Eating disorders

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This Seminar adds to the previous *Lancet* Seminar about eating disorders, published in 2003, with an emphasis on the biological contributions to illness onset and maintenance. The diagnostic criteria are in the process of review, and the probable four new categories are: anorexia nervosa, bulimia nervosa, binge eating disorder, and eating disorder not otherwise specified. These categories will also be broader than they were previously, which will affect the population prevalence; the present lifetime prevalence of all eating disorders is about 5%. Eating disorders can be associated with profound and protracted physical and psychosocial morbidity. The causal factors underpinning eating disorders have been clarified by understanding about the central control of appetite. Cultural, social, and interpersonal elements can trigger onset, and changes in neural networks can sustain the illness. Overall, apart from studies reporting pharmacological treatments for binge eating disorder, advances in treatment for adults have been scarce, other than interest in new forms of treatment delivery.

Lancet 2010; 375: 583–93

Published Online
November 19, 2009
DOI:10.1016/S0140-6736(09)61748-7

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Introduction

This Seminar adds to the previous *Lancet* Seminar about eating disorders, which was published in 2003.[1] We provide a concise review of eating disorders in young people, focusing on factors of particular relevance to the clinician such as diagnosis, epidemiology, pathogenesis, treatment, and prognosis. In this Seminar we draw attention to biological factors that could contribute to new interventions. Eating disorders also occur in prepubertal children, but studies in this age group are scarce and there is no consensus about either diagnosis or treatment.

Classification and diagnosis

Diagnosis is challenging because diagnostic symptoms and associated behaviours substantially overlap across the range of eating disorders. For example, extreme dietary restraint, binge eating, and overvalued ideas about weight and shape can be present in all forms of eating disorder. Additionally, the subjective interpretation and justification behind diagnostic behaviours is often not clear or is limited by developmental constraints (as in childhood anorexia nervosa), further complicating diagnosis.

In the diagnostic and statistical manual of mental disorders fourth edition (DSM-IV),[2] three broad categories are delineated: anorexia nervosa, bulimia nervosa, and eating disorder not otherwise specified. The international classification of diseases tenth revision (ICD-10) has three categories: anorexia nervosa, bulimia nervosa, and atypical eating disorder.[3] Briefly, anorexia nervosa is characterised by extremely low bodyweight and a fear of its increase; bulimia nervosa comprises repeated binge eating, followed by behaviours to counteract it. The category of eating disorder not otherwise specified encompasses variants of these disorders, but with subthreshold symptoms (eg, menstruation still present despite clinically significant weight loss, purging without objective binging). The panel shows some key symptoms of eating disorders in general (more detailed information about the clinical features of each disorder is available in the previous Seminar[1]). The weight criteria used for diagnosis need to be adjusted for age,[4] height, sex, and the developmental weight trajectory of the individual.

More than 50% of cases in the community fall into the category termed eating disorder not otherwise specified (or atypical).[5] Proposals to reduce the specificity of some of the diagnostic criteria in anorexia nervosa and bulimia nervosa have been made, which would reduce the proportion of cases that fall within the not-otherwise-specified category.[6] Subgroups within obesity with mental or behavioural components, such as binge eating disorder and night eating syndrome, can be delineated.[7]

Binge eating disorder is a subcategory of eating disorder not otherwise specified, and is defined as frequent binge eating distinguished from bulimia nervosa by the absence of recurrent inappropriate compensatory behaviours. Hence binge eating disorder is often associated with obesity. Transition from severe restriction into binge eating behaviour is common;[8] however, the reverse process (a shift from binge eating into restriction) is less usual. The criteria for diagnosis of binge eating disorder in DSM-IV appendix B include associated behavioural and affective features,[2] and these

Search strategy and selection criteria

We searched the Cochrane Library, Medline, and Embase up to March, 2009. We used the search terms: "anorexia nervosa", "bulimia nervosa", "binge eating disorder", and "eating disorders" in combination with the terms "treatment", "biology", "outcome", "epidemiology", "comorbidity", "personality", "osteoporosis", "medical", "neuropsychology", "neuroimaging", "psychotherapy", and "pharmacotherapy". We manually searched the main eating disorder specialist journals and reference lists of articles identified by this search strategy. Several review articles or books are included because they provide comprehensive overviews that are beyond the scope of this Seminar. We largely selected publications in the past 6 years, but did not exclude commonly referenced and highly regarded older publications, or more recent ones published during the review process and that we considered of relevance to the scope of the Seminar. Whenever possible we have cited systematic reviews on a topic.

