Adolescent Eating Disorders

Update on Definitions, Symptomatology, Epidemiology, and Comorbidity

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KEYWORDS

• Anorexia nervosa • Bulimia nervosa • Binge-eating disorder • Adolescence
• Epidemiology • Comorbidity • Diagnostic classification

KEY POINTS

- Eating disorders are some of the most prevalent disorders in adolescence, often taking a chronic and disabling course.
- Most eating disorders imply a deep dissatisfaction with the subject's own body and shape; everyday live is often unduly preoccupied by eating and weight-control practices.
- There have been major changes from DSM-IV to DSM-5, leading to an increasing prevalence of anorexia and bulimia nervosa and a decreasing prevalence of eating disorders not otherwise classified. According to DSM-5, binge-eating disorder (BED) enters a distinct category of its own.
- In adolescence and childhood, the rates of eating disorders are on the increase. Every clinician working with this age group should be familiar with their symptomatology and medical/psychiatric assessment.
- Eating disorders are associated with high and sometimes life-threatening medical and psychiatric comorbidities.
- Severe and prolonged starvation, characteristic of chronic anorexia nervosa, can have profound consequences on brain and bone development.

INTRODUCTION

Eating disorders are the third most common chronic illness among adolescents, after obesity and asthma[1]; the peak age of onset occurs between 14 and 19 years. In this article, 5 categories of eating disorder are described according to the *Diagnostic and*

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Abbreviations	
ADHD	Attention-deficit/hyperactivity disorder
AN	Anorexia nervosa
BED	Binge-eating disorder
BMI	Body mass index
BN	Bulimia nervosa
DSM-5	*Diagnostic and Statistical Manual of Mental Disorders*, 5th edition
EDNOS	Eating disorders not otherwise specified
LOC	Loss of control of eating
OCD	Obsessive-compulsive disorder
OSFED	Other specified feeding or eating disorders

Statistical Manual of Mental Disorders, 5th edition (DSM-5)[2]: Anorexia Nervosa (AN), Bulimia Nervosa (BN), Binge-Eating Disorder (BED), Other Specified Feeding or Eating Disorders (OSFED), and Unspecified Feeding or Eating Disorders. All of these disorders are thought to exist within a broader spectrum, and patients frequently move among them.[3] Recent epidemiologic studies have suggested higher prevalence rates in youth than previously thought,[4,5] with a substantial increase in unspecified eating disorders over recent years. Although approximately 10% of the general population suffers from some type of eating disorder, only a minority of these individuals ever seek treatment.[6] Children and adolescents often become adults in whom these disorders persist: the chronic and disabling courses of these conditions generate high somatic and psychiatric comorbidity rates, along with substantial personal and societal costs.

This article provides an overview of the recent developments in definitions and diagnoses, including new classification issues, medical and psychiatric comorbidities, and current trends in the prevalence of the spectrum of eating disorders.

DEFINITION AND CLASSIFICATION

Definition of Eating Disorders

Most of the spectrum of eating disorders, especially AN, BN, and some OSFED, is characterized by a fear of fatness and a pathologic preoccupation with weight and shape. Self-evaluation is predominantly based on the perception of one's own body, and everyday life is unduly influenced by weight-control practices. In BED, negative feelings related to body weight and shape are also frequently prevalent.

Anorexia Nervosa

AN is a severe psychiatric disorder with substantial morbidity and the highest mortality of all mental disorders. The standardized mortality rate for AN is approximately 6,[7] which is higher than that for asthma and diabetes mellitus type 1.[8] About one-fifth of those who die commit suicide.[7]

Extreme dissatisfaction with the size or shape of one's body or some body parts leads to weight phobia and food aversion. Whereas some patients perceive their bodies as being fat despite of severe starvation, others are able to recognize their emaciated figures but find it attractive. Low body weight is the result of a strict diet and/or excessive hyperactivity. It is pursued beyond the bounds of reason and to the exclusion of age-appropriate activities. In very young patients, especially in those

with prepubertal onset, low body weight may be achieved by increasing growth in height without corresponding weight gain. Most patients experience their symptoms as egosyntonic, and despite feeling weak and excluded from age-appropriate life, they feel distinguished by having AN.

Bulimia Nervosa

Similarly to AN, fear of fatness and attempts to lose weight are core symptoms of BN. In many patients, a body-image disturbance is present and can be characterized by a profound dissatisfaction with one's own body shape and weight. While permanently restricting calories, fasting is interrupted by binge-eating episodes accompanied by a feeling of losing control. Binges are followed by fear of weight gain and the desire to purge and, thus, compensate for the calories consumed. Patients with BN usually weigh within a normal range, although some fall in the upper or lower normal ranges. A lower body mass index (BMI; calculated as weight in kilograms divided by height in square meters [kg/m^2]) is often associated with a history of AN. However, the percentage of overweight and adiposity in BN has increased during recent years,[9,10] rendering its treatment more demanding. Overweight patients with BN seek help for bingeing and purging in addition to weight loss,[10] which in turn might promote bingeing.

Binge-Eating Disorder and Loss of Control of Eating

BED is characterized by episodes of binge eating associated with feelings of loss of control, for example, eating a large amount of food in a discrete period of time but not followed by purging behavior. BED usually starts in adolescence but may already be prevalent in children.[11] In contrast to individuals with similar high BMI, individuals with BED often present with high psychiatric comorbidities, especially mood and anxiety disorders.[12] In children and adolescents, BED or any other type of disinhibited eating is often preceded by loss of control of eating (LOC).[13,14] LOC is defined as eating with the associated experience of being unable to control the amount of food, regardless of the size of the meal.

CLASSIFICATION OF ADOLESCENT EATING DISORDERS: CHANGES FROM *DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS,* 4TH EDITION TO *DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS,* 5TH EDITION

To reduce the frequency of eating disorders not otherwise specified (EDNOS in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, text revision [DSM-IV]),[15,16] the threshold for both AN and BN has been lowered, and BED has been introduced into DSM-5. Previous research has reported the stigmatization of individuals with eating disorders by both health professionals and the general public.[17] The stigmatization of AN was most likely supported by DSM-IV items implying a deliberate attitude of the patient and willful actions, such as "refusal to maintain body weight at or above a minimally normal weight for age and height" or a "denial of the seriousness of low body weight." In DSM-5 criteria for AN (**Box 1**), these items have been replaced by more neutral terms, such as "restriction of energy intake relative to requirements" and "persistent lack of recognition of the seriousness of the current low body weight." In item A of the new DSM-5 criteria, underweight must be judged in the context of "age, sex, developmental trajectory and physical health," which is especially important for diagnosing and treating children and adolescents. Moreover, it seems to be helpful for clinicians treating younger subjects to rely on the clinical symptom "persistent behavior that interferes with weight gain" because many underweight adolescent patients or children do not

Box 1
Diagnostic criteria for anorexia nervosa according to DSM-5 (abbreviated form)

A. Restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory, and physical health. For children and adolescents, significantly low weight is defined as a weight that is less than minimally expected

B. Intense fear of gaining weight or becoming fat or persistent behavior that interferes with weight gain

C. Body image disturbance, undue influence of weight and shape on self-confidence, or persistent lack of recognition of the seriousness of the illness

Subtypes: Restricting and Binge Eating/Purging Type.

admit "an intense fear of gaining weight" or a distortion of body image.[18] However, especially in the younger patient groups, the lack of a standard or reference for the weight criterion is a problem. According to DSM-5, significantly low body weight in children and adolescents is defined as "weight that is less than minimally expected." For adults, a BMI of 18.5 is proposed as the lower limit of normal body weight,[2] which approximately corresponds to the 10th BMI percentile in United States and European adult populations. Accordingly, BMI below the 10th percentile is used in Germany[19,20] and by several United States[21] and international clinicians[22] as a weight threshold for minors.

