abstract

BACKGROUND AND OBJECTIVES: Clinicians are increasingly observing adolescents who have lost large amounts of weight, experience typical cognitions and acute medical complications of anorexia nervosa (AN), yet do not meet diagnostic criteria for AN owing to weight. We refer to this category of Eating Disorder Not Otherwise Specified as EDNOS-Wt. We set out to describe the changing incidence of EDNOS-Wt compared with AN, and to compare the characteristics of these 2 groups in a cohort that required hospitalization after weight loss.

METHODS: A 6-year retrospective cohort study (2005 to 2010) was undertaken of first admissions of 12- to 19-year-old patients to a tertiary children’s hospital using Diagnostic Statistical Manual of Mental Disorders, Fourth Edition (DSM IV) AN or EDNOS-Wt. Clinical, biochemical, and nutritional data were collected up to day 28 of admission.

RESULTS: Ninety-nine adolescents were admitted; 73 had AN and 26 had EDNOS-Wt. Mean (SD) age at admission was 15.2 years (1.3) and 87% were female. In 2005, EDNOS-Wt represented 8% of admissions; by 2009 this proportion had increased to 47%. Hypophosphatemia developed in 41% of AN and in 39% of EDNOS-Wt patients. The lowest mean pulse rate in AN was 45.1 bpm compared with 47.1 bpm in EDNOS-Wt patients.

CONCLUSIONS: We have experienced more than a fivefold increase in the proportion of adolescents who have EDNOS-Wt admitted over this 6-year period. Despite not being underweight, EDNOS-Wt patients experienced a similar profile of life-threatening complications of weight loss as patients who have AN. Higher-weight adolescents who have extensively lost weight require careful medical assessment. Pediatrics 2014;134:e758–e764

WHAT’S KNOWN ON THIS SUBJECT: Recent case reports have described acute life-threatening complications in adolescents who present to health services having lost large amounts of weight but who are not underweight. Little is known about the frequency of life-threatening complications in these adolescents.

WHAT THIS STUDY ADDS: Over 6 years, we found more than a fivefold increase in the incidence of hospitalized adolescents who, apart from not being underweight, have diagnostic features of anorexia nervosa. This group experienced a similar profile of acute complications of anorexia nervosa.
We have observed increasing numbers of adolescents who have a restrictive eating disorder who meet all diagnostic criterion for anorexia nervosa (AN) apart from low body weight. The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV) describes 4 diagnostic criterion to be diagnosed with AN, 1 of which is low body weight, defined as $<85\%$ of expected body weight. Failure to meet this low weight or other diagnostic criterion for AN results in the residual diagnosis of Eating Disorder Not Otherwise Specified (EDNOS), which is frequently perceived by clinicians and families to be less severe than AN. The recently released Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM 5) also requires a “significantly low body weight” to diagnose AN. Despite not being underweight, these patients have the psychological features of AN and can be medically compromised to the extent of requiring hospital admission. We refer to EDNOS patients who do not meet weight criteria as EDNOS-Wt.

The aim of this paper is to describe the relative incidence of adolescents who have EDNOS-Wt and those who have AN over a 6-year period. We also compare the severity of acute medical complications between these 2 diagnoses. This retrospective study based the diagnosis of AN on DSM IV, which was in use over the study period.

METHODS

Setting

The Royal Children’s Hospital (RCH) is a tertiary pediatric hospital in Melbourne, Australia, which has a specialist Eating Disorder (ED) program. All patients who have a possible ED undergo ambulatory assessment by a multidisciplinary ED team. Adolescents requiring admission are managed on the general Adolescent Ward by the same specialist team.

Ethical approval was obtained from the RCH Ethics and Research Committee and the University of Melbourne. Patient consent was waived as this study used retrospective, routinely collected data.

