 3**  
Univariate regression analyses predicting height prognosis parameter (HPP) at 6 months, 12 months and longer-term follow-up.

Variables	HPP at 6 months	HPP at 12 months	HPP at longer-term follow-up
Premorbid			
BMI percentile	0.17 ± 0.12	-0.31 ± 0.09**	-0.22 ± 0.07**
Height percentile	0.08 ± 0.09	-0.15 ± 0.08	-0.07 ± 0.06
Admission			
Age	1.67 ± 2.49	-2.18 ± 1.986	-2.45 ± 1.51
Length of disease	-4.38 ± 2.24	-0.19 ± 1.73	-3.33 ± 1.47
Weight suppression	0.14 ± 0.13	-0.35 ± 0.09**	-0.24 ± 0.08**
Discharge			
Weight suppression	0.12 ± 0.12	-0.23 ± 0.09*	-0.24 ± 0.07**
Follow-up			
Occurrence of menarche	21.66 ± 7.61**	7.7 ± 6.57	7.58 ± 3.43*

HPP: Height prognosis parameter defined as the difference between height percentile at 6, 12, and 36 ± 18 months and premorbid height percentile. Negative raw values of HPP reflect loss in height prognosis with reference to premorbid height. BMI: Body Mass Index. Weight suppression: defined as the difference between premorbid BMI percentile and BMI percentile at the time considered. Values are unstandardized beta coefficient ± standard error, \*p < .05; \*\*p < .01; \*\*\*p < .001 corrected for multiple comparison with the false discovery rate procedure.

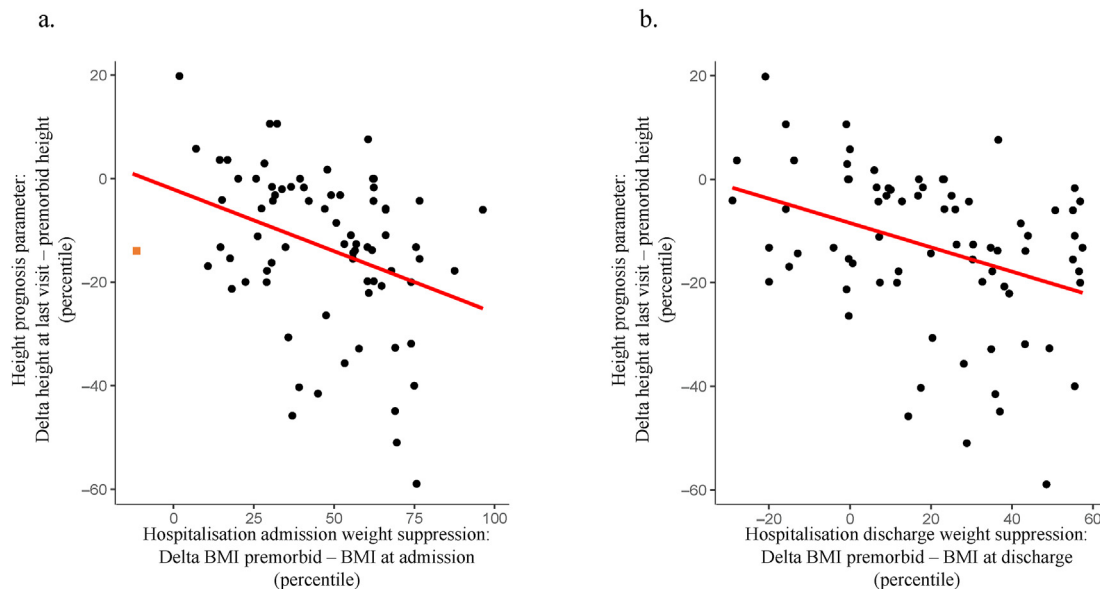
**Height prognosis**

The mean height percentile at admission (43; SD = 32) was lower than the premorbid mean height percentile (61; SD = 28), reflecting a decreased or arrested growth velocity at admission (Table 2). The