Panel: Common symptoms in eating disorders

Behaviours

Restrictive behaviour

- Cutting back on amount of food eaten
- Strict rules about eating (eg, time of day, specific macronutrient content)
- Prolonged fasting (greater than 8 waking hours)
- Ritualised behaviour associated with the purchase, preparation, and consumption of food
- Little variety in foods (eg, extreme vegan diets, avoidance of fat, etc)
- Avoidance of social eating
- Secret eating
- Social competitiveness around eating

Binge eating

- Eating an amount of food in a discrete time that is considered excessive in view of the situational context (objective)
- Eating an amount of food that is not excessive in view of the context but is considered large by the individual because of associated feelings of loss of control over eating (subjective)

Associated features of binge eating

- Eating more rapidly than normal
- Eating until uncomfortably full
- Eating large amounts when not hungry
- Eating alone because of embarrassment
- Feeling disgusted, depressed, or very guilty because of eating

Purgative behaviour

- Self-induced vomiting; spitting
- Misuse of laxatives, diuretics, diet pills, etc

Excessive exercise

- Intense, highly driven exercising of a compulsive nature
- The drive to exercise is associated with impaired social or physical function, or both

Drinking

- Limited drinking (<0·5 L per day)
- Excess drinking (>1·5 L per day)

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Body checking

- Repeated weighing
- Pinching or measuring the size of body parts (eg, circumference of wrist)
- Repeatedly checking the protrusion of specific bones
- Checking that specific clothes fit
- Mirror gazing
- Comparison with others' bodies

Body avoidance

- Avoidance of behaviours above (eg, refusal to weigh, avoidance of mirrors, wearing bulky clothes)

Psychopathology

Body image disturbance

- Weight and shape concerns (eg, preoccupation with weight, shape, or both)
- Overvaluation of shape and weight in determination of self-worth
- Minimisation or denial of symptom severity
- Disturbance in the way body is experienced
- Intense fear of weight gain, even though underweight

Physical symptoms

- Weight loss or failure of growth with associated features of starvation—eg, amenorrhoea
- Absence of at least three consecutive menstrual cycles (women)
- Reduced libido
- Reduction in waking erections (men)
- Reduced beard growth in men
- Sensitivity to cold
- Weakness, fatigue, etc

This panel outlines the most common symptoms of eating disorder. A range of symptoms caused by starvation are also present in anorexia nervosa, which are not all detailed here. All these symptoms are not usually volunteered by the patient and often have to be gently elicited or are noted by informants.

criteria have been extensively used in research in the past 15 years. Support is growing for recognition of binge eating disorder as a specific entity[9] on the basis of taxometric analyses,[10] family aggregation studies,[11] treatment response research,[12] and studies of clinical course.[13]

Furthermore, interest is growing in a transdiagnostic approach to eating disorders, both within[14] and outside the category of eating disorders, with proposals for links to the obsessive compulsive and autistic spectrum of disorders[15] and anxiety and mood disorders.[16,17] Several articles present the arguments for diagnostic change in DSM-V.[7,18]

Psychiatric comorbidity

Comorbidity is the rule rather than the exception for patients with eating disorders.[19,20] Developmental disorders (eg, those of the autistic spectrum and attention-deficit hyperactivity disorder) have been reported to affect about a fifth of patients with anorexia nervosa.[21,22] Moreover, a small proportion of adults with attention-deficit hyperactivity disorder have additional symptoms of eating disorders.[23] Obsessive compulsive traits[24,25] or disorder,[26] and anxiety disorders[27,28] and some borderline traits,[25] have been reported both before and after the onset of eating disorders, and are also diagnosed in family members.[29,30] Bulimia nervosa and binge eating disorder are associated with affective disorders[31,32] and with alcohol[33] or substance[34] misuse.

Epidemiology

Eating disorders and related behaviours are common in young people. Investigators of a study of a large sample

of American children aged 9–14 years reported that 7·1% of boys and 13·4% of girls displayed disordered eating behaviours.[35] The pivotal effect on health has led to the inclusion of eating disorders among the priority mental illnesses for children and adolescents identified by WHO.[36] Eating disorders have been reported worldwide both in developed regions and emerging economies such as Brazil and China.[37,38] The lifetime prevalence of eating disorders in adults is about 0·6% for anorexia nervosa, 1% for bulimia nervosa, and 3% for binge eating disorder.[19,20] Women are more affected than are men, and the sex differences in lifetime prevalence in adults could be less substantial than that quoted in standard texts: 0·9% for anorexia nervosa, 1·5% for bulimia nervosa, and 3·5% for binge eating disorder in women; and 0·3%, 0·5%, and 2·0%, respectively, in men.[20] Many people with eating disorders, who were detected in community studies in the USA, do not seek treatment.[20]

Pathogenesis

A comprehensive review published in 2004 summarised the risk factors for eating disorders,[39] and a position paper from the Academy of Eating Disorders outlined the evidence supporting these diseases as biologically-based forms of severe mental illnesses.[40] In this section we draw attention to some present areas of emphasis.