In comparison with DSM-IV the amenorrhea criterion has been left out of DSM-5, which was the most important step in lowering the diagnostic threshold. DSM-IV amenorrhea was not applicable to prepubescent and premenarchal girls and to females on contraceptives, and is not relevant for male patients with AN. In addition, no important differences seem to exist between those with amenorrhea and those without. A significant minority of women (up to one-fourth in clinical samples) who fulfill all other criteria for AN and need clinical attention, menstruate.[23] It must be noted, however, that existence of amenorrhea might help to distinguish between constitutional thinness and AN.

DSM-5, similarly to DSM-IV, distinguishes between 2 subtypes of AN: the restricting type and the binge-eating/purging type. The restricting type is characterized by accomplishing weight loss primarily by fasting and/or excessive exercising, whereas patients with the binge-eating/purging type may engage in bingeing and purging, only bingeing (with intermittent periods of fasting or excessive exercising) or only purging (practicing self-induced vomiting, laxative abuse, diuretics, or other weight-loss–supporting medications, such as thyroid hormones, amphetamines, or enemas). However, in contrast to DSM-IV, the time frame is more specific; instead of referencing the "current episode" of the eating disorder, a duration of at least 3 months for either symptomatology is given, thus corresponding to the definitions for bingeing in BN and BED. The subtyping of AN is important, as both subgroups differ in somatic and psychiatric comorbidities and, most likely, in outcomes.

DSM-5 criteria for BN are very similar to those of DSM-IV. However, the symptom frequency of binge eating and subsequent compensatory behavior was relaxed to once a week for 3 months instead of twice a week (**Box 2**).

The major change from DSM-IV to DSM-5 is the official diagnostic classification of BED. The publication of preliminary criteria in DSM-IV was followed by extensive research in adult and youth populations. From many empirically derived results, it

Box 2
Diagnostic criteria for bulimia nervosa according to DSM-5 (abbreviated form)

A. Recurrent episodes of binge eating
B. Recurrent inappropriate compensatory behaviors, eg, self-induced vomiting, laxative or diuretics abuse, or fasting or excessive exercise
C. Frequency of binge eating at least once a week for 3 months
D. Self-confidence is contingent on weight and shape
E. Symptoms do not only occur during episodes of anorexia nervosa

was demonstrated that BED has sufficient clinical utility and validity.[24] In children and adolescents, a consistent relationship between binge eating and overweight/obesity and current and future comorbid psychopathologies was observed (**Box 3**).[25]

Other Specified Feeding or Eating Disorder

An eating disorder is classified under this diagnostic category if it does not fulfill all diagnostic criteria for one of the aforementioned categories but causes "clinically significant distress or impairment" in different types of functioning.[2] The following disorders are subsumed under this eating disorder class: atypical AN (weight criterion not fulfilled), atypical BN of low frequency and/or limited duration (time frame not fulfilled), atypical BED of low frequency and/or limited duration (time frame not fulfilled), purging disorder, and night eating syndrome.

In a recent study, no significant differences between AN and EDNOS-AN were found according to self-report or interview measures, with the exception that participants with AN reported higher rates of binge eating and purging compared with those with EDNOS-AN and more obvious somatic sequelae, such as lower white blood cell counts.[26]

Purging disorders are defined by recurrent self-induced vomiting and/or laxative abuse or other medications to lose weight, and an overvaluation of shape and weight in the absence of binge eating and low body weight.

Night eating is diagnosed in the presence of recurrent eating after awakening from sleep or excessive food consumption after evening dinner. The patient is aware of and remembers this food consumption.

Box 3
Diagnostic criteria for binge-eating disorders according to DSM-5 (abbreviated form)

A. Recurrent episodes of binge eating
B. Binge eating is associated with eating faster until feeling uncomfortably full, eating when not feeling hungry, eating alone due to being embarrassed, or feeling disgusted or depressed
C. Marked distress because of the symptoms
D. Frequency at least once a week for 3 months
E. Symptoms are not followed by compensatory behavior and do not occur in the context of bulimia nervosa or anorexia nervosa

Unspecified Feeding or Eating Disorder

This term applies to eating disorders that cause significant impairment but do not fulfill all diagnostic criteria enumerated under the other diagnostic classes already mentioned.

Eating Disorders: DSM-IV to DSM-5

The most important change from DSM-IV to DSM-5 is the reduction of the residual diagnosis of EDNOS by introducing the new specific diagnostic category for BED and by lowering the thresholds for AN, owing to the omission of the amenorrhea criterion, and for BN, because of the reduced symptom frequency in BN.

SYMPTOMS

Anorexia Nervosa

Dieting behaviors

AN almost always begins with dieting. Girls with AN will mostly eat so-called healthy food, such as fruit, vegetables, and salad; many of them become vegetarians. Persons with AN differentiate between "good" and "bad" foodstuffs, and are often influenced by magical or superstitious thinking. Several of them celebrate their eating by setting the table in a particular manner and practicing rituals while eating. Adolescents with AN often eat very slowly and show picky eating, taking very small bites, avoiding any fat and smearing food up to avoid eating it. Many of them excessively count calories. Some develop an extensive interest in recipes and cooking, or they may urge their family members to eat large meals so that those often complain of weight gain. Younger adolescents or children may even refuse to drink because of an intense fear of becoming fat.[27] Others do not dare to even touch fat because they fear it might be absorbed by the skin.

Anorexia Nervosa Pearl

The younger the girl and the quicker the weight loss, the higher the rate of medical complications.