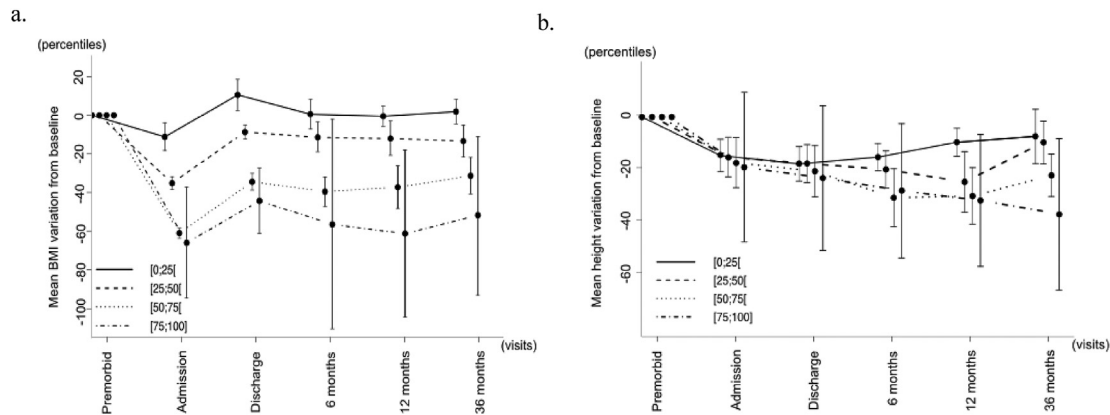
height percentile remained low at discharge (38; SD = 31), highlighting the decoupling between weight and height regains, as well as the relative increase in height loss with the patient's increased age during the hospitalization. At follow-up, the mean loss in height relative to premorbid height percentile decreased from -25 (SD = 23) at 6 months, to -22 (SD = 19) at 12 months, and to -16 (SD = 19) at longer-term follow-up, reflecting increased growth velocity after hospitalization discharge with incomplete catch-up.

**Predictors of height prognosis in EO-AN**

Univariate linear regression analyses tested the associations between premorbid, hospitalization, and follow-up parameters and HPP at 6 months, 12 months, and longer-term follow-up after discharge (Table 3). Premorbid BMI was negatively associated with HPP at 12 months and longer-term follow-up (respectively β = -0.31, p = .003 and β = -0.22, p = .007), suggesting that higher premorbid BMI predicted the worst height prognosis at follow-up. WS at admission and discharge were also negatively associated with HPP at 12 months and at the longer-term follow-up (respectively β = -0.35, p = .001 and β = -0.23, p = .02 at 12 months, and (β = -0.24, p = .007 and β = -0.24, p = .007 at longer-term follow-up) (Fig. 2), suggesting that higher WS at admission and discharge predicted a worse height prognosis at follow-up. We also observed that the occurrence of menarche during follow-up was positively correlated with HPP at 6 months and longer-term follow-up (respectively β = 21.66, p = .034 and β = 7.58, p = .045), indicating



**Fig. 2.** Linear regression slope with data points depicting the association between height prognosis parameter (delta height follow-up – height prognosis) and hospitalization admission weight suppression (delta premorbid BMI - BMI at admission) (a) and hospitalization discharge weight suppression (delta premorbid BMI - BMI at discharge) (b) among EO-AN patients. Heights and BMI were expressed in percentiles. In Fig. 2a, one patient (red square) was reported with BMI at admission higher than premorbid BMI due to pathological weight trajectory with a period of weight gain preceding EO-AN development. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 3.** Mean BMI percentile evolution (a.) and mean height percentile evolution (b.) across premorbid, admission, discharge, 6 months, 12 months, and longer-term follow-ups in subgroups classified by premorbid BMI percentile quartile.

that the onset of menarche during follow-up was associated with a better height prognosis. We did not find any significant relationship between duration of disease before admission, or age at hospitalization and HPP.