Genetic factors

The most potent risk factor is female gender. How much this association can be attributed to biological rather than social factors is uncertain. Sexual divergence is less pronounced in binge eating disorder[23] and in prepubertal anorexia nervosa.[41] Twin and family studies suggest that anorexia nervosa, bulimia nervosa, and binge eating disorder are complex genetic diseases, and for each disorder the estimated heritability ranges between 50% and 83%.[11,42,43] Linkage studies have identified loci for anorexia and bulimia nervosa and for associated behavioural traits such as compulsivity.[44–46] About a third of genetic risk for eating disorders and depression,[47] anxiety disorders,[48] and addictive disorders[49] is shared. All the above studies are limited because of low power; however, international collaborations are working at pooling cases and using newer forms of analysis such as genome-wide associations.

Biological factors

Although many of the biological findings in eating disorders can be best understood as results of starvation and disturbed eating behaviours, some are causally linked as risk or maintaining factors. The brain is particularly vulnerable to the consequences of poor nutrition since it uses around 20% of the caloric intake and is especially dependent on glucose. Therefore, poor nutrition has a general effect on brain function in addition to the specific effect on the appetite system. Most eating disorders emerge during adolescence—a vulnerable period of brain reorganisation—and malnutrition during this crucial period can negatively affect illness trajectories.

Starvation shrinks the brain and is associated with many behavioural and psychosocial disturbances such as rigidity, emotional dysregulation, and social difficulties.[50] Many symptoms resolve with weight gain and when brain mass is restored.[51] Concentrations of brain-derived neurotrophic factor, a regulator of brain plasticity, in blood are reduced in acute anorexia nervosa,[52] and genetic studies suggest a trait-related disturbance in this system.[53]

The characterisation of the central control of appetite[54,55] could improve our understanding of eating disorders. A simplified heuristic is to consider three components. First is the homoeostatic system that is centred mainly in the brain stem and hypothalamus, which integrates peripheral metabolic markers with information from the gastrointestinal tract to affect subjective states of hunger, satiety, and autonomic nervous activity. Second is the drive system, with distributed neural circuitry within the mesolimbic cortex and striatum that has afferent inputs from sense organs and neural structures that are implicated in learning and memory. This system registers the reward value associated with food and is involved in the motivation to seek food and eat. Third is the self-regulation system, within which a form of so-called top-down control contextualises appetite within life goals, values, and meaning.

Abnormal changes in all three of these systems have a role in the risk and maintenance of eating disorders. A hypothesis suggests that these disorders could result from pervasive deficits in self-regulatory systems.[56] Furthermore, eating disorder behaviours affect the drive system, as shown by models of binge eating in laboratory rodents for which scientists have replicated the conditions implicated in the increase of binge eating—ie, food restriction, gastric drainage (an analogue of vomiting), stress, and intermittent access to highly palatable food—and produced animals with an addiction to food. The investigators noted that not only did these animals binge eat, but they also showed withdrawal effects. Moreover, they had a propensity to relapse after a time, and cross-tolerance to alcohol and cocaine.[57,58] Underpinning these behavioural changes are alterations in the chemical transmitters (dopamine and opioids). Finally, the response to changes in food intake of the putative homoeostatic system could contribute—eg, anorexia nervosa is often linked to premorbid and familial leanness,[59] whereas the reverse is the case for bulimia nervosa and binge eating disorder.[60]

Brain monoamine function in eating disorders has been studied in the acute state (which can be confounded by illness effects) and after recovery with specific ligands and positron emission tomography. These findings for anorexia nervosa have been synthesised into an explanatory model.[61] 5HT2A receptors are reduced and

	Moderate risk	High risk
Nutrition		
Body-mass index (kg/m²)	<15	<13
Body-mass index centiles	<3rd	<2nd
Weight loss (kg per week)	>0·5	>1·0
Purpuric rash	..	+
Circulation		
Systolic blood pressure (mm Hg)	<90	<80
Diastolic blood pressure (mm Hg)	<60	<50
Postural drop (mm Hg)	>10	>20
Pulse rate (beats per min)	<50	<40
Oxygen saturation (%)	<90%	<85%
Extremities	..	Cyanotic
Musculoskeletal (squat test*)		
Unable to get up without use of arms for balance	+	..
Unable to get up without use of arms as leverage	..	+
Temperature		
Core temperature (°C)	<35	<34·5
Investigations		
FBC, urea , electrolytes (including phosphate), LFT, albumin, creatinine kinase, glucose	Concern if outside normal limits	Potassium <2·5 mmol/L, sodium <130 mmol/L, phosphate <0·5 mmol/L
Electrocardiograph	..	Prolonged QT interval especially in context of low potassium

+=present. FBC=full blood count. LFT=liver function test. *The instructions for the squat test are that the patient squats on her/his haunches and has to stand up without, if possible, using her/his hands.

