Anorexia nervosa in adolescents

Abstract

Anorexia nervosa is an eating disorder with peak onset in adolescence, which carries the highest mortality rate of all psychiatric illnesses. It is commonly comorbid with other physical and mental health problems, yet training on management of people with eating disorders and working knowledge of clinicians working with underweight adolescents is inconsistent. This review of anorexia nervosa in adolescents provides an overview of the presentation, aetiology and treatment of this disorder, with a particular focus on the assessment and management of physical health risks, including refeeding syndrome.

Key words: Adolescent medicine; Anorexia nervosa; Eating disorders; Refeeding syndrome

Submitted: 4 March 2020; accepted after double-blind peer review: 15 April 2020

Josephine Neale[1]

Lee D Hudson[2]

Author details can be found at the end of this article

Correspondence to:
Josephine Neale;
Josephine.neale@nhs.net

Introduction

Integrating physical and mental health is recognised as a key priority for the improvement of health care internationally (Naylor et al, 2016; NHS, 2019), and perhaps no other condition epitomises the need for such integration as anorexia nervosa. Anorexia nervosa is an eating disorder characterised by pervasive, pathological weight and shape concerns leading to restricted oral intake and consequent low weight. Although a psychiatric disorder (and indeed it is the most lethal of all of the psychiatric disorders, with mortality rates 5.86 times higher than the general population; Arcelus et al, 2011), around half of deaths are attributable to physical complications associated with starvation. At a more practical level, anorexia nervosa presents particular challenges to those who predominantly work in medical settings. Patients can frustrate with their apparent lack of desire to get better amidst busy inpatient services. Training, knowledge base and understanding of the condition and how to work with patients and their carers is frequently missing and risks are sometimes misunderstood (Hudson et al, 2013). Yet in an era of shifting epidemiology (Micali et al, 2013), better understanding and collaborations are needed more than ever for this condition, especially if care and survival is to be improved. This review provides information on the condition, but also calls for improved and collaborative care for a much misunderstood, maligned and yet simultaneously physically risky psychiatric disorder.

Epidemiology and prognosis

The peak age of onset of anorexia nervosa in both men and women is 15–19 years (Micali et al, 2013). A surveillance study of young people aged 8–17 years in the UK and Ireland found incidence rates of 13.68 per 100 000 population (95% confidence interval 12.88–14.52), with rates of 25.66 (95% confidence interval 24.09–27.30) for young women and 2.28 (95% confidence interval 1.84–2.79) for young men (Petkova et al, 2019). The estimated lifetime prevalence for anorexia nervosa in women is 3.64% (95% confidence interval 2.81–4.72) (Micali et al, 2017).

The aetiology of anorexia nervosa is complex and multifactorial. Although there is a clear genetic risk factor, with twin studies demonstrating high heritability (Hinney and Volckmar, 2013), there is evidence of interaction of genetic risk with other identified risk factors, including anxiety, perfectionism, cognitive rigidity, and early feeding problems (Treasure et al, 2015). As understanding of the genetic basis of anorexia nervosa develops, it has been proposed that the significant genetic correlations with psychiatric disorders, physical activity and metabolic traits warrant viewing anorexia nervosa as a ‘metabo-psychiatric disorder’ (Watson et al, 2019). Anorexia nervosa was once considered developmental, given

How to cite this article:
Neale J, Hudson LD. Anorexia nervosa in adolescents. Br J Hosp Med. 2020. https://doi.org/10.12968/hmed.2020.0099

that peak onset coincides with puberty, but the early onset of cases as young as 8 years of age (Petkova et al, 2019) demonstrates the complex nature of the aetiology. In contrast to bulimia nervosa, sexual abuse or assault are not thought to be risk factors for anorexia nervosa (Wonderlich et al, 2001).

In terms of prognosis, an estimated 50% of patients achieve full recovery, 30% improve and the remaining 20% remain chronically ill (Steinhausen, 2002).