Weight control and exercise

Patients with AN step on the scales several times a day and look in mirrors to assess their shape. Their moods will be heavily influenced by weight gain; often the pursuit of thinness escalates with increasing weight loss. Approximately 30% to 80% of individuals with AN can be characterized as hyperactive.[28] Many of them practice sports or commit themselves to fitness training or gymnastics. Exercise often becomes ritualized and may be used for regulating mood states, such as anxiety, anger, and depression. With increasing weight loss, active sports are often replaced or complemented by restlessness, which may express itself in a constantly active posture, fidgeting, or inability to sit still. Exercise is not only voluntarily driven; it is also induced by prolonged semistarvation. In the advanced stages of the illness, hyperactivity is largely triggered by hypoleptinemia[29,30] and other metabolic changes.[31] Hyperactive individuals with AN suffer from higher relapse rates[32] and often fall ill at a younger age.[30]

Physical Hyperactivity and Anorexia Nervosa

Hyperactivity is associated with

a. More severe psychopathology[33]
b. Lower BMI[29]
c. Higher dissatisfaction with one's own body[34]
d. Worse response to treatment[35]
e. A more chronic course[36]

Body image disturbance

Slade[37] defined body image as the "picture we have in our minds of the size, shape and form of our bodies; and our feelings concerning these characteristics and our constituent body parts." Today the conception of body image is based on a combination of perceptual, affective, and cognitive components with behavioral features. Although the results are somewhat contradictory in reports on adolescent patients, many individuals with AN (and BN) overestimate their body size in comparison with healthy controls. Certain body parts are more overestimated than others, especially the thighs and waist. Patients with the binge/purging type of AN seem to be more affected than those with the restrictive subtype. Some patients practice checking rituals, such as touching body parts repetitively or controlling their shape in the mirror (for a review see Legenbauer and colleagues[38]).

Bulimia Nervosa

Girls and young women with BN share the fear of obesity and exaggerated wish of thinness with individuals suffering from AN. Although body-image distortion is less pronounced than in emaciated AN, several patients with BN also tend to overestimate their body size. In most cases, BN starts with a longer episode of fasting, which is terminated by a loss of control resulting in binge attacks followed by an extreme fear of gaining weight and weight-loss practices, such as vomiting, laxative abuse, diuretics, the abuse of other medications, or, more rarely, the use of non-purging strategies, such as exercising. Thus, a vicious circle is started. Binges and purges are mostly practiced in secret. Failure to adhere to a planned small amount of food is sometimes deliberately followed by a binge to facilitate vomiting. For the same purpose, patients drink fluid copiously during meals. A binge attack might comprise up to more than 10,000 calories and mostly consists of cold food that is easy to swallow, such as desserts, cake, and chocolate. In contrast to objective binges with high amounts of food, some patients may engage in so-called subjective binges with only small quantities of food, which nevertheless cause them to experience a loss of control. In short, a binge is the violation of one's personal conception of the amount and type of food he or she is allowed to eat. In the beginning, binge attacks and compensatory behaviors are often preceded by emotional stress and feelings of loneliness; during the course of the disorder, they become more and more habitual and are sometimes regularly scheduled in everyday life. Binges may occur from once a week to several times a day, with a higher medical risk associated with the latter. Some patients combine vomiting with taking laxatives. In contrast to AN patients, many individuals with BN can hide their disorder and avoid treatment for many years.[27]

Binge-Eating Disorder

BED in children and adolescents refers to eating an objectively large amount of food while experiencing a sense of loss of control. Similarly to BN, children and adolescents with BED seek food in the absence of hunger for example, after a full meal. Some of them use bingeing to regulate negative effects or as a reward; they may also hoard or hide food. However, several researchers have pointed out that BED is not easy to conceptualize in childhood, largely because of the difficult definition of "a large amount of food" in childhood or adolescence; for example, whether 3 pieces of cake would be too large for a 12-year old boy might be judged differently. In addition, the amount of food might be limited by caretakers so that the real quantity the child would have eaten cannot be assessed. Moreover, some children report a decreased awareness during the meal, resulting in a biased recall of the amount eaten. Tanofsky-Kraff and colleagues[39] have therefore proposed to better refer to "loss of control of eating" independently, rather than as measured by the quantity eaten, as they believe the former constitutes a more reliable criterion for an eating disorder in younger age groups. Indeed, recent studies have shown that LOC and not overeating was predictive of later overweight and obesity, and depression.[25] Children with LOC develop more general and eating disorder psychopathologies than those without LOC, and gain more weight over time.[40] Moreover, children with LOC make significantly higher use of dysfunctional emotion-regulation strategies.[41]

EPIDEMIOLOGY

Anorexia Nervosa

Very few community studies have assessed the incidence of eating disorders. Comparing these incidence rates with those of primary care, the former are significantly higher because the latter implies a bias caused by selection processes on the way to treatment.[42]

In Finnish community studies based on a twin register, incidence rates of 270 to 450 per 100,000 (depending on a narrow or broad definition) were found in 15- to 19-year-old females during the 1990s.[43] The incidence rates derived from primary care are shown in **Table 1**. Several studies were able to demonstrate that the highest incidence rates are found in this age group, with approximately 40% of all new cases appearing in this period.[5,42] In children between 5 and 12 years of age, the incidence rates for restrictive eating disorders (not all fulfilling DSM-IV criteria for AN) were estimated at 1 to 2.5,[44,45] although they seem to be on the increase.[46,47] While the incidence rates are stable in the adult group, they seem to be increasing in adolescents and children (for reviews see Smink and colleagues[42] and Favaro and colleagues[48]).

In adolescent samples, most studies found point and 12-month prevalence rates of AN, according to DSM-IV, of between 0.3 and 0.9[4,42,49] (including an epidemiologic

Table 1
Epidemiology of adolescent eating disorders

	AN		BN		BED (DSM-IV EDNOS)	
	Female	Male	Female	Male	Female	Male
Incidence[a]	40–100	1–4	40–50	2–3	70	10
12-month prevalence (%)	0.3–0.9	0.1–0.3	1–2.0	0.3–0.5	1.5–2.0	0.4–0.8

[a] Eating disorder per 100, 000 15–19-year-olds in primary care.
Data based on Refs.[4,5,51] and reviews by Refs.[42,89]

study investigating a nationally representative sample of 10,120 adolescents in the United States between 13 and 18 years and a median age at onset of 12.4 years). Point prevalence is defined by the prevalence at a given point in time and assessed according to the current standard of a 2-stage selection model. In this model, an epidemiologic sample is primarily investigated by means of a screening questionnaire to select for persons at risk. The at-risk individuals are then usually interviewed personally by a general or disorder-specific diagnostic instrument. The 12-month prevalence is the number of cases in a given year.

Bulimia Nervosa

Similarly to AN, community studies are scarce. In a Finnish epidemiologic study of BN, the incidence rate was measured at 200 per 100,000 females aged 16 to 20 years.[50] In studies based on primary care rates, incidence in adult individuals seemed to decrease, which can most likely be explained by an increasing number of treatment options in the community (eg, self-help group vs medical care). Alternatively, the initially high rates in the 1990s were due to the announcement and detection of the new diagnosis of "BN." Nevertheless, in young females and males the incidence rates of BN remain stable.[5,51] Some investigations even indicate that individuals with BN have been diagnosed at increasingly young ages.[48] Recent studies have reported controversial results as to whether the prevalence of BN is also decreasing (in accordance with incidence rates) (for a review see Smink and colleagues[42]).

Binge-Eating Disorder and Eating Disorder Not Otherwise Specified

To the author's knowledge there are no incidence studies in BED, as up to recently no DSM criteria existed. A recent study reports on the increasing incidence of EDNOS, including BED, in the United Kingdom between 2000 and 2009.[5] According to this study, EDNOS is the most prevalent eating disorder.