Study Design and Sample

A 6-year retrospective cohort study (2005 to 2010) was undertaken of 12- to 19-year-old patients admitted to hospital for the first time with an ED and weight loss. Admission data were retrieved from dietician encounters in the hospital database. Study participants were categorized with either DSM IVAN (including restricting and binge-purge subtypes) or EDNOS-Wt. That is, eligible patients met all criteria for the diagnosis of AN or were not sufficiently underweight at 85% or more of median BMI (%MBMI) and diagnosed with EDNOS-Wt.

Patients in the study were admitted to hospital after ambulatory assessment or after presentation to the hospital’s emergency department. The main admission criterion was acute medical complications if the treating team felt the patient was too unwell to be safely managed as an outpatient (eg, sinus bradycardia).

Over the 6-year period there were 174 admissions for an ED. Patients were excluded if their primary diagnosis was bulimia nervosa (BN, $N = 9$), the admission was not the first admission (to any hospital) for an ED ($N = 20$), they had menstruated in the previous 3 months ($N = 9$), they had no AN cognitions ($N = 10$), they were <$12$ years old ($N = 9$), or because of lack of beds on the adolescent ward they were admitted elsewhere and not managed according to clinical protocols ($N = 18$). Four patients admitted for <$7$ days were excluded, as they were transferred to another hospital for ongoing care. This study was based on the remaining 99 patients.

Inpatient Refeeding Protocol for AN

After assessment of recent dietary intake, a minimum of 1900 kcal per day was prescribed by the dietician, gradually increasing up to 2700 kcal on day 5. Patients deemed at significant risk for refeeding syndrome were commenced on rehydration therapy or modified meal plan. Regular food and drinks were offered; nasogastric feeding was used when patients were unable to eat the prescribed amount. Prescribed meal plans were analyzed with Foodworks Professional, Version 4, 1998–2005.

Outcome Measures

Retrospective data were collected on clinical features and investigations from clinical records. Data were collected from Day 1 of admission to discharge, to a maximum of 28 days. For longer admissions, final discharge data were also recorded. Weight and height were measured at admission, with weight then measured twice weekly before breakfast, after voiding and wearing a gown. Patients and families were asked to report the maximum premorbid weight; medical confirmation was used when available. Centers for Disease Control and Prevention (CDC) growth charts were used to calculate age- and gender-specific percentiles for height, weight, and BMI. Weight is reported as z score. BMI is reported as z score, percentile, and percentage of median BMI (%MBMI). Overweight was defined as BMI percentile 85.0 to 94.99 and obesity as 95.0 or above.

At admission, pulse rates were measured throughout the day and night by cardiac monitor (3 lead, Phillips MP-30) or pulse oximetry (Nellcor N-395) until clinically indicated to cease. Vital signs were measured at least daily by nursing staff throughout the admission. Data recorded for analysis included lowest lying pulse rate (bpm), lowest systolic blood pressure (mm/hg), and lowest body temperature (Celsius). Serum phosphate, magnesium, and potassium were measured throughout the admission. Liver function tests were only measured at admission unless...
abnormal. Biochemistry reference ranges were based on our hospital pathology guidelines.

**Statistical Analysis**

The number of EDNOS-Wt patients is presented as a proportion of the total AN plus EDNOS-Wt patients, along with a line of best fit. All clinical and outcome data are summarized separately for AN and EDNOS-Wt patients, reported using means and SD for quantitative characteristics (medians and interquartile ranges [IQR] for non-normal data), and numbers and percentages for categorical characteristics. Comparisons between AN and EDNOS-Wt adolescents were made using linear regression for continuous variables, reported as differences in means and their 95% confidence intervals (CI), or using a nonparametric rank sum test for non-normal data, and a difference in proportions and its 95% CI for binary variables. All analyses were performed by using Stata 12.0 (Stata Corp, College Station, TX).