#### Subgroup analysis

We then performed a subgroup analysis in participants with complete premorbid BMI data ( $n = 65$ ) using premorbid BMI percentile quartiles to study the trajectory of BMI and height over the follow-up period. The premorbid BMI distribution did not differ from a normal distribution expected in the general population ( $p = .33$ ). We found 15% of patients ( $n = 10$ ) in the first premorbid percentile BMI quartile [0–25], 38.5% ( $n = 25$ ) in the second quartile [25–50], 38.5% ( $n = 25$ ) in the third quartile [50–75] and 8% ( $n = 5$ ) in the last one [75–100] (including premorbid obese participant  $n = 1$ ). We considered the mean of the premorbid BMI percentile as a baseline for each subgroup (Fig. 3a). At longer-term follow-up, the mean WS of patients belonging to the first quartiles [0–25] did not differ significantly from 0 ( $-2$   $p = .67$ ), similar to the mean HPP, which also did not significantly differ from 0 ( $-8$   $p = .13$ ). In contrast, at longer-term follow-up, patients belonging to quartiles [25–50], [50–75] and [75–100] presented with higher WS, significantly different from 0 (respectively 13,  $p = 3.9e-7$ ; 31,  $p = 3.9e-14$ ; 52,  $p = 1.5e-3$ ) (Fig. 3a). They also presented with lower HPP significantly different from 0, at longer-term follow-up (respectively  $-10$   $p = 1.07e-4$ ;  $-21$ ,  $p = 2.40e-10$ ;  $-35$ ,  $p = .037$ ) (Fig. 3b), reinforcing evidence that higher premorbid BMI was associated with worse weight suppression and height prognosis after inpatient treatment.

#### Discussion

Our study provides important guidance for determining an adequate target discharge weight for a better height prognosis in children with EO-AN. A higher premorbid BMI trajectory and higher WS negatively impacted height prognosis at follow-up. Consistent with other studies [29], we observed an initial delay in height catch-up after weight regain. At 6 months after discharge we observed a loss in height percentile relative to the premorbid height percentile ( $-25$ ;  $SD = 22$ ), since patients increased in age with no or low catch-up in height. During follow-up, the loss in height percentile decreased to  $-22$  ( $SD = 19$ ) at 12 months and  $-16$  ( $SD = 19$ ) at longer-term follow-up, reflecting a partial height catch-up over time. We also found that height prognosis was

negatively associated with WS at discharge, such that a larger difference between premorbid and discharge BMI was associated with worse height catch-up at 12 months and at longer-term follow-up. EO-AN patients with a higher premorbid BMI, higher WS at admission and at discharge also displayed poorer height prognosis at follow-up. Better height prognosis was associated with occurrence of menarche during follow-up.

Growth retardation is an early sign of EO-AN [30] and many patients with EO-AN or AN in adolescence have incomplete height catch-up even after nutritional recovery [3,11,12], however detailed data regarding growth rate and change in height percentiles, and prognostic factors, is lacking. In adolescents and adults with AN, recent studies report that higher WS at discharge is associated with a poorer prognosis and a worsening of eating disorder symptoms over time [31]. Higher WS at discharge has been linked to the persistence of restrictive symptoms among adolescents with AN [24], and the worsening of purging behaviors over follow-up among adult women with AN [31]. Experts in the fields of adult and childhood AN have questioned whether the definition of a weight restoration target ought to be aligned with the patient's premorbid weight trajectory rather than a weight standardized for sex, age, and height [32,33]. Our results support defining target discharge weight of EO-AN with reference to the premorbid weight trajectory to improve height prognosis. Hormonal adaptations to weight loss [34,35] contribute to growth retardation and amenorrhea in patients with AN [36,37]. AN is associated with acquired growth hormone (GH) resistance - increased GH secretion and decreased systemic IGF-1, as observed at hospital admission in our population - responsible for impaired growth and described to be partially reversible with weight gain [37]. Persistent high WS is associated with persistent hormonal dysregulation [38]. Reducing WS by targeting premorbid BMI trajectory reversed hormonal disturbance and led to an increased growth velocity to establish growth catch-up [38].

