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"Long-Term Outcomes of Anorexia Nervosa in Adolescents and Young Adults"

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Long-Term Outcomes of Anorexia Nervosa in Adolescents and Young Adults

1. **Introduction**

Food and behaviours associated with food consumption play an important role in many spheres of our lives - how we perceive ourselves, socialize with others and care for our health in general. More specifically, higher diet quality has been associated with a positive self-concept (Schafer, 1979). Healthy eating behaviours have been linked to enhanced self-compassion and, in part, higher body esteem (Carbonneau et al., 2021). Eating in the company of others, especially our loved ones, can promote the feelings of being loved, understood and connected. Children learn about the importance of food and eating practices through their families. This learning process reflects the social and cultural values of children's immediate surroundings and serves as a basis for their relationship with food and eating throughout their lives (Block et al., 2011). Apart from that, a balanced, healthy diet reduces the risk of various life-threatening conditions, including cardiovascular diseases, obesity and some forms of cancer (De Ridder et al., 2017).

Having healthy eating patterns and positive food attitudes might be something many of us work towards. However, what happens when our eating patterns become so dysfunctional that they severely affect our physical and mental well-being? What happens when our relationship with food is disrupted to the extent that our self-worth is based on what we see on a scale? Or when we become so infatuated with thoughts about eating, calories and external appearance that it interferes with our life quality? The present study follows a sample of adolescent and young adult women with previously diagnosed anorexia nervosa. It focuses on assessing the current eating disorder-specific psychopathology, psychiatric comorbidities and possible predictors to explore the long-term course of the disorder.

1.1 Classification, Symptomatology and Differential Diagnosis of Anorexia Nervosa

Within the field of psychiatry, eating disorders represent a group of mental conditions characterised by abnormalities in eating behaviours, eating habits and attitudes towards food. According to the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association, 2013) and the International Statistical Classification of Diseases and Related Health Problems (11th ed.; ICD-11; World Health Organisation, 2019), anorexia nervosa (henceforth named AN) is one of the most common eating disorders, especially among females in adolescence and early adulthood. Primary symptoms of AN include: 1.) food intake restriction, 2.) intense fear of weight gain and 3.) distorted body

image. More particularly, patients suffering from AN limit the number of calories and types of food they consume, leading to progressive weight loss. A frequently used threshold of low body weight is the body mass index (or shortly BMI). Significantly low body weight is reached when the value of BMI is less than 18.5 kg/m² (for adult patients) or age-adjusted BMI is below the 5th percentile (for children and adolescents). Patients continue to engage in behaviours that encourage further weight loss (such as excessive exercise or vomiting) despite significantly reduced body weight and skinny appearance. Thus, they are unable to perceive themselves and their bodies accurately – body weight and shape play an essential role in their self-evaluation and are central to their self-concept (American Psychiatric Association, 2013; World Health Organisation, 2019).

According to the DSM-5 (American Psychiatric Association, 2013), two subtypes of AN have been identified – restrictive and binge eating/purging types. Patients diagnosed with restrictive AN use predominantly fasting, dieting and/or excessive exercise to control their weight, whereas binge eating/purging AN patients additionally engage in behaviours such as vomiting or laxative abuse to promote weight loss. Three categories emerge based on the degree of symptom severity and remission status – full remission, partial remission and ongoing or acute AN. Acutely ill patients show all three primary symptoms. Despite a successful weight restoration, partially remitted patients still show one or two of the remaining primary symptoms. Fully remitted patients show no primary symptoms for a sustained period of time (American Psychiatric Association, 2013).

Various related psychiatric conditions should be considered when diagnosing a patient with AN due to symptomatic overlaps. This especially stands for other known eating disorders (such as bulimia nervosa) and obsessive-compulsive disorders (such as body dysmorphic disorder). For instance, although engaging in binge eating and/or purging behaviours is seen as a characteristic symptom of both AN and bulimic patients, the two disorders differ markedly in patients' current body weight. Whereas AN patients can be distinguished based on their low body weight, bulimic patients usually fall within a normal weight range. However, AN patients can keep experiencing episodes of binge eating and/or purging even after reaching a healthy weight. In this case, a change of diagnosis may be considered. Additionally, persistent preoccupations with appearance and distorted body image are central clinical features of both AN and body dysmorphic disorder. The main difference between the conditions is that AN patients are more concerned about the shape and figure-related aspects of their appearance with subsequent weight loss and dysfunctional eating patterns. In contrast, patients suffering from body dysmorphic disorder focus on other

seemingly noticeable flaws (such as specific body parts) and usually do not have low body weight or exhibit disrupted eating behaviours (American Psychiatric Association, 2013; World Health Organisation, 2019).

1.2 Epidemiology and Prognosis of Anorexia Nervosa

This section presents a short overview of the epidemiology and prognosis of AN. Rising incidence rates, high mortality risk and suboptimal prognosis for affected patients underline the importance of research on AN, improvement of the existing therapy options and development of new treatment approaches.

In a recent review, van Eden et al. (2021) reported that up to 4% of females and 0.3% of males might develop AN during their lifetime, with females being far more frequently affected by the disorder than males. They demonstrated the stability of AN incidence rates in the last decades, with a rising trend observed in the younger population. Nevertheless, the authors warn against precipitant conclusions since this trend may result from diagnostic advancements, increasing public awareness and reducing stigma surrounding the disorder rather than the actual increase in AN cases.

Prior research suggests that AN is one of the most serious and potentially lethal psychiatric disorders. In a review of studies conducted throughout the second half of the 20th century, Steinhausen (2002) reported a mortality rate of 5%. Fichter and Quadflieg (2016) argued that an AN diagnosis implies a five times higher mortality rate than the expected mortality rate in the general population. Furthermore, they reported significantly higher mortality rates in AN patients than those suffering from other eating disorders. The mortality risk seems to be higher in individuals who received inpatient treatment compared to treatment within an outpatient setting (Micali & Herle, 2023; van Eden et al., 2021). The leading causes of high mortality rates are suicide and complications due to severe malnutrition (Meczekalski et al., 2013).

AN has been acknowledged as a highly persistent psychiatric disorder, meaning that many individuals never fully recover (Andrés-Pepiñá et al., 2020; Herpertz-Dahlmann et al., 2001; Lo Sauro et al., 2013; Pla & Toro, 1999). Longitudinal studies are of growing importance in accurately estimating successful remission rates. In a recent study by Andrés-Pepiñá et al. (2020), most women diagnosed with AN during adolescence achieved remission at a 20-year follow-up assessment. More specifically, 66% had fully remitted and 8% were in partial remission. Earlier studies obtained similar results. For example, Lo Sauro et al. (2013) reported that 54.4% of patients achieved full remission and 26.1% partially remitted at a 6-year follow-up. Herpertz-Dahlmann et al. (2001) assessed patients ten years after the

beginning of treatment and claimed that 69% of women showed full remission. Pla and Toro (1999) observed that 67% of patients achieved full and 4% partial remission eight years after the beginning of treatment. Although these results suggest that most patients achieve full or partial remission, it is important to emphasize that in about one-third of affected patients, AN runs a chronic course.

1.3 History of Anorexia Nervosa

Eating disorders, in general, and AN, in particular, have been attracting considerable interest within the scientific community in recent decades. Although the psychological phenomena specific to AN (such as severe weight loss, phobia-like attitudes regarding normal body weight and denial of being ill) are acknowledged as modern and culture-specific by some researchers, a closer look at the literature on this topic reveals that dysfunctional eating habits and negative attitudes towards food have accompanied humankind for centuries (Habermas, 2005). The following paragraphs focus on conditions associated with or formerly believed to be a form of AN and emphasize the contributions of societal expectations on the emergence and course of this psychiatric disorder.

In his review, Bemporad (1996) attempted to describe forms of self-starvation prior to the modern medical understanding of AN based on available reports from prominent historians, physicians and clinicians throughout history. For instance, deliberately abstaining from food was not uncommon in ancient times. During this period, a widespread notion about the material world as a source of evil separating an individual from God and its spiritual nature emerged. It was believed that one could achieve the liberation and purification of the soul by refraining from indulging in physical pleasures. This refrained lifestyle has been known as asceticism and fasting was its essential component since it served as a means of withdrawing from bodily pleasures, temptations and sins. Throughout the Middle Ages and early Renaissance, similar behaviours have been reported. To preserve the purity of the eternal soul temporarily trapped in a physical body, fasting was honoured as a form of selfdenial in the name of God, along with other types of torture, such as self-flagellation. During the same period, demonic possession was introduced as a possible explanation for what we now identify as anorectic behaviours. However, during the 17th and 18th centuries, the focus shifted to physiological malfunctions as a cause of these behavioural patterns. Advancements in modern medicine paved the way for a systematic description and differentiation of the symptoms associated with AN as well as its classification as a separate psychiatric disorder. For the first time in 1873, AN was formally separated from other conditions involving forms of self-starvation through physicians William Gull and Ernst-Charles Lasègue. The main

clinical features they identified, involving refusal to eat, the onset in early adulthood or adolescence and patients' indifference to their declining health, are nowadays still used in research and clinical practice.

A critical problem with much of the literature on the history of AN is the inconsistent empirical evidence on whether AN has been continuously present or is a relatively new psychiatric condition. Our understanding of phenomena around us becomes redefined in response to the advances in scientific knowledge. It is, therefore, not uncommon for the same disorder to be expressed through a different combination of clinical symptoms or for disorder definitions to change accordingly (Brumberg, 1985). Thus, many experts now insist that AN has indeed been accompanying humankind for centuries, though presenting itself through somewhat different complaints and underlying motives. For example, while voluntary fasting was motivated by religious beliefs and spirituality, this can nowadays be rooted in weight phobia (Brumberg, 1985; Habermas, 2005; Habermas, 2015).

