Familial predispositions among children and adolescents with an eating disorder

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Baggrund: Spiseforstyrrelser udgør en række lidelser, som kan have alvorlige psykiske og somatiske konsekvenser, som kan forringe patientens psykiske og fysiske sundhed samt påvirke den psykosociale funktion. Disse lidelser udgør et voksende folkesundhedsproblem blandt børn og unge i mange vestlige lande. Nationale og internationale undersøgelser indikerer, at antallet af henvisninger til børne- og ungdomspsykiatriske afdelinger er stigende, hvilket gør det afgørende, at undersøge de potentielle risikofaktorer, der ligger til grund for udviklingen af en spiseforstyrrelser. Spiseforstyrrelser er komplekse og ætiologien bag er endnu uklar, men involverer et samspil mellem psykologiske, genetiske, sociale, kulturelle og biologiske faktorer. Akkumulerende evidens fra familie, tvilling og genetiske studier, har dog i de seneste år fundet, at der er en øget genetisk risiko og familiær prædisposition i udviklingen af disse lidelser. Forskningen har vist, at børn og unge med en forælder som har eller har haft en spiseforstyrrelse, har højere risiko for selv at udvikle en spiseforstyrrelse, end deres jævnaldrende. Få studier har dog undersøgt, hvorvidt antallet af slægtninge eller graden af disse, kan have indflydelse på den symptomatologi, der er knyttet til spiseforstyrrelsen hos barnet eller den unge.

Formål: Det overordnede formål med dette projekt var at undersøge forekomsten og indflydelsen af spiseforstyrrelser hos slægtninge til børn og unge med en spiseforstyrrelse.

Metode: Projektet består af en rammesættende del samt en tværsnitsundersøgelse. Den rammesættende del blev anvendt til at belyse nuværende forskning vedrørende den familiære prædisposition hos børn og unge, samt til at identificere og understøtte metodemæssige overvejelser, i relation til den tværsnitsundersøgelse, der har tilvejebragt projektets empiriske grundlag. I tværsnitsundersøgelsen blev data indsamlet retrospektivt ud fra patientjournaler af børn og unge (N = 282), henvist til afdelingen for spiseforstyrrelser på Aalborg Universitetshospital, Nordjylland, Danmark, i perioden fra 2009 til 2014. Under udredningen, som en del af det standardiserede assesment batteri anvendt i enheden, blev forældre inkluderet, for at tilgå både deres egen, men også øvrige slægtninges forekomst af en spiseforstyrrelse. Den statistiske analyse blev udført ved brug af lineær regression til at undersøge potentielle sammenhænge mellem debutalder og symptomsværhedsgrad hos børn og unge uden, dem som havde én og dem som havde to eller flere slægtninge med en spiseforstyrrelse.

Resultater: Baseret på de børn og unge, som har en familiær prædisposition (N = 84), havde 61 (72,62%) mindst én påvirket slægtning, mens 23 (27,38%) havde to eller flere.

Tooghalvtreds (63,68%) havde en familiær prædisposition blandt førstegradsslægtninge, mens 23 (27,38%) var af anden grad og 30 (35,71%) var af tredje grad. Børn og unge med to eller flere familiære prædispositioner udviste en tendens, til at score højere (op til 1,17 point) målt på symptomsværhedsgrad, sammenlignet med patienter uden familiær prædisposition. Herudover, havde drenge med familiær prædisposition en betydeligt højere symptomsværhedsgrad, sammenlignet med drenge uden familiær prædisposition. Det begrænsede antal drenge med familiær prædisposition, gjorde det dog ikke muligt at kunne foretage sammenligninger baseret på køn, eller drage endegyldige konklusioner af dette fund. Ud fra den statistiske analyse, blev der ikke fundet nogen signifikant sammenhæng mellem familiære prædispositioner, debutalder og symptomsværhedsgrad.

Konklusion: Forekomsten af familiær prædisposition var sammenlignelig med øvrige studier og højere end den estimeret baggrundspopulation. Metoden der blev anvendt i projektet, muliggjorde en undersøgelse af en repræsentativ, unik mængde data fra en yderst sårbar befolkningsgruppe, hvilket gav værdifuld indsigt i prævalensen af spiseforstyrrelser hos slægtninge til børn og unge med en spiseforstyrrelse. På trods af den øgede familiære risiko, er der mange børn og unge der ikke udvikler en spiseforstyrrelse, og en betydelig andel af dem, der udvikler en spiseforstyrrelse, har ikke en familiær prædisposition. Dette understreger kompleksiteten i ætiologien bag spiseforstyrrelser, hvorfor udviklingen af en spiseforstyrrelse bør forstås ud fra et komplekst samspil mellem genetiske og miljømæssige faktorer, hvor den familiære risiko kan udtrykkes i nærværet af miljømæssig risiko eller beskyttende faktorer.

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1. Background

Eating disorders (EDs) are potentially life-threatening illnesses associated with a severe and persistent disturbance in eating behavior and preoccupation with body image, food and weight to such an extent, that it can have a significant impact on the psychological, physical and psychosocial functioning of the affected individual (Academy of Eating Disorders, 2021). EDs are often accompanied with psychiatric and somatic comorbidities (Udo & Grilo, 2019), impaired quality of life (Van Hoeken & Hoek, 2020) and increased mortality rates, due to medical complications and suicide (Chesney, Goodwin, and Fazel 2014; Hambleton et al., 2022). The prevalence of EDs have been rising, especially in mid- and high- income countries, with childhood and adolescence representing a high-risk period for the onset of these disorders (American Psychiatric Association, 2013; Silén & Keski-Rahkonen, 2022; Smink et al., 2012; Sundhedsstyrelsen, 2005; Treasure et al., 2020). Based on a systematic review and meta-analyses, pooled lifetime prevalence rates of any ED in the general population have been estimated at 0.91%, while lifetime prevalence rates of anorexia nervosa (AN), bulimia nervosa (BN) and binge-eating disorder (BED) have been reported at 0.16%, 0.63% and 1.53%, respectively (Qian et al., 2022). Point prevalence estimates from Western countries suggests, that between 5.5% and 17.9% of young females and between 0.6% and 2.4% of young males, experience either a full or subthreshold ED before reaching early adulthood (Silén & Keski-Rahkonen, 2022). Moreover, an increase of 66% in the ED prevalence from 2010 to 2018 have been reported in Denmark with children and adolescents accounting for more than half of all new ED cases (Sundhedsdatastyrelsen, 2020). These data have prompted increased attention to these disorders and their effects among children and adolescents. Although a significant amount of research have been made into developmental factors (I. C. Campbell et al., 2011), early identification efforts and treatment approaches (Grange & Loeb, 2007), a substantial proportion of ED patients experience a chronic course (Van Hoeken & Hoek, 2020). However, EDs are treatable and full recovery is always possible (Academy of Eating Disorders, 2021), thus, early detection and an early response to treatment, have been associated with improved effects on the prognosis (Austin et al., 2021; Le Grange et al., 2010; Madden et al., 2015). Nevertheless, the adverse health consequences of EDs makes treatment challenging and prolonged, which is not only debilitating for the affected individual, but also requires an extensive amount of resources from the healthcare system (Mairs & Nicholls, 2016). To provide health-care professionals with the necessary knowledge for planning targeted interventions and facilitate early detection strategies,

understanding the etiology of these disorders seems crucial for further investigation. The etiology of EDs is complex and involves an intersection of several biological, psychological and sociocultural factors (Garner & Garfinkel, 1980; Van Hoeken & Hoek, 2020). Although numbers of presumed risk factors contributing to the development of EDs have been increasing, findings from research have not been conclusive (Rikani et al., 2013). However, accumulated evidence from family, twin and genetic molecular studies have shown, that EDs run in families and are substantially heritable indicating a strong genetic component in the development of these disorders (Bulik, Yilmaz, and Hardaway 2015). Research have shown, that relatives of individuals with an ED, are more likely to be, or have been affected with an ED, compared to relatives of individuals without an ED (Hudson et al., 2006; Lilenfeld et al., 1998; Strober et al., 2000, 2001). Twin studies have found increased concordance rates among monozygotic twins compared to dizygotic twins (Fichter & Noegel, 1990; Holland et al., 1988), further supporting a familial transmission of these disorders. Additionally, heritability of functional alterations of serotonin have been suggested by showing anomalous peripheral uptake of serotonin in unaffected first-degree relatives of BN patients (Rikani et al., 2013). Several studies have explored causes and effects of ED psychopathology among children and adolescents (K. Campbell & Peebles, 2014). However, relatively few studies have investigated whether the number or degree of the relatives to children and adolescents with an ED, has any impact on the clinical manifestation of the ED, such as an earlier onset or a greater clinical severity (Dissing and Rasmussen, 2025, submitted)[1]. Based on these empirical and theoretical considerations, this thesis aims to create a nuanced and in-depth framework of familial predispositions among children and adolescents with EDs. Thus, following problem formulation, hypotheses and research questions have been made.

1.1 Problem formulation and hypotheses

The objective of this thesis is to investigate the prevalence and impact of EDs among first-, second-, and third-degree relatives of children and adolescents assessed with an ED. The problem-formulation is as following:

What is the prevalence of familial predisposition of eating disorders among children and adolescents with an eating disorder? What are the associations between familial predisposition, age of onset and disease severity, respectively?

[1] [1]This population: *Josefine Jul Dissing, Emma Torp Rasmussen, Kirstine Kahr Nilsson & Gry Kjaersdam Telléus (2024). Familial predispositions to an eating disorder: A Systematic Review and Meta-analysis.* Have been submitted to the Journal of Eating Disorders and was written as a part of the 9th semester project by Josefine Dissing and Emma Rasmussen.

It is hypothesized that:

1. *Greater illness severity and earlier age of onset will be associated with a greater number of familial predispositions and/or a closer degree of relatedness (i.e., first-degree)*
2. *No gender differences will be found*

1.2 Research questions

To investigate the above-mentioned problem formulation and hypotheses, following research questions will be examined:

1. *What is the prevalence of EDs among first-, second-, and third-degree relatives of children and adolescents with an ED?*
2. *What is the age of onset and severity of EDs among children and adolescents without any familial predispositions compared to those with familial predispositions?*
3. *What are the differences in the age of onset and disease severity among children and adolescents with familial predispositions among first-degree relatives, compared to those without any familial predisposition?*
4. *Is a closer degree of relatedness among first-degree relatives associated with an earlier age of onset and greater severity?*
5. *Are there any differences in familial predispositions, when comparing females to males?*

1.3 Operational measures

The above-mentioned problem formulation, associated hypotheses and research questions have been based on the existing literature of familial predispositions to EDs. Although EDs can affect individuals of all ages, genders, ethnicities and socioeconomic backgrounds (Academy of Eating Disorders, 2021), this thesis have been concentrated on children and adolescents. Children and adolescents have received limited attention in regards to familial predispositions compared to adult populations (Dissing & Rasmussen, 2025), and the rising prevalence among this population makes it an important area of study. The hypotheses and research questions will be sought examined through a retrospective cross-sectional study design. Thus, considerations regarding this design will be explained in the framework part of this thesis. The article contains an aim and hypotheses which have been based on the problem formulation and hypotheses of the thesis. Although various approaches, such as cognitive, developmental, and behavioral perspectives, may offer

valuable insights into the etiology of EDs (Kjærsdam Telléus et al., 2016; Møhl & Jensen, 2017), this thesis will primarily focus on familial predispositions, while other perspectives are going to serve as contextualizing a multifactorial framework of EDs. The problem formulation contains no limitations in terms of gender or subcategories of EDs, as this enables a broad study of the phenomenon. The data collection method is based on journal data from children and adolescents assessed with an ED, who retrospectively have been diagnosed with an ED based on the criteria from the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5). DSM-5 is the most widely used diagnostic manual in the research literature. It is therefore considered advantageous to base the findings on these criteria, as this allows for comparisons with other research articles to be made. Parents have been included during assessment of the child or adolescent, which is a method that has been accounted for creates greater validity and reliability of the findings, providing a higher accuracy of the prevalence (Dissing & Rasmussen, 2025). Family, twin and molecular genetic studies have been included in the framework part to identify environmental and genetic factors relevant for understanding the etiology of EDs. These findings will be discussed in relation to the findings from the study conducted within this thesis, hereby emphasizing the strengths and limitations of the method and methodology used. To ensure a rigorous investigation, conceptual definitions should be clearly defined (Launsø et al., 2017, p. 82f). Thus, the next section will provide a detailed description of the terminology and concepts related to EDs and familial predispositions.

2. Terminology and concepts

This following section will contain a definition of EDs and its subcategories. Moreover, the concept of familial predisposition and basis for the use of this term, will be explained.

2.1 Eating disorders

EDs are usually in research classified according to the criteria of the DSM-5, published by the American Psychiatric Association (APA, 2013). However, in Denmark, clinical practice and secondary mental health care primarily rely on the International Classification of Diseases (ICD-11), published by the World Health Organization (Sundhedsstyrelsen, 2005, p. 20; World Health Organization, 2022). References between the two classification systems are therefore presented.