For BED, prevalence rates are also scarce; the prevalence data in adolescents according to the earlier proposed DSM-5 criteria are estimated to be approximately 1% to 5%.[4,52] In a longitudinal study, the prevalence of BED increased significantly in girls between 14 and 20 years of age.[52] The prevalence in males was lower than in females; however, the gap between the sexes was less pronounced than in AN and BN.

Changes in Epidemiology from Diagnostic and Statistical Manual of Mental Disorders, 4th edition to Diagnostic and Statistical Manual of Mental Disorders, 5th edition

Recent studies demonstrate that the revised version of eating disorders in DSM-5 alters the frequency of disorders previously reported according to DSM-IV. In all studies, AN and BN rates increased in children and adolescents when using DSM-5; in a clinical eating disorder sample, the proportions of AN and BN rose from 30% to 40% and from 7% to 12%, respectively.[53] An increase was also found in epidemiologic studies when comparing DSM-IV prevalence rates with the prevalence rates obtained according to DSM-5.[52,54] In the clinical sample by Ornstein and colleagues,[53] the percentage of EDNOS was reduced by nearly half when applying DSM-5 criteria. A significant reduction was also found in epidemiologic studies. All of the investigators agree that DSM-5 criteria effectively restricted the residual diagnosis of EDNOS and better assigned eating-disordered individuals to specific and homogeneous diagnostic categories.

COMORBIDITY

Medical Comorbidity

As already mentioned, eating disorders have a high rate of medical comorbidity. In a recent meta-analysis based on 36 studies, the standardized mortality rates (ratio of

observed to expected deaths) were 5.86 for AN, 1.93 for BN, and 1.92 for EDNOS (according to DSM-IV criteria). The mortality rates for AN showed a significant association with age but not with BMI, underlining the danger of a long-lasting illness.[7] The severity and consequences of somatic sequelae depend on the extent and rapidity of weight loss, the current degree of underweight, the duration of the eating disorder, the intensity of purging, and the age of the patient. In general, because of a smaller amount of fat mass, children suffer from more medical comorbidities in comparison with adolescents. In contrast to adult patients, children and adolescents with AN experience severe effects on their pubertal development and growth. The most important somatic changes and dysfunctions are described in **Table 2**.

In AN, signs of malnutrition often make diagnosis easy, whereas BN patients are of normal weights and often deny their symptoms. AN patients present with emaciated limbs, a wasting of the subcutaneous fat tissue and muscles, bony prominences, and protruding ribs. Dental assessment might show erosion of dental

Table 2
Medical alterations in adolescent eating disorders

	AN	BN
Physical examination findings	Dry skin Lanugo hair formation (only with severe weight loss) Acrocyanosis Alopecia Low body temperature Dehydration Retardation of growth and pubertal development	Erosion of dental enamel Parotid/salivary gland enlargement Scars on the skin of the back of the hand resulting from inducing the gag reflex Dehydration
Cardiovascular system	Bradycardia ECG abnormalities (mostly prolonged QT interval) Pericardial effusion Edema (before or during refeeding)	ECG abnormalities (cardiac arrhythmia, prolonged QT interval)
Gastrointestinal system	Impaired gastric emptying Pancreatitis Constipation	Esophagitis Pancreatitis Delayed gastric emptying
Blood	Leukocytopenia, thrombocytopenia Anemia	
Biochemical abnormalities	Hypokalemia Hyponatremia Hypomagnesemia Hypocalcemia Hypophosphatemia (during refeeding) Low glucose levels AST ↑, ALT ↑ (with severe fasting or beginning of refeeding) Cholesterol	Hypokalemia Hyponatremia Hypomagnesemia (caused by diarrhea) Hypocalcemia Metabolic alkalosis (in case of severe purging) Metabolic acidosis (in case of severe laxative abuse)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ECG, electrocardiographic.

Data from Herpertz-Dahlmann B. Adolescent eating disorders: definitions, symptomatology, epidemiology and comorbidity. Child Adolesc Psychiatr Clin N Am 2009;18(1):31–47.

enamel, which is a characteristic of vomiting in AN and BN patients. The effect of starvation on the heart and low thyroid hormones explain the bradycardia, low body temperature, hypotension, and orthostatic problems. Fluid and electrolyte abnormalities may be especially serious in binge/purge AN or BN patients. Hypokalemia is especially frequent in the latter disorder, and represents a harmful complication that might result in cardiac arrest. Gastrointestinal complications are also frequent in AN and BN, including dysfunctions of the pancreas and the liver and increased levels of amylase, lipase, and liver enzymes. The usually mild elevations described here may be the result of severe malnutrition or a consequence of refeeding. The hallmark of refeeding syndrome is hypophosphatemia associated with neurologic and cardiac adverse events. Renal dysfunction may be revealed by elevated levels of creatinine or blood urea nitrogen. Persistently elevated creatinine levels may point to a chronic renal abnormality. Many patients with AN, especially those who drink large amounts of water to appease their hunger, have problems concentrating their urine and exhibit disturbed osmoregulation. Recent studies have reported abnormalities in vitamin blood levels, such as vitamin D deficiencies and high levels of vitamin A.[55] Many patients complain of hair loss, brittle nails, constipation, headache, or fatigue (for a review see Katzman[56]). A full medical assessment is recommended (**Box 4**).

AN and, to a lesser degree, BN lead to endocrine changes. In general, these abnormalities are a consequence of semistarvation, abnormal eating behaviors, or both, and are regarded as adaptive mechanisms to conserve energy. The most important (but not all) of the changes are listed in **Table 3**.

Osteopenia and Osteoporosis

As shown later, AN (and, to a lesser degree, BN and OSFED) is characterized by widespread endocrinologic abnormalities, such as hypogonadotropic hypogonadism, hypercortisolemia, low level of insulin-like growth factor 1, deficits in adipocyte hormones, including leptin, and changes in gut hormones, including ghrelin. All of these contribute to the uncoupling of bone formation and bone resorption, resulting in an impaired bone structure and reduced bone strength (see **Box 4**). Low bone density is generally not completely reversible, even after weight rehabilitation. Several studies have demonstrated that adolescent AN is associated with a 2- to 7-fold higher fracture risk later in life (for a review see Fazeli and Klibanski[57]). Osteoporosis is not only a problem of females but also of male patients, owing to their deficits in gonadal hormones.[58]

Box 4
Medical assessment of eating disorders

- Physical assessment (heart rate, blood pressure, body temperature)
- Complete blood count
- Biochemical profile (sodium, potassium, calcium, chloride, magnesium, phosphate, creatinine, urea, serum proteins, glucose, liver enzymes, amylase, lipase)
- Electrocardiogram
- Electroencephalography, magnetic resonance imaging, computed tomography (in case of atypical eating disorder, eg, boys, children, or manifestation of seizures)

Data from Herpertz-Dahlmann B. Adolescent eating disorders: definitions, symptomatology, epidemiology and comorbidity. Child Adolesc Psychiatr Clin N Am 2009;18(1):31–47.