**RESULTS**

Ninety-nine adolescents fulfilled the inclusion criteria, of whom 73 met diagnostic criteria for AN and 26 for EDNOS-Wt. The mean (SD) admission age was 15.2 years (1.3) and 87% were female. The median length of stay for AN was 21 days (IQR, 15 to 29) compared with 14.5 days for EDNOS-Wt (IQR, 10 to 21), \( P < .001 \).

Figure 1 demonstrates the increasing proportion of adolescents admitted with EDNOS-Wt compared with AN over 6 years. In 2005, EDNOS-Wt represented 1 of 13 (8%) first admissions. By 2009, this proportion had increased to 9 of 19 (47%) first admissions.

**Clinical Characteristics**

As expected, adolescents who had AN had lower admission weights, with a mean (SD) admission weight z score of \(-2.06 (1.25)\) compared with \(-0.01 (1.78)\) in adolescents who had EDNOS-Wt (mean difference = 2.05; 95% CI, 1.42 to 2.69; \( P < .001 \)). Adolescents who had AN had a mean (SD) %MBMI of 74.5 (7.1) compared with 93.0 (5.3) in EDNOS-Wt patients (mean difference = 18.5; 95% CI, 15.4 to 21.5; \( P < .001 \)). As expected, AN patients had a lower BMI centile and z score compared with EDNOS-Wt patients (both \( P < .0001 \)) (Table 1).

Eighty-six adolescents had their pre-morbid weight recorded. Over a third of patients who had EDNOS-Wt were previously overweight (17%) or obese (29%). In comparison, less than one-fifth of AN patients were previously overweight (11%) or obese (7%). There was no statistical difference in the amount of weight lost or duration of weight loss before admission between the 2 diagnoses (\( P = .84 \) and 0.18, respectively). One eligibility criteria was lack of menstruation in the 3 months before admission. Menstrual status was compared in females (\( N = 86 \)) by diagnosis. Fifteen (23%) of the 64 girls who had AN were premenarchal, whereas 3 (14%) of the 22 girls who had EDNOS-Wt were premenarchal. The remaining percentages had secondary amenorrhea.

**Severity of Acute Medical Complications**

There was no statistical difference in the severity of acute medical complications between the 2 groups, including lowest pulse rate, severity of sinus bradycardia, or incidence of hypophosphatemia (Table 2). More importantly, the 95% CIs are reasonably narrow. For example, the mean (SD) lowest pulse rate was 45.1 (9.9) bpm in AN patients and 47.1 (13.7) bpm in EDNOS-Wt patients. Similarly, in patients who experienced severe sinus bradycardia during the admission (pulse rate <40 bpm), there was no statistical difference in the mean (SD) pulse rate, being 35 (4.8) in patients who had AN and 34 (5.71) in patients who had EDNOS-Wt. The 1 exception was a statistical difference between the lowest lying systolic blood pressure, which was lower in AN patients (\( P = .0005 \)).

**Nutritional Intake**

The mean (SD) daily maximum energy prescribed for a minimum weight gain of 1 kg per week up to day 28 was 3086 (336) kcal in patients who had AN and 2977 (475) kcal in patients who had...
EDNOS-Wt (mean difference = 109; 95% CI, −258 to 1179; \( P = .21 \)). Twenty (30%) patients who had AN and 10 (38%) patients who had EDNOS-Wt required enteral feeding (difference in proportions, 0.03; 95% CI, 0.23 to 0.17; \( P = .76 \)).

**DISCUSSION**

We have observed a dramatic increase in restrictive EDs in adolescents who met all diagnostic criteria for AN apart from low weight. These adolescents required hospital admission because of acute medical complications of weight loss, despite not meeting the low weight criteria. We also found that inpatients who had EDNOS-Wt experienced a similar profile of life-threatening complications as adolescents who had AN, including early refeeding syndrome. This builds on the study by Peebles et al., who were the first to demonstrate that medical complications from weight loss can occur in adolescents who do not meet diagnostic criteria for DSM IV AN. Their retrospective study compared the medical severity of 8- to 19-year-old females diagnosed with AN, BN, and EDNOS. Of those who had EDNOS, a proportion had lost >25% of their premorbid weight. Although not underweight, this group was more medically compromised in some outcomes than the AN group. Our study reinforces the Peebles' conclusion that malnutrition at “multiple weights” can