Anorexia nervosa (AN) has one of the highest mortality rate of any psychiatric disorder (Academy of Eating Disorders, 2021, p. 1). Symptoms of this disorder includes low

weight, an intense fear of weight gain and body image disturbances (American Psychiatric Association, 2013). Both the DSM-5 and ICD-11 have provided weight cut-offs and severity specifiers with the body weight criterion being at least 15% below the expected weight in the context of age, height and developmental stage, or from having a body mass index (BMI) below 18.5 kg/m^2, indicating severe weight loss or failure to achieve expected body weight. Additionally, weight gain is prevented and weight loss is intentionally maintained by the affected individual, due to behavior such as dieting or fasting, excessive exercising or from compensatory behavior such as self-induced vomiting, misuse of laxatives, diuretics or enemas (American Psychiatric Association, 2013; World Health Organization, 2022). AN has a mean peak age of onset of 14 to 17 years (Møhl & Jensen, 2017, p. 487), and denial and minimization of malnutrition, appears to be a common symptom of AN, especially in younger patients (Couturier & Lock, 2006). Individuals with bulimia nervosa (BN) present with recurrent episodes of binge eating, which is defined as; the consumption of an objectively large amount of food, within a short period of time (Academy of Eating Disorders, 2021, p. 2). Binge-eating episodes are accompanied by a sense of loss of control over eating followed by compensatory behavior such as fasting outside of binge episodes, self-induced vomiting or excessive exercising. Binge-eating and compensatory behavior needs to have been present once a week or more for at least three months, in order to make a clinical diagnosis (American Psychiatric Association, 2013; World Health Organization, 2022). Binge-eating disorder (BED) involves, as in BN, recurring episodes of binge-eating with a sense of loss of control over eating, but is distinguished from BN by the absence of compensatory behavior (Academy of Eating Disorders, 2021, p. 2). Binge-eating episodes in BED are associated with eating more rapidly, eating until uncomfortably full, continuous eating regardless of hunger and/or eating alone due to the amount of food consumed (American Psychiatric Association, 2013). These episodes are often followed by significant physical and psychological discomfort such as feelings of shame or guilt (Academy of Eating Disorders, 2021, p. 2). BN and BED have most commonly been reported as having a later age of onset than AN, most frequently during late adolescence or early adulthood (Møhl & Jensen, 2017, p. 487). However, clinical observations have shown, that individuals with BN often report of initial symptom onset as early as eight to ten years of age (Møhl & Jensen, 2017, p. 488). Avoidant-restrictive food intake disorder (ARFID) involves food restriction or avoidance, but unlike other EDs, this disorder is not primarily related to weight and shape concerns (American Psychiatric Association, 2013). Instead, ARFID is associated with selective eating with some patients experiencing hypersensitivity to food texture,

appearance and taste, or from having disturbed appetite cues or fears regarding consequences of eating, such as swallowing or choking, which contributes to the food avoidance (American Psychiatric Association, 2013). These symptoms interferes with the psychosocial functioning of the affected individual, due to the persistent failure to meet appropriate caloric and/or nutritional needs (Academy of Eating Disorders, 2021, p. 2). The diagnostic classification of other feeding or eating disorder (OSFED) involves individuals, who experience eating behavior such as restricting food intake, purging or binge eating, but who do not meet full threshold criteria for either one of the above-mentioned subtypes. The diagnosis of unspecified feeding and eating disorders (UFED) involves cases in which ED behavior is present, but insufficient information makes a more specific diagnosis challenging (American Psychiatric Association, 2013; World Health Organization, 2022).

2.2 Familial predisposition

The term *familial predisposition* refers to an increased probability or risk of developing an ED, based on the presence of full or suggestive traits among relatives of individuals with an ED (Dissing and Rasmussen, 2025). Although it is acknowledged, that the term *genetic predisposition* has been more widely used throughout the research literature, genetics by definition requires the use of methods capable of quantifying specific environmental factors or genetic components contributing to the development of EDs (Bulik et al., 2016; Hoek, 2016). However, since the data and methods used within this thesis do not allow for causal inferences to be made, the term of familial predisposition was evaluated as a more accurate term. Additionally, to delimit this thesis, it has been relevant to use a term or concept that specifically seeks to determine familial relationships. This is derived from the operationalization of clearly defined variables. Individuals are defined in terms of a specific index, as to whether these are known to be either affected or not affected with an ED, combined with their degree of relatedness as following:

- 1st degree relatives (parents, children and sisters/brothers) and
- 2nd degree relatives (grandparents, grandchildren, half-siblings and biologically related uncles/aunts) and
- 3rd degree relatives (cousins, great-grandparents, great-aunts etc.)

From the use of the term familial predisposition, it is emphasized that having a familial predisposition to an ED does not imply that an individual will necessarily develop the disorder. Rather, an increased vulnerability from having a familial predisposition may or,

conversely may not, contribute to the understanding of the etiology of EDs to some extent, reflecting the complexity and multifactorial nature of EDs. This aspect is further elaborated in the next section, where theoretical and empirical literature regarding the role of genetic and environmental factors for EDs is presented.

3. Multifactorial aspects of eating disorders

In this section, the multifactorial model of the etiology of EDs is presented. Furthermore, a second generation of research will provide a state of the art in relation to familial predispositions, providing further insights into the etiology of EDs.

3.1 The multidimensional model

For the past decades, an extensive amount of research have suggested that EDs are multifactorial, involving several biological, psychological and socioenvironmental risk factors, which can predispose, precipitate and perpetuate the ED (Garner & Garfinkel, 1980; Jacobi et al., 2004; Striegel-Moore & Bulik, 2007). Risk factors refers to a characteristic, event or internal experience, that precedes the onset of a disorder, maintenance or severity (Jacobi et al., 2004; Striegel-Moore & Bulik, 2007, Kraemer et al., 1997). These factors are essential in identifying high-risk groups for targeted interventions, and useful to inform assessment, prevention and treatment (Bakalar et al., 2015; Barakat et al., 2023). This multifactorial interaction has been described by Garner and Garfinkel (1980) in their multifactorial model of the etiology of EDs, which is illustrated in **figure 1**.

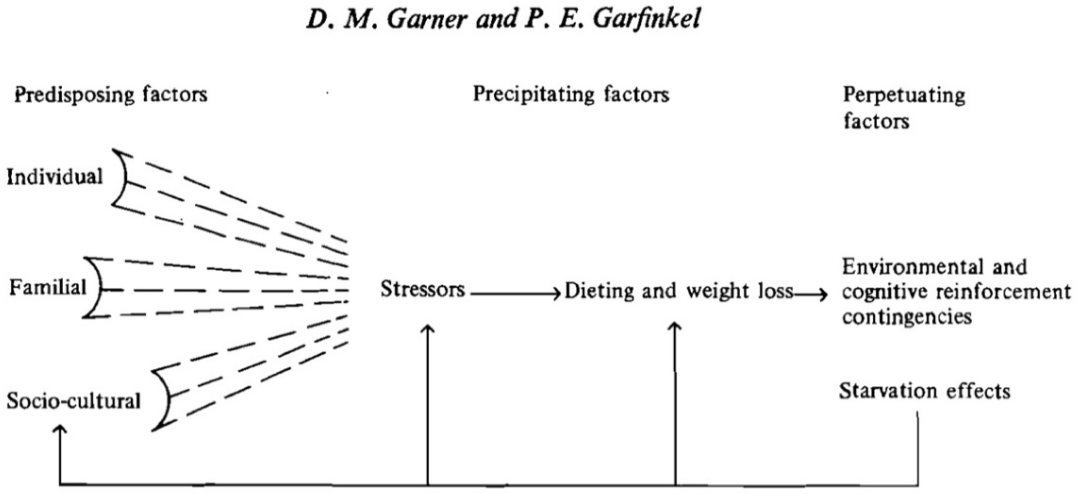

Figure 1. *The multifactorial model of eating disorders (Garner & Garfinkel, 1980)*

According to Garner and Garfinkel (1980) predisposing factors can be individual, familial and sociocultural. Individual risk factors, in which an individual is made vulnerable to

the development of an ED can be biological or psychological. Biological risk factors include a range of individual attributes, such as the genetic profile, a proclivity towards overweight, or early maturity. Psychological factors include, and can be expressed from, characteristics of the individual (e.g., negative self-evaluation, body image disturbances, perfectionism), the family (e.g., having a family history of EDs) or in adverse life events, with recent evidence emphasizing an increased vulnerability to the exposure of non-specific trauma (Garner & Garfinkel, 1980; Johnsen et al., 2024). Other familial risk factors involves different interactional patterns and value-laden, most often negatively, attitudes towards weight, shape or fitness within families (Garner & Garfinkel, 1980). Sociocultural risk factors includes living in a modern, urbanized and globalized society, where specific body images are idealized and promoted through different forms of media and peer pressure (Garner & Garfinkel, 1980; Treasure et al., 2020). Garner and Garfinkel (1980) have proposed, that an individual can possess several predisposing factors and that these may become pathogenetic, within the context of precipating factors. Precipating factors such as stressful life events, interpersonal loss or conflict, high achievement expectations, criticism regarding body, weight or shape, or physical and emotional changes during puberty, have been identified as triggering behavior such as dieting and weight loss (Garner & Garfinkel, 1980). Physical consequences of weight-related behavior, have been noticed to produce feedback mechanisms such as praise, approval or negative commentary about appearance, weight or shape, which serves as perpetuating the disorder (Garner, 1993; Garner & Garfinkel, 1980; Hetherington, 2000). On a psychological level, the ED may therefore serve as a coping strategy, providing a sense of control, relief or increase feelings of self-worth, making food and control of eating even more imperative (Garner, 1993; Garner & Garfinkel, 1980). On a biological level, starvation induces secondary symptoms, such as reduced stomach capacity and delayed gastric emptying, causing bloating when eating and creating physical discomfort. Inadequate food intake can thereby result in stomach pain and disrupted hunger, making weight restoration and regular eating particularly challenging (Hetherington, 2000). Although Garner and Garfinkel (1980) through their multifactorial model of EDs acknowledged the role of biological influences, recent research has emphasized that the genetic component in the etiology of EDs may be stronger than initially proposed. Thus, this aspect will be elaborated further in the following section.

3.2 State of the art: Family, twin and molecular genetic studies

Findings from family, twin and molecular genetic studies have indicated that AN, BN and

BED aggregates in families and that genetic effects, contributes to the variance in liability of these disorders (Yilmaz et al., 2015, p. 4). Family studies have shown that first-degree relatives of individuals with an ED have a seven- to ten- fold increased risk of developing an ED themselves, compared to the general population (Bulik, 2005, p. 336). Prevalence rates of 5.9% of any ED in second-degree relatives and 4.4% in third-degree relatives also have been reported (Dissing and Rasmussen, 2025), suggesting of a continuum of transmitted liability within at-risk families. Female relatives of AN patients have been reported up to 11 times more likely to develop AN than individuals who do not have relatives with AN (Strober et al., 2000). Research have shown, that the lifetime prevalence of AN, BN and BED in first-degree relatives of individuals with an ED ranges from 2% to 12%, compared to 0% to 4% in relatives of unaffected controls (Hudson et al., 2006; Kassett et al., 1989; Kuntz et al., 1992; Lee et al., 1999; Lilenfeld et al., 2008; Strober et al., 2000; Thornton et al., 2010). Individuals who have a relative with AN or BN are at an elevated risk for developing either disorder and a diagnostic crossover between the two presentations have been evident (Lilenfeld et al., 1998; Strober et al., 2000), suggesting some genetic correlation between AN and BN. However, no cases of BN were found in relatives of individuals who had the restrictive subtype of AN in one study (Grigoroiu-Serbanescu et al., 2003), suggesting that the genetic correlation may be restricted to specific subcategories of EDs. Additionally, in a study conducted by Field et al. (2008) it was demonstrated that females younger than 14 years of age whose mother had a history of an ED, were approximately three times more likely to develop and engage in bulimic behaviour than their peers. However, this association was not found among older adolescent females or males, suggesting that maternal history of an ED is a risk factor among younger adolescent females. However, since family studies do not distinguish between environmental and biological contributions of risk, further insights into the familial transmission of EDs have been provided from studies using twin designs. Most of these studies, have aimed at assessing the degree of genetic contributions, such as additive genetic factors, shared- or non-shared environmental influences (Thornton et al., 2010). Additive genetic factors represent the cumulative effects of more than one gene, contributing to the phenotype, with small to moderate effect commonly referred to as heritability (Bulik et al., 2006). Twin-based heritability estimates of AN have been reported ranging from 0.38 to 0.78 (Klump et al., 2001; Kortegaard et al., 2001; Wade et al., 2000) indicating that 78% of the phenotypic variation can be explained by additive genetic factors. Heritability of BN have been estimated to be between 0.50 to 0.85 (Bulik et al., 1998; Walters et al., 1992, 1993). Additionally, heritability for BED have been estimated to be between 0.39-0.45

(Javaras et al., 2008; Mitchell et al., 2010), and although less well-documented, heritability of a broad ARFID phenotype at 0.79 have been estimated (Dinkler et al., 2019). Shared and non-shared environmental factors contribute to the understanding of twin similarity, such as events influencing both members of the twin pair (e.g., starting school at the same age), and likewise events, only influencing one member of the twin pair (e.g, peer-groups) (Klump et al., 2002). Twin studies have indicated, that non-shared environmental influences contributes significantly greater to the development of EDs, compared to shared environmental factors (Bulik et al., 1998; Kendler et al., 1991; Klump et al., 2001; T. D. Wade et al., 2000). The presence of non-shared environmental experiences within families includes, amongst others, treatment by parents and siblings, family constellation variables (e.g., birth order), life events and individual characteristics (Klump et al., 2002).