Presentation

Diagnostic criteria for anorexia nervosa changed with the publication of DSM-5 (American Psychiatric Association, 2013) (Table 1). The latest diagnostic criteria have removed the criterion of amenorrhoea, as this cannot be assessed in men or pre-menarcheal females. Typical characteristics of anorexia nervosa include distorted perceptions of being overweight, target weights, target calorie intakes, specific foods that should or should not be eaten, as well as target levels of excessive exercise or other compensatory behaviours, such as self-induced vomiting. That said, by its nature, anorexia nervosa can be covert and presentations may be hidden for long periods of time. Moreover in younger patients, where cognitive development is not sufficiently mature, the initial presentation may be with weight loss as a result of food refusal alone.

It is important to recognise that, because of the wide range of physical and psychological symptoms, anorexia nervosa can present across a variety of settings, including primary care, secondary care (in particular cardiology, endocrinology and gastroenterology), schools and dietetic clinics, with anorexic cognitions only becoming evident on questioning. Alternative reasons for reduced intake or weight loss should be considered as part of the assessment, and potential differential diagnoses are listed in Table 2.

Acute physical health risks

Anorexia nervosa can pose significant acute physical risk, with rapid weight loss and significant underweight the most immediately concerning. Rate of weight loss may be as important as absolute weight at presentation (Hudson et al, 2012). A thorough history should include questions about the rate and amount of weight loss, compensatory behaviours (fasting, self-induced vomiting, use of laxatives or diuretics), exercise, menstrual history and questions to identify physical symptoms of underweight or weight loss, such as cold intolerance, fatigue, dizziness or fainting, chest pain and palpitations.

Key signs to look for on examination include pallor, lanugo hair, dehydration (mucous membranes, skin turgor), poor dentition and parotid gland enlargement. Examination should also include measurement of weight and height. In the field, body mass index has become the benchmark for underweight, with anyone with an absolute body mass index of less than 18.5 kg/m^2 being considered underweight in adults; however, in children and young people the focus is on standardised body mass index for age and sex, sometimes called ‘weight for height’, which relates to a percentage of the average body mass index for age and sex, aligned with World Health Organization measures of wasting (de Onis and Blössner, 1997). In itself, body mass index is unhelpful, in that most medically unwell patients are at a higher range of body mass index and being physically unwell is more likely

Table 1. DSM-5 diagnostic criteria for anorexia nervosa

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
Intense fear of gaining weight or of becoming fat, or persistent behaviour that interferes with weight gain, even though at a significantly low weight
Disturbance in the way in which one’s body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight

From American Psychiatric Association (2013)

Table 2. What other common differentials might there be for reduced intake or weight loss?	
Other mental health problems or psychological dysfunction	Depression
	Anxiety
	Obsessive compulsive disorder
	Avoidant/restrictive food intake disorder
	Illicit substance misuse
Bowel pathology	Inflammatory bowel disease
	Coeliac disease
	Malabsorption syndrome
Systemic medical illness	Diabetes mellitus
	Addison's disease
	Thyroid dysfunction
	Systemic lupus erythematosus
	Malignancies
	Infection
Iatrogenic (ie loss of appetite secondary to medication side effects)	

related to weight loss, although very low body mass index is a specific measure for medical instability at presentation (Hudson et al, 2012). When there is concern about weight loss, it is crucial that key risk parameters are identified and documented and guidance on assessment and management of physical risk is provided by Junior MARSIPAN (Royal College of Psychiatrists, 2012) (Table 3). Cardiovascular instability is the most common clinical finding, and simple vital observations can provide swift indicators of risk: bradycardia, hypotension, postural hypotension and hypothermia signify compromise secondary to underweight. An electrocardiogram should be reviewed for bradycardia, prolonged QTc and other arrhythmias.

Blood tests can be used to assess both physical risk from underweight as well as other possible medical diagnoses, but it must be recognised that even in the most acute of medical presentations, blood tests are frequently normal (Hudson, 2019). Below are listed some useful blood tests for assessing the effects of anorexia nervosa, with urea and electrolytes being the most commonly measured.