Based on the omnipresence of AN symptomatology in history highlighted in the previous paragraphs, the question arises as to which aspects of societal expectations encourage the emergence of these symptoms in individuals, especially among girls and young women. Bemporad (1996) suggested that women's position within society could offer a possible explanation for their vulnerability to AN. He argued that, for most of human history, women's role had been centred around marriage, childbirth and family life. In other words, they were rarely involved in decisions concerning the choice of a life partner, having children or pursuing a career, resulting in an inability to control their own lives. Consequently, fasting and other behaviours associated with AN may have given women the control and autonomy they craved by liberating them from the pains of menstruation and childbirth, forced sexual relationships and submissiveness to men. Furthermore, a more profound conflict between the historical status of women and the societal role of women in the industrialized era might have been created through growing opportunities for them to be an active part of the working force. Self-starvation may have made them feel successful and independent during rapid economic changes. Nowadays, AN may provide patients with feelings of self-control, security and power. It may be seen as an escape from the female body ideal, emerging adolescence and feminity, as well as means of resolving individuals' conflicts with their psychological environment, as suggested by various researchers (Bemporad, 1996; Brumberg, 1985; Habermas, 2015).

Ultimately, advances in clinical research and practice enable us to gain valuable insights into symptom presentation in our contemporary world. However, apart from a

thorough examination of the clinical symptomatology and the resulting burden of suffering, it is important to investigate the possible causes and motives that may lead to AN onset. The following sections give a brief overview of the underlying factors of AN linked to the development and maintenance of this psychiatric disorder, including biological aspects, personal characteristics and environmental determinants.

1.4 Causes of Anorexia Nervosa

Empirical findings on factors that can be identified as causes, onset triggers or risk factors of AN are inconsistent, leading to little general agreement on this topic within the scientific community. Nevertheless, recent studies provide considerable evidence for the association between various specific factors and AN.

Woerwag-Mehta and Treasure (2008) differentiate between biological, psychological and social determinants that play a role in the pathogenesis, onset and maintenance of AN. For instance, they described genetic factors and neurodevelopmental complications as predispositions underlying this eating disorder. Heritability of anorexic behaviours, pregnancy complications and prematurity fall within this category. The authors defined personality traits, such as perfectionism, harm avoidance, anxiety and detail orientation, as both predisposing and maintaining factors. Additional studies corroborate these conclusions, with a particular emphasis on perfectionism and harm avoidance as the most prominent personality traits (Atiye et al., 2014; Cassin & von Ranson, 2005; Cloninger et al., 1993; Farstad et al., 2016; Thornton et al., 2017; Tozzi et al., 2003; Wonderlich et al., 2005). Besides, the relationship between AN and the five dimensions of personality, as proposed by McCrae and Costa (1992) (also known as the Big Five), has been examined. The most robust evidence was found for the association between neuroticism and extraversion and AN symptomatology. More precisely, AN patients scored significantly higher on neuroticism and lower on extraversion than healthy control participants. Results on openness to experience, agreeableness and conscientiousness appear inconsistent and suggest opportunities for future research (Farstad et al., 2016; Garrido et al., 2018).

In addition to biological and individual determinants, family dynamics and influences in one's social surroundings may also facilitate the progress and maintenance of AN. Studies examining the role of family interactions and parenting styles have reported contradictory findings. Parental neglect and possessive overprotection have been recognized as the two parenting style extremes, potentially leading to AN (Matt Lacoste, 2017; Tozzi et al., 2003; Woerwag-Mehta & Treasure, 2008). Likewise, internalized body image ideals imposed by the modern media and peer pressure frequently motivate engaging in unhealthy eating

behaviours, such as extreme dieting (Tozzi et al., 2003; Woerwag-Mehta & Treasure, 2008). Adverse life events, trauma and exposure to different types of abuse have also been identified as critical components in AN development (Matt Lacoste, 2017; Tozzi et al., 2003; Woerwag-Mehta & Treasure, 2008).

In his work, Matt Lacoste (2017) argued that AN emerges as a response to psychological conflicts within the patient. In a series of interviews with AN patients, the author identified family problems and sexual abuse as the two most important causes of AN, corroborating the abovementioned findings. He further focused on these two causes to explain the meaning that patients ascribe to AN in gaining back the power over their lives and their own bodies. Simply put, when faced with dysfunctional communication patterns and other family difficulties, patients may develop AN to preserve family unity. Family members commonly unite to support their loved ones on their way to a successful recovery from the disorder. At the same time, AN may be seen as an escape from adolescence and emerging adulthood. It preserves the lack of adult responsibilities, carelessness and parental care, creating an opportunity for affected individuals to be heard, understood, and continuously taken care of. In line with these assumptions, AN may arise as a response to different types of abuse, especially sexual abuse. The author proposed that the separation of the mind and physical body is achieved through extremely restricted dieting as means of expressing pain and psychological distress stemming from the experienced assault. Due to food deprivation, numerous physiological disturbances and complications occur, some directly affecting AN patients' sexuality. In other words, by impeding the development of distinguishable secondary sexual characteristics, AN patients restore the stolen privacy and power over their bodies. Thereby, AN might be seen as an essential tool in protecting oneself from being desired, vulnerable and abused again. The study by Matt Lacoste (2017) validates the conclusions proposed by Bemporad (1996), highlighting the significance of this specific eating disorder in restoring patients' autonomy despite challenging circumstances.

1.5 Effects of Anorexia Nervosa on Physical, Psychological and Social Development

1.5.1 Physical Complications of Anorexia Nervosa.

Numerous adverse effects have been identified during and after the course of this eating disorder, often making it challenging to accept AN diagnosis and learn how to live with it. Not only does AN alter patients' current physical well-being, but it may also interfere with the normal functioning of the affected individuals for months and years after the onset. Physical complications associated with AN can be divided into three main categories based

on whether they emerge due to severe malnutrition, pathological anorectic behaviours or refeeding syndrome (Gosseaume et al., 2019).

According to Gosseaume et al. (2019), somatic complications resulting from severe malnutrition represent the group of phenomena that arise directly as a consequence of extreme weight loss and caloric restriction in AN patients. Diverse cardiopulmonary, gastrointestinal and gynaecological problems, endocrine abnormalities and neurological impairments fall within this category. For example, a growing body of evidence shows that AN patients are at a higher risk of experiencing sinus bradycardia, atrophy of tissues supporting the heart, decreasing heart rate variability and sudden cardiac death (Cass et al., 2020; Gosseaume et al., 2019; Meczekalski et al., 2013; Puckett et al., 2021). They more frequently develop pulmonary complications such as weakening of the respiratory muscles and reduction of lung capacity (Puckett et al., 2021). Concerning gynaecological problems, most female patients experience the absence of menstruation and/or ovulation. They face an increased risk of infertility and pregnancy complications (Cass et al., 2020; Puckett et al., 2021). Besides, it is common for female patients to suffer from miscarriages and display negative attitudes towards pregnancy (Meczekalski et al., 2013). Gastrointestinal disturbances, including delays in gastric emptying, constipation and early satiety, are also prevalent among the affected patients (Cass et al., 2020; Gosseaume et al., 2019; Meczekalski et al., 2013; Puckett et al., 2021).

In spite of the fact that most of the complications mentioned above remit entirely or to a great extent once a successful weight restoration is achieved, some problems may remain preserved. This especially stands for endocrine dysregulation and neurological disturbances. The most common consequence of a severe endocrine disruption is the reduction of bone mineral density, potentially leading to a life-long elevated bone fracture risk. Both maturation of bone mineral density and AN onset peak during adolescence; therefore, it is unsurprising that disrupted bone formation is mostly irreversible (Puckett et al., 2021). Similarly, deficits in cognitive flexibility and set-shifting resulting from the alterations of the brain tissues may persist for a sustained period after the AN onset (Cass et al., 2020).

Pathological behaviours associated with AN may also promote a range of physical complications. Frequent vomiting and laxative abuse may induce mineral and electrolyte deficiencies, possibly culminating in sudden death (Gosseaume et al., 2019).

Finally, refeeding can trigger adverse effects in AN patients equivalent to those caused by severe malnutrition and pathological anorectic behaviours. Simply put, the refeeding syndrome may occur due to a sudden increase in caloric intake in malnourished

individuals. Abrupt fluid, electrolyte and fat changes may lead to potentially lethal changes in bodily homeostasis (Cass et al., 2020; Gosseaume et al., 2019).

1.5.2 Psychological Effects of Anorexia Nervosa.

A considerable body of literature has recognized the profound impact of AN on mental health and the onset of other psychiatric disorders. Meczekalski et al. (2013) concluded that a previous AN diagnosis is strongly linked to a higher lifetime prevalence of psychiatric comorbidities. Salbach-Andrae et al. (2007) pointed out that up to 73.3% of AN patients suffered from at least one comorbid psychiatric disorder. Among commonly reported psychiatric disorders is depression, the most frequent psychiatric condition accompanying AN, followed by other mood disorders, anxiety disorders, obsessive-compulsive disorders and substance abuse (Meczekalski et al., 2013; O'Brien & Vincent, 2003; Salbach-Andrae et al., 2007). Suicidality (Mereu et al., 2022; Moskowitz & Weiselberg, 2017) and personality disorders (Himmerich et al., 2019; Meczekalski et al., 2013; Moskowitz & Weiselberg, 2017) have also been frequently observed.