**TABLE 1** Comparison of Weight Measures Between Patients Who Have AN and Those Who Have EDNOS-Wt

<table>
<thead>
<tr>
<th></th>
<th>AN (( N = 62))</th>
<th>EDNOS-Wt (( N = 24))</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum premorbid BMI centile</td>
<td>84.5 (30.1 to 82.9)</td>
<td>83.0 (75.9 to 97.5)</td>
<td>.0005</td>
</tr>
<tr>
<td>Admission BMI centile</td>
<td>0.3 (0.03 to 3.18)</td>
<td>25.6 (17.07 to 38.41)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Admission BMI z score</td>
<td>−2.7 (−3.4 to −1.9)</td>
<td>−0.7 (−0.9 to −0.5)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Duration of weight loss from lifetime maximum to admission (mo)</td>
<td>9.3 (5.4 to 13.1)</td>
<td>6.1 (3.5 to 12.4)</td>
<td>.18</td>
</tr>
<tr>
<td>Weight loss from lifetime maximum to admission (kg)</td>
<td>12.7 (7.8 to 18.8)</td>
<td>13.2 (6.8 to 18.4)</td>
<td>.84</td>
</tr>
<tr>
<td>Mean wt gain per day (kg)</td>
<td>0.16 (0.1)</td>
<td>0.18 (0.7)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**TABLE 2** Comparison of Clinical Measures Between Inpatients Who Have AN and Those Who Have EDNOS-Wt

<table>
<thead>
<tr>
<th></th>
<th>AN (( N = 73))</th>
<th>EDNOS-Wt (( N = 26))</th>
<th>Estimate of Difference</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission signs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest pulse rate</td>
<td>45.1 (9.9)</td>
<td>47.1 (13.7)</td>
<td>2.0</td>
<td>.45</td>
</tr>
<tr>
<td>Pulse rate &lt;40 bpm</td>
<td>35 (4.8)</td>
<td>34 (5.3)</td>
<td>1.0</td>
<td>.60</td>
</tr>
<tr>
<td>Lowest body temperature (°C)</td>
<td>35.9 (0.41) (0.4)</td>
<td>34.8 (0.71) (0.7)</td>
<td>1.1</td>
<td>.09</td>
</tr>
<tr>
<td>Lowest systolic blood pressure</td>
<td>84 (80–90)</td>
<td>91 (87–94)</td>
<td></td>
<td>.0005</td>
</tr>
<tr>
<td>Investigations at admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>30 (41%)</td>
<td>10 (38%)</td>
<td>0.03</td>
<td>.81</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td>8 (11%)</td>
<td>1 (4%)</td>
<td>0.07</td>
<td>.27</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>4 (5%)</td>
<td>0 (0%)</td>
<td>0.05</td>
<td>.22</td>
</tr>
<tr>
<td>Phosphate nadir (mg/dL)</td>
<td>3.5 (0.4)</td>
<td>3.6 (0.6)</td>
<td>0.1</td>
<td>.50</td>
</tr>
<tr>
<td>Magnesium nadir (mg/dL)</td>
<td>2.1 (2.1)</td>
<td>1.9 (0.1)</td>
<td>0.2</td>
<td>.54</td>
</tr>
<tr>
<td>Potassium nadir (mEq/L)</td>
<td>4.0 (0.4)</td>
<td>4.2 (0.3)</td>
<td>0.2</td>
<td>.03</td>
</tr>
<tr>
<td>Alkaline phosphatase (IU) (( N = 99))</td>
<td>62.0 (57.0 to 86.5)</td>
<td>85.0 (66.0 to 111.0)</td>
<td></td>
<td>.14</td>
</tr>
<tr>
<td>( \gamma )-glutamyltransferase (IU) (( N = 98))</td>
<td>14.0 (10.5 to 18.0)</td>
<td>12.0 (11.0 to 16.0)</td>
<td></td>
<td>.85</td>
</tr>
<tr>
<td>Alanine aminotransferase (IU) (( N = 98))</td>
<td>55 (25.0 to 42.0)</td>
<td>34 (28.0 to 39.0)</td>
<td></td>
<td>.86</td>
</tr>
</tbody>
</table>
result in medical compromise. Two studies of early onset ED also identified that low weight is not the only risk factor for medical instability. In a British review of 208 cases of children <12 years old, Hudson et al reported that 41% were medically unstable yet not underweight. Similarly, a Canadian study of 161 children <13 years of age also identified children who did not meet criteria for AN but were medically compromised.