Table 3
Endocrinologic changes in AN and BN

	AN	BN
Thyroid axis	↓ fT3, n (↓) fT4	n (↓)
Gonadal axis	↓ FSH	n (↓)
	↓ LH pulsatility	n (↓)
	↓ Estrogens	n (↓)
	↓ Androgens	n (↓)
Adrenal axis	↑ Cortisol	n (↑)
	n DHEAS	n
Growth hormone	GH resistance (↑ GH/↓ IGF-1)	n (↑)
Appetite-regulating hormones	↓ Leptin	n (↓)
	↑ Ghrelin (fasting)	↑
	↑ (n) PYY (fasting)	n

Abbreviations: DHEAS, dehydroepiandrosterone; FSH, follicle-stimulating hormone; fT3, free triiodothyronine; fT4, free thyroxine; GH, growth hormone; IGF-1, insulin-like growth factor type 1; LH, luteinizing hormone; n, normal; PYY, peptide YY; ↑, elevated; ↓, reduced.

Data from Miller KK. Endocrine dysregulation in anorexia nervosa update. J Clin Endocrinol Metab 2011;96(10):2939–49; and Herpertz-Dahlmann B, Holtkamp K, Konrad K. Eating disorders: anorexia and bulimia nervosa. Handb Clin Neurol 2012;106:447–62.

Implications of Anorexia Nervosa for Brain Development

In the starved state, AN leads to reduced volumes of gray and white matter in the brain. Although these reductions do improve on weight restoration, the completeness of the brain-volume rehabilitation remains equivocal. Studies in adolescent AN have shown larger effects for brain-volume changes than in adult AN.[59,60] There is also recent evidence that long-lasting starvation-induced hormone deficits may be linked to the disturbed development of certain brain regions, especially the volumes of the amygdala and hippocampus.[61] These disruptions are most likely responsible for the neuropsychological deficits, such as impaired memory and learning and reduced cognitive flexibility that render psychotherapy difficult during acute stages of the illness (see later discussion on neuropsychological impairment).

Psychiatric Comorbidity

Eating disorders are often accompanied by other psychiatric disorders, either before or during the acute state of the illness or in the long-term course. Clinicians should conduct a thorough psychiatric assessment focusing on comorbid disorders, continuing through treatment. Onset patterns (eg, which disorder preceded the other) might also be important. The rates of concurrent affective and anxiety disorders are high in both females and males.[58] In an 18-year follow-up study of 51 former adolescents with AN, based on an epidemiologic sample, 1 in 4 did not have paid employment owing to psychiatric problems.[62]

Physical Comorbidity and Eating Disorders

Greater negative long-term outcomes of eating disorders seem to be associated with additional psychiatric disorders.

Anorexia Nervosa

In clinical and epidemiologic samples, the lifetime prevalence rates of at least 1 comorbid condition according to DSM-IV range from 45% to 97%.[4,63] The most prevalent disorders are mood and anxiety disorders, obsessive-compulsive disorder (OCD), substance abuse, and personality disorders. In general, adolescents with AN seem to display lower rates of comorbid disorders than do adults.[64]

The 2 subtypes of AN, the restricting type and the binge-purging type, display different patterns of comorbid conditions, with the binge/purge subtype more closely resembling the pattern of BN than that of the restricting type of AN.

In more recent studies, up to 60% of adolescent patients with AN display some type of mood disorder,[65–67] with usually higher rates in clinical than in epidemiologic samples.[4] Patients complain of depressed mood, emotional emptiness, social withdrawal, anhedonia, loss of libido, and low self-esteem. In standard depression inventories, they usually score in the mild to moderate range, with the bingeing type scoring higher than the restrictive type. Several studies found an association between weight loss and depression; for example, patients with a high degree of starvation also felt more depressed. Mood is substantially affected by starvation; thus, clinicians should always question whether depressive states are primarily the result of acute AN and might thus be alleviated by nutritional rehabilitation, or whether depression preceded or outlasted the eating disorder.

Anxiety disorders other than OCDs are very common in AN. About one-fourth of patients with acute AN report 1 or more anxiety disorders, with no significant differences in clinical or epidemiologic samples.[4,65] The most frequent anxiety disorders are specific phobias, separation anxiety disorders, and social phobia. In many cases, the anxiety disorders begin in childhood and predate the eating disorder.[68]

In DSM-5, OCD is no longer subsumed among anxiety disorders but instead constitutes a separate entity. Its onset often occurs in childhood. OCD in AN mostly manifests as ordering or washing rituals, in addition to being obsessed with the thought that things are going wrong. These genuine OCD phenomena must be differentiated from eating disorder–related obsessions and compulsions, such as certain rituals or eating strictly at the same time of day. In addition, there are some traits in AN patients that are related to obsessive-compulsive personality disorder, such as perfectionism, rigidity, and scrupulosity. It remains undetermined whether OCD symptoms are more prevalent in restrictive or binge/purging AN.

A similar debate is ongoing regarding substance abuse. About one-fourth of AN patients suffer from substance abuse, with a ratio between restricting AN and binge/purging AN of 1:2.[69] Some investigators even go so far as to consider AN a protective factor against substance abuse.[70] The most prevalent substance abuse is amphetamine and cocaine dependence, but many patients also abuse nicotine.[71,72]

As mentioned earlier, the most common personality disorders in adults with AN are Cluster-C personality disorders, which include OCD and avoidant personality disorder.[73]

Suicidality

Suicidality is one of the most important reasons for premature death in AN. Suicidal ideation is found in about half of adolescent AN patients, and suicidal attempts are observed in 3% to 7%. There are few studies on adolescent AN that investigate suicidal ideation. Although suicidality is much lower in adolescent AN than in adult AN, a strong association between depression, the binge/purge subtype of AN, and the duration of illness has been reported.[66,67]

Suicidal Ideation and Eating Disorders

Suicidal ideation should be carefully assessed in eating-disordered adolescent patients, especially in those with depressive mood, bingeing, and self-harm behavior.

Neuropsychological impairment

Several studies addressing flexibility have described an impaired set-shifting ability (ie, concrete and rigid behaviors in reaction to changing patterns) in adult patients with AN, which was found to be independent of nutritional and body-weight status (for review see Friederich and Herzog[74]). In adolescent patients, deficits in set shifting are less pronounced and are correlated with perfectionistic traits.[64] Poor achievement in set-shifting tasks has also been reported in patients with OCD and those with obsessive-compulsive personality traits, consistent with the personality model of anorexic patients who exhibit high perfectionism, harm avoidance, rigidity, and obsessive traits (see earlier discussion).

