



## Review

## Long-term consequences of anorexia nervosa

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## ABSTRACT

Anorexia nervosa (AN) is a psychiatric disorder that occurs mainly in female adolescents and young women. The obsessive fear of weight gain, critically limited food intake and neuroendocrine aberrations characteristic of AN have both short- and long-term consequences for the reproductive, cardiovascular, gastrointestinal and skeletal systems. Neuroendocrine changes include impairment of gonadotropin releasing-hormone (GnRH) pulsatile secretion and changes in neuropeptide activity at the hypothalamic level, which cause profound hypoestrogenism. AN is related to a decrease in bone mass density, which can lead to osteopenia and osteoporosis and a significant increase in fracture risk in later life. Rates of birth complications and low birth weight may be higher in women with previous AN. The condition is associated with fertility problems, unplanned pregnancies and generally negative attitudes to pregnancy. During pregnancy, women with the condition have higher rates of hyperemesis gravidarum, anaemia and obstetric complications, as well as impaired weight gain and compromised intrauterine foetal growth. It is reported that 80% of AN patients are affected by a cardiac complications such as sinus bradycardia, a prolonged QT interval on electrocardiography, arrhythmias, myocardial mass modification and hypotension. A decrease in bone mineral density (BMD) is one of the most important medical consequences of AN. Reduced BMD may subsequently lead to a three- to seven-fold increased risk of spontaneous fractures. Untreated AN is associated with a significant increase in the risk of death. Better detection and sophisticated therapy should prevent the long-term consequences of this disorder. The aims of treatment are not only recovery but also prophylaxis and relief of the long-term effects of this disorder. Further investigations of the long-term disease risk are needed.

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## 1. Defining anorexia nervosa

Anorexia nervosa (AN) is a psychiatric disorder characterized by abnormal eating behaviours that result in weight loss. Criteria are set out in, for example, the fourth edition of the Diagnostic and Statistical Manual produced by the American Psychiatric Association (DSMIV) [1]. They include failure to maintain weight above 85% of the ideal, a distorted body image or denial of the seriousness of low body weight, fear of gaining weight, and amenorrhoea [1].

Three types of the disorder have been identified: the restricting type, characterized by a marked reduction in food intake; the binge and purging type, characterized by self-induced vomiting, laxative or diuretic misuse, or strenuous physical exercise; and a type 'as yet not classified' [2].

## 2. Prevalence

AN most commonly afflicts female adolescents or young women and has potentially serious medical consequences [2]. It affects 0.3–3% of women and is the third most prevalent chronic disease in adolescent girls [3].

The prevalence of AN is often underestimated [4]. Lifetime prevalence is defined as the proportion of people who have a specific disorder at any point in their life [4]. According to Isomaa et al. 2009 [5] the lifetime prevalence rate of AN among women is probably between 2.0% and 3.0%, and for men 0.24%, [6] although there is some evidence that in males AN is more frequently undetected than in females [7]. The mean age at onset of the disorder in women is approximately 19 years [8]. Only 33% of sufferers are reported to recover fully [9].

## 3. Time course: short-term versus long-term disease

AN is a chronic and severe eating disorder. During its course, many complications may occur. Immediate effects include dizziness, headaches, brain foginess, cold, nausea, weakness and blurred vision [9]. The long-term effects are osteoporosis, cardiovascular disturbances, diabetes mellitus, thyroid disorders, gastrointestinal disorder, fertility and pregnancy problems, and other psychiatric disorders [9].

## 4. Life expectancy

There are few reports on life expectancy in AN. Harbottle et al. [10] studied 954 patients and using statistical tools estimated years of life remaining after the onset of AN versus normal life. According to this study, women diagnosed with AN at the age of 15 years are likely to live 25 years less than predicted for the normal population; women diagnosed at the age of 20 are predicted to have 36.6 years of life remaining, versus 60.5 for the normal population; and for those in whom AN starts at the age of 25 the estimate of years of life remaining is 32.2, versus 55.5. Further studies are required to evaluate this problem.

## 5. Mortality rates

Patients with AN have a mortality rate for all causes of death six times higher than the general population [11], and higher than the mortality rate seen in other types of eating disorder [11]. The American Psychiatric Association [1] reported that 5% of patients with AN die within the first 4 years of diagnosis; where the illness lasts for more than 20 years the mortality rate (as a direct result of the illness) is 20%, with many deaths occurring suddenly. According to a recently published meta-analysis, the standardized mortality ratio (SMR) for AN is 5.9 [12] (the SMR has the death rate in the

general population as the denominator or divisor and is standardized for any particular population).

A long-term retrospective Swedish cohort study of 201 patients with eating disorders reported a high SMR in patients with AN [13]. Huas et al. [14] similarly found that patients with AN are at a high risk of death, and that this risk can be predicted by both the chronicity and the severity of the illness upon hospitalization.

Published mortality rates vary widely, partly because of differences in the attribution of death. Anorexic patients can die due to 'natural' causes, such as severe heart problems, organ failure, malnutrition, or 'unnatural' causes, such as suicide [12]. A recent meta-analysis revealed that approximately 20% of the deaths of AN patients are the result of suicide [12]. Eating disorders have the highest mortality rate of any mental illness [15].

The association between childbearing in AN patients and mortality has been studied. Overall, women with AN who have never been pregnant present a six-fold higher mortality rate due to natural causes and a nine-fold higher mortality due to unnatural causes in comparison with the normal population [11] but childbearing decreases this mortality rate by 60%. Among parous women with AN only rates of death from unnatural causes, not natural causes, were higher than in the normal population [11].

## 6. Psychiatric disorders in anorexia nervosa

Psychiatric co-morbidity is common in eating disorders. For instance, in clinical studies the lifetime prevalence of mood disorders varies from 31.0% to 88.9% in patients with AN [16,17]. Depression is the single most common psychiatric disorder among patients with eating disorders, with a prevalence rate of approximately 40–45% [18], but a range of anxiety disorders (including bipolar affective disease) are seen in more than 60%. Additionally, social phobia or obsessive-compulsive disorder are common in AN [19]. AN patients often show obsessive personality manifestations. Notably, borderline and avoidant personality disorders are common. Substance misuse is another psychiatric comorbidity observed in patients with eating disorders [20].

Additionally, sexual assaults, physical abuse in childhood and post-traumatic stress disorder have been frequently reported in patients with AN [21].

## 7. Cardiovascular disease

It is reported that cardiac complications appear in 80% of patients with eating disorders [22]. The main cardiovascular consequences of AN include a prolonged QT interval, sinus bradycardia, evident on electrocardiography (ECG), myocardial mass modification, hypotension and arrhythmias [23].

The most frequent cardiovascular disorder and the most common arrhythmia among patients with AN is sinus bradycardia [23]. It is a serious condition, particularly when it coexists with other ECG abnormalities such as arrhythmias or a prolongation of the QTc interval. Sinus bradycardia may be associated with sudden death [23]. Cooke et al. [24] found that there was a substantial prolongation of the QT interval in patients with AN and also a significant reversion to normal after refeeding. Sinus bradycardia is presumably an effect of vagal hyperactivity, which subsequently decreases the cardiac output [25]. It is thought that most sudden cardiac deaths in anorexic patients arise from arrhythmia [26]. Other cardiac problems, including premature ventricular complexes, ectopic atrial foci and first-degree heart block, are also characteristic in patients suffering from AN [26].

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