- Full blood count (anaemia, thrombocytopenia and low white cell count are common in anorexia nervosa representing a marrow response to starvation)
- Urea and electrolytes (potassium and sodium levels may be deranged and the risk of electrolyte imbalance and cardiac side effects can be worsened by vomiting; urea levels are frequently raised)
- Liver function tests (a raised alanine aminotransferase level is common in starvation)
- Calcium, magnesium and phosphate levels.

The decision to perform blood investigations for alternative medical diagnoses should be based on clinical findings – and it is the authors' view that there are no mandatory tests. Importantly, it should be remembered that eating disorders and medical conditions are not mutually exclusive. Indeed, in some medical conditions, such as type 1 diabetes mellitus, eating disorders are more common (Pursey et al, 2020). Important examples of where additional medical tests should be performed in the context of an eating disorder is for coeliac disease (using tissue transglutaminase as a screen) where there is weight loss and typical symptoms of coeliac disease (eg abdominal pain), and where there are symptoms and signs of thyroid disease this should prompt the measurement of thyroid function tests. It should be remembered that sick euthyroid is common in anorexia nervosa and underweight states

Table 3. What puts a young person with anorexia nervosa at high risk of serious illness or death?
Percentage median body mass index <70% (approx. below 0.4th body mass index centile)
Recent loss of weight of 1 kg of more/week for 2 consecutive weeks
Heart rate (awake) <40 bpm
History of recurrent syncope, marked orthostatic changes
Irregular heart rhythm or electrocardiogram abnormalities
Severe dehydration
Temperature <35.5°C tympanic
Low serum levels of phosphate, potassium, albumin, glucose, sodium or calcium
Acute food refusal or estimated calorie intake 400–600 kcal per day
Violence to or from parents
>2 hours per day of uncontrolled exercise
Suicidal ideation with moderate to high risk of suicide
Unable to complete sit-up squat-stand test
Confusion, delirium, acute pancreatitis
Gastric or oesophageal rupture

adapted from Junior MARSIPAN (Royal College of Psychiatrists, 2012)

(Usdan et al, 2008). Other diagnoses should also be considered where the presentation of an eating disorder is considered unusual by mental health professionals, and in particular in younger patients where typical cognitions of eating disorder pathology may be reduced as a result of immaturity (Hudson and Court, 2012). There are no published data on the sensitivity or specificity of usual tests performed for possible medical conditions in the context of eating disorders beyond those published where suspicion is sufficient for testing in other settings (Rostom et al, 2005). The reader is directed to Hudson and Court (2012) for a more detailed description of medical conditions that may mimic anorexia nervosa in causing underweight.

Refeeding syndrome

During assessment, current dietary intake, recent rate of weight loss and presence of vomiting provide important information regarding the risk of refeeding syndrome, a potentially fatal complication of anorexia nervosa. The use of the multidisciplinary team is key here, in particular the involvement of a dietitian. On reintroduction of nutrition after starvation, phosphate requirements increase as the body switches back to carbohydrate metabolism, depleting the body's phosphate stores. The so-called refeeding syndrome is a potentially serious complication of reintroduction of calories. In addition to biochemical evidence of low phosphate levels, clinical signs may include resting tachycardia, oedema and confusion. Treatment consists of phosphate replacement and electrolyte correction, and cardiac monitoring is advised if clinical signs or electrolyte abnormalities are present. In a review of 1039 adolescents with anorexia nervosa, the incidence of refeeding hypophosphataemia ranged from 0% to 38%, with an average incidence of 14% (O'Connor and Nicholls, 2013). The highest risk period for refeeding syndrome is within the first few days of refeeding, although it can occur up to 2 weeks after, and intensive clinical and biochemical monitoring is required during this time. It is important to recognise that underfeeding syndrome – frequently seen because of a lack of recognition or reluctance to commence feeding because of fear of refeeding syndrome – is more commonly seen than refeeding syndrome and the consequences are potentially more severe (Nicholls et al, 2011).