Genetic contributions to EDs such as binge-eating, self-induced vomiting and dietary restraint have been estimated to involve a heritable component between 46% to 72% (Rutherford et al., 1993; Sullivan et al., 1998), while pathological attitudes such as body dissatisfaction, eating and weight concerns, have shown heritability estimates between 32% to 72% (Klump & Culbert, 2007; Rutherford et al., 1993; T. Wade et al., 1998, 1999). Given the importance of genetic factors in the development of EDs, recent molecular genetic studies have aimed to examine the extent of genes involved in the vulnerability of these disorders (Klump & Culbert, 2007). Findings have implicated monoaminergic functioning in both AN and BN, which have led researchers to target serotonin (5-hydroxytryptamin, 5-HT) and dopamine-related genes (Berrettini, 2004, p. 23). Some of these studies, have found increased frequencies of specific alleles of the 5-HT2A receptor gene in women with AN compared to controls, implicating this neurotransmitter system in appetite and mood regulation, which may influence the heritability of EDs, through changes in serotonin functioning (Van Der Veen et al., 2007). Furthermore, the neurotransmitter dopamine, have been receiving growing attention, due to its receptors in brain regions and neurocircuitry implicated in food craving, decision making, executive functioning and impulsivity, commonly associated with binge eating (Yu et al., 2022, p. 2). However, studies investigating dopamine receptor genes (D3 and D4) have failed to establish clear associations with AN, and these genes remain under-investigated in BN populations (Berrettini, 2004, p. 23f). Although several biological systems may be implicated in the etiology of EDs, limited studies exist per gene, small sample sizes predominate and non-replicating results have been most prominent within the research literature (Mazzeo & Bulik, 2009, p. 10f). However, it is now generally accepted that both genes and

environment interact to influence the ED risk, and environmental factors have been proposed to precipitate ED in individuals, with a biological or genetic vulnerability to an ED (Mazzeo & Bulik, 2009, p. 11; Møhl & Jensen, 2017, p. 491). However, modern biology and natural sciences questions, through its own results, contradictions between genetic and environmental factors, which necessitates a broader epistemological framework, that reaches beyond purely biological explanations (Andersen, 2006, p. 166f). Thus, next section will present the scientific theory informing this thesis.

4. Scientific theory

The following section provides an elaboration on the ontological and epistemological underpinnings of the medical research paradigm, as studying the prevalence of familial predispositions may have important implications for clinical decision-making.

Medical philosophy of science examines fundamental assumptions about concepts such as health and disease, which have been of significant debate in the medical research literature (Andersen, 2006, p. 228). Several theoretical frameworks have been suggested, which have introduced some philosophical considerations about how scientific knowledge is generated and interpreted (Juul et al., 2017, pp. 54–60). One of such frameworks is the one of the philosopher Christopher Boorse whose approach to health, labelled the biostatistical theory, originates from a biological and objective perspective (Andersen, 2006, p. 231). According to the Boorse, health is defined as the absence of disease. Health should be considered within a range of normality, which is determined statistically, while levels of functioning should be determined biologically. To determine whether an individual is within the range of normality, a reference class must be assigned, which consists of individuals within a relevant age group and gender (Andersen, 2006, p. 231f). However, another perspective on the concepts of health and disease have been offered by the philosopher Richard Hare (1986) who proposed, that health should not be viewed merely in the absence of disease, but is shaped by evaluative attitudes, cultural contexts and individual experiences. Thus, health and disease must be understood as a dynamic, normative construct, where subjective factors are of importance in its definition. In this thesis, a more objective approach has been applied, due to the study population being a clinical population, operationalized from the objective criteria of DSM-5. However, this position does not seek to challenge the importance of subjectivity, as the complexity of health and disease requires attention to both. Epistemological principles underlying medical research and practice is often identified within the framework of evidence-based medicine

(Andersen, 2006, p. 232f). Evidence-based medicine is based on the ethical and clinical ideal of identifying the best available evidence, when making decisions about the care of individual patients (Hróbjartsson & Lundh, 2022, p. 24f). Thus, emphasis is placed on finding, analyzing and communicating results from clinical research, where the preferences of the patient must be central in the clinical decision-making process (Hróbjartsson & Lundh, 2022, p. 26). In medical research, the hierarchy of evidence is often used to assess the quality and effect of studies and results (Hróbjartsson & Lundh, 2022, p. 32). Systematic reviews, meta-analyses and randomized controlled trials, have been deemed as having the highest quality evidence (Wallace et al., 2022, p. 784). Further down the hierarchy are study designs such as cohort studies, case-control studies and cross-sectional studies and at the bottom of the hierarchy, are expert judgements or individual expertise (Hróbjartsson & Lundh, 2022, p. 32f). For ethical reasons, it is often challenging to conduct randomized controlled trials in psychology, due to difficulties with blinding, and the complexity of measuring psychological interventions (Juul et al., 2017, pp. 208–210). Additionally, since the time frame and resources of this thesis did not allow for a cohort or case-control study to be made, the following project will be based on a cross-sectional study design (further addressed in paragraph 6.1). From conducting such research, several ethical considerations have been made and is presented in the next section.

5. Ethical considerations

Ethics are guiding principles that shapes the conduct of researchers and ensures careful planning of scientific research (Miteu, 2024, p. 2395). Researchers must be aware of their own responsibilities, beyond their own interests, to ensure that implications from scientific findings can be relied upon (Pedersen et al., 2015, p. 6).

Ethical standards within medical research are to protect and ensure respect for all human subjects and protect their health and rights which include, but are not limited to, confidentiality, anonymity, privacy, honesty and transparency of the entire research process to enhance the integrity of the findings (Miteu, 2024; Pedersen et al., 2015). Observational studies do not involve interventions and are therefore considered as studies of minimal risk to the individual. However, it is important that such research is conducted only after considerations and approval of a research ethics committee (World Medical Association, 2013, p. 2193). The article conducted within this thesis has obtained legal and ethical approvals from the Danish Health Data Authority, which approved data access. The study is based on data from journal records, which generates utility from the assessment of

health-related outcomes. Such data contains sensitive information including diagnostic information and family medical history. This form of data is incorporated into a broader scope of personal information in the European Union, as defined by the General Data Protection Regulation (GDPR) (Hoofnagle et al., 2019). Additionally, this level of detail in data, may increase the risk of reidentification if the data is unique for the individuals involved (Lane & Schur, 2010). To ensure confidentiality and protect against reidentification, several measures can be taken, including anonymization and pseudonymization (Voigt & Von Dem Bussche, 2024, p. 14f). Pseudonymization have been applied during the stages of data collection and analysis, hence any sensitive information or personal specifiers, have been replaced with a unique pseudonym and quantified. Moreover, to protect the privacy and confidentiality of the study population, data needs to be protected against unauthorized access, loss, destruction and stored in secure databases to protect the integrity and anonymity of the patient (Voigt & Von Dem Bussche, 2024, p. 41). Restricted data access has been employed. All data have been securely stored on a specialized network drive at Aalborg University Hospital, North Denmark, which is a dedicated database for research data, that complies with the legal requirements for handling personal data. It is also important to consider that retrospective patient record data may contain errors. To avoid information bias, due to potential registration errors, the diagnosis codes for EDs have been identified, based on the DSM-5 criteria and verified through the evaluation of experienced clinicians. Studies examining children and adolescents raises additional ethical concerns, especially due to the sensitivity of this study population. All data has therefore been anonymised through a quantitative generalization of data, in which all personal information has been either modified or removed and the analysis conducted have been based on groups rather than individuals. To ensure honesty and integrity throughout the entire research process, a research protocol has been made beforehand (see appendix A), which outlines the rationale for the study, its objective and methods used. Additionally, all findings will be shared. Moreover, to ensure transparency of the study, the methodology and methods used, will be presented in the next section.

6. Methodology and method

The following section is going to provide a detailed description and considerations of the study design, data collection and statistical methods relevant when managing and analysing quantitative data.

6.1 Study design

Quantitative research is a structured approach, which enables the collection of numerical data and the quantification of variables to systematically investigate or identify certain trends or relationships within a phenomenon (Watson, 2015, p. 44f). There are various types of quantitative research designs, including cohort, case-control and cross-sectional studies, which each encompasses distinct characteristics and ways of collection, analyzing and interpret data results (Watson, 2015, p. 45). These types of study designs are often referred to as observational studies, as they are based on observations rather than interventions carried out by the researcher. Cohort studies are a type of a longitudinal study, which includes a temporal sequence, commonly used for determining incidence, causes and prognosis (Mann, 2003, p. 54). Case-control studies are frequently used retrospectively, to evaluate factors associated with diseases and outcomes between groups (Mann, 2003, p. 57). Cross-sectional studies are primarily used to determine prevalence, which involves collecting data about a population or group, from a specific point in time (Mann, 2003, p. 56; Wang & Cheng, 2020). This study design enables a thorough examination of multiple associations within the study population simultaneously, making it possible to address the problem statement and associated hypotheses of this thesis. Consequently, this type of study design cannot be used to establish causality, as the temporal sequence does not allow for such interpretations to be made. In this thesis, data will be derived from the assessment of children and adolescents at the Unit for Eating Disorders, Psychiatry at Aalborg University Hospital. Notably, any claims of causal inferences within the context of using retrospective journal records, thus, such claims would essentially be considered methodologically inadequate, as the temporal onset of EDs among affected relatives of children and adolescents cannot be established. Hence, next section will provide further considerations of the data collection method.

6.2 Data collection

As mentioned, evidence-based healthcare is based on the view that clinical decision-making should be based on the best available evidence. This approach has, among others, increased demands for objectivity and reliability in the clinical assessment work, leading to a greater focus on the assessment tools used to ensure adherence to clinical standards (Hróbjartsson & Lundh, 2022, p. 25f). Several family studies of familial predispositions to EDs have indicated that obtaining a psychiatric family history of EDs through interviews with probands are more likely to underestimate the prevalence of EDs in relatives, when compared to studies using direct interviews with relatives (Halmi, 1991; Logue et

al., 1989). Hence, direct interviews with relatives have been accounted for as creating greater validity across several studies (Dissing and Rasmussen, 2025). In this thesis, the data has been based on retrospective journal records from children and adolescents assessed with an ED and their relatives, strengthening the validity and improving the accuracy of the findings. Several assessment tools can be used as a part of the clinical evaluation process and for the purpose of documenting and evaluating treatment. Findings from both clinical practice and the research literature have demonstrated that the *Eating Disorder Examination* (EDE) is one of the most frequently used assessment tools for the examination of EDs (Clausen et al., 2012, p. 589). In Denmark, the EDE version 16 is included and incorporated in the assessment of anorexia and bulimia (BAB-A) in order to provide a comprehensive diagnostic evaluation (Sundhedsstyrelsen, 2005, p. 44). The EDE-16 provides data on key behavioral features of EDs, in terms of numbers of episodes and in some instances, number of days in which the behavior has occurred (Clausen et al., 2012, p. 589). Furthermore, the subscale items of restraint, eating, weight and shape concerns reflects the severity of the psychopathology and encompasses both current and developmental stages of EDs, which allows for a systematic coverage of the various subcategories of EDs (Sundhedsstyrelsen, 2005, p. 44). Additionally, several other semi-structured interviews can be used to obtain anamnestic information such as somatic information (BAB-S), background information (BAB-B) and information regarding both the development and course of EDs from interviews with the parents of the child or adolescent (BAB-F) (Sundhedsstyrelsen, 2005, p. 44). In this thesis, data from both the BAB-A and BAB-F regarding ED psychopathology and familial predispositions have been used to systematically examine the proportion and distribution of relatives who have experienced an ED themselves, which also applies to information regarding other distant relatives.

6.3 Statistics

Following section contains a description of prevalence and levels of measurement. Additionally, linear regression and the reasoning behind using this statistical analysis will be explained.