Hilde Bruch reported a "narrow range of emotional reactions" in her AN patients.[75] Some researchers have suggested an overlap between AN and autism spectrum disorder, indicating their corresponding cognitive styles, such as impaired weak central coherence, set shifting, and an impairment of theory-of-mind capacities. These impairments seem to be independent of the starved state and instead are stable characteristics of individuals with AN. In an 18-year follow-up study of adolescent AN subjects, difficulties in mentalizing tasks remained in several subjects after recovery and were independent of body-weight loss and the duration of the eating disorder.[76] In this study, autistic traits in childhood were found to be predictive of a poor global outcome in the eating disorder in adulthood.[62] Moreover, the author's own study of adolescent patients, hypoactivations in the brain networks supporting the theory of mind functions were associated with a poor clinical outcome 1 year later.[77]

Bulimia Nervosa

The prevalence rates of mood disorders are similar to those in AN (50%–70%).[61] In a large epidemiologic study, 50% of individuals with BN suffered from some type of mood disorder, and 66% from some type of anxiety disorder.[4] In this study, specific phobias were the most prevalent, followed by posttraumatic stress disorder and social phobia. Suicidality was high. More than half of the adolescents with BN recalled an instance of lifetime suicidality; more than a third had a history of suicide attempts. While some investigators argue that OCD is more strongly related to AN, others report similar prevalence rates.[78,79] Substance abuse also seems to affect a substantial proportion of patients with AN. In the aforementioned study, 20% of adolescents with BN reported some sort of substance abuse. In a meta-analysis, bulimic individuals with purging behaviors had the highest rates of abuse.[80]

Some more recent research supports an important association between BN and attention-deficit/hyperactivity disorder (ADHD). Blinder and colleagues[63] found that 9% of 882 patients with BN also had ADHD; however, this study did not use standardized tools to diagnose BN or ADHD. Yates and colleagues[81] examined 37 female inpatients with BN and 97 female inpatients with binge/purge AN, and found that 6.7% of all participants met a diagnosis of childhood-onset ADHD. In the author's own study, approximately 20% of adolescent and adult patients with BN met the criteria for previous childhood ADHD, compared with 2.5% of healthy controls. The risk for adult ADHD was also significantly higher than for healthy controls. Most importantly, patients with BN and previous childhood ADHD were more impulsive and

inattentive than patients with BN alone. These patients also displayed more severely disordered eating patterns and more general psychopathological symptoms in comparison with those without ADHD.[82]

Comparable with ADHD, many bulimic patients display impulsive behavior. Thus, in addition to Cluster-C disorders, the most prevalent personality disorders in BN are Cluster-B disorders, including borderline personality disorder.[83]

Binge-Eating Disorder and Loss of Control of Eating

As mentioned earlier, LOC often precedes BED. In 10-year-old youths, LOC was associated with the development of BED 4 years later; in addition, these children developed more disordered eating attitudes and depressive symptoms than those without LOC, even after controlling for body mass growth.[25,84] LOC was also predictive of higher weight gain[39] and drug abuse.[25] Other studies have also reported of a higher risk of binge drinking.[85]

Because BED was only just established as a category of its own in DSM-5, studies on comorbidity are scarce.

Most studies have found an association between binge eating and purging on one side and feelings of depression and ineffectiveness, negative self-esteem, and somatic complaints on the other.[86,87] In a large epidemiologic study on more than 10,000 adolescents between 13 and 18 years of age, 45% of individuals with BED had a comorbid mood disorder; about one-third had an anxiety disorder; and one-fourth had a substance abuse disorder.[4] In approximately 10%, ADHD was diagnosed.

According to a recent meta-analysis, the most frequent personality disorders were Cluster-C and Cluster-B disorders.[88]

Evidence-based treatment strategies for adolescent eating disorders are limited. Family-based therapy is considered to be an effective treatment for adolescent AN. Given the expanding knowledge of the neurobiology and psychological mechanisms underlying the development of these disorders, clinicians should intensify efforts to generate more effective treatment interventions for this age group, keeping in mind that outcomes may be influenced by early diagnosis and support.

REFERENCES

1. Gonzalez A, Kohn MR, Clarke SD. Eating disorders in adolescents. Aust Fam Physician 2007;36(8):614–9.
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 5th edition (DSM-5). Washington, DC: American Psychiatric Press; 2013.
3. Fairburn CG, Harrison PJ. Eating disorders. Lancet 2003;361(9355):407–16.
4. Swanson SA, Crow SJ, Le Grange D, et al. Prevalence and correlates of eating disorders in adolescents. Results from the national comorbidity survey replication adolescent supplement. Arch Gen Psychiatry 2011;68(7):714–23.
5. Micali N, Hagberg KW, Petersen I, et al. The incidence of eating disorders in the UK in 2000-2009: findings from the general practice research database. BMJ Open 2013;3(5). pii:e002646.
6. Hudson JI, Hiripi E, Pope HG Jr, et al. The prevalence and correlates of eating disorders in the national comorbidity survey replication. Biol Psychiatry 2007; 61(3):348–58.
7. Arcelus J, Mitchell AJ, Wales J, et al. Mortality rates in patients with anorexia nervosa and other eating disorders. A meta-analysis of 36 studies. Arch Gen Psychiatry 2011;68(7):724–31.

8. Powers PS, Cloak NL. Failure to feed patients with anorexia nervosa and other perils and perplexities in the medical care of eating disorder patients. Eat Disord 2013;21(1):81–9.
9. Villarejo C, Fernandez-Aranda F, Jimenez-Murcia S, et al. Lifetime obesity in patients with eating disorders: increasing prevalence, clinical and personality correlates. Eur Eat Disord Rev 2012;20(3):250–4.
10. Bulik CM, Marcus MD, Zerwas S, et al. The changing "weightscape" of bulimia nervosa. Am J Psychiatry 2012;169(10):1031–6.
11. Lamerz A, Kuepper-Nybelen J, Bruning N, et al. Prevalence of obesity, binge eating, and night eating in a cross-sectional field survey of 6-year-old children and their parents in a German urban population. J Child Psychol Psychiatry 2005;46(4):385–93.
12. Pauli-Pott U, Becker K, Albayrak O, et al. Links between psychopathological symptoms and disordered eating behaviors in overweight/obese youths. Int J Eat Disord 2013;46(2):156–63.
13. Tanofsky-Kraff M, Yanovski SZ, Schvey NA, et al. A prospective study of loss of control eating for body weight gain in children at high risk for adult obesity. Int J Eat Disord 2009;42(1):26–30.
14. Tanofsky-Kraff M. Binge eating among children and adolescents. In: Jelalian E, Steele RG, editors. Handbook of Childhood and Adolescent Obesity. New York: Springer Science; 2008.
15. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Washington, DC: American Psychiatric Association; 1994.
16. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Text revision. 4th edition. Washington, DC: American Psychiatric Association; 2000.
17. Maier A, Ernst JP, Muller S, et al. Self-perceived stigmatization in female patients with anorexia nervosa—results from an explorative retrospective pilot study of adolescents. Psychopathology 2014;47(2):127–32.
18. Focker M, Knoll S, Hebebrand J. Anorexia nervosa. Eur Child Adolesc Psychiatry 2013;22(Suppl 1):S29–35.
19. Herpertz SH, Fichter M, Tuschen-Caffier B, et al. S3-Leitlinie Diagnostik und Behandlung von Essstörungen. Heidelberg (Germany): Springer-Verlag; 2011.
20. Hebebrand J, Himmelmann GW, Herzog W, et al. Prediction of low body weight at long-term follow-up in acute anorexia nervosa by low body weight at referral. Am J Psychiatry 1997;154(4):566–9.
21. Lock J, Le Grange D, Agras WS, et al. Randomized clinical trial comparing family-based treatment with adolescent-focused individual therapy for adolescents with anorexia nervosa. Arch Gen Psychiatry 2010;67(10):1025–32.
22. Beumont PJ, Touyz S. Relevance of a standard measurement of undernutrition to the diagnosis of anorexia nervosa: use of Quetelet's body mass index (BMI). Int J Eat Disord 1988;7:399–405.
23. Uher R, Rutter M. Classification of feeding and eating disorders: review of evidence and proposals for ICD-11. World Psychiatry 2012;11(2):80–92.
24. Wonderlich SA, Gordon KH, Mitchell JE, et al. The validity and clinical utility of binge eating disorder. Int J Eat Disord 2009;42(8):687–705.
25. Sonneville KR, Horton NJ, Micali N, et al. Longitudinal associations between binge eating and overeating and adverse outcomes among adolescents and young adults: does loss of control matter? JAMA Pediatr 2013;167(2):149–55.
26. Le Grange D, Crosby RD, Engel SG, et al. DSM-IV-defined anorexia nervosa versus subthreshold anorexia nervosa (EDNOS-AN). Eur Eat Disord Rev 2013;21(1):1–7.