Eating disorder-specific psychopathology may impair healthy emotional responses to external influences. The adverse effects of AN on emotional regulation in affected individuals have been explored in prior studies. Meule et al. (2021) investigated the relationship between emotional regulation and emotional eating in patients suffering from eating disorders. When experiencing negative emotions, AN subjects were prone to restrained eating, providing strong evidence for self-starvation as a dysfunctional emotional regulation strategy linked to AN. These findings are consistent with a previous study by Naumann et al. (2016), which showed that patients affected by eating disorders exhibited maladaptive emotional regulation strategies, such as suppression and rumination, more frequently than their healthy counterparts.

As discussed in the previous paragraph, emotional regulation difficulties may extend to other spheres of an individual's inner world. Oldershaw et al. (2019) considered that AN emerges following overwhelming emotional experiences, detaching the person from their identity and authentic self. This lost sense of emotional self then becomes replaced by the false sense of self stemming from AN. The authors concluded that the inability to form a coherent sense of identity during adolescent years might provide a solid foundation for holding onto AN and a need to continuously rely on external validation and acceptance from others.

1.5.3 Social Implications of Anorexia Nervosa.

Patients' difficulties in regulating their emotions may extend to the interactions within their social surroundings. Meneguzzo et al. (2020) argued that AN patients had distorted cognitive and emotional interpretations of social situations, expressing a higher sensitivity to negative social interactions and rejection. Therefore, they not only struggle to perceive their emotions, but it may also be difficult for them to communicate these feelings to others. Such findings confirm earlier empirical results reported by Hamatani et al. (2016), who demonstrated that AN patients struggle to predict other people's intentions. Difficulties in social function are not limited to the acute phase of the illness and may persist even after remission (Bentz et al., 2017).

The significance of this psychiatric disorder within the social context is best reflected in lower quality of and higher dissatisfaction with interpersonal relationships. Namely, friendship difficulties may develop before the AN onset and intensify over the years. Westwood et al. (2016) stated that AN has adverse effects on starting and maintaining friendships, resulting in elevated anxiety and reduced social contact. However, the authors accentuated various positive qualities and emotions AN patients associate with their friends, emphasizing the importance of a supportive social circle on the way to recovery. These findings have been corroborated by Lukas et al. (2022) and Newton et al. (2005), implying a lower parental and peer relationship quality as well as pronounced dissatisfaction with romantic relationships, respectively.

Deep dissatisfaction with romantic and sexual relationships may be rooted in altered approaches to sexuality and disturbances in sexual functioning specific to eating disorders. Gonidakis et al. (2015) examined sexual function in women with AN, bulimia nervosa and without an eating disorder. Although sexual functioning was impaired in both groups affected by an eating disorder, women with a previously diagnosed AN reported the highest sexual disturbances among the three groups, being far less likely to engage in sexual relationships. Body image distortion and body dissatisfaction have been identified as the underlying aspects of eating disorder-specific psychopathology that impede the establishment of meaningful intimate relationships and sexual pleasure (Gonidakis et al., 2016).

1.6 Predictors of Adverse Anorexia Nervosa Outcomes

The previous paragraphs aimed to address the clinical symptomatology, possible causes and far-reaching consequences of AN in an effort to deepen the understanding of this psychiatric disorder. The following sections provide a short review of notable predictors

associated with poorer AN outcomes, including higher relapse rates, increased mortality and poorer treatment results, before transitioning to the importance of longitudinal studies in AN research and, finally, stating the aim of the present study.

1.6.1 Sociodemographic Variables.

The risk of getting diagnosed with specific psychiatric disorders, including eating disorders, and differences in treatment outcomes may stem from the diverse sociodemographic characteristics of the individual patients. Migration background has been evaluated as one such variable, yielding inconsistent findings. For instance, White et al. (2003) reported opposing reasons for dieting behaviours in Caucasian and African American patients. Caucasian girls engaged in dieting behaviours due to excessive body shape and weight concerns, whereas these behaviours were unrelated to such concerns in African American girls. Lindberg and Hjern (2003) examined migration background within a sample of European AN patients and found significant differences depending on their parents' ethnicity. More specifically, having northern, central and eastern European parents was associated with an increased susceptibility to AN, whereas having southern or non-European parents was identified as a protective factor against AN. In a study by Mustelin et al. (2017), the risk of being diagnosed with an eating disorder was investigated in first and secondgeneration immigrants compared to the native populations. Being a first-generation immigrant or having two foreign-born parents served as a protective factor against eating disorders, halving the risk of developing AN. In contrast with these findings, Cheng et al. (2019) found no significant differences in eating disorder prevalences and factors predicting future onset among ethnic minorities.

Parental educational background has been shown to predict eating disorders. Goodman et al. (2014) recognized a strong connection between a family history of education and eating disorders. Their findings draw attention to greater educational levels in parents and maternal grandparents as predictors of all eating disorders. Furthermore, these findings were observed across multiple generations and increased over time. These conclusions confirm the results by Ahrén et al. (2012), who linked higher maternal education to a higher hospitalization risk in patients suffering from AN.

Mixed results have been reported on the role of a family history of a psychiatric disorder in predicting AN. In their review of family characteristics in eating disorders, Kog and Vandereycken (1985) mentioned parental somatic illnesses, affective disorders and alcoholism as factors increasing vulnerability to AN. Lindberg and Hjern (2003) proposed an

increased risk of developing AN in patients whose parents had previously been discharged from the hospital due to a psychiatric disorder. In line with these conclusions, the results reported by Forsberg et al. (2017) showed that higher levels of baseline psychological symptomatology in mothers and subsequent reduction of these symptoms through treatments targeting mothers and children suffering from AN predicted better weight outcomes in children one year after finishing the treatment. However, Garfinkel et al. (1983) found no higher levels of psychopathology in parents of AN patients compared to parents of healthy controls.

1.6.2 Illness Severity.

A large number of existing studies in the broader literature have examined clinical phenomena indicative of more pronounced illness severity in patients suffering from AN. The patient's BMI is one of the most significant predictors of an AN outcome. The majority of studies investigating the effects of BMI have been conducted in an inpatient setting. A lower BMI at admission to the inpatient ward significantly predicted higher treatment dropout (Gregertsen et al., 2019; Hubert et al., 2013) and poorer prognosis (Carrot et al., 2017), whereas a higher BMI at admission predicted positive treatment outcome (Wales et al., 2016). Lower desired BMI also indicated higher treatment dropout (Huas, Godart et al., 2011) and increased mortality (Huas, Caille et al., 2011). A higher BMI at discharge from the inpatient ward predicted lower relapse rates (Frostad et al., 2022) and healthy weight maintenance (Glasofer et al., 2020). Similar results have been observed in individuals treated within an outpatient setting (Wild et al., 2016).

Eating disorder-specific psychopathology may change over time, facilitating remission or enhancing the chances for a relapse. In terms of overall eating disorder-specific psychopathology, Gregertsen et al. (2019) argued that greater symptomatology before treatment predicts poorer treatment response in individuals affected by AN. Huas, Caille et al. (2011) stated that more pronounced clinical symptomatology at admission is linked to elevated mortality risk. These findings correlate with a recent study by Frostad et al. (2022), who showed that the higher eating disorder-specific symptoms at discharge from the inpatient ward predicted future relapse. Regarding specific symptoms, Roux et al. (2016) reported that patients expressing lower restraint concern were at higher risk of dropping out from inpatient treatment, reflecting patients' unawareness of their illness severity. Calugi et al. (2018) observed that starvation symptoms before treatment affected the course of patients' eating

and weight concerns at the end of and six months after treatment. A greater reduction in starvation symptoms contributed to improved eating and weight concerns.

Besides BMI and eating disorder-specific psychopathology, other illness severity markers are worth paying attention to when exploring long-term AN trajectories. Previous history of hospitalization (Hubert et al., 2013), older age at admission (Huas, Caille et al., 2011; Hubert et al., 2013) and longer AN duration (Glasofer et al., 2020; Huas, Caille et al., 2011; Meule et al., 2022; Wild et al., 2016) also increased the odds of poorer AN outcome.

1.6.3 Psychiatric Comorbidity.

Psychiatric disorders may not only arise as a consequence of AN but can also precede it, reflecting an individual's increased vulnerability to AN and acting as markers of worse AN outcomes. The contribution of mood disorders, especially depression, to the development and poor prognosis of eating disorders has still been insufficiently explored. Despite the fact that some authors found no evidence for the predictive value of depression (Carrot et al., 2017; Himmerich et al., 2019; Huas, Godart et al., 2011), others offered compelling evidence for the role of depression in predicting poorer treatment outcome (Schlegl et al., 2016), lower BMI (Wild et al., 2016) and lower remission rates (Franko et al., 2018; Wild et al., 2016).

Similarly, the effects of anxiety disorders on eating disorder-specific psychopathology remain to be addressed. Whereas Carrot et al. (2017) confirmed the importance of anxiety disorders, especially social phobia and agoraphobia, in reduced quality of life and increased eating disorder-related symptoms, Lloyd et al. (2019) found no association between specific anxiety disorders and the development of or recovery from AN. Still, the latter reported a possible elevated risk of AN development when previously diagnosed with any anxiety disorder.

Ultimately, various other disorders have been discussed as predictive of a poorer AN prognosis, including substance abuse (Himmerich et al., 2019; Huas, Godart et al., 2011), suicidality (Huas, Caille et al., 2011; Huas, Godart et al., 2011), obsessive-compulsive disorders (Carrot et al., 2017), autism (Leppanen et al., 2022) and personality disorders (Himmerich et al., 2019; Råstam et al., 1995).