Studying height prognosis requires defining a normative reference height which is then compared with the patient's height. Previous studies have reported different approaches for analyzing a patient's final height percentile by comparing it with: the calculated target height  $[(\text{maternal height} + \text{paternal height} \pm 13 \text{ cm})/2]$  [3] or the mean height percentile for age and sex in the general population [36]. These approaches do not take into account individual trajectories, and studies reported wide variability in prediction of adult height from the calculated target height [39,40]. One of the strengths of our study is that, similar to WS's definition, which is defined with reference to premorbid BMI percentile, we

determined the HPP with reference to premorbid height percentile. HPP allowed us to evaluate the relative loss in height percentile after disease onset, with reference to premorbid height percentile. Although our study included a long follow-up of 36 months post-discharge, full adult height is not expected in our population at the time of evaluation. Thus, future research studies involving longer follow-ups to final height, and with reference to normative height-for-age trajectories, will be helpful for informing discussions about appropriate target discharge weight for EO-AN.

The present study has indicated that target discharge weight should restore the individual's premorbid BMI trajectory to achieve a better height prognosis in children with EO-AN, rather than defining target discharge weight as the 25th percentile of BMI for age and sex. Yet, restoring weight to premorbid BMI trajectory at discharge can imply increased duration of inpatient care. Duration of hospitalization is already long in AN [41], and reducing disruption to school, social and family life, and financial cost of treatment are important considerations. Future research is needed to develop alternative care and to target reduced WS with limited hospitalization duration. Research comparing longitudinal weight and height outcomes in EO-AN patients randomized to continued inpatient treatment versus day-patient treatment (partial hospitalization) after short inpatient care would be valuable. Among adolescents aged 11–18 with AN, day treatment after short inpatient care was comparable to continued inpatient care on BMI at discharge and 12 months, but long-term data on height were unavailable [42].

Our results must be interpreted in light of several limitations. First, although we used a consecutive hospital population sample to reduce sample bias by recruiting all inpatients with EO-AN, missing data in clinical records or from attrition over follow-up was not negligible. We thus performed multiple imputations using the standard protocols [28] for approximately 10–30% of the data depending on the follow-up time point. However, we replicated our results concerning the regression analysis by including only patients with complete data with similar results (Suppl Table 2). Second, as in most previous studies, the patients were not followed to their final adult height [3,29], yet, a longer follow-up would allow for better prediction. We cannot rule out the possibility that patients with a higher premorbid BMI or for whom menarche had not been observed before the last follow-up might perform their growth catch-up later. Additionally only one patient with premorbid obesity was reported in our population sample, we cannot conclude on target discharge weight in premorbid obese patients. Finally, although our sample (n = 74) is one of the largest to study height prognosis in EO-AN, it remains limited. Our study may lack power to identify some of the clinical characteristics associated with height prognosis in patients with EO-AN.

## Conclusion

WS at hospitalization discharge negatively impacts height prognosis at follow-up. Target discharge weight should be tailored to fully restore individual premorbid BMI trajectory for a better height prognosis in children with EO-AN. The difficulties in facilitating long-term weight recovery in this population represent a major challenge, especially in patients with EO-AN. Providing psychoeducation to patients and families about EO-AN and its deleterious effects upon growth is encouraged; the best possible height prognosis can be achieved when weight regain at discharge restores the patient's premorbid trajectory. Restoring weight to premorbid BMI trajectory at discharge can imply increased inpatient care duration, yet day patient care after short inpatient treatment may prove a viable alternative.

## Statement of authorship

All authors contributed to the conception/design of the study. AA and MD contributed to data acquisition. AA and HP contributed to data analysis and all authors contributed to data interpretation. All authors drafted the manuscript, revised the draft critically and approved the final draft.

## Declaration of competing interest

Drs Ayrolles, Clarke, Dechaux, Lefebvre, Cohen, Stordeur, Peyre, Bargiacchi, Godart, Watson, Delorme report no biomedical financial interests or potential conflicts of interest related to this work.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnesp.2023.01.025>.