27. Herpertz-Dahlmann B. Adolescent eating disorders: definitions, symptomatology, epidemiology and comorbidity. Child Adolesc Psychiatr Clin N Am 2009;18(1):31–47.
28. Hebebrand J, Exner C, Hebebrand K, et al. Hyperactivity in patients with anorexia nervosa and in semistarved rats: evidence for a pivotal role of hypoleptinemia. Physiol Behav 2003;79(1):25–37.
29. Holtkamp K, Herpertz-Dahlmann B, Hebebrand K, et al. Physical activity and restlessness correlate with leptin levels in patients with adolescent anorexia nervosa. Biol Psychiatry 2006;60(3):311–3.
30. Kostrzewa E, van Elburg AA, Sanders N, et al. Longitudinal changes in the physical activity of adolescents with anorexia nervosa and their influence on body composition and leptin serum levels after recovery. PLoS One 2013; 8(10):e78251.
31. Duclos M, Ouerdani A, Mormede P, et al. Food restriction-induced hyperactivity: addiction or adaptation to famine? Psychoneuroendocrinology 2013;38(6): 884–97.
32. Steinhausen HC, Grigoroiu-Serbanescu M, Boyadjieva S, et al. Course and predictors of rehospitalization in adolescent anorexia nervosa in a multisite study. Int J Eat Disord 2008;41(1):29–36.
33. Bratland-Sanda S, Sundgot-Borgen J, Ro O, et al. "I'm not physically active - I only go for walks": physical activity in patients with longstanding eating disorders. Int J Eat Disord 2010;43(1):88–92.
34. Solenberger SE. Exercise and eating disorders: a 3-year inpatient hospital record analysis. Eat Behav 2001;2(2):151–68.
35. Dalle Grave R, Calugi S, Marchesini G. Compulsive exercise to control shape or weight in eating disorders: prevalence, associated features, and treatment outcome. Compr Psychiatry 2008;49(4):346–52.
36. Strober M, Freeman R, Morrell W. The long-term course of severe anorexia nervosa in adolescents: survival analysis of recovery, relapse, and outcome predictors over 10-15 years in a prospective study. Int J Eat Disord 1997; 22(4):339–60.
37. Slade PD. Body image in anorexia nervosa. Br J Psychiatry Suppl 1988;2:20–2.
38. Legenbauer T, Thiemann P, Vocks S. Body image disturbance in children and adolescents with eating disorders. Z Kinder Jugendpsychiatr Psychother 2014;42(1):51–9.
39. Tanofsky-Kraff M, Marcus MD, Yanovski SZ, et al. Loss of control eating disorder in children age 12 years and younger: proposed research criteria. Eat Behav 2008;9(3):360–5.
40. Boutelle KN, Tanofsky-Kraff M. Treatments targeting aberrant eating patterns in overweight youth. New York: Guilford Press; 2011.
41. Czaja J, Rief W, Hilbert A. Emotion regulation and binge eating in children. Int J Eat Disord 2009;42(4):356–62.
42. Smink FR, van Hoeken D, Hoek HW. Epidemiology of eating disorders: incidence, prevalence and mortality rates. Curr Psychiatry Rep 2012;14(4):406–14.
43. Keski-Rahkonen A, Hoek HW, Susser ES, et al. Epidemiology and course of anorexia nervosa in the community. Am J Psychiatry 2007;164(8):1259–65.
44. Pinhas L, Morris A, Crosby RD, et al. Incidence and age-specific presentation of restrictive eating disorders in children: a Canadian paediatric surveillance program study. Arch Pediatr Adolesc Med 2011;165(10):895–9.
45. Nicholls DE, Lynn R, Viner RM. Childhood eating disorders: British national surveillance study. Br J Psychiatry 2011;198(4):295–301.