Table 1: **An abridged set of markers of nutritional and cardiovascular decompensation that signal the need for increased or urgent care in people with eating disorders**

5HT1A receptors are increased in both the acute and recovered state, and dopamine receptors (DA2) within the striatum are increased after recovery.[62] Less research has been done into binge eating disorders and bulimia nervosa, but anomalies in the dopamine system could heighten food reward.[63]

Abnormalities in both illness-related (food and body shape) and non-illness-related information processing are detected in eating disorders. An attentional bias is evident towards food and body shape[64] associated with increased activation in distributed neural networks connected with self-regulation and hedonic motivation.[61,65] General problems include difficulties in decision making,[66] abnormal striatal activation by reward,[67,68] reduced flexibility[69] associated with decreased activation in the striatum and associated areas,[70] a bias towards focusing on detail at the expense of seeing the general picture (weak central coherence),[71] problems in social cognition,[72] and dysfunctional emotional regulation.[73] These functional anomalies can maintain eating disorder behaviours. For example, an eye for detail and inflexibility can allow an individual to understand the laws of thermodynamics in relation to energy intake and expenditure and succeed in weight loss, whereas impaired social and emotional regulation could isolate the individual.

Environmental context

The environment shapes the developmental course of the individual beginning at the time of conception. For example, mothers of people who later develop an eating disorder might be more exposed to stress during pregnancy.[74] Birth-related perinatal complications (eg, cephalohaematoma) and premature delivery increase the risk of development of an eating disorder.[75] Epigenetic mechanisms or damage to the brain from hypoxia can also mediate these effects.

In some developed countries, the excess value placed on thinness encourages extreme dieting and weight control practices. Negative comparisons between an individual's body shape and that of the ideal contributes to poor self-esteem.[76] Criticism, teasing, and bullying focused on food, weight, and shape issues specifically increase the risk of developing an eating disorder.[77] The tension between the stigmatisation of fatness, idealisation of thinness, and easy access to highly palatable foods, perhaps eaten in secret, could lead to weight control behaviours that can have a destabilising effect on the biology of appetite control. In addition to food-related and weight-related harmful experiences, general adversity (neglect and physical and sexual abuse) also increases the risk of developing an eating disorder.

Interactions between the environment and individual biology

The postpubertal years are a crucial time of vulnerability. Developmental changes of puberty (the hormonal fluxes and synaptic pruning and myelination within the brain), stressful events, and challenges (eg, changes in social affiliation and ranking) could trigger eating disorder behaviours. The consequent nutritional deficits can induce factors that maintain the illness. These factors have been grouped into four broad domains: the medical effect on the body and brain, the interpersonal effect, the exaggeration of avoidant coping, and obsessive compulsive traits.[78]

Treatment

Medical complications

Although eating disorders can begin in adulthood, the highest incidence is between 10 and 19 years of age,[79] potentially disrupting optimum growth and development. Most pathophysiological complications are reversible with improved nutritional status or remittance of abnormal eating and purging behaviours. However, some physical consequences can be life-threatening, such as electrolyte imbalances (eg, hypokalaemia) due to excessive vomiting or laxative and diuretic misuse. Additionally, nutritional deficiencies increase the risk of cardiac arrhythmias and intercurrent infection. Comprehensive reviews[80,81] and the previous Seminar[1] discuss the physical abnormalities of eating disorders in great depth.

Many practice guidelines discuss how to measure and assess medical risk.[82–84] Children and adolescents have

less nutritional reserve than do adults, so their risk can rapidly escalate. Body-mass index (BMI) is not a useful index of nutritional compromise for men, children, tall and muscular individuals, and those with water retention. Other comorbid medical disorders also increase vulnerability and might need regular monitoring, such as diabetes mellitus, which can increase risk at any level of BMI. Apart from these caveats, standard forms present a means of giving both personalised and normative feedback on medical risk. (Examples include the Maudsley BMI chart and the Risk Assessment in Eating Disorders). Table 1 shows an abridged set of markers of nutritional and cardiovascular decompensation that signal the need for increased or urgent care. These markers should be considered in the context of the complete clinical picture, expertise of the treating team, and local availability of eating disorder units. Signs of increased medical risk suggest the need for immediate specialist consultation or inpatient treatment, or both, especially in people with a recent, acute onset.