Chronic physical health risks

Growth impairment and delay of puberty is often seen in adolescents with anorexia nervosa, which is influenced by the timing of their underweight with regard to their pubertal development. There is evidence for catch-up growth in the majority of those with anorexia nervosa and growth impairment, although not all. Possible risk factors for growth delay and potential growth stunting include younger age and longer duration of illness (Neale et al, 2020). Fertility can be affected; women with a history of anorexia nervosa experience delayed first birth and lower parity relative to the general population (Tabler et al, 2018) and are more likely to have seen a doctor for lifetime fertility problems than those without anorexia nervosa (Easter et al, 2011). However, sexually active women should be reminded that amenorrhoea in anorexia nervosa is not a guarantee of infertility, with evidence for higher rates of accidental pregnancy and termination in women with anorexia nervosa (Bulik et al, 2010).

Bone mineral density may also be disturbed with chronic underweight, particularly in childhood and adolescence, periods of development that see increased accumulation of bone mineral content. Measurement of bone mineral density should be considered when a young person has been underweight for over a year, or earlier if they have bone pain or recurrent fractures (National Institute for Health and Care Excellence, 2017). Importantly, assessment of bone mineral density should only be organised by someone qualified to interpret this, and also only after discussion with patients and carers as to whether or not it will be of value. Adolescents with anorexia nervosa may also be at greater risk of fractures, even in the presence of normal bone mineral density values (Faje et al, 2014). Weight restoration is the first-line treatment of low bone mineral density in the context of underweight in anorexia nervosa, although this is not always successful in achieving a bone mineral density of normal range (Misra and Klibanski, 2014). Attention should be paid to adequate calcium intake and vitamin D. Although there are reported benefits for bone mineral density in physiological dose replacement of oestrogen in underweight young women with anorexia nervosa, the effects are minimal (Misra et al, 2011). A systematic review showed that use of the oral contraceptive pill does not positively impact on bone mineral density recovery (Bergström et al, 2013) and may cause confusion with an artificial return of periods.

Treatment

Treatment requires the input of a multidisciplinary team experienced in the management of eating disorders and dietetic input is crucial, providing appropriate meal plans and guidance on energy needs, as well as advice on supplementary vitamins and minerals and support with refeeding. Generally a healthy % weight for height is considered to be above 95%, but individualised care approaches are needed. Young people with confirmed or suspected anorexia nervosa should be referred to a specialist secondary care eating disorders service for children and young people, and these services have been shown to improve outcomes and cost effectiveness, reducing the need for inpatient admissions (NHS England, 2015). Over the last few years there has been investment in development and training of community eating disorders teams for children and young people, and NHS England standards dictate that young people with eating disorders should be able to access emergency treatment within 24 hours, urgent help within 1 week and treatment within 4 weeks (NHS England, 2015).

For those who are medically stable and managed in the community, anorexia nervosa-focused family therapy is first-line treatment for children and young people (National Institute for Health and Care Excellence, 2017), which emphasises the role of the family in helping the young person to recover. Initial sessions focus on weight restoration, with parents being empowered to achieve this. Over time, the responsibility shifts towards the young person as they feel more able to make independent decisions about meals, finishing with sessions geared towards relapse prevention. These may be delivered as single-family or multi-family therapy sessions and typically consist of 18–20 sessions over a year. Therapy includes psychoeducation on aspects of nutrition and this is important in maintaining recovery. Alternative therapies for adolescents with anorexia nervosa, where anorexia

nervosa-focused family therapy is contraindicated or not effective, include individual cognitive behavioural therapy or adolescent-focused psychotherapy for anorexia nervosa.

From a physical and mental health point of view, early intervention in adolescents with anorexia nervosa is essential. Unless treatment is provided within the first 3 years of illness, outcomes are poor, even when treatment is ultimately provided (Treasure and Russell, 2011). Early therapeutic alliance with adolescents predicts better end of treatment outcomes (Pereira et al, 2006) and weight gain during the first four sessions of family-based treatment predicts restoration to a higher weight and remission at end of treatment, as well as 12-month follow up (Madden et al, 2015). Recovery can be lengthy and physical symptoms often remit before psychological symptoms.