1.7 Knowledge Gap

AN received much attention over the past few decades and the growing research on the topic deepened our understanding of this psychiatric disorder. However, some questions regarding AN still remain unanswered. Longitudinal studies of AN patients are scarce. More specifically, no study so far has focused on investigating the long-term course of AN in a sample of Austrian patients only. Such studies are challenging due to longer data collection periods and potentially high dropout. The number of follow-up years varies considerably from study to study, making it difficult for researchers to compare the findings directly.

Previous works have provided inconsistent findings of remission, partial remission and chronicity rates in patients suffering from AN. Fichter et al. (2017) argued that higher remission rates are associated with higher follow-up years. In other words, there is a tendency to report higher remission rates when following a specific sample over longer periods. This was corroborated by earlier studies (Herpertz-Dahlmann et al., 2001; Lo Sauro et al., 2013; Pla & Toro, 1999). Nevertheless, there is no general agreement on the exact estimation of remission, partial remission and chronicity rates over the course of the illness.

The factors predicting a poorer AN outcome are still insufficiently explored and different authors propose different predictors (Andrés-Pepiña et al., 2020; Fichter et al., 2017; Löwe et al., 2001; Saccomani et al., 1998; Strober et al., 1997). Future research should further explore the role of patients' sociodemographic characteristics, illness severity and comorbidities in the long-term outcome of AN.

The abovementioned evidence suggests that many hypotheses concerning the long-term course of AN, estimates of remission rates and predictive factors are still questionable, thereby highlighting the importance of longitudinal research in answering the open questions. The present study aimed to fill the knowledge gap on the course of AN in adolescent and young adult patients by evaluating the existing hypotheses about long-term outcomes, remission and chronicity rates, psychiatric comorbidities and predictive factors accompanying the illness.

The current study is a part of the *AN-bel project*, a collaboration project between the Eating Disorders Research Unit of the Department of Child and Adolescent Psychiatry of the Medical University of Vienna and the Faculty of Psychology of the University of Vienna. It follows a sample of Austrian patients that had previously received psychotherapy treatment in a study conducted by the Eating Disorders Research Unit of the Department of the Child and Adolescent Psychiatry of the Medical University of Vienna. Each patient participating in the current study has previously taken part in the *MANTRa study* – an evaluation study of a manualized treatment program, the *Maudsley Model of Anorexia Nervosa Treatment for Adolescents and Young Adults (MANTRa)* (Wittek et al., 2021).

1.8 Research Questions and Hypotheses

The overall research question to be addressed in this study is whether and how the course of AN changes over time. Consequently, the following three research questions with specific hypotheses emerge:

<u>RQ1</u>: How do BMI, eating disorder-specific psychopathology and psychiatric comorbidities in AN patients change over time?

- H1: BMI changes significantly from T0 to T4.
- H2: Eating disorder-specific psychopathology changes significantly from T0 to T4.
- H3: Psychiatric comorbidities change significantly from T0 to T4.

<u>RQ2</u>: How many patients diagnosed with full syndrome AN at T0 are in full or partial remission at T4?

<u>RQ3</u>: Do sociodemographic characteristics, illness severity¹ and psychiatric comorbidities at T0 predict the AN outcome² at T4 in AN patients?

- H4: Sociodemographic characteristics significantly predict the outcome at T4 in patients with AN.
- H5: The illness severity at T0 significantly predicts the outcome at T4 in patients with AN.
- H6: Psychiatric comorbidities at T0 significantly predict the outcome at T4 in patients with AN.

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¹ Estimation of illness severity is based on the patient's BMI and eating disorder-specific psychopathology at the beginning of the treatment (T0).

² The outcome is defined as the total EDE score at T4.

2. **Methods**

2.1 Study Design

The longitudinal design of the present study allowed a comprehensive evaluation of the long-term AN outcomes. Within the *MANTRa* study, participants have undertaken psychological assessments at four time points – assessment before the beginning of the treatment (T0), assessment after six months (T1), after twelve months (T2) and eighteen months (T3). The present study collected a fifth timepoint (T4). The fifth assessment occurred approximately two to four years after the first assessment.

2.2 Participants

Initially, thirty-five female patients, who expressed their interest in taking part in future research projects during their participation in the *MANTRa* study, were contacted via email by the scientific staff, clinical psychologists or psychiatrists of the Eating Disorders Research Unit of the Department of Child and Adolescent Psychiatry of the Medical University of Vienna. Some of these patients expressed no interest in participating in the present study, while others did not respond to the invitation. Therefore, the present study sample consisted of twenty female patients between 15 and 22 years of age (M = 18.25; SD = 1.92).

2.3 Sample Considerations

Due to the generally high dropout in longitudinal studies, it was assumed that not all thirty-five patients would participate in the present study. For this reason, a sample of twenty-five patients was planned. A sensitivity analysis was performed with G*Power to calculate the effect size (change in the total EDE score between all five time points). Using repeated measures analysis of variance (repeated measures ANOVA), a medium effect size (f = 0.22) could be identified with 80% power at a significance level of $\alpha = .05$.

However, our sample consisted of only twenty participants. With this smaller sample, a medium effect size (f = 0.25) could be identified with 80% power at a significance level of $\alpha = .05$.

2.4 Materials

The following sections contain brief descriptions of measurements and psychological instruments used for the assessment of sociodemographic characteristics, illness severity and psychiatric comorbidities, respectively.

2.4.1 Sociodemographic Characteristics.

The sociodemographic characteristics of study participants were collected at T0 through a case report form. The characteristics of interest included age, migration background, age of eating disorder onset, duration of illness, maternal and paternal highest educational attainment as well as lifetime prevalence of psychiatric disorders in the family.

2.4.2 Illness Severity.

Body Mass Index (BMI): A measurement calculated by dividing the patient's weight (expressed in kilograms) by the square of their height (expressed in meters) and subsequently comparing this value to a fixed threshold. BMI is a marker of significantly low body weight and, when low, is one of the three main symptoms of AN. Adult patients having a BMI of less than 18.5 kg/m² can be described as significantly underweight (American Psychiatric Association, 2013; World Health Organisation, 2019).

Body Mass Index – Standard Deviation Score (BMI-SDS): A measurement calculated by dividing the patient's weight (expressed in kilograms) by the square of their height (expressed in meters) and subsequently comparing this value to the typical value of other individuals matched in age and sex. Whereas BMI is used for adults, BMI-SDS is used for reporting significantly low body weight in children and adolescents. If the patient's BMI-SDS is one or more standard deviations lower than that of other children similar in age and sex, it can be assumed that the patient has a significantly low body weight (Engelhardt et al., 2021).

Eating Disorder Examination (EDE) (Hilbert & Tuschen-Caffier, 2016): A German version of the semi-structured clinical interview used to classify and evaluate eating disorder-specific psychopathology in children and adults. The interview encompasses four subscales – Restraint, Eating Concern, Weight Concern and Shape Concern. The Restraint subscale consists of items denoting dietary restriction and eating avoidance. The other three subscales cover different eating disorder-specific concerns, including eating-related worries (Eating Concern subscale), dissatisfaction and preoccupations with one's weight (Weight Concern subscale) and dissatisfaction and worries associated with one's figure (Shape Concern subscale). The questions target distorted behaviours typical for an eating disorder during the last twenty-eight days. The answers are represented through a seven-point scale, from zero, implying no eating disorder-specific behaviours, to six, marking eating disorder-specific behaviours present every day during the last twenty-eight days. Aside from subscale scores, a total EDE score encompassing all of the subscale scores can be calculated. Higher scores

reflect a greater eating disorder-specific psychopathology. The EDE interview has excellent reliability (total EDE score: Cronbach's $\alpha = .93$).

Eating Disorder Inventory (EDI-2) (Rathner & Waldherr, 1997): A German version of the self-report questionnaire used to classify and evaluate eating disorder-specific psychopathology in children and adults. The questionnaire comprises ninety-one questions allocated to eleven subscales – *Drive for Thinness, Bulimia, Body Dissatisfaction, Perfectionism, Interpersonal Distrust, Interoceptive Awareness, Maturity Fears, Asceticism, Impulse Regulation* and *Social Insecurity*. The questions target distorted cognitions and behaviours typical for an eating disorder at the present moment. The answers are represented through a six-point scale, from one, indicating never experiencing eating disorder-specific cognitions and behaviours, to six, implying always experiencing eating disorder-specific cognitions and behaviours. Aside from subscale scores, a total EDI-2 score encompassing all of the subscale scores can be calculated. Higher scores reflect a greater eating disorder-specific psychopathology. Like the EDE interview, EDI-2 has excellent internal consistency (total EDI-2 score: Cronbach's $\alpha = .90$).

2.4.3 Psychiatric Comorbidities.

Beck Depression Inventory (BDI-2) (Hautzinger et al., 2009): A German version of the self-report questionnaire used to assess symptoms and severity of depression in children and adults. The questionnaire consists of 21 questions about the patient's mood in the past two weeks. Each question can be answered with one of the four possible responses, ranging from zero, suggesting the absence of the questioned symptom, to three, implying the high intensity of the specific symptom. Higher scores reflect greater depressive symptomatology and higher illness severity. The questionnaire has excellent internal consistency (Cronbach's $\alpha = .92$) (Besier et al., 2007).