## References

- [1] American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub; 2013.
- [2] Herpertz-Dahlmann B, Dempfle A, Egberts KM, Kappel V, Konrad K, Vloet JA, et al. Outcome of childhood anorexia nervosa—the results of a five-to-ten-year follow-up study. *Int J Eat Disord* 2018;51(4):295–304.
- [3] Lantzooui E, Frank GR, Golden NH, Shenker RI. Reversibility of growth stunting in early onset anorexia nervosa: a prospective study. *J Adolesc Health* 2002;31(2):162–5.
- [4] Mainz V, Schulte-Rüther M, Fink GR, Herpertz-Dahlmann B, Konrad K. Structural brain abnormalities in adolescent anorexia nervosa before and after weight recovery and associated hormonal changes. *Psychosom Med* 2012;74(6):574–82.
- [5] Clarke J, Peyre H, Alison M, Bargiacchi A, Stordeur C, Boizeau P, et al. Abnormal bone mineral density and content in girls with early-onset anorexia nervosa. *J Eat Disord* 2021 Jan 10;9(1):9.
- [6] Jagielska G, Wolanczyk T, Komender J, Tomaszewicz-Libudziec C, Przedlacki J, Ostrowski K. Bone mineral density in adolescent girls with anorexia nervosa. *Eur Child Adolesc Psychiatr* 2002;11(2):57–62.
- [7] Pfeiffer RJ, Lucas AR, Ilstrup DM. Effect of anorexia nervosa on linear growth. *Clin Pediatr* 1986;25(1):7–12.
- [8] Swenne I. Weight requirements for return of menstruations in teenage girls with eating disorders, weight loss and secondary amenorrhoea. *Acta Paediatr* 2004;93(11):1449–55.
- [9] Nussbaum M, Baird D, Sonnenblick M, Cowan K, Shenker IR. Short stature in anorexia nervosa patients. *J Adolesc Health Care* 1985;6(6):453–5.
- [10] Root AW, Powers PS. Anorexia nervosa presenting as growth retardation in adolescents. *J Adolesc Health Care* 1983;4(1):25–30.
- [11] Modan-Moses D, Yaroslavsky A, Pinhas-Hamiel O, Levy-Shraga Y, Kochavi B, Iron-Segev S, et al. Prospective longitudinal assessment of linear growth and adult height in female adolescents with anorexia nervosa. *J Clin Endocrinol Metab* 2021 Jan 1;106(1):e1–10.
- [12] Modan-Moses D, Yaroslavsky A, Novikov I, Segev S, Toledano A, Miterany E, et al. Stunting of growth as a major feature of anorexia nervosa in male adolescents. *Pediatrics* 2003;111(2):270–6.
- [13] American Psychiatric Association. Practice guideline for the treatment of patients with eating disorders. *Am J Psychiatr* 2006;163:4–54.
- [14] Beumont P, Hay P, Beumont D, Birmingham L, Derham H, Jordan A, et al. Australian and New Zealand clinical practice guidelines for the treatment of anorexia nervosa. *Aust N Z J Psychiatr* 2004 Sep;38(9):659–70.
- [15] Autorité de Santé Haute. Anorexie mentale: prise en charge. Paris HAS; 2010.
- [16] National Institute for Health and Care Excellence. Eating disorders: recognition and treatment. NICE; 2017.
- [17] Vandereycken W. The place of inpatient care in the treatment of anorexia nervosa: questions to be answered. *Int J Eat Disord* 2003;34(4):409–22.
- [18] Rozé C, Doyen C, Le Heuzey MF, Armoogum P, Mouren MC, Léger J. Predictors of late menarche and adult height in children with anorexia nervosa. *Clin Endocrinol* 2007;67(3):462–7.
- [19] Golden NH, Jacobson MS, Sterling WM, Hertz S. Treatment goal weight in adolescents with anorexia nervosa: use of BMI percentiles. *Int J Eat Disord* 2008;41(4):301–6.
- [20] Elamin A, Hussein O, Tuvemo T. Growth, puberty, and final height in children with Type 1 diabetes. *J Diabet Complicat* 2006 Aug;20(4):252–6.