While inpatient care for adolescents with anorexia nervosa has long been considered the most appropriate treatment option, and those admitted to inpatient care at a higher body mass index tend to have a better prognosis (Toulany et al, 2015), inpatient admissions are costly with a high rate of relapse, so this method of management of adolescents with anorexia nervosa remains controversial (Gowers et al, 2007; Hay et al, 2019). Day-patient care may be a safe and less costly alternative to lengthy inpatient admissions (Herpertz-Dahlmann et al, 2014). National Institute for Health and Care Excellence (2017) guidelines advise against the use of an absolute weight or body mass index threshold when deciding whether to admit those with eating disorders to day-patient or inpatient care. If long-term psychiatric admissions for adolescent anorexia nervosa can be avoided, brief paediatric admissions may be necessary to address medical concerns and this should be guided by risk assessment using the Junior MARSIPAN guidelines (Royal College of Psychiatrists, 2012). In particular, intravenous fluids and nasogastric tube feeding may be necessary and, in some cases where young people are at serious physical risk and not consenting to treatment, ongoing treatment may need to be given under the legal framework of the Mental Health Act.

Medication is not recommended as the sole treatment of anorexia nervosa (National Institute for Health and Care Excellence, 2017) although commonly comorbid illnesses such as depression, anxiety and obsessive-compulsive disorder should be treated appropriately (with treatments used for those comorbidities alone) and this may have a considerable impact on symptoms of anorexia nervosa. However, symptoms of low mood and anxiety can improve with weight restoration so it is important to take a careful history and discuss treatment plans and options with young people and their families. Concern over physical development, delayed puberty or impairment of growth should prompt referral for specialist review.

Future initiatives

As an illness which crosses both physical and mental health, it is vital that treatment is collaborative between child and adolescent psychiatrists and paediatricians. Clinicians encountering young people with anorexia nervosa should be aware that it may be difficult for the young person to engage and they are vulnerable to stigma and shame (National Institute for Health and Care Excellence, 2017).

Trials for new treatments for anorexia nervosa include cognitive remediation therapy and non-invasive neuromodulation (Brockmeyer et al, 2018), although these have not been specific to adolescents. Further research is needed to provide evidence for the most appropriate treatment setting in addition to treatment options. In addition to this, treatments addressing eating disorders and their mental health comorbidities will be important to explore, given the high rate of comorbidity seen in anorexia nervosa.

Author details

[1]Priory Hospital Ticehurst House, East Sussex, UK

[2]UCL Great Ormond Street Institute of Child Health, London, UK

Conflicts of interest

The authors declare no conflicts of interest.

Key points

- Early recognition and intervention for adolescents with anorexia nervosa is crucial to achieve good outcomes.
- It is important to monitor and recognise refeeding syndrome in all clinical settings.
- There are both acute and chronic physical health implications to being underweight.

References

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th edn. Washington (DC): American Psychiatric Association; 2013

Arcelus J, Mitchell AJ, Wales J, Nielsen S. Mortality rates in patients with anorexia nervosa and other eating disorders. A meta-analysis of 36 studies. Arch Gen Psychiatry. 2011;68(7):724–731. https://doi.org/10.1001/archgenpsychiatry.2011.74

Bergström I, Crisby M, Engström A-M et al. Women with anorexia nervosa should not be treated with estrogen or birth control pills in a bone-sparing effect. Acta Obstet Gynecol Scand. 2013;92(8):877–880. https://doi.org/10.1111/aogs.12178

Brockmeyer T, Friederich H-C, Schmidt U. Advances in the treatment of anorexia nervosa: a review of established and emerging interventions. Psychol Med. 2018;48(8):1228–1256. https://doi.org/10.1017/S0033291717002604

Bulik CM, Hoffman ER, Von Holle A et al. Unplanned pregnancy in anorexia nervosa. Obstet Gynecol. 2010;116(5):1136–1140. https://doi.org/10.1097/AOG.0b013e3181f7efdc

de Onis M, Blössner M. WHO global database on child growth and malnutrition. Geneva: WHO; 1997