In the Minnesota Starvation Experiment of 1943–44, 36 previously healthy men were fed 3200 calories per day for 3 months, then 1800 calories for 6 months. Most men lost >25% of their body weight over this period. In response, they developed decreased heart rate and blood pressure. Fatigue, apathy, dizziness, hair loss, and psychological and personality changes were also observed. The men were reported to become obsessed with food, and developed unusual behaviors around food.

In our study there was a similar amount and duration of weight loss in the 2 groups, despite the fact that 1 group was underweight and the other was not. Given this, it may be that the clinical features we observed in AN and EDNOS-Wt patients are less attributable to underweight and more a physiologic response to extreme weight loss over a short period, which was apparent in both groups. Additional research is required to explore this further.

The fact that severely underweight children and adolescents can experience life-threatening cardiovascular complications continues to pose a challenge for clinical educators. For example, a recent British study showed that most pediatric trainees were unable to identify any cardiovascular complications of severe underweight and that only half knew that refeeding syndrome can lead to hypophosphatemia. That a similar profile of complications can be experienced in patients who have lost considerable weight without being significantly underweight will provide an even greater challenge for educators.

As many clinicians are not aware of the cardiovascular risks associated with underweight, or that weight loss itself may result in medical instability, it is not surprising that there are extensive delays in diagnosing adolescents who have EDs who are not underweight. Sim et al reported 2 cases of previously obese adolescents; 1 was a 14-year-old boy who had lost over 50% of his body weight. Despite 13 medical encounters, increasing food restriction, social withdrawal, cold intolerance, bloating, constipation and fatigue, and clinical signs of sinus bradycardia and dehydration, there was no clinical discussion of his weight loss over this time. At his mother’s request, he was referred for an ED assessment and the diagnosis was finally made, but only after the patient had lost sufficient weight to meet diagnostic criteria for AN. In contrast, Whitelaw et al reported that although a pediatric emergency department did not consider an ED within the differential diagnosis of an overweight adolescent who presented after losing 17 kg in a few months and was found to have severe bradycardia, EDNOS-Wt was promptly diagnosed after admission to hospital under the care of an adolescent medicine team with extensive ED experience. In this latter case, an ED was diagnosed without the patient having to lose sufficient weight to meet diagnostic criteria for AN. Our retrospective study reinforces the message of these case reports: that cardiovascular assessment is a critical component of the clinical assessment of significant weight loss, regardless of a patient’s actual weight.

In the context of the obesity epidemic, EDNOS-Wt has rapidly emerged as an ED in adolescents who have lost large amounts of weight but who are not underweight at the time they present to health services. In this study, EDNOS-Wt patients had higher premorbid weights; however, some AN cases were also premorbidly overweight or obese. It is noteworthy that some of the patients in the current study had been advised by a health professional that they should lose weight, but no advice or follow-up was provided. None of the patients were engaged with any medical or professional service at the time they lost weight. This highlights the need for supervision of appropriate weight loss efforts in overweight adolescents to ensure it is physiologically safe.