<u>Diagnostic Interview for Mental Disorders (DIPS)</u> (Margraf et al., 2017): A structured clinical interview for mental disorders based on the DSM-5 diagnostic criteria across the lifespan in adults. The interview consists of a series of questions on prominent symptoms of major psychiatric disorders, including anxiety disorders, depression, obsessive-compulsive disorders, trauma and stress-related disorders, disorders related to the use of psychoactive drugs and substance abuse, suicidality and non-suicidal self-injury disorder. The questions enable a thorough exploration of the patient's current and lifetime psychiatric disorders. The psychiatric symptomatology was assessed at T0, T2 and T4.

<u>Diagnostic Interview for Mental Disorders in Children and Adolescents (Kinder-DIPS)</u> (Schneider et al., 2017): A structured clinical interview for mental disorders based on the DSM-5 diagnostic criteria across the lifespan in children and adolescents. This psychological instrument is equivalent to DIPS interview for adults and allows a comprehensive exploration of the patient's current and lifetime history of mental disorder symptomatology. The psychiatric symptomatology was assessed at T0, T2 and T4.

Obsessive-Compulsive Inventory (OCI-R) (Gönner et al., 2007): A German version of the self-report questionnaire used to evaluate obsessive-compulsive symptomatology in children and adults. The questionnaire contains eighteen questions allocated to six scales – *Checking, Washing, Ordering, Hoarding, Obsessing* and *Neutralizing*. The questions refer to a series of situations during the last month that can make patients distressed or bothered. Each question can be answered on a five-point scale, from zero, meaning not being distressed or bothered by the situation at all, to four, implying being extremely distressed or bothered by the situation during the last month. Aside from subscale scores, a total OCI-R score encompassing all of the subscale scores can be calculated. Higher scores are indicative of more severe obsessive-compulsive symptomatology. The questionnaire has excellent internal consistency (total OCI-R score: Cronbach's $\alpha = .86$).

State-Trait Anxiety Inventory (STAI) (Laux et al., 1981): A German version of the self-report questionnaire intended to assess state and trait anxiety in children and adults. The questionnaire has forty items – twenty items estimating state anxiety and twenty items estimating trait anxiety. Each item depicts a statement that may describe someone to a lesser or a greater extent. Patients are encouraged to rate themselves in regard to each of these statements on a four-point scale. Concerning state anxiety, the ratings range from one, implying that the statement does not describe the specific patient at all, to four, meaning that the statement describes the specific person very much. Concerning trait anxiety, the ratings range from one, indicating that the person almost never feels in such a way, to four, meaning that the person almost always feels that way. Higher scores reflect higher anxiety. Like other instruments used in the present study, this questionnaire has excellent internal consistency (Cronbach's $\alpha \ge .89$).

2.5 **Procedure**

Ethical approval was obtained from the Ethics Committee of the Medical University of Vienna prior to the start of the study (EK 2005/2017 and EK 1670/2021).

The psychological assessment for T4 was carried out by trained scientific staff at the Department of Child and Adolescent Psychiatry of the Medical University of Vienna. Each

participant was required to sign an informed consent form and complete an online questionnaire before the on-site assessment. In case the participant was underage, an informed consent form was also signed by their parent(s) or legal guardian(s). The online questionnaire sent to the participants prior to the on-site assessment encompassed EDI-2 (Rathner & Waldherr, 1997), BDI-2 (Hautzinger et al., 2009), OCI-R (Gönner et al., 2007) and STAI questionnaires (Laux et al., 1981), which were used for assessment of eating disorder, depressive, obsessive-compulsive and anxiety symptomatology, respectively. After completing the online questionnaire, a scientific staff member arranged an individual on-site appointment with the participant via e-mail or a telephone call.

During the on-site assessment, the weight and height of the participant were measured for BMI or BMI-SDS estimation, followed by the semi-structured EDE interview (Hilbert & Tuschen-Caffier, 2016). Additionally, the structured DIPS interview was conducted based on the participant's age, either the adult version (Margraf et al., 2017) or the child and adolescent version (Schneider et al., 2017). At the end of the experiment, potential questions regarding the psychological assessment were clarified and participants received an incentive in the form of a voucher for their participation in the study.

2.6 Data Analysis

The first research question – how BMI, eating disorder-specific psychopathology and psychiatric comorbidities change over time – was statistically explored using repeated measures ANOVA. Additionally, t-tests were performed to explore the changes between T0 and T4 as well as T3 and T4. The effect sizes (defined as Cohen's *d*) were calculated. Cohen's *d* values of 0.2, 0.5 and 0.8 can be interpreted as small, medium and large effect sizes (Sawilowsky, 2009).

The second research question – how many patients diagnosed with full AN syndrome at T0 are in full remission or partial remission at T4 – was answered through descriptive statistics.

Ultimately, the question of whether sociodemographic characteristics, illness severity and psychiatric comorbidities at T0 predict the AN outcome (total EDE score) at T4 was answered using univariate and hierarchical linear regressions. Firstly, a series of univariate linear regressions was conducted to detect the impact of each predictor. In these analyses, each sociodemographic characteristic, illness severity marker and psychiatric comorbidity at T0 was included as a separate predictor to investigate whether it predicted the AN outcome at T4. Subsequently, sociodemographic characteristics, illness severity markers and psychiatric

comorbidities were included in the hierarchical linear regression model as separate blocks, possibly predicting the outcome variable.

Before statistically exploring the research questions, underlying assumptions were tested (e.g. visual inspection of variable distributions, collinearity of predictors). The assumptions were not violated in this study; therefore, parametric tests were used and no predictor was omitted. In the case of lack of sphericity, the Greenhouse-Geisser correction was used. A significance level of $\alpha = .05$ was used in all analyses. Data analysis was conducted with Statistical Package for the Social Sciences (SPSS).

3. **Results**

3.1 Sociodemographic and Clinical Characteristics of the Study Sample

A brief overview of the participants' sociodemographic and clinical characteristics at the first time point assessment is presented in Table 1. Worth noting are the high rates of inpatient treatment (50%), current psychiatric comorbidity (40%) and a lifetime prevalence of psychiatric disorders (50%) in the present sample. In addition, a university degree was the most prevalent educational attainment of participants' parents, with 50% of mothers and 65% of fathers reporting obtaining a university degree. The time between the first and the last time point assessment ranged from nineteen to fifty-two months (M = 37.35; SD = 9.33).

Table 1Sociodemographic and Clinical Characteristics of the Sample at T0

Variable	Mean (SD)
Age (in years)	15.72 (1.64)
Age of eating disorder onset (in years)	14.33 (1.82)
Duration of illness (in months)	13.89 (10.47)
BMI	17.08 (1.12)
BMI-SDS	-1.55 (0.77)
	N (%)
Sex	
Female	20 (100%)
Inpatient treatment	
Yes	10 (50%)
No	10 (50%)
AN subtype	
Restrictive	16 (80%)
Binge eating / purging	4 (20%)
Current psychiatric comorbidity	
Any	8 (40%)
Anxiety disorder	2 (10%)
Obsessive-compulsive disorder	3 (15%)
Depression	2 (10%)
Non-suicidal self-injury	5 (25%)
Lifetime prevalence of psychiatric disorder	
Yes	10 (50%)

No	10 (50%)
Migration background	
Yes	3 (15%)
No	17 (85%)
Maternal migration background	
Yes	5 (25%)
No	15 (75%)
Paternal migration background	
Yes	5 (25%)
No	15 (75%)
Lifetime prevalence of eating disorders in the family	
Yes	4 (20%)
No	16 (80%)
Lifetime prevalence of psychiatric disorders in the family	
Yes	8 (40%)
No	12 (60%)
Maternal highest educational attainment	
No school leaving qualification	5 (25%)
School leaving qualification	5 (25%)
University	10 (50%)
Paternal highest educational attainment	
No school leaving qualification	5 (25%)
School leaving qualification	2 (10%)
University	13 (65%)
Remission status	
Full syndrome	12 (60%)
Partial remission	8 (40%)

3.2 Longitudinal Changes

The first research question addressed the changes in BMI, eating disorder-specific psychopathology and psychiatric comorbidities in AN patients over time. The following sections present the results of longitudinal changes from T0 to T4 for BMI, eating disorder-specific psychopathology and psychiatric comorbidities, respectively.

3.2.1 **BMI.**

The changes in BMI and BMI-SDS values from T0 to T4 are shown in Table 2. A repeated measures ANOVA with a Greenhouse-Geisser correction determined that both BMI (p < .001, partial $\eta^2 = .328$) and BMI-SDS values (p = .027, partial $\eta^2 = .185$) increased

significantly between T0 and T4. A medium effect was found regarding the changes in BMI from T0 to T4 (d = 0.60) and small effects were identified for the changes in BMI from T3 to T4 (d = 0.40), the changes in BMI-SDS from T0 to T4 (d = 0.26) and the changes in BMI-SDS from T3 to T4 (d = 0.27).