- [21] Gasparetto M, Guariso G. Crohn's disease and growth deficiency in children and adolescents. *World J Gastroenterol* 2014 Oct 7;20(37):13219–33.
- [22] Autorité de Santé Haute. Anorexie mentale: prise en charge. Paris HAS; 2010.
- [23] Organization WH. WHO child growth standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: methods and development. 2006.
- [24] Swenne I, Parling T, Ros HS. Family-based intervention in adolescent restrictive eating disorders: early treatment response and low weight suppression is associated with favourable one-year outcome. *BMC Psychiatr* 2017;17(1):333.
- [25] Dempfle A, Herpertz-Dahlmann B, Timmesfeld N, Schwarte R, Egberts KM, Pfeiffer E, et al. Predictors of the resumption of menses in adolescent anorexia nervosa. *BMC Psychiatr* 2013;13(1):308.
- [26] van Noort BM, Lohmar SK, Pfeiffer E, Lehmkuhl U, Winter SM, Kappel V. Clinical characteristics of early onset anorexia nervosa. *Eur Eat Disord Rev* 2018. Sep;26(5):519–25.
- [27] Benjamini Y, Yekutieli D. False discovery rate—adjusted multiple confidence intervals for selected parameters. *J Am Stat Assoc* 2005 Mar 1;100(469):71–81.
- [28] Rubin DB. Multiple imputation for survey nonresponse. New York: Wiley; 1987.
- [29] Swenne I. Weight requirements for catch-up growth in girls with eating disorders and onset of weight loss before menarche. *Int J Eat Disord* 2005;38(4):340–5.
- [30] Swenne I, Thurjell B. Clinical onset and diagnosis of eating disorders in premenarcheal girls is preceded by inadequate weight gain and growth retardation. *Acta Paediatr* 2003;92(10):1133–7.
- [31] Bodell LP, Racine SE, Wildes JE. Examining weight suppression as a predictor of eating disorder symptom trajectories in anorexia nervosa. *Int J Eat Disord* 2016;49(8):753–63.
- [32] Föcker M, Bühren K, Timmesfeld N, Dempfle A, Knoll S, Schwarte R, et al. The relationship between premorbid body weight and weight at referral, at discharge and at 1-year follow-up in anorexia nervosa. *Eur Child Adolesc Psychiatr* 2015 May 1;24(5):537–44.
- [33] Yilmaz Z, Gottfredson NC, Zerwas SC, Bulik CM, Micali N. Developmental premorbid body mass index trajectories of adolescents with eating disorders in a longitudinal population cohort. *J Am Acad Child Adolesc Psychiatry* 2019;58(2):191–9.
- [34] Anastasiou CA, Karfopoulou E, Yannakoulia M. Weight regaining: from statistics and behaviors to physiology and metabolism. *Metabolism* 2015;64(11):1395–407.
- [35] Sumithran P, Prendergast LA, Delbridge E, Purcell K, Shulkes A, Kriketos A, et al. Long-term persistence of hormonal adaptations to weight loss. *N Engl J Med* 2011;365(17):1597–604.
- [36] Modan-Moses D, Yaroslavsky A, Kochavi B, Toledano A, Segev S, Balawi F, et al. Linear growth and final height characteristics in adolescent females with anorexia nervosa. *PLoS One* 2012;7(9):e45504.
- [37] Schorr M, Miller KK. The endocrine manifestations of anorexia nervosa: mechanisms and management. *Nat Rev Endocrinol* 2017;13(3):174.
- [38] Leroy JL, Frongillo EA, Dewan P, Black MM, Waterland RA. Can children catch up from the consequences of undernourishment? Evidence from child linear growth, developmental epigenetics, and brain and neurocognitive development. *Adv Nutr* 2020;11(4):1032–41.
- [39] Luo ZC, Low LC, Karlberg J. A comparison of target height estimated and final height attained between Swedish and Hong Kong Chinese children. *Acta Paediatr Oslo Nor* 1999 Mar;88(3):248–52. 1992.
- [40] Cole TJ, Wright CM. A chart to predict adult height from a child's current height. *Ann Hum Biol* 2011 Nov;38(6):662–8.
- [41] Glasofer DR, Muratore AF, Attia E, Wu P, Wang Y, Minkoff H, et al. Predictors of illness course and health maintenance following inpatient treatment among patients with anorexia nervosa. *J Eat Disord* 2020 Dec 2;8(1):69.
- [42] Herpertz-Dahlmann B, Schwarte R, Krei M, Egberts K, Warnke A, Wewetzer C, et al. Day-patient treatment after short inpatient care versus continued inpatient treatment in adolescents with anorexia nervosa (ANDI): a multi-centre, randomised, open-label, non-inferiority trial. *Lancet* 2014 Apr 5;383(9924):1222–9.