Easter A, Treasure J, Micali N. Fertility and prenatal attitudes towards pregnancy in women with eating disorders: results from the Avon longitudinal study of parents and children. BJOG. 2011;118(12):1491–1498. https://doi.org/10.1111/j.1471-0528.2011.03077.x

Faje AT, Fazeli PK, Miller KK et al. Fracture risk and areal bone mineral density in adolescent females with anorexia nervosa. Int J Eat Disord. 2014;47(5):458–466. https://doi.org/10.1002/eat.22248

Gowers S, Clark A, Roberts C et al. Clinical effectiveness of treatments for anorexia nervosa in adolescents: randomised controlled trial. Br J Psychiatry. 2007;191(5):427–435. https://doi.org/10.1192/bjp.bp.107.036764

Hay PJ, Touyz S, Claudino AM et al. Inpatient versus outpatient care, partial hospitalisation and waiting list for people with eating disorders. Cochrane Database Syst Rev. 2019;1(1):CD010827. https://doi.org/10.1002/14651858.CD010827.pub2

Herpertz-Dahlmann B, Schwarte R, Krei M et al. Day-patient treatment after short inpatient care versus continued inpatient treatment in adolescents with anorexia nervosa (ANDI): a multicentre, randomised, open-label, non-inferiority trial. Lancet. 2014;383(9924):1222–1229. https://doi.org/10.1016/S0140-6736(13)62411-3

Hinney A, Volckmar AL. Genetics of eating disorders. Curr Psychiatry Rep. 2013;15(12):423. https://doi.org/10.1007/s11920-013-0423-y

Hudson LD. Spotlight: physical health risks of patients with an eating disorder. Br J Fam Med. 2019. https://www.bjfm.co.uk/physical-health-risks-of-patients-with-an-eating-disorder (accessed 5 May 2020)

Hudson LD, Court AJ. What paediatricians should know about eating disorders in children and young people. J Paediatr Child Health. 2012;48(10):869–875. https://doi.org/10.1111/j.1440-1754.2012.02433.x

Hudson LD, Cumby C, Klaber RE et al. Low levels of knowledge on the assessment of underweight in children and adolescents among middle-grade doctors in England and Wales. Arch Dis Child. 2013;98(4):309–311. https://doi.org/10.1136/archdischild-2012-303357

Hudson LD, Nicholls D, Lynn R, Viner R. Medical instability and growth of children and adolescents with early onset eating disorders. Arch Dis Child. 2012;97(9):779–784. https://doi.org/10.1136/archdischild-2011-301055

Madden S, Miskovic-Wheatley J, Wallis A et al. Early weight gain in family-based treatment predicts greater weight gain and remission at the end of treatment and remission at 12-month follow-up in adolescent anorexia nervosa. Int J Eat Disord. 2015;48(7):919–922. https://doi.org/10.1002/eat.22414

Micali N, Hagberg KW, Petersen I, Treasure J. The incidence of eating disorders in the UK in 2000–2009: findings from the General Practice Research Database. BMJ Open. 2013;3(5):e002646. https://doi.org/10.1136/bmjopen-2013-002646

Micali N, Martini MG, Thomas JJ et al. Lifetime and 12-month prevalence of eating disorders amongst women in mid-life: a population-based study of diagnoses and risk factors. BMC Med. 2017;15(1):12. https://doi.org/10.1186/s12916-016-0766-4

Misra M, Katzman D, Miller KK et al. Physiologic estrogen replacement increases bone density in adolescent girls with anorexia nervosa. J Bone Miner Res. 2011;26(10):2430–2438. https://doi.org/10.1002/jbmr.447

Misra M, Klibanski A. Anorexia nervosa and bone. J Endocrinol. 2014;221(3):R163–R176. https://doi.org/10.1530/JOE-14-0039

National Institute for Health and Care Excellence. Eating disorders: recognition and treatment (NG69). London: National Institute for Health and Care Excellence; 2017

Naylor C, Das P, Ross S et al. Bringing Together Physical and Mental Health. London: The King's Fund; 2016