The deficits in anorexia nervosa gradually evolve and are general rather than specific. Therefore they should be rectified slowly, orally, and with food supplemented with multivitamin and multimineral preparations. In the first phase (3–7 days), a soft diet of about 5–10 kcal/kg per day with thiamine and vitamin B co-strong in small portions throughout the day, and foods with high phosphorus content (eg, milk-based products) accords with guidelines from the UK National Institute for Health and Clinical Excellence (NICE) describing refeeding of severely undernourished patients, and reduces the risk of refeeding syndrome.[85] On special units with skilled nursing, feeding by tube is rarely necessary. At moderate levels of risk the aim is to produce a weight gain between 250 g and 450 g per week in outpatients, and around 1 kg in those treated in hospital.[83]

Some weight change strategies—such as vomiting or misuse of diuretics, laxatives, or caffeinated and carbonated drinks—can result in underhydration or overhydration and electrolyte imbalance. Acute renal failure can occur in severe cases. Oral replacement is usually the first line of management, but the full clinical diagnosis and level of risk (table 1) decide the appropriate setting and method of replacement. Persistent hypokalaemia can be linked to low calcium and magnesium (which also need rectification), or to sustained purging behaviours. Proton-pump inhibitors to inhibit gastric acid secretion reduce metabolic alkalosis and help to conserve potassium.[86] They can also prevent oesophageal and tooth damage.

Long-term effects on physical health

Some medical consequences of eating disorders can be irreversible or have later repercussions on health, especially those affecting the skeleton, the reproductive system, and the brain. Dental problems, growth retardation, and osteoporosis are some of the long-term problems. Bone loss in lumbar spine, radius, and proximal femur can be detected within a year of illness and progresses to produce fractures, kyphoscoliosis, and chronic pain. Weight gain alone improves bone density, especially if it is sufficient to restore menses. Several treatments have been investigated, including antiresorptive agents, oestrogens, insulin growth factor, and calcium supplementation, but none can be recommended on the basis of present evidence.[87]

The fertility and maternity rate of women with anorexia nervosa is reduced; a Swedish study[88] suggested that the rate of fertility was 70% of that in the general population. Infant birthweight is lower in mothers with anorexia nervosa[89] but higher in those with bulimia nervosa.[90] The miscarriage rate for women with bulimia nervosa is higher than for healthy women—those with bulimia nervosa were twice as likely to have two or more miscarriages compared with the general population.[89] Perinatal problems can be increased,[91] and feeding difficulties reducing infant growth have been reported.[92] Infertile and pregnant women should be screened for eating disorders and offered treatment to optimise the wellbeing of their offspring.[82]

For more about the **Maudsley BMI chart and the Risk Assessment in Eating Disorders** see http://www.iop.kcl.ac.uk/sites/edu/?id=73

Pathways of care

High levels of health-care use are common across all forms of eating disorders.[93] The management of bulimia nervosa and binge eating disorder can be complicated by medical (eg, diabetes and obesity) and psychiatric (eg, affective disorders and addictions) comorbidity, but acute medical risk is less of a problem than it is for anorexia nervosa, and care is typically delivered on an outpatient basis in adult services.

NICE guidelines recommended that people with anorexia nervosa should first be offered outpatient treatment[82] and that inpatient care be used for those who do not respond or who present with high risk and little psychosocial resources. Whether inpatient admissions should be short to alleviate acute risk or prolonged to attain full weight restoration (thought to reduce relapse) is controversial.[94] Models of day treatment provide an intermediate service model.[95]

Practice recommendations emphasise the importance of specialised care for the treatment of eating disorders, but such care is not often accessible. Hence, new forms of service delivery (eg, e-mailing, text-messaging) with use of treatment directed via mobile phones, the internet, or telemedicine (eg, cognitive behavioural therapy [CBT] delivered by a therapist via the internet) are being assessed.[96–99] A systematic review[98] of self-help interventions (computerised or manual) modelled after empirically validated approaches concluded that with professional oversight (guided self-help) these interventions could have benefit in bulimia nervosa and binge eating disorder, although some uncertainty still remains.[98,100,101]