6.3.1 Measurement of variables

The main characteristic of an analytical cross-sectional study is that it collects data on both independent (exposure) and dependent (outcome) variables at a single point in time (A. Field, 2018, pp. 9–11). However, in retrospective studies researchers do not

manipulate variables, as it typically would be expected with independent variables, instead, observations are made. In this context, the terms of predictor variables and effect variables provides a more accurate framework, as these terms do not imply that causal inferences can be made (A. Field, 2018, p. 10). It has been hypothesized that familial predispositions have an impact on various outcomes in children and adolescence, such as an earlier age of onset or greater symptom severity. Additionally, the relationship between familial predispositions and gender, is examined through hypothesis testing, where the null hypothesis (H0) suggests that there are not any differences, while the alternative hypothesis (H1) suggests that such differences exist. ED psychopathology among children and adolescents have been measured by age of onset, gender, EDE global score, duration of illness and body mass index (BMI). Prevalence is defined as the proportion of individuals within a population, exhibiting a specific condition at a specific point in time (Juul et al., 2017, p. 27). Following formulae have been applied, which express prevalence as a percentage of the total population:

$$\text{Prevalence} = \frac{\text{Number of the cases in the population}}{\text{Total number of individuals in the population}} \text{x } 100$$

Studies using prevalence as a measurement of characteristics within groups can provide indications of individuals who may be more at risk of developing certain diseases. To ensure that the estimates of prevalence represent the true value within the study population, as support of the alternative hypotheses (H_1), and that the findings are not due to chance or systematically errors, it is crucial to establish the level of measurement of the variables involved (Juul et al., 2017, p. 24). The level of measurement determines which statistical tests that are appropriate to apply, during analysis of the data (A. Field, 2018, p. 10). There are four main levels of measurement: nominal, ordinal, interval and ratio scales. Nominal- and ordinal scales are classified as categorical variables. This type of data is often divided into categories or distinct groups, such as binary variables (i.e., yes/no) but does not indicate any value between them. In contrast, interval- and ratio levels are continuous variables, which can have an infinite number of values on the measurement scale used (A. Field, 2018, p. 11f). In the study conducted within this thesis, the predictor variable familial predisposition has been categorised into three levels, (1) none, (2) one affected relative and (3) two or more affected relatives. These variables have been treated as categorical variables, which also have allowed for the categorisation of first-, second-, and third-degree relatives to be applied. Several effect variables such as the global EDE score, age of onset and duration of illness, are continuous variables and

treated at an interval scale, due to the continuous measure of ED psychopathology. Since these are continuous, they are examined at a parametric level.

6.3.2 Statistical tests

The statistical tests were conducted from using the statistical software program Stata, which provides a comprehensive use of statistical tools, including descriptive statistics, inferential statistics and data visualisation (Statacorp, 2025). Descriptive statistics has been used to analyse data. Furthermore, inferential statistics was carried out from the use of linear regression, to test the relationship between the predictor and effect variables. In this context, regression have been applied to assess whether familial predispositions have an impact on the age of onset, the global EDE score and duration of illness. The linear model estimates a regression coefficient (i.e., mean difference) which allows for comparisons to be made between the effect and predictor variable (A. Field, 2018, p. 372). The formulae for a linear model with several effect variables is:

$$Y_i = (b_0 + b_1 X_{1\mathrm{i}} + b_2 X_{2\mathrm{i}}) + \varepsilon_i$$

The formula represents the effect variable as Y, such as the age of onset, EDE score or symptoms in months, while X represents the predictor variable, which is the familial predisposition. B_0 is the intercept for the reference group (i.e., those without familial predispositions). $B_1$is the regression coefficient, representing the mean difference between the groups, while ε is a random error term (A. Field, 2018, p. 372f). To determine whether the difference in data can be assumed to have occurred by chance, a threshold value for the p-value is usually set at 0.05, indicating that findings below this value, can be considered significant, providing support for the alternative hypothesis (Juul et al., 2017, p. 69f).

In the next section, the article part of this thesis is being presented, which have been set up according to the American Psychological Association (APA) guidelines (APA Publications and Communications Board Working Group on Journal Article Reporting Standards, 2008). The final format of the article, including word count, tables, and figures, will be adjusted in accordance with the submission requirements of the targeted journal.

RESEACH ARTICLE

Familial predispositions among children and adolescents with an eating disorder: a retrospective cross-sectional study of prevalence, age of onset and symptom severity

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ABSTRACT

Objective: Accumulated evidence from family, twin and molecular genetic studies indicate that eating disorders (EDs) run in families and are substantially heritable. This study aimed to assess the prevalence and impact of familial predispositions, as to whether the number of relatives and/or closer degree of relatedness (i.e., first-degree) would be associated with an earlier age of onset and greater illness severity in a clinical sample of children and adolescents.

Method: This retrospective cross-sectional study included 282 children and adolescents assessed for an ED in a specialized ED unit at Aalborg University Hospital, Denmark.

Results: A total of 84 children and adolescents had any familial predisposition to an ED, whereas 79 (94.05%) were females and five were males (5.95%). Sixty-one (72.62%) patients had at least one familial predisposition, while 23 (27.38%) had two or more familial predispositions. Fifty-two (63.68%) had ED-affected first-degree relatives, 23 (27.38%) had second-degree relatives and 30 (35.71%) had third-degree relatives with EDs. No significant association was found between familial predispositions and the age of onset, global EDE score, or symptom duration. However, a tendency towards having two or more familial predispositions and a high global EDE score was found (95%CI [-0.07, 1.17]), which could have clinical relevance.

Conclusions: A high prevalence of familial predispositions among children and adolescents was found. The findings suggest that having multiple ED-affected relatives may influence the severity of these disorders, emphasizing the importance of early detection and prevention programs among children and adolescents with EDs.

Keywords *familial predisposition, relatives, eating disorder, prevalence, severity, age of onset*

Background

Eating disorders (EDs), including anorexia nervosa (AN), bulimia nervosa (BN), binge-eating disorder (BED) and avoidant/restrictive food intake disorder (ARFID) have become a major public health concerns in most mid- and high-income countries with their increasing prevalence and adverse health consequences (1–3). These disorders are severe, potentially life-threatening, and can have a significant impact on the physical health, psychosocial functioning and development in children and adolescents. Based on the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), lifetime prevalence rates among children and adolescents (aged 11-19 years) in population-based studies of AN, BN and BED have been estimated at 0.29%, 2% and 3%, respectively (4,2). Despite limited research, varying prevalence rates of ARFID have also been reported, ranging from 1.98% in population studies to 22.5% in specialized ED units (5,6). EDs are often chronic and have many negative outcomes, such as long-term functional impairment, somatic complications and increased suicide risk (7). Early detection and early intervention have been associated with higher rates of recovery (8), thus, emphasizing the need to identify target groups at risk of developing of these disorders.

Although the etiology of EDs is complex, it is generally accepted that these disorders are multifactorial, influenced by several biological, psychological and sociocultural factors (9). Family, twin and molecular genetic studies, have throughout the past decades found that EDs run in families and are substantially heritable, emphasizing a genetic component in the development of these disorders (10–12). Family studies on both AN and BN have demonstrated that first-degree relatives of individuals with an ED have a greater lifetime risk of an ED, compared to relatives of unaffected individuals (13–16). In a study of 99 first-degree relatives of 24 patients with AN, and 265 unaffected control subjects, Gershon et al. (17) found that the lifetime risk among relatives was 6% compared to 1% among relatives of controls. Similarly, Strober, Morrell, Burroughs, Salkin and Jacobs (18) reported the presence of either definite ED or suggestive traits in at least one first- or second-degree relative among 27% of patients with AN, compared to only 6% in controls. Some of the highest prevalence rates have been reported among sisters of individuals with AN, ranging from 3% to 18% (16,19,20), exceeding rates in the general population. Female relatives of individuals with AN have been reported as 11 times more likely to develop AN than relatives of individuals without AN (16). Findings have suggested that relatives of individuals with BN are approximately four to nine times more likely to develop BN, compared to individuals without any family history of this disorder (14,16). In a family study of 102 first-degree relatives of 25 females with BN and of 101 first-degree relatives in the control group, Kuntz, Groze and Yates (21) found that the lifetime risk of any ED in relatives was 9.8% compared to 2.97% among relatives of controls. Findings from Stein et al. (22) demonstrated that the prevalence of lifetime ED was significantly greater among mothers and sisters of patients with BN, compared to relatives of unaffected patients. Recently, elevated rates of BED in first-degree relatives of individuals with AN, BN and BED have been reported (23). In two family studies conducted by Hudson, Jonas, Pope, Yurgelun-Todd and Frankenburg (24) and Lee et al. (25), a higher prevalence of BED in first-degree relatives among patients with BED was found, compared to

both relatives of controls and relatives with AN and BN. Moreover, in a study by Bertrand et al. (26) on 100 children with ARFID, reported that 51 (51%) relatives had experienced either full or subthreshold symptoms of ARFID. In contrast to most other EDs, males seem to be as frequently affected by ARFID as females (6). However, familial predispositions have been less well documented among this population compared to other EDs, emphasizing the need for further research within this area of interest.

Research has shown, that when both parents have the same disorder, the risk of the disorder developing in the offspring is increased (27). Several studies have reported associations between parental – primarily maternal – ED and the development of an ED in their daughters (28–30). A recent systematic review of 32 studies examining the impact of maternal ED found that children of mothers with an ED are at an increased risk of developing feeding problems, temperamental challenges and several psychological disturbances, such as cognitive inefficiencies (31). One study conducted by Cimino et al. (32) found that children with both parents affected by BED, showed higher affective, anxiety, oppositional/defiant and autism spectrum problems, when compared to children with only one affected parent, indicating that a greater genetic load, may have an impact on ED psychopathology. Studies of the psychopathology among child offspring of parents affected by EDs, are considered highly relevant, as these provides knowledge on early developmental psychopathology, relevant for planning targeted intervention and facilitating early detection strategies. As only a few studies have examined this relationship between male patients and male relatives. Hence, this is an area of interest which requires further investigation.

Several twin studies have been conducted, since family studies cannot distinguish between environmental and genetic contributions to the familial transmission of EDs. These twin studies have found increased concordance rates of AN, BN, or both, among monozygotic twins compared to dizygotic twins. Heritability estimates range from between approximately 0.48 and 0.83 in both disorders (33–38). Similarly, twin studies of BED report heritability estimates between 0.39 and 0.45 (39,40). Furthermore, a high twin-based heritability of a broad ARFID phenotype of 0.79 has also been identified (41), with the remaining variance being primarily attributed to non-shared environmental factors. Currently, research from molecular and genetic studies, have indicated some biological systems, such as the serotonin (5-HT) receptor, in both the acute and recovered illness states of AN and BN, as well as in mood, appetite and body weight regulation (42). This suggests that some of the ED variance can be explained by specific genetic effects. However, these studies have been conducted with small samples, unreplicated findings and inconsistent definitions of diagnoses, symptoms, and traits (42). Thus, while findings from these studies may have important implications in the aspect of familial predispositions to EDs, this is beyond the scope of this article and will therefore not be addressed in greater details.

Most research on familial predisposition of EDs has faced several limitations, as most studies have focused on AN, BN or BED, and only a few have included other less specific categories of EDs, including ARFID and Other Specified Feeding or Eating Disorders (OSFED) (43). Additionally, prevalence rates of EDs among relatives remain highly uncertain, due to small study groups, low statistical

power and broad confidence intervals, limiting the reliability of the findings (43). Most studies have used retrospective self-reported or register-based data instead of conducting direct interviews with the relatives. The use of self-reported data from ED affected children or adolescents has demonstrated to limit the validity and reliability of the findings, particularly due to the risk of recall and information bias (43–45). Only a few studies have been conducted explicitly on children and adolescents, compared to adults, tending to focus more on EDs among females than males (43).

Throughout the literature, it has been established, that an earlier age of onset can lead to severe medical instability (46), secondary to malnutrition, with significant impact upon growth and development of children and adolescents (47). Early detection and prevention strategies are essential, as later recognition and treatment of EDs have been associated with greater clinical severity, including longer illness duration, higher risk of relapse and poorer treatment outcomes (48). However, the extent of whether an earlier age of onset or disease severity is associated with a greater number of familial predispositions or a closer degree of relatedness in relation to first-, second-, and third-degree relatives among children and adolescents affected by an ED have not been well documented. Thus, it is imperative to investigate this area further, as research into such ED risk factors advances knowledge of the etiology and possibilities of identifying high-risk groups. This knowledge is needed for early detection and prevention program.

Aim of the study

The overall aim of this study was to examine the prevalence and the impact of familial predispositions among patients with an ED.

Thus, the objective of this retrospective cross-sectional study was to estimate the prevalence of EDs among first-, second-, and third-degree relatives. Another objective was to examine whether an earlier age of onset and greater clinical severity, had any impact on the familial predisposition in relation to the number of relatives, degree of relatedness and gender. These findings were sought compared to children and adolescents without any familial predispositions. The primary hypotheses were:

1. Greater illness severity and earlier age of onset would be associated with a greater number of familial predisposition and closer degree of relatedness (i.e., first-degree)
2. No gender differences would be found

Ethical considerations

Ethical and legal approval for conducting this study, has been received from the North Denmark Region Committee on Health Research Ethics and the Danish health data authority (the North Denmark Region), which granted data access (id number: 1-45-72-256-25). Informed or written consent has not been obtained nor required due to the retrospective and observational study design. Data have been stored in a secure specialized network drive at Aalborg University Hospital, North Denmark Region. Furthermore, all data processing has been conducted pseudo-anonymously to ensure the safety of the patients. Special attention has been paid to groups consisting of fewer than five patients, which have been either modified or removed, due to microdata and the risk of reidentification.

Methods

Study population

The study population consisted of children and adolescent referred to the Unit for Eating Disorders at Aalborg University Hospital, North Denmark Region, Denmark, between the years of 2009 and 2014. This interdisciplinary and specialized ED unit provides both in- and outpatient treatment to children, adolescents and adults with an ED. The included children and adolescents were all assessed for an ED. In connection with the assessment, the parents of the child or adolescent was interviewed about familial predispositions. The diagnostic categorization was conducted retrospectively, according to the DSM-5 criteria (49) based on the diagnostic interviews conducted at the time of diagnosis. In total, 282 children and adolescents, both female and males, were included.