Neale J, Pais SMA, Nicholls D, Chapman S, Hudson LD. What are the effects of restrictive eating disorders on growth and puberty and are effects permanent? A systematic review and meta-analysis. J Adolesc Health. 2020;66(2):144–156. https://doi.org/10.1016/j.jadohealth.2019.08.032

NHS. The NHS Long Term Plan. London: NHS; 2019

NHS England. Access and waiting time standard for children and young people with an eating disorder: commissioning guide. London: NHS England; 2015

Nicholls D, Hudson L, Mahomed F. Managing anorexia nervosa. Arch Dis Child. 2011;96(10):977–982. https://doi.org/10.1136/adc.2009.177394

O'Connor G, Nicholls D. Refeeding hypophosphatemia in adolescents with anorexia nervosa: a systematic review. Nutr Clin Pract. 2013;28(3):358–364. https://doi.org/10.1177/0884533613476892

Pereira T, Lock J, Oggins J. Role of therapeutic alliance in family therapy for adolescent anorexia nervosa. Int J Eat Disord. 2006;39(8):677–684. https://doi.org/10.1002/eat.20303

Petkova H, Simic M, Nicholls D et al. Incidence of anorexia nervosa in young people in the UK and Ireland: a national surveillance study. BMJ Open. 2019;9(10):e027339. https://doi.org/10.1136/bmjopen-2018-027339

Pursey KM, Hart M, Jenkins L, McEvoy M, Smart CE. Screening and identification of disordered eating in people with type 1 diabetes: a systematic review. J Diabetes Complications. 2020;34(4):107522. https://doi.org/10.1016/j.jdiacomp.2020.107522

Rostom A, Dubé C, Cranney A et al. The diagnostic accuracy of serologic tests for celiac disease: a systematic review. Gastroenterology. 2005;128(4):S38–46. https://doi.org/10.1053/j.gastro.2005.02.028

Royal College of Psychiatrists. Junior MARSIPAN: management of really sick patients under 18 with anorexia nervosa. CR168. London: Royal College of Psychiatrists; 2012

Steinhausen HC. The outcome of anorexia nervosa in the 20th century. Am J Psychiatry. 2002;159(8):1284–1293. https://doi.org/10.1176/appi.ajp.159.8.1284

Tabler J, Utz RL, Smith KR, Hanson HA, Geist C. Variation in reproductive outcomes of women with histories of bulimia nervosa, anorexia nervosa, or eating disorder not otherwise specified relative to the general population and closest-aged sisters. Int J Eat Disord. 2018;51(2):102–111. https://doi.org/10.1002/eat.22827

Toulany A, Wong M, Katzman DK et al. Cost analysis of inpatient treatment of anorexia nervosa in adolescents: hospital and caregiver perspectives. CMAJ Open. 2015;3(2):E192–E197. https://doi.org/10.9778/cmajo.20140086

Treasure J, Russell G. The case for early intervention in anorexia nervosa: theoretical exploration of maintaining factors. Br J Psychiatry. 2011;199(1):5–7. https://doi.org/10.1192/bjp.bp.110.087585

Treasure J, Zipfel S, Micali N et al. Anorexia nervosa. Nat Rev Dis Primers. 2015;1(1):15074. https://doi.org/10.1038/nrdp.2015.74

Usdan LS, Khaodhiar L, Apovian CM. The endocrinopathies of anorexia nervosa. Endocr Pract. 2008;14(8):1055–1063. https://doi.org/10.4158/EP.14.8.1055

Watson HJ, Yilmaz Z, Thornton LM et al. Genome-wide association study identifies eight risk loci and implicates metabo-psychiatric origins for anorexia nervosa. Nat Genet. 2019;51(8):1207–1214. https://doi.org/10.1038/s41588-019-0439-2

Wonderlich SA, Crosby RD, Mitchell JE et al. Eating disturbance and sexual trauma in childhood and adulthood. Int J Eat Disord. 2001;30(4):401–412. https://doi.org/10.1002/eat.1101