Table 2

Changes in BMI from T0 to T4

Outcome	Mean (SD)					Repeated measures ANOVA	Effect sizes (Cohen's d)	
	T0	T1	T2	T3	T4	F(df), p	Т0-	Т3-
							T4	T4
BMI	17.14	17.70	17.19	18.21	19.38	7.824(2.35, 37.62),	0.60	0.40
	(1.16)	(1.30)	(1.60)	(1.95)	(2.56)	<.001		
BMI-SDS	-1.51	-1.30	-1.69	-1.25	-0.81	3.631(2.48, 39.73),	0.26	0.27
	(0.82)	(0.62)	(0.87)	(0.96)	(1.03)	.027		

Note. BMI = Body Mass Index; BMI-SDS = Body Mass Index - Standard Deviation Score

3.2.2 Eating Disorder-Specific Psychopathology.

The changes in eating disorder-specific psychopathology from T0 to T4 are shown in Table 3. The results of a repeated measures ANOVA showed that total EDE score (p = < .001, partial $\eta^2 = .474$), EDE *Restraint* score (p = < .001, partial $\eta^2 = .277$), EDE *Eating Concern* score (p = < .001, partial $\eta^2 = .327$), EDE *Weight Concern* score (p = < .001, partial $\eta^2 = .356$) and total EDI-2 score (p = .011, partial $\eta^2 = .173$) decreased significantly from T0 to T4. Additionally, a repeated measures ANOVA with a Greenhouse-Geisser correction determined that EDE *Shape Concern* score (p = < .001, partial $\eta^2 = .447$) showed a statistically significant decrease from T0 to T4. With regard to changes from T0 to T4, large effects were found for EDE total score (d = -1.36), EDE *Restraint* score (d = -0.84), EDE *Eating Concern* score (d = -1.20), EDE *Weight Concern* score (d = -1.12) and EDE *Shape Concern* score (d = -1.17). A medium effect was found for changes in EDI-2 total score between T0 and T4 (d = -0.58). Concerning the changes between T3 and T4, a small effect was identified for the EDE *Restraint* score (d = -0.18). No other significant effect sizes could be identified for the changes between T3 and T4.

Table 3Changes in Eating Disorder-Specific Psychopathology from T0 to T4

Outcome	Mean (SI	D)				Repeated measures	Effect	sizes
						ANOVA	(Cohe	n's <i>d</i>)
	T0	T1	T2	Т3	T4	F(df), p	Т0-	Т3-
							T4	T4
EDE Total	3.66	2.81	2.34	2.11	1.87	14.432(4, 64), <.001	-1.36	-0.10
Score	(0.93)	(1.12)	(1.07)	(1.02)	(0.94)			
EDE	3.20	2.45	2.19	1.81	1.45	6.121(4, 64), <.001	-0.84	-0.18
Restraint	(1.42)	(1.24)	(1.05)	(1.23)	(1.18)			
EDE Eating	2.77	2.13	1.79	1.35	1.19	7.779(4, 64), <.001	-1.20	-0.02
Concern	(1.00)	(1.52)	(1.36)	(1.12)	(0.98)			
EDE Weight	3.90	2.96	2.36	2.18	1.98	8.850(4, 64), <.001	-1.12	0.00
Concern	(1.23)	(1.40)	(1.60)	(1.59)	(1.15)			
EDE Shape	4.77	3.71	3.04	3.10	2.85	12.918(2.51, 40.13),	-1.17	-0.11
Concern	(1.05)	(1.23)	(1.26)	(1.39)	(1.37)	<.001		
EDI-2 Total	88.50	84.83	66.94	66.44	64.44	3.563(4, 68), .011	-0.58	0.00
Score	(45.47)	(49.94)	(40.69)	(46.67)	(42.32)			

Note. EDE = Eating Disorder Examination; EDI-2 = Eating Disorder Inventory

3.2.3 Psychiatric Comorbidities.

The changes in psychiatric comorbidities from T0 to T4 are shown in Table 4. A repeated measures ANOVA identified statistically significant decreases in total BDI-2 score $(p = .015, \text{ partial } \eta^2 = .164)$ between T0 to T4. No significant changes in STAI State score (p = .175), STAI Trait score (p = .053) or OCI-R score (p = .186) were determined between the two time points. Medium effects were found for the changes in BDI-2 total score (d = -0.55) and STAI State score (d = -0.46) and small effects were identified for the changes in STAI Trait score (d = -0.42) and OCI-R score (d = -0.26) between T0 and T4. No significant effect sizes were found for any psychiatric comorbidity between T3 and T4.

Table 4Changes in Psychiatric Comorbidities from T0 to T4

Outcome	Mean (Sl	D)				Repeated measures ANOVA	Effect (Cohe	
	T0	T1	T2	T3	T4	F(df), p	Т0-	Т3-
							T4	T4
BDI-2 Total	25.33	21.94	16.33	17.83	17.56	3.331(4, 68), .015	-0.55	-0.01
Score	(12.53)	(14.55)	(12.18)	(13.41)	(11.34)			
STAI State	51.44	47.78	45.72	46.83	44.83	1.635(4, 68), .175	-0.46	-0.11
Score	(13.01)	(13.25)	(13.39)	(14.26)	(10.21)			
STAI Trait	53.28	52.67	47.17	48.44	47.39	2.461(4, 68), .053	-0.42	0.00
Score	(11.52)	(13.46)	(11.12)	(15.83)	(13.74)			
OCI-R Score	21.22	23.33	19.33	19.72	18.11	1.593(4, 68), .186	-0.26	-0.01
	(13.46)	(17.28)	(15.65)	(15.57)	(15.17)			

Note. BDI-2 = Beck Depression Inventory; STAI = State-Trait Anxiety Inventory; OCI-R = Obsessive- Compulsive Inventory

The results from Kinder-DIPS / DIPS interviews are shown in Figure 1. A tendency for anxiety disorders, post-traumatic stress disorder and depressive disorders to increase from T0 to T4 was observed. Obsessive-compulsive disorders remained stable between T0 and T4. Complete remission of the symptomatology from T0 to T4 was observed only for non-suicidal self-injury.

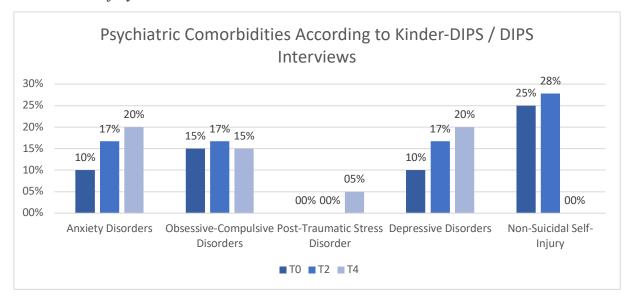


Figure 1

Psychiatric Comorbidities Based on Kinder-DIPS / DIPS Interviews

3.3 **Remission Status**

The second research question investigated the differences in remission status across time. More specifically, it examined how many patients with full syndrome AN at T0 were in full remission or partial remission at T4.

As illustrated in Figure 2, 60% of participants had been diagnosed with a full syndrome AN and 40% of them were in partial remission at T0. None of them had achieved full remission at that time point.

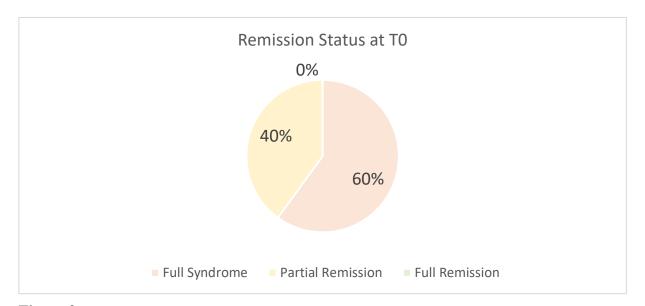


Figure 2

Remission Status at TO

The remission status at T4 is presented in Figure 3. It can be observed that 35% of participants still had a full syndrome AN diagnosis and 45% of them were in partial remission at T4. In contrast to T0, when no full remission could be observed, 20% of participants were classified as fully remitted at T4.

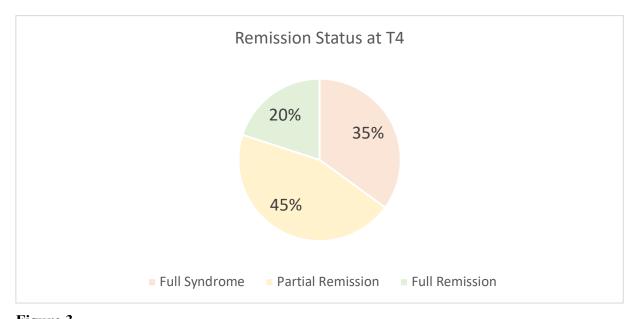


Figure 3

Remission Status at T4

3.4 **Outcome Predictors**

The third research question investigated whether specific sociodemographic characteristics, illness severity and psychiatric comorbidities at T0 predict the AN outcome at T4 in AN patients.

3.4.1 Sociodemographic Characteristics.

The results from a univariate linear regression between participants' sociodemographic characteristics at T0 (acting as independent variables) and total EDE score at T4 (acting as dependent variable) are shown in Table 5. No statistically significant predictive values of age (p = .591), migration background (p = .235), age of eating disorder onset (p = .994) and duration of illness (p = .441) were found. Moreover, maternal (p = .804) and paternal (p = .460) highest educational attainments as well as lifetime prevalence of psychiatric disorders within the family (p = .355) were not predictive of the total EDE score at T4.

Table 5
Sociodemographic Characteristics at T0 as Predictors of the AN Outcome at T4

Predictor	b(SE)	Beta	<i>t</i> -value	p
Age (in years)	-0.087 (0.158)	-0.128	-0.548	.591
Migration background ¹	0.632(0.515)	0.278	1.227	.235
Age of eating disorder onset (in years)	0.001(0.161)	0.002	0.007	.994
Duration of illness (in months)	-0.022(0.027)	-0.194	-0.790	.441
Maternal highest educational attainment ²	-0.129(0.510)	-0.059	-0.252	.804
Paternal highest educational attainment ³	0.398(0.528)	0.175	0.755	.460
Lifetime prevalence of psychiatric disorders in the family ⁴	0.484(0.509)	0.218	0.950	.355

¹coded as follows: 0 = no, 1 = yes; ²coded as follows: 0 = no university degree, 1 = university degree; ³coded as follows: 0 = no university degree, 1 = university degree; ⁴coded as follows: 0 = no, 1 = yes

3.4.2 Illness Severity.

Table 6 presents a univariate linear regression results between different illness severity markers at T0 (acting as independent variables) and total EDE score at T4 (acting as dependent variable). No significant predictive values of BMI-SDS (p = .783), EDE score (p = .170) or EDI score (p = .516) could be determined.