Diagnostic assessment of ED in children and adolescents

Children and adolescents were assessed for an ED according to a standardized assessment battery used at the ED unit for assessing psychopathology according to the Eating Disorder Examination, edition 16.0D (EDE-16) (50). The EDE-16 is a semi-structured interview with measurements to establish the frequency and ED key behavioral features in terms of number of episodes and days of ED behavior. The frequency is measured over a 28-day period (50). Moreover, the subscale scores restraint, eating concern, shape concern and weight concern, reflect the severity of ED psychopathology and are scored on a 7-point scale (0-6), which provides a global score of an overall index of the severity of ED symptoms (51), with higher scores indicating greater symptom severity. The assessment also included information regarding the onset and developmental trajectories of the ED, as well as a medical examination including both clinical observations and patient-reported symptoms. The EDE-16 has a good internal consistency, discriminate and concurrent validity and inter-rater reliability (52). However, as it was originally developed for the adult populations, modifications is required, when administered to children and adolescents (53). These modifications involve, amongst others, an adaption in language and the assessment of intent rather than behavior with the use of ranking tasks (53). All assessment tools were administered by highly experienced and trained clinicians, ensuring the validity and reliability of the findings.

Assessment of familial predispositions

The ED assessment battery also included a semi-structured interview entailing a parental interview to collect anamnestic data and familial predispositions of EDs. During the assessment of the child or adolescent, parents have been asked about any known familial predispositions to EDs, and whether these have been of first-, second-, and/or third-degree relatives. The parents have therefore been the primary source of information, both about their own familial predispositions to an ED and of familial predispositions amongst other relatives. This information source has been considered the most valid and reliable way to obtain the prevalence of familial predispositions (43), enhancing the overall validity of the findings.

Statistical approach

Description of variables

To rigorously investigate familial predispositions to EDs, all diagnostic categories representing exclusive classifications, including AN, BN, BED, ARFID and OSFED were initially included during initial assessment. Some of the ED subcategories were pooled into broader categories. The AN broad category included both patients who met full diagnostic

criteria for AN, with restrictive eating behavior, binge-purge, and those who did not meet the low-weight criterion (i.e., atypical AN). Similarly, the BN broad category encompassed both patients who met full diagnostic criteria for BN, with some individuals having a low frequence and/or limited duration of illness (i.e., atypical BN). Diagnostic subcategories of BED and ARFID were excluded entirely from the statistical analysis. These decisions were made to ensure data confidentiality and minimize the risk of reidentification due to microdata.

As mentioned, the semi structured interview with the child or adolescent provided information regarding ED psychopathology. The age of onset, which is also the time of inclusion in the study, was defined as the age at time of diagnostic assessment with the EDE-16. The age of onset for AN and atypical AN was defined as the onset of restrictive eating behavior and for BN and atypical BN, as the onset of binge eating, purging and/or weight-controlling behavior. The onset of the first ED behavior of the above-mentioned symptoms was chosen. Body mass index (BMI) was calculated based on height and weight measures, obtained during the medical examination. If these measures were not available, self-reported measures obtained through the EDE-16 were used. Since the study population included children and adolescents, the WHO standards for weight-for-age and gender were used to compare the patient's BMI for diagnostic criteria. The severity of the ED was calculated from the global EDE-16 score. The duration of ED symptoms in months was defined as the difference between the reported date of onset (e.g., regulation in food intake, binge eating or purging behavior) and the date of the diagnostic interview. All the above-mentioned variables were treated as continuous.

Information from the parental interviews was used to define the binary variable as to whether the child or adolescent had any familial predisposition (variable "do you know anyone in your family with an ED yes/no"). The variable "yes" was then used to determine the categorical variables, which were divided into three categories of "first-degree", "second-degree" and "third-degree". First-degree relatives were defined as parents and siblings. It was presumed that first-degree relatives, being more closely related to the child or adolescent both genetically and environmentally, would provide a separate indication of the severity. Second-degree relatives were defined as half-siblings, biological related uncles/aunts and grandparents. Since the obtained journal data did not differentiate between maternal and paternal grandparents, these were pooled together for the statistical analysis. Third-degree relatives were defined as cousins, great-aunts, great-grandparents etc. These categories were used to summarize the number of relatives of each patient, which were classified into broader categories as either having (1) none, (2) one or (3) two or more familial predispositions. Those without any familial predispositions were considered as a reference group for patients with familial predispositions.

Statistical analysis

All statistical analyses were performed in Stata19 (54). For categorical variables, the number of cases and percentages are reported. For continuous variables, the mean and standard deviation are reported, except for highly skewed variables, which were summarized using median, and interquartile range [p25, p75]. The association between number of familial

predispositions, and the age of onset, and the EDE-16 global score and the duration of symptoms in months was investigated using linear regression. To handle deviations from the model assumptions (i.e., linearity, normality of residuals and no heteroskedasticity), all mean differences were calculated by the Hubert/White sandwich estimator to robustly calculate the standard error. A sensitivity analysis was performed to test the robustness of the results, in relation to grandparent variables, which had a determining role for the categorization of patients with an ED. Results with p-values below 0.05 are considered statistically significant.

Results

A total of 282 children and adolescents (91.92% females and 8.08% males) and their parents were assessed and included in the study. **Table 1** presents the characteristics of the study population divided by patients without any familial predisposition and patients

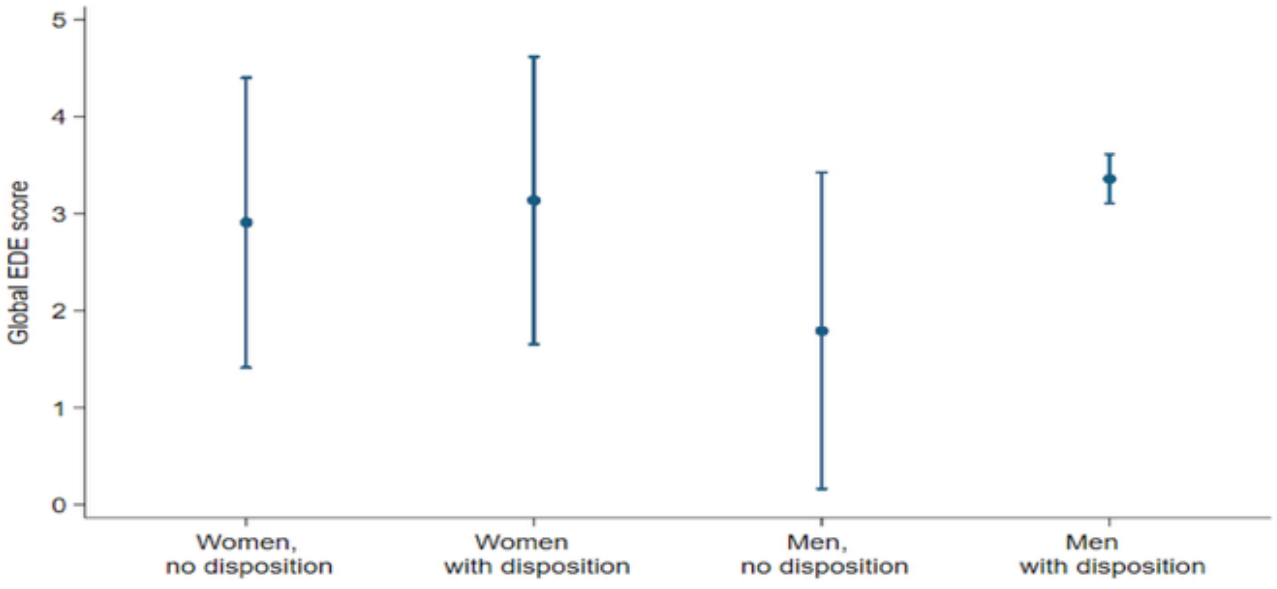
Table 1 Characteristics of the study population

	No disposition			Any disposition		
			n			N
Global EDE score	2.82	(1.53)	197	3.15	(1.44)	84
BMI	17.51	(2.91)	174	18.41	(3.10)	76
Age of onset	13.57	(2.21)	176	13.60	(1.98)	78
Duration of symptoms in months	14.00	[7.00, 28.00]	163	17.00	[8.00, 29.00]	71
Gender						
Female	182	91.92%	198	79	94.05%	84
Male	16	8.08%	198	5	5.95%	84
AN Broad	72	71.29%	101	47	75.81%	62
BN Broad	29	28.71%	101	15	24.19%	62
Number of relatives with disposition						
0	198	100.00%	198	0	0.00%	84
1	0	0.00%	198	61	72.62%	84
2+	0	0.00%	198	23	27.38%	84
First-degree relatives with disposition						
No	198	100%	198	30	36.14%	83
Yes	0	0.00%	198	53	63.86%	83
Second-degree relatives with disposition						
No	198	100.00%	198	61	72.62%	84
Yes	0	0.00%	198	23	27.38%	84
Third-degree relatives with disposition						
No	198	100.00%	198	54	64.29%	84
Yes	0	0.00%	198	30	35.71%	84

Numbers are mean (SD), median and [p25, p75] or frequency and percentage as appropriate

with familial ED predispositions. Seventy-nine females (94.05%) and five males (5.95%) had any familial predisposition to an ED, corresponding to approximately 30% had a familial predisposition to an ED (N = 84). Forty-seven (75.81%) patients had familial predispositions in the AN broad category, and 15 (24.19%) patients had familial predispositions in the BN broad category. Sixty-one (72.62%) patients had at least one familial predisposition, while 23 (27.38%) had two or more familial predispositions. Among patients with any familial predisposition, 53 (63.68%) were of first-degree, 23 (27.38%) were of second-degree, while 30 (35.71%) were of third-degree. As to the degree of relatives, data could not support differentiating between genders, and fewer than five patients reported that both parents were affected by an ED. Most of the included patients of the sample were children and adolescents, with 254 patients aged between 10 and 17 years (90%), while 28 patients (10%) were 18 years or above. Mean age at time of diagnosis among those with familial predispositions were 13.60 years (SD = 1.98) spanning just above 10 years and below 30 years old of age. The BMI of those with familial predisposition was 18.41 (SD = 3.10), which was slightly higher than the BMI reported among those without any familial predisposition of 17.51 (SD = 2.91). The global mean EDE score was higher among those with any familial predisposition of 3.15 (SD = 1.44) compared to those without familial predisposition 2.82 (SD = 1.53), while the median duration of illness at time of diagnosis was 17 months [8.00, 29.00]. Among both groups, some patients had demonstrated symptoms for a few months and others for several years, before receiving a formal diagnosis. Children and adolescents were compared in relation to differences in the global EDE between genders, from mean scores and standard deviation (**Figure 1)**. Females without any familial predisposition had a global EDE mean score of 2.91 (SD = 1.50), while females with any familial predisposition had a global EDE score of 3.14 (SD = 1.48). Males without any familial predisposition had a global EDE mean score of 1.79 (SD = 1.63), which was lower than both female groups, while males with familial predisposition had a global EDE mean score of 3.36 (SD = 0.25), suggesting that males with a familial predisposition present with a greater

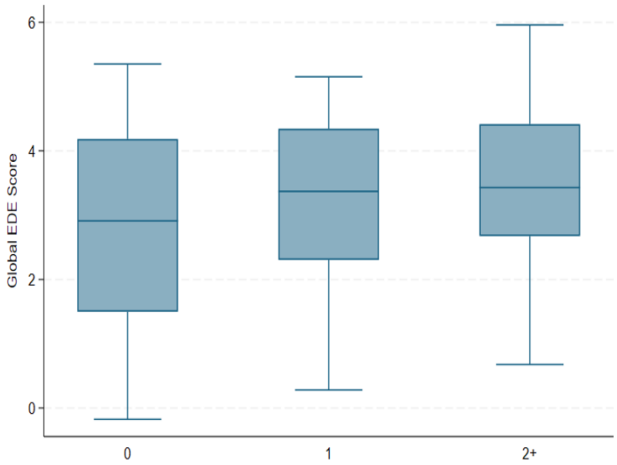
Figure 1. *Global EDE score among females with and without familial predisposition and males with and without familial predisposition. Interpretation for males should be made with caution, due to the limited number of male patients.*



severity, when compared to males without any familial predisposition.

The global EDE score between patients without, and with one or with two or more familial predisposition, did not reveal any statistical significance (**table 2)**. The mean difference was 0.25 (95%CI [-0.17 to 0.67]) between not having any familial predisposition and having one familial predisposition. Moreover, there was a mean difference between not having a familial predisposition and having two or more familial predispositions of 0.56 (95%CI [-0.07 to 1.17]). This finding indicates that patients with two or more affected relatives, could score up to 1.17 points higher on the EDE-16, compared to patients without any familial predisposition. **Figure 2** illustrates this distribution and the tendency of patients with two or more relatives having a greater clinical severity, than those without any familial predisposition. Additionally, those with two or more relatives tended to have a greater clustering of EDE scores at the upper interquartile range, compared to those with less and without any familial predisposition. Furthermore, the age of onset among patients with two or more familial predispositions had a mean difference of

Figure 2. *Differences between global EDE score and having no, one or two or more familial predisposition*



0.46 years lower compared to patients without any familial predisposition (95%CI [-1.43, 0.50]). There was a mean difference of 5.45 months in duration of symptoms, compared to those without any familial predisposition (95%CI [-5.19, 16.08]). However, the wide confidence intervals indicate a high degree of uncertainty.