	Anorexia nervosa		Bulimia nervosa		Binge eating disorder	
	Evidence	Effect	Evidence	Effect	Evidence	Effect
Pharmacological treatment						
Antidepressants (acute phase)	Weak	–	Strong	+	Moderate	+
SSRIs	Weak*	–	Strong*	+	Moderate	–/+
TCAs	Weak*	–	Weak*	+	Weak	+
Other classes	..	..	Weak*	–/+	..	..
SNRIs (atomoxetine)	..	..	..	..	Weak	+
Antidepressants (relapse prevention)	Weak*	–/+	Weak	–/+	Weak	–/+
Antipsychotic: olanzapine	Weak*	–/+	..	..	..	..
Zinc	Weak*	–/+	..	..	..	..
Drugs for osteoporosis/osteopenia	Weak*	–	..	..	..	..
Anticonvulsant: topiramate	..	..	Weak	+	Moderate	++
Appetite suppressor: sibutramine	..	..	..	..	Moderate	++
Obesity drug: orlistat	..	..	..	..	Weak	+
Behavioural treatment						
Cognitive behavioural therapy	Weak*	+	Strong*	++	Moderate	+++
Interpersonal psychotherapy	Weak*	+	Moderate	+	Weak	++
Cognitive analytical therapy	Weak	+	..	..	..	..
Dialectical behavioural therapy	..	..	Weak	+	Weak	+
Psychodynamic therapies	Weak	+	Weak	–/+	..	..
Behavioural therapies	Weak	–/+	Moderate	+	..	..
Family-based therapy (Maudsley)	Moderate*	++	Weak*	+	..	..
Specialist clinical management	Weak*	+	..	..	..	..
Nutritional counselling (alone)	Weak*	–	Weak	–/+	Weak	+
Behavioural weight loss therapy	..	..	..	..	Weak	++
Self-help interventions (GSH/PSH)	..	..	Weak*	+	Weak	+
Mobile/internet/telemedicine	..	..	Weak	–/+	Weak	–/+

SSRIs=selective serotonin reuptake inhibitors. TCAs=tricyclic antidepressants. SNRIs=serotonin-norepinephrine reuptake inhibitors. GSH=guided self-help. PSH=pure self-help. Evidence grades: ··=non-existent or not applicable; grades weak/moderate/strong. Beneficial effect (reduction of symptoms or behaviours or maintenance of improvements): ··=no randomised controlled trial available; –=no beneficial effect; –/+=mixed results or still inconsistent results (possible beneficial effect); +=slight beneficial effect; ++=moderate beneficial effect; +++=strong beneficial effect. *At least one trial included adolescents (<18 years).

Table 2: **Treatments for anorexia nervosa, bulimia nervosa, and binge eating disorder and strength of their empirical support**

Evidence-based treatments

Anorexia nervosa

The evidence base relating to the treatment of anorexia nervosa is meagre.[82] Two main factors contribute to difficulties in trials of treatment for this disease: clinician-instigated protocol withdrawal because of failure to stabilise risk, and patient withdrawal and difficulties in recruitment because of poor acceptability of treatments. Thus, treatment guidelines rely on expert recommendations. These recommendations emphasise the importance of a multidisciplinary approach including medical, nutritional, social, and psychological components.[82–84] Psychotherapy can be delivered individually or with the family. The involvement of families in treatment depends on several factors—eg, age of the patient, living arrangements, the patient's level of risk and dependence, and the ethos of the treatment team.

For adolescents with anorexia nervosa, family psychotherapy as practised according to the Maudsley method is recommended (table 2).[102] 6 months of treatment can be sufficient unless there is obsessive compulsive comorbidity or non-intact families.[103] Families with extremes of overprotection or criticism have better outcomes in separated family therapy (child and parents seen separately) than in combined family therapy.[104] Parents are distressed and burdened by symptoms and behaviours of eating disorders.[105] These feelings can be alleviated by group educational interventions.[106]

A Cochrane collaboration review (updated in 2008) concluded that the evidence accumulated so far does not lend support to any one particular psychotherapeutic method for adults with anorexia nervosa, although support from a non-specialist clinician might be less efficacious than might that from a specialist delivering a specific form of psychotherapy.[107]

No strong evidence lends support to drug treatment either in the acute or maintenance phases of the illness.[108,109] A few randomised controlled trials have been done since the last Seminar. The previous expectation that fluoxetine could have a role in prevention of relapse in anorexia nervosa[110] weakened after the negative findings from a large and thorough study.[111] Interest has been renewed in the potential use of atypical antipsychotic drugs to target dopaminergic dysregulation and comorbid features of this disease.[112] The idea is that by reducing distorted cognitions and anxiety symptoms, resistance to weight gain decreases. Initial, small randomised studies[113,114] report decreases in obsessive symptoms and an increased rate of weight gain. Larger trials are necessary, however, to substantiate these benefits and elucidate harms with this drug, such as a potential increase of QTc interval with the risk of cardiac arrhythmias.