More ecological approaches have been recommended with a shift away from weight as a primary determinant for treatment of overweight. Recent risks have been described from school-based obesity intervention studies. For example, Pinhas et al reported 4 cases in which school interventions that included teaching healthy eating were temporally associated with dietary restriction and disordered eating. Three of 4 cases required hospital admission for medical stabilization.

The current study has a number of limitations. Data were collected retrospectively, which reduces reliability. In particular, data about the maximum premorbid weight were not routinely sought during the study period and we cannot be certain of the reliability of the reported weights. Over the 6 years, our admission criteria relied increasingly on strict medical instability, which may have led to an increased recognition of this condition over the study period. Although this could partly explain the increasing number of EDNOS-Wt cases over this period, this change in admission criteria would have affected both AN and EDNOS-Wt patients alike. Family Based Treatment was introduced at the RCH during the study period. However, because only first hospital admissions are included, which typically occur before the...
commencement of treatment, this was unlikely to have influenced our findings. All adolescents who had EDNOS-Wt in the current study were clinically assessed by our psychiatrist to have similar cognitions as adolescents who had AN. This is consistent with Fairburn and Bohn’s study that compared the psychological profile of AN patients with EDNOS patients, finding no differences between the 2. Similarly, Eddy et al compared 57 AN and 46 EDNOS patients and found no differences of Eating Disorder Examination Questionnaire results or self-reported measures of depression and self-esteem between the 2 groups. It is interesting to contemplate the validity of psychometric measures when patients are not underweight, a topic that warrants further research.

Despite significant weight loss and a psychological profile consistent with AN, adolescents who had EDNOS-Wt were not sufficiently underweight to be classified as AN according to DSM IV criteria (Fig 2). The recent DSM 5 has removed the numerical weight requirement of <85% expected body weight for AN. The requirement for amenorrhea has also been removed. However, individuals must still have a “significantly low” body weight to be diagnosed with AN. Determining the definition of low weight is complex in adolescents owing to variations in pubertal status and growth. The DSM 5 recommends less than the fifth percentile for CDC BMI-for-age as suggestive of low weight, while advising clinicians to also assess somatotype, weight history, and physiologic disturbances. Atypical AN is the new terminology to describe those who fail to meet the weight criteria for AN under DSM 5, a diagnosis within the larger diagnostic group of Other Specified Feeding or Eating Disorder. Despite our EDNOS-Wt cohort being physically unwell, they did not reach diagnostic criteria for AN in either manual. Indeed, were we to retrospectively apply the CDC suggestion of low weight at less than fifth percentile BMI to our cohort, 11 fewer would be diagnosed with AN than using DSM IV. Although further studies are required to explore the incidence, clinical severity, and prognosis of adolescents who are not underweight yet otherwise have diagnostic features of AN, the current study supports further broadening the diagnostic criteria of AN by removing reference to low weight.

Dietary restraint, body dissatisfaction, weight concerns, and pursuit of the thin ideal have each been identified as risk factors for dieting and the development of disordered eating, which can lead to an ED. Both BN and binge ED, another common ED, can be experienced in those who are overweight and obese. Although the causes of EDs are likely multifactorial, neurobiological risk factors are increasingly believed to contribute in those who are genetically vulnerable. Indeed, weight loss itself may trigger the cascade that leads to AN in those who are neurobiologically or genetically vulnerable.

CONCLUSIONS
We have observed a fivefold increase in adolescents diagnosed with EDNOS-Wt over a 6-year period who required hospital admission because of acute medical complications. Regardless of their actual weight, clinicians consulting with adolescents who have lost a large amount of weight should, among other tasks, review the patient’s weight loss strategies to ensure they are sustainable and safe. They should also carefully assess the patient’s cardiovascular health and consider the development of an ED.

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Restrictive Eating Disorders Among Adolescent Inpatients
Melissa Whitelaw, Heather Gilbertson, Katherine J. Lee and Susan M. Sawyer

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