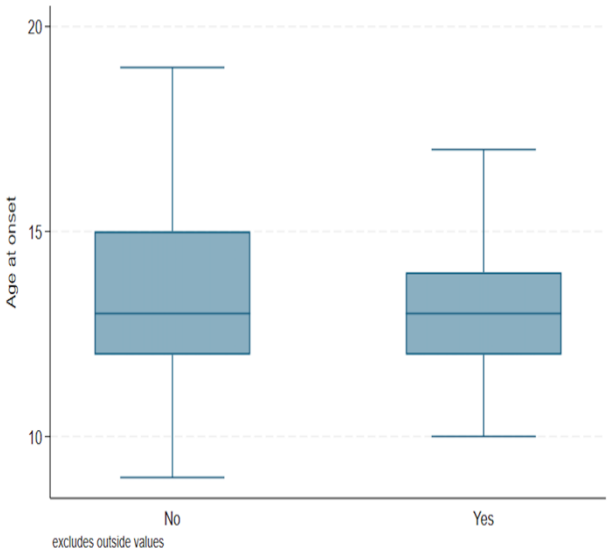
To prove the hypothesis that having a closer degree of relatedness would be associated with an earlier onset and greater clinical severity, a sub analysis of first-degree relatives was conducted (**Table 3)**. Patients with familial predispositions among first-degree relatives was

Table 2 Linear regression

	Mean difference	95% CI	p-value
Global EDE score			
One relative	0.25	[-0.17, 0.67]	0.242
Two or more relatives	0.55	[-0.07, 1.17]	0.083
Age of onset			
One relative	0.21	[-0.39, 0.80]	0.493
Two or more relatives	-0.47	[-1.43, 0.50]	0.340
Duration of symptoms in months			
One relative	0.21	[-5.78, 6.21]	0.944
Two or more relatives	5.45	[-5.19, 16.08]	0.314

Association between EDE global score, age of onset and duration of symptoms for individuals with one relative, two or more relatives compared to individuals without any familial predisposition

Figure 3. *Difference between the age of onset and children and adolescents without and with familial predispositon in first-degree relatives*



compared to those without any familial predisposition and showed a small increase in the global EDE score, with a mean difference of 0.28 (95%CI [-0.16, 0.27]). Additionally, a mean difference in age of onset of -0.13 years (95% CI: -0.72, 0.47), and a symptom duration of 0.21 months (95%CI [-5.78, 6.21]) was found. However, none of these findings had any statistical significance and the wide confidence intervals prevent any clear findings, regarding the direction. The age of onset among individuals with first-degree relatives, are illustrated in **Figure 3.** Although patients with no familial predisposition and those with any familial predisposition, had a similar overall distribution, patients with familial predispositions in first-degree relatives had a narrower interquartile range, as compared to patients without any familial predisposition. This suggests a clustered, perhaps younger age distribution in this group, possibly reflecting an earlier onset or earlier referral among those with affected first-degree relatives, compared to those without any familial predisposition. However, no clear association can be made. Patients with affected first-degree relatives had a mean difference of 3.55 months (95% CI: -3.35, 10.45), which compared to patients with two or more affected relatives was lower. The overall findings did not change from the sensitivity analyses (**Table 4)** although reaching statistical significance in the EDE global score. Individuals with two or more familial predispositions ($p < 0.5$), had a mean difference of 0.65 (95% CI: 0.04, 1.26, $p = 0.038$), suggesting that the effect is robust regarding the model specification, supporting the notion of a greater illness severity among this group, this is unlikely to be due to random error effects.

Discussion

The aim of this retrospective cross-sectional study was to assess the prevalence and impact of familial predispositions among children and adolescents with an ED. Approximately 30% had any familial predisposition to an ED, with 63.86% being of first-degree, 27.38% being of second-degree, and 35.71% being of third-degree. These findings align with most other family studies, reporting a prevalence between 10% and 20% or above, with the vast majority being of first-degree relatives (43). However, the high prevalence of familial predispositions

Table 3 Subanalysis of first-degree relatives

	Mean difference	95% CI	p-value	N
Global EDE score	0.28	[-0.16, 0.72]	0.209	250
Age of onset	-0.13	[-0.72, 0.47]	0.672	226
Duration of symptoms in months	3.55	[-3.35, 10.45]	0.312	211

Association between EDE global score, age of onset and duration of symptoms for any first-degree relatives with familial predisposition, as compared to no familial predisposition. Please note, that those with relatives of second and third degree have been removed.

Table 4 Sensitivity analysis on grandparent disposition

	Mean difference	95% CI	p-value
Global EDE score			
One relative	0.30	[-0.12, 0.71]	0.164
Two or more relatives	0.65	[0.04, 1.26]	0.038
Age of onset			
One relative	0.24	[-0.36, 0.84]	0.434
Two or more relatives	-0.47	[-1.43, 0.50]	0.340
Duration of symptoms in months			
One relative	0.21	[-5.78, 6.21]	0.944
Two or more relatives	5.45	[-5.19, 16.08]	0.314

Association between EDE global score, age of onset and duration of symptoms for individuals with one relative, two or more relatives compared to individuals without any familial predisposition

found in this study is to some extent exceeding prevalence estimates found in other studies (17,18,21). This may be explained by several methodological differences. One explanation may be that all patients in the study population were included regardless of age and gender. This contrasts with most other studies of familial predispositions, which have tended to focus more on adult populations and females (43). Another explanation may be, that the clinical diagnosis of relatives was based on direct interviews with the parents. This may have improved the detection of subclinical or undiagnosed cases among relatives, thus revealing a higher prevalence compared to other studies, as some studies using methods such as self-reports, chart reviews and registers have not found any associations of familial predispositions (55). Thus, the absence, or near absence, of familial predispositions in two prior studies (56,57) is likely to be the results of small study populations, not being able to detect familial predisposition with enough statistical power, supporting the notion of having a representative sample size and an appropriate data collection method, when assessing a clinical population with EDs. Thus, the large number of children and adolescents, and their relatives, included in this study, coupled with semi-structured interview data obtained directly from the parents, permitted a more accurate and comprehensive investigation of familial predispositions among children and adolescents with an ED enhancing the overall validity and reliability of the findings.

Some studies have suggested that EDs cluster within families, not only in the form of full syndromes, but also as milder subclinical variants (16), supporting the notion that these disorders may exist along a continuum, where familial predispositions may influence, not only the likelihood of developing an ED, but also the clinical severity of these disorders. From the findings within this study, exclusive diagnostic categories were included during assessment; however, due to ethical concerns, microdata could not be included, and as a result, only individuals diagnosed with the AN broad subcategory and BN broad subcategory were examined. In accordance with other findings within the literature (43), there was a higher prevalence of the AN broad subcategory (75.81%) as compared to the BN broad subcategory (24.19%). This lower prevalence in the BN broad subcategory may be explained by the

later onset of BN (i.e., young adulthood) as compared to AN (i.e., early childhood and adolescence). Thus, children and adolescents with AN and their relatives may have been more available at the specialized hospital unit.

The hypothesis that familial predispositions are associated with an earlier age of onset or greater clinical severity, could not be supported with sufficient degree of confidence. However, a tendency, towards having two or more relatives with an ED and greater clinical severity based on the global EDE score (95% CI: -0.07, 1.17) was found, although not statistically significant, but a clinical significance. The findings and methods used within this study, did not allow for causal inferences to be made, regarding the role of genetic and environmental influences on familial predispositions. However, this finding could potentially, to some extent, be explained in accordance with the multifactorial model of EDs (9). First, if one were to focus exclusively on individual biological factors such finding could indicate that a genetic vulnerability to the development of EDs is influenced by the number of affected relatives, whereas those with multiple familial predispositions may inherit a greater predisposition towards more severe psychopathology. Second, it could also be presumed that the presence of several EDs among family members, especially if these are of first-degree, who share the same home environment with the child or adolescent, may act as either an individual psychological or as a perpetuating factor (i.e., family dynamics, relationship with eating, weight and shape). This could potentially create less adaptive coping models during development, influencing the clinical presentation and severity of the ED. Finally, it is interesting, that children and adolescents with two or more familial predispositions had broader confidence intervals for symptom duration (95% CI: -5.19, 16.08) compared to those with only one familial predisposition (95% CI: -5.78, 6.12), which firstly, and most likely, reflects differences in sample sizes of the subgroups and greater heterogeneity, as compared to those without or with one familial predisposition. Another explanation for this finding, although even more speculative, is that if there is a stronger underlying genetic risk among those with multiple affected family members, this impact may not be fully recognized or underestimated within families, hence help-seeking may be delayed, potentially resulting in longer symptom durations before diagnosis, which may result in a greater clinical severity. However, it is also interesting, that children and adolescents with first-degree relatives, had a slightly, although insignificant, earlier age of onset, with a mean difference of 0.13 years (95%CI [-072, 0.47]) compared to those without any familial predisposition. Since the study population included approximately 90% of children and adolescents under the age of 17 years, and children and adolescents are generally referred and diagnosed at an early stage, compared to adult populations, due to parental involvement and interdisciplinary efforts (i.e., schools) (58), this could, although speculative, also have led to a shorter symptom duration among the younger subgroups, hence influence an earlier age of onset. Young adults, although only a few were included in this study, have been reported to more often experiencing longer delays, compared to children and adolescents, before initial assessment and diagnosis (59). The inclusion of these individuals may therefore have added variability to the data. Thus, differences in developmental stages and age, may have reduced the ability to detect significant effects.

It was also hypothesized that there would be no gender differences in the study population. This hypothesis could not be sufficiently statistically tested due to the unequal representation of males and females with familial predispositions. However, although results should be interpreted with caution, gender differences may be evident to some extent. Thus, males with any familial predisposition compared to males without any familial predisposition, had a greater severity on the EDE global score. As such, the null hypothesis cannot be confirmed, and support for the alternative hypothesis cannot be confirmed either. However, this aspect requires further investigation, potentially with a larger subgroup of males. The high prevalence of familial predispositions among females (94.05% versus 91.92%) compared to males (5.95% versus 8.08%) is, nevertheless, consistent with most previous studies, differentiating between gender among children and adolescents (18,60,61). In comparison to several other studies, which excluded male patients and male relatives due to small samples, this present study was able to include males, enhancing the generalizability of the findings. Previous research has shown that despite similar duration of illness and familial predispositions to EDs, males are more often seen referred to inpatient care by external or internal providers, rather than seeking specialized treatment themselves (55). Although, all males were included in this study, this likely reflects an underrepresentation of males in general in clinical settings. Female relatives of males diagnosed with an ED, in a study by Strober (16), had nearly double as many affected relatives, as compared to female relatives of females with an ED (6.1% vs. 3.4%). This might implicate, that a greater loading of genes or adverse environmental effects are required for EDs to be expressed in males, compared to females. Research has also shown, that males in general experience diagnostic delays, due to greater self-stigma of seeking psychological help, thus underdiagnosed more often than females (62). Since the study population is based on children and adolescents, alongside their relatives, this could therefore potentially have influenced the number of males included in the study. Thus, the number of males included is likely to reflect true referral and treatment patterns at the specialized hospital unit, rather than selection bias in the study, as all referred male patients were included during the study period.

The distinction between genetic and environmental factors is not dichotomous. It is more likely, a combination of a complex interplay between which should be considered when interpreting the results. It is also important to note, that many individuals with a familial predisposition do not necessarily experience greater illness severity, and likewise not all individuals with a familial predisposition will necessarily develop an ED. Based on these considerations, it would be relevant for future research to examine whether the number of familial predispositions is differentially associated with the age of onset across specific age, perhaps narrower age groups, to indicate whether the familial predispositions may be associated with an earlier onset of EDs. Furthermore, it would be relevant to investigate protective factors involved in the development of EDs, particularly among individuals with a known familial predisposition.

Strengths and limitations

There are both strengths and limitations in this retrospective cross-sectional study, which should be considered. One of the strengths is the inclusion of a representative number of unique data from children and adolescents, and

their relatives who were assessed for an ED, which have made it possible to examine a highly vulnerable patient group. Additionally, the use of an exclusive diagnostic classification system and a validated and reliable assessment tool allowed for a rigorous and comprehensive investigation of the proposed hypotheses. Besides this, all referred children and adolescents were included, regardless of age, gender and specific ED diagnosis. However, some limitations should be mentioned. The lack of a control group matched for age and gender composition to the study population poses a challenge when interpreting the prevalence. However, since the risk of EDs in the general population is relatively low, it is unlikely that the use of comparison subjects would have altered the results substantially. Another limitation in relation to the inclusion of children and adolescents, selected from a special ED treatment unit, is that this may represent a specific subgroup of individuals, not necessarily generalizable to other subgroups. However, in the absence of a systematic ascertainment of individuals from the general population, the degree of such bias remains unknown. Thus, this was addressed through incorporating other available data from the background population and other research findings among this population. Furthermore, patient reported data may, which always is the case in retrospective studies, create a risk of recall bias, due to the accuracy of lifetime diagnoses being dependent on the patients' abilities to recall earlier experienced symptoms. This was addressed by including information from parents to ensure that familial predispositions were reported as accurately and as closely to the family member as possible. Lastly, only biologically assigned gender were included in this study. However, it is important to emphasize that other gender-minorities and gender-diverse individuals also constitutes a relevant, although small, proportion among ED populations (63). Thus, this area of interest is relevant for future research.