46. German Institute for Federal Statistics. Diagnosedaten der Krankenhäuser ab 2000. Available at: www.destatis.de, www.gbe-bund.de. Accessed May 29, 2013.
47. Health and Social Care Information Centre. Provisional monthly hospital episode statistics for admitted patient care. Outpatient and accident and emergency data—April to June 2012. Topic of interest: eating disorder. Available at: https://catalogue.ic.nhs.uk/publications/hospital/monthly-hes/prov-mont-hes-admi-outp-ae-apr-jun-12/prov-mont-hes-admi-outp-ae-apr-jun-12-toi-rep.pdf. Accessed May 29, 2013.
48. Favaro A, Caregaro L, Tenconi E, et al. Time trends in age at onset of anorexia nervosa and bulimia nervosa. J Clin Psychiatry 2009;70(12):1715–21.
49. Machado PP, Machado BC, Goncalves S, et al. The prevalence of eating disorders not otherwise specified. Int J Eat Disord 2007;40(3):212–7.
50. Keski-Rahkonen A, Hoek HW, Linna MS, et al. Incidence and outcomes of bulimia nervosa: a nationwide population-based study. Psychol Med 2009; 39(5):823–31.
51. Currin L, Schmidt U, Treasure J, et al. Time trends in eating disorder incidence. Br J Psychiatry 2005;186:132–5.
52. Allen KL, Byrne SM, Oddy WH, et al. Early onset binge eating and purging eating disorders: course and outcome in a population-based study of adolescents. J Abnorm Child Psychol 2013;41(7):1083–96.
53. Ornstein RM, Rosen DS, Mammel KA, et al. Distribution of eating disorders in children and adolescents using the proposed DSM-5 criteria for feeding and eating disorders. J Adolesc Health 2013;53(2):303–5.
54. Machado PP, Goncalves S, Hoek HW. DSM-5 reduces the proportion of EDNOS cases: evidence from community samples. Int J Eat Disord 2013;46(1):60–5.
55. Higgins J, Hagman J, Pan Z, et al. Increased physical activity not decreased energy intake is associated with inpatient medical treatment for anorexia nervosa in adolescent females. PLoS One 2013;8:e61559.
56. Katzman DF. Assessment of eating disorders in children and adolescents. New York: Guilford Press; 2011.
57. Fazeli PK, Klibanski A. Bone metabolism in anorexia nervosa. Curr Osteoporos Rep 2014;12(1):82–9.
58. Norris ML, Apsimon M, Harrison M, et al. An examination of medical and psychological morbidity in adolescent males with eating disorders. Eat Disord 2012;20(5):405–15.
59. Seitz J, Buhren K, von Polier GG, et al. Morphological changes in the brain of acutely ill and weight-recovered patients with anorexia nervosa. Z Kinder Jugendpsychiatr Psychother 2014;42(1):7–18.
60. Castro-Fornieles J, Bargallo N, Lazaro L, et al. A cross-sectional and follow-up voxel-based morphometric MRI study in adolescent anorexia nervosa. J Psychiatr Res 2009;43(3):331–40.
61. Mainz V, Schulte-Ruther M, Fink GR, et al. Structural brain abnormalities in adolescent anorexia nervosa before and after weight recovery and associated hormonal changes. Psychosom Med 2012;74(6):574–82.
62. Wentz E, Gillberg IC, Anckarsater H, et al. Adolescent-onset anorexia nervosa: 18-year outcome. Br J Psychiatry 2009;194(2):168–74.
63. Blinder BJ, Cumella EJ, Sanathara VA. Psychiatric comorbidities of female inpatients with eating disorders. Psychosom Med 2006;68(3):454–62.
64. Buhren K, Mainz V, Herpertz-Dahlmann B, et al. Cognitive flexibility in juvenile anorexia nervosa patients before and after weight recovery. J Neural Transm 2012;119(9):1047–57.

65. Salbach-Andrae H, Lenz K, Simmendinger N, et al. Psychiatric comorbidities among female adolescents with anorexia nervosa. Child Psychiatry Hum Dev 2008;39(3):261–72.
66. Fennig S, Hadas A. Suicidal behavior and depression in adolescents with eating disorders. Nord J Psychiatry 2010;64(1):32–9.
67. Buhren K, Schwarte R, Fluck F, et al. Comorbid psychiatric disorders in female adolescents with first-onset anorexia nervosa. Eur Eat Disord Rev 2014;22(1): 39–44.
68. Godart NT, Flament MF, Lecrubier Y, et al. Anxiety disorders in anorexia nervosa and bulimia nervosa: co-morbidity and chronology of appearance. Eur Psychiatry 2000;15(1):38–45.
69. Root TL, Pinheiro AP, Thornton L, et al. Substance use disorders in women with anorexia nervosa. Int J Eat Disord 2010;43(1):14–21.
70. Kaye WH, Wierenga CE, Bailer UF, et al. Nothing tastes as good as skinny feels: the neurobiology of anorexia nervosa. Trends Neurosci 2013;36(2):110–20.
71. Thompson-Brenner H, Eddy KT, Franko DL, et al. Personality pathology and substance abuse in eating disorders: a longitudinal study. Int J Eat Disord 2008;41(3):203–8.
72. Barbarich-Marsteller NC, Foltin RW, Walsh BT. Does anorexia nervosa resemble an addiction? Curr Drug Abuse Rev 2011;4(3):197–200.
73. Herpertz-Dahlmann B, Muller B, Herpertz S, et al. Prospective 10-year follow-up in adolescent anorexia nervosa–course, outcome, psychiatric comorbidity, and psychosocial adaptation. J Child Psychol Psychiatry 2001;42(5):603–12.
74. Friederich HC, Herzog W. Cognitive-behavioral flexibility in anorexia nervosa. Curr Top Behav Neurosci 2011;6:111–23.
75. Herpertz-Dahlmann B, Seitz J, Konrad K. Aetiology of anorexia nervosa: from a "psychosomatic family model" to a neuropsychiatric disorder? Eur Arch Psychiatry Clin Neurosci 2011;261(Suppl 2):S177–81.
76. Gillberg IC, Billstedt E, Wentz E, et al. Attention, executive functions, and mentalizing in anorexia nervosa eighteen years after onset of eating disorder. J Clin Exp Neuropsychol 2010;32(4):358–65.
77. Schulte-Ruther M, Mainz V, Fink GR, et al. Theory of mind and the brain in anorexia nervosa: relation to treatment outcome. J Am Acad Child Adolesc Psychiatry 2012;51(8):832–41.e1.
78. Swinbourne JM, Touyz SW. The co-morbidity of eating disorders and anxiety disorders: a review. Eur Eat Disord Rev 2007;15(4):253–74.
79. Kaye WH, Bulik CM, Thornton L, et al. Comorbidity of anxiety disorders with anorexia and bulimia nervosa. Am J Psychiatry 2004;161(12):2215–21.
80. Calero-Elvira A, Krug I, Davis K, et al. Meta-analysis on drugs in people with eating disorders. Eur Eat Disord Rev 2009;17(4):243–59.
81. Yates WR, Lund BC, Johnson C, et al. Attention-deficit hyperactivity symptoms and disorder in eating disorder inpatients. Int J Eat Disord 2009;42(4):375–8.
82. Seitz J, Kahraman-Lanzerath B, Legenbauer T, et al. The role of impulsivity, inattention and comorbid ADHD in patients with bulimia nervosa. PLoS One 2013; 8(5):e63891.
83. Lilenfeld LR, Stein D, Bulik CM, et al. Personality traits among currently eating disordered, recovered and never ill first-degree female relatives of bulimic and control women. Psychol Med 2000;30(6):1399–410.
84. Tanofsky-Kraff M, Shomaker LB, Olsen C, et al. A prospective study of pediatric loss of control eating and psychological outcomes. J Abnorm Psychol 2011; 120(1):108–18.

85. Field AE, Sonneville KR, Micali N, et al. Prospective association of common eating disorders and adverse outcomes. Pediatrics 2012;130(2):e289–95.
86. Pasold TL, McCracken A, Ward-Begnoche WL. Binge eating in obese adolescents: emotional and behavioral characteristics and impact on health-related quality of life. Clin Child Psychol Psychiatry 2013;19(2):299–312.
87. Glasofer DR, Tanofsky-Kraff M, Eddy KT, et al. Binge eating in overweight treatment-seeking adolescents. J Pediatr Psychol 2007;32(1):95–105.
88. Friborg O, Martinsen EW, Martinussen M, et al. Comorbidity of personality disorders in mood disorders: a meta-analytic review of 122 studies from 1988 to 2010. J Affect Disord 2014;152–154:1–11.
89. Smink FR, van Hoeken D, Hoek HW. Epidemiology, course, and outcome of eating disorders. Curr Opin Psychiatry 2013;26(6):543–8.