Table 6 *Illness Severity at T0 as Predictor of the AN Outcome at T4*

Predictor	b(SE)	Beta	<i>t</i> -value	p
BMI-SDS	0.095(0.338)	0.066	0.280	.783
EDE Total Score	0.384(0.268)	0.320	1.431	.170
EDI-2 Score	0.004(0.006)	0.154	0.663	.516

Note. BMI-SDS = Body Mass Index – Standard Deviation Score; EDE = Eating Disorder Examination; EDI-2 = Eating Disorder Inventory

3.4.3 Psychiatric Comorbidities.

The results from a univariate linear regression between participants' psychiatric comorbidities at T0 (acting as independent variables) and total EDE score at T4 (acting as dependent variable) are shown in Table 7. Only OCI-R score at T0 was identified as a significant predictor of the total EDE score at T4 (b(SE) = 0.037(0.015), t-value = 2.439, p = 0.25). More specifically, a higher OCI-R score at T0 predicted a higher total EDE score at T4. No other variable significantly predicted total EDE score at last time point.

Table 7Psychiatric Comorbidities at T0 as Predictors of the AN Outcome at T4

Predictor	b(SE)	Beta	t-value	p
Kinder-DIPS / DIPS ¹	0.235(0.519)	0.106	0.453	.656
BDI-2 Score	0.020(0.021)	0.216	0.936	.362
STAI State Score	0.025(0.020)	0.278	1.226	.236
STAI Trait Score	0.033(0.022)	0.329	1.479	.156
OCI-R Score	0.037(0.015)	0.498	2.439	.025

 $^{^{1}}$ coded as follows: 0 = no psychiatric comorbidity at the moment, 1 = any psychiatric comorbidity at the moment

Note. Kinder-DIPS = Diagnostic Interview for Mental Disorders in Children and Adolescents; DIPS = Diagnostic Interview for Mental Disorders; BDI-2 = Beck Depression Inventory; STAI = State-Trait Anxiety Inventory; OCI-R = Obsessive-Compulsive Inventory

3.4.4 Hierarchical Linear Regression Analysis.

Finally, the results of a hierarchical linear regression are summarized in Table 8. No significant predictive value of sociodemographic characteristics (p = .773), illness severity (p = .861) or psychiatric comorbidities (p = .638) at T0 on the total EDE score at T4 could be found. Worth noting is, however, that 68.5% of the variance was explained through the model when all three blocks were included in the analysis. The biggest increase in the explained variance was observed when psychiatric comorbidities were included in the model as predictors of the total EDE score at T4 ($\Delta R^2 = .394$), followed by sociodemographic

predictors ($\Delta R^2 = .225$), whereas illness severity predictors had only a minor impact on the changes in explained variance ($\Delta R^2 = .066$).

Table 8Results of the Hierarchical Linear Regression Analysis

Block	R	R ²	ΔR^2	p
Block 1: Sociodemographic predictors	.475	.225	.225	.773
Block 2: Illness severity predictors	.540	.291	.066	.861
Block 3: Psychiatric comorbidities predictors	.828	.685	.394	.638

4. **Discussion**

The main aim of the present study was to fill in the knowledge gap on the long-term course of AN in female adolescent and young adult patients by evaluating the existing hypotheses about lasting outcomes, remission status, associated psychiatric comorbidities and factors predictive of the outcome of this eating disorder. The following sections critically discuss the study's main results, underline the practical relevance of these results in clinical practice, highlight the strengths and limitations of this study and acknowledge possible directions for future research.

4.1 **Discussion of the Main Results**

The first research question investigated the long-term changes in AN patients' BMI, eating disorder-specific psychopathology and psychiatric comorbidities. Herein, BMI increased significantly from the first to the last time point, confirming the first hypothesis, which assumed that BMI would change significantly between these two time points. This finding was expected since reaching a healthy body weight and maintaining a stable BMI over time are important treatment goals, especially in the case of inpatient treatment, and some of the first milestones towards overcoming this severe psychiatric disorder (Fichter et al., 2017; Herpertz-Dahlmann & Dahmen, 2019; Madden et al., 2015; World Health Organisation, 2019).

The second hypothesis regarding the first research question centred around changes in eating disorder-specific psychopathology over time, assuming that it would change significantly from the first to the last time point. In line with the previous findings, the present study provides empirical evidence for the decrease in eating disorder-specific psychopathology over the years (Bachner-Melman et al., 2006; Fichter et al., 2017; Lo Sauro et al., 2013). According to several authors, an overall improvement in eating disorder-specific psychopathology is reflected in improvements in both behavioural and cognitive symptomatology (Bachner-Melman et al., 2006; Bardone-Cone et al., 2010; Lo Sauro et al., 2013; Mairhofer et al., 2021). The authors suggest that while behavioural components of AN, including dietary restriction and eating avoidance, often improve in the short-term, distorted cognitions, such as body image disturbances, may persist for a sustained period after the AN onset and/or physical recovery. These assumptions are indicative of promptly improved physical and behavioural symptomatology and longer-lasting residual cognitive disturbances. However, the present study identified no such patterns. Quite the contrary, the most significant reduction was observed in distorted cognitive attitudes towards food and patients' appearance. More specifically, the largest effects were found for changes in eating concerns,

followed by shape and weight concerns. A large effect was also found for the change in eating disorder-specific restraint, yet this effect was much smaller compared to the eating, shape and weight concerns. Important to note is that the patients, who formerly participated in the MANTRa study, were only included if they already reached a certain weight threshold (Wittek et al., 2021). In other words, the study did not include the most severely affected and extremely underweight patients requiring immediate inpatient treatment. Therefore, an alternative explanation of the current findings concerning changes in eating disorder-specific psychopathology may be that the present sample consisted of individuals whose restraint behaviours and physical manifestations were already improved at the baseline assessment when compared to other study samples, including most severely affected individuals within an inpatient setting (Mairhofer et al., 2021). Furthermore, the present sample consisted of highly motivated individuals willing to participate in a longitudinal study over several years. As proposed by Gregertsen et al. (2019), the high motivation and engagement of the study participants may be the key to explaining more significant reductions in the eating, shape and weight concerns observed in the current study, reflecting not only remission of visible restrictive behaviours and improvements in physical symptoms but also long-term adaptive modifications of distorted cognitions associated with this eating disorder.

The third hypothesis concerning the first research question concentrated on changes in psychiatric comorbidities over time. It was hypothesized that psychiatric comorbidities would change significantly from the first to the last time point. This hypothesis was partially confirmed. Half of the participants reported a lifetime prevalence of psychiatric disorder and current psychiatric comorbidity was observed in forty per cent of them. These results support previous findings on the high prevalence of psychiatric comorbidities before the onset of, throughout and after the course of AN (Meczekalski et al., 2013; Salbach-Andrae et al., 2007). The present study investigated the changes in symptomatology representative of five major psychiatric disorders frequently associated with AN, including anxiety, depressive and obsessive-compulsive disorders, post-traumatic stress disorder and non-suicidal self-injury (Meczekalski et al., 2013; O'Brien & Vincent, 2003; Salbach-Andrae et al., 2007). The results from Kinder-DIPS and DIPS interviews (Margraf et al., 2017; Schneider et al., 2017) indicate a tendency for anxiety, depressive and post-traumatic stress disorder-specific symptomatology to increase over time, whereas non-suicidal self-injury symptoms remitted entirely between the first and the last time point assessment. When the results of different psychological questionnaires were considered, a significant reduction of disorder-specific psychopathology over time was observed only for depressive symptoms, as assessed with the

BDI-2 questionnaire (Hautzinger et al., 2009). A medium effect for the reduction of depressive symptoms based on the BDI-2 questionnaire was in contrast with the increase in depressive symptomatology identified with the Kinder-DIPS and DIPS interviews. A possible explanation for this discrepancy may lie within the method used to assess the underlying disorder-specific psychopathology. On the one hand, BDI-2 is a self-report questionnaire that may reflect respondents' inability to accurately report their feelings or the magnitude of the experienced symptoms (Salbach-Andrae et al., 2008). On the other hand, Kinder-DIPS and DIPS interviews involve not only an interviewee but also an experienced interviewer skilled in detecting respondents' reactions and tendencies, including nonverbal signals, selfpresentation strategies or cognitive biases. Therefore, the interviewer might come to a conclusion regarding the actual symptomatology, which might oppose the patient's selfperception. Another alternative explanation revolves around the severity of the prominent depressive symptomatology. Patients may indeed have experienced a significant reduction of the overall depressive symptomatology between the first and the last time point, as reported in the BDI-2 questionnaire; however, the symptoms may still, to some extent, persist over the years. Although the Kinder-DIPS and DIPS interviews enable severity differentiation of psychiatric symptomatology, in the current study, only the information about the presence of prominent psychopathology was used. For this reason, it is possible that overall depressive symptomatology declined over time but not to the degree that it would suggest a complete absence of the salient clinical picture.