Conclusions

In conclusion, the study found that approximately 30% of all children and adolescents assessed with an ED, had a familial predisposition. This finding supports previous studies that EDs transmit within families. Furthermore, a higher prevalence of familial predispositions among first-degree relatives, as compared to second-, and third-degree relatives, both in relation to the background population, and other studies was found. No significant associations could be found regarding familial predispositions, and the age of onset, and the clinical severity. However, a tendency towards having two or more affected relatives and higher EDE global scores, seems prevalent to an extent that makes it clinically relevant to address, when developing early detection and prevention programs for children and adolescents with EDs. The findings of this study did not provide support for the hypothesis regarding that no gender differences would be found due to the limited number of males with familial predispositions, which was insufficient to detect such differences. However, males with familial predispositions had higher EDE goal scores compared to males without familial predispositions, indicating that there may be a greater clinical severity among this group. Thus, it would be relevant for future research to investigate this aspect further, to provide a more balanced gender representation.

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7. Discussion

Following section is going to discuss the key findings (cf. article) in relation to the multifactorial framework and state of the art review of EDs, as well as the strengths and limitations of this thesis.

This thesis aimed to investigate the prevalence and impact of familial predispositions among children and adolescents with EDs. It was hypothesized that a greater illness severity and earlier age of onset would be associated with a greater number of familial predispositions and/or a greater degree of relatedness (cf. article). The findings did, to some extent, support this hypothesis with about 30% of the total study population having ED-affected first-, second-, and third-degree relatives (cf. article). The method used within this thesis, allowed for a representative number of unique data from a highly vulnerable patient group to be examined. The inclusion of parents of children and adolescents provided valuable insights into the ED prevalence, enhancing the ecological validity of the overall findings. Although previous research have shown that first-degree relatives have a greater lifetime risk of EDs (Strober et al., 2000), no statistically significant association could be found between the degree of familial predispositions and ED psychopathology among children and adolescents with familial predispositions. However, a tendency between having multiple ED-affected relatives and a higher EDE global score was found (cf. article), suggesting that an increased genetic load may result in more severe clinical outcomes. Nonetheless, many individuals without any known family history of an ED are still being diagnosed with an ED, and individuals with a family history of an ED may not necessarily develop an ED. These findings suggest that the impact of familial predispositions may be limited to specific high-risk groups in which and ED may, or may not, develop. For children and adolescents with a familial predisposition who do develop an ED, several biological, genetic, environmental and familial risk factors have been proposed as contributing to the etiology of these disorders (Garner and Garfinkel, 1980). Gene-environment (GxE) interactions and correlations may be potential explanatory models in this aspect, extending the multifactorial understanding of EDs, as to how inherited risk may be expressed in the presence of certain environmental risk or protective factors (Bulik., 2005; Klump et al., 2007). Although interpretations of these models should be done with caution, as biological underpinnings of EDs and their causative role remains highly speculative, the GxE interaction model may offer some explanations as to how individuals with a greater familial load are more vulnerable to environmental risk factors. According

to this model, individuals are differentially vulnerable to weight-related behavior such as dieting, because of differences in their genotype. For instance, individuals with a lesser genetic load may try dieting, find it unpleasant and return to normal eating habits, while those with a higher genetic load may find dieting rewarding or reinforcing, contributing to a greater risk of EDs (Bulik, 2005, p. 337). In addition, findings from research have suggested, that EDs may be transmitted from parents to their children due to either indirect effects such as the parents' preoccupation with food, shape or weight, or from direct effects such as the influences of food choices that parents make (Patel et al., 2002). This potentially creates a high-risk environment among individuals whose specific genotype, biological and psychological responses, may be genetically vulnerable to the development of an ED. Furthermore, since EDs historically have been conceptualized as predominantly affecting young Western females, most research have been conducted among these populations. However, EDs have gradually been reported increasing in non-Western countries, due to the increasing globalization and exposure to Western media (Makino et al., 2004). This is an interesting aspect, as the prevalence of EDs in the general population is relatively low, thus, GxE interactions may potentially explain, how individuals with a genetic vulnerability in non-Western cultures gradually may have become more widely exposed to Western cultural ideals, increasing the vulnerability to disorder onset. Thus, previous protective cultural contexts in non-Western cultures may have become risk-enhancing, revealing genetic vulnerabilities not previously expressed or underestimated. However, more research in this area of interest is needed as eating, weight and body image concerns present differently in different cultures (Makino et al., 2004), making the theoretical influence of familial predispositions uncertain.

It was furthermore hypothesized that no gender differences would be found in this thesis, however males with familial predispositions had a greater clinical severity of EDs, compared to males without familial predispositions (cf. article), which may be of clinical relevance. Most research within the field of familial predispositions of EDs have found, that children of mothers with EDs are more likely to develop ED themselves, with less research attention focusing on the relationship between fathers and their children (Bould, Sovio, et al., 2015; Kothari et al., 2013). Studies examining the effects on maternal EDs have shown, that mothers with an ED, have a negative impact on the cognitive and psychological development of their children (Martini et al., 2020; Micali et al., 2015). Accumulated evidence have suggested, that paternal EDs may contribute to similar risks in children, with some studies indicating gender-specific patterns in the transmission of disordered ED behavior in early childhood (Lydecker & Grilo, 2016). For instance, high

levels of concerns with weight and negative commentary about weight from fathers, have been shown to be a significant predictor of the onset of binge eating among adolescents (A. E. Field et al., 2008, p. 5). Moreover, psychosocial factors in relation to gender, such as peer interactions, have been accounted for as influencing heritability through active GxE correlations, where an individual, who are predisposed to an ED, seeks out an environment, which enhances pre-existing genetic vulnerabilities, most commonly recognised in weight-oriented or high-achievement sports (Klump et al., 2007; Trace et al., 2013). However, in a study conducted by Vo et al. (2016) which included a total of 33 outpatients males, only 35.4% had a history of sport participation. Although the study had a relatively small sample size, this propose an interesting aspect, as to whether similar patterns would emerge in a larger and more diverse study population, such as among inpatient males, as familial predisposition may be enhanced within those settings (Meijsen et al., 2024).

It has been suggested, that nonspecific early responses among children and adolescents, may be associated with familial psychopathology, as parental mental illness can be a major stressor for the family (Bould, Koupil, et al., 2015), and affect family functioning (O'Neil et al., 2010). Evidence from twin studies have suggested, that the majority of environmental variance of EDs may be influenced by non-shared environmental factors (Bulik., 2005). However, one of the limitations of twin studies could be short follow-up periods, as some cases that are not concordant, may turn to be concordant later. Small sample sizes is another limitation, which may prohibit researchers to study wide ranges of non-shared and shared environmental effects, which potentially could overestimate the heritability. Thus, genetic differences may provide mechanisms by which non-shared environment exerts its influence. Although adoption studies have been scarce within this area of research, existing findings have demonstrated substantial genetic effects in EDs, similar to those found in twin studies (Klump et al., 2009), supporting that genetic and non-shared environmental factors are of significant role in the etiology of EDs. Additionally, when considering the specific genetic variations thought to contribute to the increased familial ED risk, genetic associations between EDs and other psychiatric conditions have been reported. Familial high-risk studies have in particular, been investigated within the field of psychosis, where it with relatively high success, have been possible to identify children at risk of developing their first psychotic episode (Ellersgaard et al., 2018). However, within the field of EDs there have been inconsistency in the findings, due to the complexity of these disorders. Psychiatric comorbidity have been reported higher among individuals with EDs than the general population (Momen et al., 2022). Although proposed as a non-specific risk factor for the onset of these disorders (Bakalar

et al., 2015), psychiatric comorbidity have been associated with more severe ED symptomatology (Spindler & Milos, 2007), suggesting that some genes may predispose the individual to more than one psychiatric disorder. High prevalence rates of anxiety disorders, attention deficit/hyperactivity disorders and mood disorders among children and adolescents with an ED have been reported (Convertino & Blashill, 2022; Sundhedsstyrelsen, 2005, p. 29). Notably, elevated rates of depressive disorders, anxiety disorders and certain personality traits have been reported among first-degree relatives of individuals with an ED (Bould, Koupil, et al., 2015, p. 201), indicating that EDs might share transmitted liabilities with other psychiatric disorders within families, emphasizing that EDs rarely occur isolated. It has been suggested that comorbidity reinforces the maintenance of ED psychopathology, from the creation of self-perpetuating circles (Spindler & Milos, 2007, p. 371). For instance, an anxious patient may engage in binge-eating to encounter negative emotions, which might initially serve as a coping strategy to reduce anxiety, but the resulting distress, such as shame and stigma, enhances the anxiety, creating cognitive distortions regarding perception of self and the environment (Spindler & Milos, 2007, p. 371ff). Furthermore, family studies have suggested that children and adolescents, and their relatives with AN, display elevated rates of obsessive-compulsive personality disorder (OCPD) (Lilenfeld et al., 1998), indicating that characteristics such as perfectionism, may be associated with an increased vulnerability to the development of AN. Consequently, familial predispositions and differential outcomes in relation to ED psychopathology may result from genetic differences, environmental differences, or most likely, a combination of the two. It is important to emphasize that none of the epidemiological or neurobiological findings in the literature, have been established beyond doubt, and their causative role remains speculative. Moreover, the cross-sectional design does not allow to determine causality of the variables assessed, since both exposure and outcome is measured simultaneously. Thus, these results are within the framework of evidence-based medicine, often considered less robust, requiring further validation (Juul, 2017, p. 213f). Future research could expand these results employing prospective longitudinal designs, addressing the potential mediating role of familial predispositions in the etiology and clinical course of EDs. Future research should therefore investigate familial predispositions further, in relation to gender, culture, personality, cognition and other relevant factors, to gain a comprehensive understanding of the etiology EDs.

8. Conclusion

Family, twin and molecular genetic studies have emphasized that EDs transmit within families, indicating a strong genetic component in the development of these disorders. The method used within this thesis, enabled the examination of a representative unique amount of data from a highly vulnerable population of children and adolescents with EDs. From the inclusion of parents during assessment reliable estimates of the prevalence were provided, reducing the likelihood of bias or underreporting, enhancing the overall reliability and validity of the findings. The findings indicated that approximately 30% of the patients with an ED had an ED-affected relative, of whom 63.68% were of first-degree, 27.38% were of second-degree and 35.71% were of third-degree. A higher EDE global mean score was found among children and adolescents with more than two ED-affected relatives. However, no statistical associations were found between the degree of relatives, the age of onset and global EDE score, indicating that hypothesis 1 could only be partially confirmed. There was an observable tendency, indicating that males with familial predispositions had a higher global EDE mean score, compared to males without any familial predisposition. However, no comparisons could be made between females and males, due to the limited number of males with familial predispositions, thus, hypothesis 2 could therefore not be supported, nor denied. Thus, these findings indicate that the inclusion of a larger subgroup of males would be highly relevant for future research. Although it is not possible to determine what familial predispositions that are particularly potent for which individuals, with what specific genetic vulnerability to an ED, familial predispositions may in combination with environmental factors, increases the risk of developing an ED. This supports a multifactorial framework in which the combination of both genes and the environment, may act as predisposing, precipating and perpetuating of an ED.

In conclusion, a higher genetic load of familial predispositions may contribute to the clinical manifestations of an ED among children and adolescents, emphasizing the importance of being aware of familial predispositions in the assessment, early detection and prevention of EDs.