Bulimia nervosa

The evidence base[115] for the original CBT model of bulimia nervosa[116] and its use as the first-line treatment is strong. Although CBT has good acceptability, binge remission rates (cessation of binge eating or purging) at the end of treatments are only 30–40%.[117,118] An enhanced form of CBT with a broader focus including interpersonal factors, emotional tolerance, perfectionism, and self-esteem did not substantially improve this outcome.[119] Furthermore, combining antidepressants (tricyclics or fluoxetine) with CBT did not significantly add to the effect of CBT alone.[117] Interpersonal therapy is efficacious as a treatment alternative, although it showed a slower response of symptom change than did CBT (similar results to CBT only after 1 year of follow-up).[115,117] Other models of treatment are being considered for use in bulimia nervosa, such as those with a focus on emotional regulation (eg, dialectical behaviour therapy).[120]

Two studies have assessed the role of family-based psychotherapy for adolescent bulimia nervosa.[121,122] One suggested that guided CBT could have advantages

compared with family-based treatment in terms of cost and speed of response,[121] whereas the other suggested that family-based treatment had advantages compared with individual supportive therapy.[122]

A 2004 review of treatment for bulimia nervosa and binging included seven trials in which participants with the form of eating disorder not otherwise specified that was similar to bulimia nervosa formed part of the sample.[123] The conclusion from this and from a recent trial[119] is that CBT is as effective for non-specified eating disorder similar to bulimia nervosa as it is for bulimia nervosa itself.

Pharmacotherapy has been recommended in the treatment of bulimia nervosa and binge eating disorder, especially if psychotherapy is either unavailable or unacceptable.[82,83] Evidence from pharmacological trials in bulimia nervosa is strong, and it is increasing in studies of binge eating disorder, but this finding mainly indicates efficacy in the acute stage after short-term treatment. Overall, evidence for long-term effects after medication is scarce. Additionally, pharmacological agents have been mainly tested in adults, and the results might not be generalised to adolescents and children. Moreover, use of antidepressant drugs in children and young people is controversial because of increased suicidal risk.[124]

Three systematic reviews detected strong evidence for the use of antidepressants to treat bulimia nervosa in the short term (around 8 weeks).[115,117,125] However, the pooled effect from one meta-analysis (with eight studies, 901 patients) was judged only moderate for clinical improvement, which was defined as the number of patients with 50% or more reduction of binge eating (57% of patients receiving antidepressants *vs* 33% receiving placebo), and remission rates with antidepressants were usually less than 20% (similar to placebo).[125] Overall acceptability of antidepressant treatment is low (around 40% dropout rates) when drugs are given alone.[125] Fluoxetine is the main drug tested in trials and approved for use in bulimia nervosa by health regulatory agencies; it is recommended in a dose (60 mg per day) that is higher than is usually necessary to treat depression (20–40 mg per day).[115] There is less evidence of efficacy for other serotonin reuptake inhibitors (citalopram, sertraline, fluvoxamine).[117,126] Whether antidepressant treatment can prevent relapse in bulimia nervosa is not yet known, since the few trials that were done were limited by their high attrition rates.[115,117,127] Topiramate can be effective in reduction of bulimic and purging symptoms, but the safety profile of this drug still needs to be established in this disease.[117,128,129]

Binge eating disorder

Psychological interventions that have shown efficacy in treatment of bulimia nervosa have also been tested in binge eating disorder with positive results, particularly modified CBT, interpersonal therapy, and dialectical behaviour therapy.[130] Large effect sizes in a metaanalysis have been reported for CBT compared with a control for reduction of binge frequency and for binge abstinence.[100] An additional challenge in the treatment of binge eating disorder is weight management, since individuals are often classified as being overweight or obese. So far, psychological interventions for this disorder have not consistently shown clinically relevant weight losses.[100] However, behavioural weight loss treatments have shown a moderate reduction in weight and improvement in binge abstinence.[100] Binge abstinence is an important treatment goal because it has been associated with increased weight loss in both psychological and pharmacological trials.[131,132] A few studies with long-term follow-up suggest that abstinence from bingeing could persist for 12 months[132,133] and 24 months.[134]