The second research question tackled the differences in remission status across time. While sixty per cent of participants had full syndrome AN and forty per cent were in partial remission at the first time point assessment, these proportions changed over time. More precisely, the fifth assessment revealed that fewer participants were diagnosed with a full syndrome AN since only thirty-five per cent fell within this category. Meanwhile, the proportion of the sample in partial remission increased, with forty-five per cent of the participants being categorized as partially remitted at the last time point assessment. In addition, twenty per cent of participants were classified as fully remitted at the end of the study. These results are consistent with the earlier studies on long-term changes in remission status and confirm that in approximately one-third of the affected patients, AN runs a chronic course (Andrés-Pepiña et al., 2020; Herpertz-Dahlmann et al., 2001; Lo Sauro et al., 2013; Pla & Toro, 1999).

The third and final research question addressed possible predictors of the long-term AN outcome. The fourth hypothesis investigating whether sociodemographic characteristics

assessed at the first time point significantly predicted the AN outcome at the last time point was not confirmed. Similarly, the fifth hypothesis examining whether illness severity at the first time point assessment significantly predicted the AN outcome at the last time point assessment was also not confirmed. The sixth and last hypothesis addressing psychiatric comorbidities as significant predictors of the AN outcome at the last time point was partially confirmed. Among numerous psychiatric comorbidities examined, only obsessivecompulsive symptomatology significantly predicted the AN outcome. The presence of obsessive-compulsive symptomatology at the first time point assessment was associated with a higher total EDE score at the last time point assessment. The present findings indicate the link between obsessive-compulsive symptoms and higher long-term eating disorder-specific psychopathology, implying a poorer AN outcome. These results confirm the previous findings by Carrot et al. (2017), who affirmed that obsessive-compulsive disorders were predictive of a poorer AN prognosis. Although the results of a hierarchical linear regression revealed no significant predictive value of the three blocks, including sociodemographic characteristics, illness severity and psychiatric comorbidities, it should be noted that the model explained a considerable amount of variance when all of the blocks were included in the analysis. In addition, despite not reaching statistical significance, the inclusion of psychiatric comorbidities in the analysis accounted for the biggest increase in the explained variance of the model. These results corroborate the findings reported by numerous other researchers investigating psychiatric comorbidities as significant predictors of the AN outcomes (Carrot et al., 2017; Himmerich et al., 2019; Huas, Caille et al., 2011; Huas, Godart et al., 2011; Leppanen et al., 2022; Råstam et al., 1995; Schlegl et al., 2016).

4.2 **Practical Implications**

The findings mentioned in the previous section have great practical value. They reflect the severity and complexity of AN, highlighting the high rates of chronicity and psychological strain still present years after the onset of the illness. Therefore, clinicians and therapists should constantly educate themselves and remain informed of the newest scientific findings and advancements in the field of AN research with an aim to provide their patients with care according to the highest standards. Moreover, the current study's results emphasize the importance of treating not only AN but also other premorbid and/or accompanying psychiatric disorders since they clearly play an essential role in the long-term course of this eating disorder. It can be said with confidence that including other present psychiatric disorders in the therapy from early on may lessen the overall symptomatology and psychosocial burden in the affected patients.

4.3 Strengths and Limitations

The present study has multiple notable strengths. Firstly, the longitudinal study design enabled a thorough assessment of participants' sociodemographic characteristics, illness severity and psychiatric comorbidities at five different time points, following the same sample for an average of three years. The current AN research draws attention to the growing need for longitudinal studies allowing a long-term evaluation of the course of and adverse effects accompanying AN. On that account, the present study's findings provide a valuable contribution to the existing body of literature on the lasting effects of this severe eating disorder. Secondly, this is the single long-term follow-up study of Austrian adolescent and young adult females previously diagnosed with AN. Given that no study so far focused on long-term AN outcomes within this specific patient group, the findings of the present study lay the foundation for understanding the development and progression of AN in Austria and offer a possibility for researchers to compare the Austrian sample with other European samples and/or communities around the world. Lastly, the broad selection of psychological instruments used in the present study allowed a comprehensive assessment of different psychiatric disorder-specific symptomatologies. This especially stands for the evaluation of eating disorder-specific psychopathology, assessed through a combination of diagnostic goldstandard methods, EDE interview and EDI-2 questionnaire, respectively.

Several limitations may have influenced the results obtained from this study. The first is the relatively small sample size, impeding the detection of small effect sizes and the extrapolation of the observed results on other populations. The findings should, therefore, be interpreted cautiously since including more participants could lead to different results. The second limitation restricting the generalizability of the present results is the inclusion of female participants only. Although females are much more frequently diagnosed with AN than males (World Health Organisation, 2019), including more male participants in clinical research would shed some light on possible differences between females and males concerning the expression of the underlying eating disorder-specific psychopathology. The third disadvantage is the missing subgroup analysis (e.g. regarding therapy forms, AN subtype and remission status) due to a relatively small sample size, hindering a finer differentiation of the individual AN trajectories. Another possible source of bias is the variability in time passed from the first to the last time point, potentially limiting the visible overall improvements of the clinical picture in participants assessed within the shorter timeframe.

4.4 Suggestions for Future Research

The results of the present study are promising and should be validated by a larger sample size. Future studies should target not only females affected by AN but also include male participants to explore the possible gender differences in symptomatic expression and course of this eating disorder. Furthermore, Fichter et al. (2017) argued that higher remission rates are associated with higher follow-up years. Thereby, further research is needed to precisely estimate full remission, partial remission and chronicity rates in relation to the number of follow-up years. Finally, further work is recommended to investigate the role of possible predictors associated with adverse effects on affected patients, with a particular emphasis on the predictive value of comorbid psychiatric disorders in explaining poorer AN outcomes.

5. References

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8. List of Abbreviations

AN anorexia nervosa ANOVA analysis of variance B BDI-2.....Beck Depression Inventory BMI body mass index BMI-SDS body mass index – standard deviation score D DSM-5......Diagnostic and Statistical Manual of Mental Disorders (5th edition) \mathbf{E} EDE Eating Disorder Examination EDI-2 Eating Disorder Inventory Ī K Kinder-DIPS......Diagnostic Interview for Mental Disorders in Children and Adolescents M MANTRa......Maudsley Model of Anorexia Nervosa Treatment for Adolescents and Young Adults.....Young Adults 0 OCI-R......Obsessive-Compulsive Inventory STAI.....State-Trait Anxiety Inventory T T0......assessment before the beginning of the treatment T2......assessment after twelve months T3.....assessment after eighteen months

9. **Abstract (English Version)**

Anorexia nervosa (AN) is a severe psychiatric disorder associated with numerous adverse effects interfering with the physical, psychological and social functioning of the affected individuals. The present study aimed to explore the long-term course of this eating disorder by evaluating lasting changes in remission status, eating disorder-specific and general psychopathology as well as factors predictive of the AN outcome. Twenty female patients from Austria between 15 and 22 years of age were assessed at five different time points across several years. The results revealed significant changes in overall psychopathology across time, including a steady increase in body mass index and a decrease in overall eating disorder-specific and self-reported depressive symptomatology. Major changes were observed concerning remission status, with full remission and partial remission rates increasing over time. Among the multiple predictors examined, only obsessivecompulsive symptomatology predicted a poorer AN outcome. Still, the inclusion of psychiatric comorbidities as predictors in the analysis accounted for the biggest increase in the explained variance of the model. The findings emphasize the long-lasting effects closely linked to this eating disorder and the role of comorbid psychiatric disorders in shaping individual AN trajectories. Practical implications and future research directions concerning the long-term course of AN are discussed.

10. Abstract (German Version)

Anorexia nervosa (AN) ist eine der schwerwiegendsten psychiatrischen Erkrankungen, welche mit einer Vielzahl an negativen Auswirkungen assoziiert ist und das physiologische, psychologische und soziale Funktionieren der Betroffenen massiv beeinträchtigen kann. Die vorliegende Studie zielte darauf ab, die langfristigen Folgen dieser Erkrankung zu untersuchen, indem die dauerhaften Veränderungen des Remissionsstatuses, der essstörungsspezifischen und der allgemeinen Psychopathologie sowie die möglichen Prädiktoren für den Verlauf einer AN evaluiert wurden. Zwanzig weibliche Patientinnen aus Österreich zwischen 15 und 22 Jahren wurden über mehrere Jahre hinweg zu fünf unterschiedlichen Messzeitpunkten untersucht. Die Ergebnisse zeigten signifikante Veränderungen der allgemeinen Psychopathologie über die Messzeitpunkte hinweg, einschließlich einer stetigen Zunahme des Body-Mass-Indexes und einer Verringerung der essstörungsspezifischen Symptomatik sowie selbstberichteten depressiven Symptomatik. Bedeutende Veränderungen wurden in Bezug auf den Remissionsstatus festgestellt, wo es über die Zeit hinweg zu einem Zuwachs an vollständig remittierten und teilremittierten Personen kam. Unter den zahlreich untersuchten Prädiktoren stellte sich lediglich die Zwangssymptomatik als signifikant für den Verlauf der Erkrankung heraus. Allerdings kam es durch den Einschluss der psychiatrischen Komorbiditäten zum größten Anstieg der erklärten Varianz. Die Studienergebnisse unterstreichen die langanhaltenden Auswirkungen, die eng mit dieser Essstörung verbunden sind, sowie die Rolle psychiatrischer Komorbiditäten beim Verlauf dieser Erkrankung. Es werden praktische Implikationen und zukünftige Forschungsrichtungen in Bezug auf den Langzeitverlauf der AN diskutiert.