Systematic reviews[130] and meta-analyses[100,135] of treatments for binge eating disorder suggest that drug treatments show, at least, a moderate effectiveness in reduction of binge frequencies and promotion of binge remission in the short term, with a remission rate of 48·7% reported with pharmacotherapy (including antidepressants, anticonvulsants, and obesity drugs) compared with 28·5% with placebo.[135] Several guidelines recommend short-term treatment with antidepressants (mainly serotonin reuptake inhibitors) as an alternative first approach to CBT. Although antidepressants are usually effective in reducing binges,[100,135] some studies have reported negative findings,[130,136] and their effect on depressive symptoms and on weight is uncertain.[135,137]

Modest weight loss and binge remission have been reported with drugs approved for use in obesity,[135] such as sibutramine[138,139] and orlistat,[140] and with drugs associated with weight loss, such as topiramate,[141] zonisamide,[142] and atomoxetine.[143] Sibutramine and topiramate have both been tested in multicentre trials and showed binge remission rates greater than with serotonin reuptake inhibitors compared with placebo.[138,139,144] Supplementation of CBT or behavioural weight loss treatments with the obesity drug orlistat[145] or topiramate[144] might increase weight loss.[146] Although these drugs can be considered as part of the available regimen to treat binge eating disorder, the short-term duration of trials (12–24 weeks), high dropout rate, and placebo-response rates restrict the conclusions about their use.[100,130] Additionally, the risk–benefit balance is uncertain since intolerable adverse effects have been reported with some drugs (eg, zonisamide, topiramate).[117,130,142]

Prognosis

Recovery from anorexia nervosa becomes much less likely the longer that the illness has persisted. This finding contrasts with that of bulimia nervosa, for which the chance of recovery becomes higher the longer the illness duration.[147] A systematic review[148] has compiled data for all outcomes for eating disorders and reported

an increased mortality rate for anorexia nervosa (the reported range is wide, varying with case mix and length of follow-up) and persistent psychiatric problems in many cases.

In anorexia nervosa, a young age at onset and short duration of illness was associated with a good outcome, and somatic and psychiatric comorbidity with a poor outcome.[149] This disease disrupts education[150] and vocational functioning, which contributes to difficulties in independent living in 20% of cases up to 10–20 years after the onset of the illness.[88] Less is known about the effect of other eating disorders in this domain of life.

Little research has been done into the long-term outcome of bulimia nervosa and binge eating disorder. Of a cohort of patients with both these diseases admitted for hospital treatment in Germany, a third had an eating disorder diagnosis 12 years later; 36% of patients with binge eating disorder and 3·6% with bulimia nervosa had a BMI greater than 30 kg/m².[151]

Conclusions

This Seminar has attempted to synthesise new developments in eating disorders that have arisen since the previous *Lancet* Seminar, and to integrate these developments into the knowledge that is relevant for clinicians. The diagnostic criteria for anorexia nervosa and bulimia nervosa are under consideration and could be broadened in DSM-V, reducing the size of the population in the category for eating disorders not otherwise specified. Binge eating disorders will probably be accepted as an additional form of eating disorder.

Eating disorders arise from an interaction between environmental events and the biological and developmental features of the individual. Abnormal eating behaviours produce both medical and psychosocial results. The psychosocial consequences derive partly from the effects of starvation on the brain and can perpetuate the illness. Several treatments and their combinations have been tested for binge eating disorder, with possible efficacy in the short term. New forms of treatment delivery have also been tested for bulimia nervosa and binge eating disorder with promising results. Progress has been made in treatment of adolescent anorexia nervosa, although not for the adult expression of this disorder.

Contributors

All authors contributed to the search and selection of the literature and to the writing of the Seminar.

Conflicts of interest

JT has written several books on eating disorders for which she receives royalties. AMC has received honoraria as speaker for Meddley and Janssen-Cilag pharmaceutical industries, and has participated in multicentre trials supported by Abbott and Janssen-Cilag (without grants) between 2001 and 2007. NZ declares that she has no conflicts of interest.

Acknowledgments

We thank the anonymous reviewers for their comments on early drafts of this Seminar. JT was partly funded by a UK Department of Health National Institute for Health Research (NIHR) Programme Grant for Applied Research (reference number RP-PG-0606-1043) and receives support from the NIHR Specialist Biomedical Research Centre for Mental Health award to the South London and Maudsley NHS Foundation Trust and the Institute of Psychiatry, King's College London. The views expressed herein are not necessarily those of the Department of Health or NIHR. AMC was funded by CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior), Ministry of Education, Brazil, with a post-doctoral grant at the Institute of Psychiatry, King's College London, during 2008 (during the writing and review process of this Seminar). NZ is partly funded by the US National Institutes of Health (K23-MH-070418).

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