References used in the article:

1. Pastore M, Indrio F, Bali D, Vural M, Giardino I, Pettoello-Mantovani M. Alarming Increase of Eating Disorders in Children and Adolescents. J Pediatr. 2023 Dec;263:1–4.
2. Smink FRE, Van Hoeken D, Hoek HW. Epidemiology of Eating Disorders: Incidence, Prevalence and Mortality Rates. Curr Psychiatry Rep. 2012 Aug;14(4):406–14.
3. Treasure J, Duarte TA, Schmidt U. Eating disorders. The Lancet. 2020 Mar;395(10227):899–911.
4. Kjeldbjerg ML, Clausen L. Prevalence of binge-eating disorder among children and adolescents: a systematic review and meta-analysis. Eur Child Adolesc Psychiatry. 2023 Apr;32(4):549–74.
5. Sanchez-Cerezo J, Nagularaj L, Gledhill J, Nicholls D. What do we know about the epidemiology of avoidant/restrictive food intake disorder in children and adolescents? A systematic review of the literature. Eur Eat Disord Rev J Eat Disord Assoc. 2023 Mar;31(2):226–46.
6. Van Buuren L, Fleming CAK, Hay P, Bussey K, Trompeter N, Lonergan A, et al. The prevalence and burden of avoidant/restrictive food intake disorder (ARFID) in a general adolescent population. J Eat Disord. 2023 Jun 29;11(1):1–10.
7. Van Hoeken D, Hoek HW. Review of the burden of eating disorders: mortality, disability, costs, quality of life, and family burden. Curr Opin Psychiatry. 2020 Nov;33(6):521–7.
8. Stice E, Johnson S, Turgon R. Eating Disorder Prevention. Psychiatr Clin North Am. 2019 Jun;42(2):309–18.
9. Garner DM, Garfinkel PE. Socio-cultural factors in the development of anorexia nervosa. Psychol Med. 1980 Nov;10(4):647–56.
10. Fairburn CG. Risk Factors for Bulimia Nervosa: A Community-Based Case-Control Study. Arch Gen Psychiatry. 1997 Jun 1;54(6):509–17.
11. Fairburn CG, Doll HA, Welch SL, Hay PJ, Davies BA, O'Connor ME. Risk Factors for Binge Eating Disorder: A Community-Based, Case-Control Study. Arch Gen Psychiatry. 1998 May 1;55(5):425–32.
12. Fairburn CG, Cooper Z, Doll HA, Welch SL. Risk Factors for Anorexia Nervosa: Three Integrated Case-Control Comparisons. Arch Gen Psychiatry. 1999 May 1;56(5):468–76.
13. Hudson JI, Pope HG, Jonas JM, Yurgelun-Todd D, Frankenburg FR. A controlled family history study of bulimia. Psychol Med. 1987 Nov;17(4):883–90.
14. Kassett JA, Gershon ES, Maxwell ME, Guroff JJ, Kazuba DM, Smith AL, et al. Psychiatric disorders in the first-degree relatives of probands with bulimia nervosa. Am J Psychiatry. 1989 Nov 1;146(11):1468–71.

15. Kendler KS, MacLean C, Neale M, Kessler R, Heath A, Eaves L. The genetic epidemiology of bulimia nervosa. Am J Psychiatry. 1991 Dec;148(12):1627–37.

16. Strober M, Freeman R, Lampert C, Diamond J, Kaye W. Controlled Family Study of Anorexia Nervosa and Bulimia Nervosa: Evidence of Shared Liability and Transmission of Partial Syndromes. Am J Psychiatry. 2000 Mar 1;157(3):393–401.

17. Gershon SE, Schreiber JL, Hamovit JR, Kaye. Clinical findings in patients with anorexia nervosa and affective illness in their relatives. Am J Psychiatry. 1984 Nov 1;141(11):1419–22.

18. Strober M, Morrell W, Burroughs J, Salkin B, Jacobs C. A controlled family study of anorexia nervosa. J Psychiatr Res. 1985;19(2–3):239–46.

19. Crisp AH, Toms DA. Primary Anorexia Nervosa or Weight Phobia in the Male: Report on 13 Cases. BMJ. 1972 Feb 5;1(5796):334–8.

20. Strober M, Freeman R, Lampert C, Diamond J, Kaye W. Males with anorexia nervosa: A controlled study of eating disorders in first-degree relatives. Int J Eat Disord. 2001 Apr;29(3):263–9.

21. Kuntz B, Groze V, Yates WR. Bulimia: A Systemic Family History Perspective. Fam Soc J Contemp Soc Serv. 1992 Dec;73(10):604–12.

22. Stein D, Lilenfeld LR, Plotnicov K, Pollice C, Rao R, Strober M, et al. Familial aggregation of eating disorders: Results from a controlled family study of bulimia nervosa. Int J Eat Disord. 1999 Sep;26(2):211–5.

23. Lilenfeld, Ringham R, Kalarchian MA, Marcus MD. A family history study of binge-eating disorder. Compr Psychiatry. 2008 May;49(3):247–54.

24. Hudson JI, Lalonde JK, Berry JM, Pindyck LJ, Bulik CM, Crow SJ, et al. Binge-Eating Disorder as a Distinct Familial Phenotype in Obese Individuals. Arch Gen Psychiatry. 2006 Mar 1;63(3):313–9.

25. Lee YH, Abbott DW, Seim H, Crosby RD, Monson N, Burgard M, et al. Eating disorders and psychiatric disorders in the first-degree relatives of obese probands with binge eating disorder and obese non-binge eating disorder controls. Int J Eat Disord. 1999 Nov;26(3):322–32.

26. Bertrand V, Tavolacci M, Bargiacchi A, Leblanc V, Déchelotte P, Stordeur C, et al. Analysis of feeding and eating disorders in 191 children according to psychiatric or gastroenterological recruitment: The PEDIAFED cohort study. Eur Eat Disord Rev. 2024 May;32(3):589–605.

27. Hosman CMH, Van Doesum KTM, Van Santvoort F. Prevention of emotional problems and psychiatric risks in children of parents with a mental illness in the Netherlands: I. The scientific basis to a comprehensive approach. Aust E-J Adv Ment Health. 2009 Jan;8(3):250–63.

28. Field AE, Javaras KM, Aneja P, Kitos N, Camargo CA, Taylor CB, et al. Family, Peer, and Media Predictors of Becoming Eating Disordered. Arch Pediatr Adolesc Med. 2008 Jun 2;162(6):574–9.

29. Bould H, Sovio U, Koupil I, Dalman C, Micali N, Lewis G, et al. Do eating disorders in parents predict eating disorders in children? Evidence from a S wedish cohort. Acta Psychiatr Scand. 2015 Jul;132(1):51–9.

30. Kothari R, Solmi F, Treasure J, Micali N. The neuropsychological profile of children at high risk of developing an eating disorder. Psychol Med. 2013 Jul;43(7):1543–54.

31. Martini MG, Barona-Martinez M, Micali N. Eating disorders mothers and their children: a systematic review of the literature. Arch Womens Ment Health. 2020 Aug;23(4):449–67.

32. Cimino S, Cerniglia L, Porreca A, Ballarotto G, Marzilli E, Simonelli A. Impact of parental binge eating disorder: Exploring Children's emotional/behavioral problems and the quality of parent - child feeding interactions. Infant Ment Health J. 2018 Sep;39(5):552–68.

33. Bulik CM, Sullivan PF, Kendler KS. Heritability of binge-eating and broadly defined bulimia nervosa. Biol Psychiatry. 1998 Dec;44(12):1210–8.

34. Klump KL, Miller KB, Keel PK, McGUE M, Iacono WG. Genetic and environmental influences on anorexia nervosa syndromes in a population–based twin sample. Psychol Med. 2001 May;31(4):737–40.

35. Kortegaard LS, Hoerder K, Joergensen J, Gillberg C, Kyvik KO. A preliminary population-based twin study of self-reported eating disorder. Psychol Med. 2001 Feb;31(2):361–5.

36. Wade TD, Bulik CM, Neale M, Kendler KS. Anorexia Nervosa and Major Depression: Shared Genetic and Environmental Risk Factors. Am J Psychiatry. 2000 Mar 1;157(3):469–71.

37. Walters EE, Neale MC, Eaves LJ, Heath AC, Kessler RC, Kendler KS. Bulimia nervosa and major depression: a study of common genetic and environmental factors. Psychol Med. 1992 Aug;22(3):617–22.

38. Walters EE, Neale MC, Eaves LJ, Heath AC, Kessler RC, Kendler KS. Bulimia nervosa: A population-based study of purgers versus nonpurgers. Int J Eat Disord. 1993 Apr;13(3):265–72.

39. Javaras KN, Laird NM, Reichborn-Kjennerud T, Bulik CM, Pope HG, Hudson JI. Familiality and heritability of binge eating disorder: Results of a case-control family study and a twin study. Int J Eat Disord. 2008 Mar;41(2):174–9.

40. Mitchell KS, Neale MC, Bulik CM, Aggen SH, Kendler KS, Mazzeo SE. Binge eating disorder: a symptom-level investigation of genetic and environmental influences on liability. Psychol Med. 2010 Nov;40(11):1899–906.

41. Dinkler L, Taylor MJ, Råstam M, Hadjikhani N, Bulik CM, Lichtenstein P, et al. Association of etiological factors across the extreme end and continuous variation in disordered eating in female Swedish twins. Psychol Med. 2019 Apr;51(5):750–60.

42. Trace SE, Baker JH, Peñas-Lledó E, Bulik CM. The Genetics of Eating Disorders. Annu Rev Clin Psychol. 2013 Mar 28;9(1):589–620.

43. Dissing J, Rasmussen ET., Nilsson KK & Kjaersdam Telléus G. Familial predispostions to Eating Disorders: A Systematic Review and Meta-Analysis. 2024 p. 1–32. Report No.: Submitted.

44. Logue CM, Crowe RR, Bean JA. A family study of anorexia nervosa and bulimia. Compr Psychiatry. 1989;30(2):179–88.

45. Halmi KA. Comorbidity of Psychiatric Diagnoses in Anorexia Nervosa. Arch Gen Psychiatry. 1991 Aug 1;48(8):712–8.

46. Peebles R, Hardy KK, Wilson JL, Lock JD. Are Diagnostic Criteria for Eating Disorders Markers of Medical Severity? Pediatrics. 2010 May 1;125(5):e1193–201.

47. Nicholls D, Hudson L, Mahomed F. Managing anorexia nervosa. Arch Dis Child. 2011 Oct 1;96(10):977–82.

48. Le Grange D, Lock J, Loeb K, Nicholls D. Academy for eating disorders position paper: The role of the family in eating disorders. Int J Eat Disord. 2010 Jan;43(1):1–5.

49. American Psychiatric Association. Feeding and Eating Disorders. In: Diagnostic and Statistical Manual of Mental Disorders [Internet]. Fifth Edition. American Psychiatric Association; 2013 [cited 2024 Nov 25]. p. 329–54. Available from: https://psychiatryonline.org/doi/book/10.1176/appi.books.9780890425596

50. Cooper Z, Cooper PJ, Fairburn CG. The Validity of the Eating Disorder Examination and its Subscales. Br J Psychiatry. 1989 Jun;154(6):807–12.

51. Fairburn CG, Cooper Z, O'Connor M. Eating Disorder Examination (Edition 16.0D). In: Cognitive Behavior Therapy and Eating Disorders. New York: Guilford Press; 2008. p. 1–8.

52. Fairburn CG. Psychotherapy and Bulimia Nervosa: Longer-term Effects of Interpersonal Psychotherapy, Behavior Therapy, and Cognitive Behavior Therapy. Arch Gen Psychiatry. 1993 Jun 1;50(6):419-28.

53. Bryant-Waugh RJ, Cooper PJ, Taylor CL, Lask BD. The use of the eating disorder examination with children: A pilot study. Int J Eat Disord. 1996 May;19(4):391–7.

54. Statacorp. Stata Statistical Software: Release 19. 2025.

55. Matthews A, Gordon K, Kramer R, Lin J, Ziv A. Clinical characteristics of medically hospitalized youth with anorexia nervosa/atypical anorexia nervosa and premorbid overweight/obesity (a). Eat Disord. 2023 May 4;31(3):201–11.

56. Logue CM, Crowe RR, Bean JA. A family study of anorexia nervosa and bulimia. Compr Psychiatry. 1989 Mar;30(2):179–88.

57. Lilenfeld LR, Kaye WH, Greeno CG, Merikangas KR, Plotnicov K, Pollice C, et al. A Controlled Family Study of Anorexia Nervosa and Bulimia Nervosa: Psychiatric Disorders in First-Degree Relatives and Effects of Proband Comorbidity. Arch Gen Psychiatry. 1998 Jul 1;55(7):603-11.

58. Danish Health Authority. Spiseforstyrrelser: Anbefalinger for organisation og behandling. 2005:4-40.

59. Austin A, Flynn M, Richards K, Hodsoll J, Duarte TA, Robinson P, et al. Duration of untreated eating disorder and relationship to outcomes: A systematic review of the literature. Eur Eat Disord Rev. 2021 May;29(3):329–45.

60. Rost S, Kappel V, Salbach H, Schneider N, Pfeiffer E, Lehmkuhl U, et al. Psychiatric Disorders and Personality Styles in Mothers of Female Adolescent Patients with Eating Disorders. Z Für Kinder- Jugendpsychiatrie Psychother. 2017 Sep 1;45(5):361–9.

61. Vo M, Lau J, Rubinstein M. Eating Disorders in Adolescent and Young Adult Males: Presenting Characteristics. J Adolesc Health. 2016 Oct;59(4):397–400.

62. Griffiths S, Mond JM, Li Z, Gunatilake S, Murray SB, Sheffield J, et al. Self-stigma of seeking treatment and being male predict an increased likelihood of having an undiagnosed eating disorder. Int J Eat Disord. 2015 Sep;48(6):775–8.

63. Rasmussen SM, Clausen L, Højgaard AD, Pop ML, Kjeldsen MK, Egedal JM, et al. Transgender and gender-diverse identity in patients with eating disorders: A national cross-sectional study. Eur Eat Disord Rev. 2025 Mar;33(2):239–53.

In total: 655 pages

References used in the framing part:

Academy of Eating Disorders. (2021). *Eating Disorders: A Guide to Medical Care* (4th edition; pp. 1–22).

American Psychiatric Association. (2013). Feeding and Eating Disorders. In *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition, pp. 329–354). American Psychiatric Association. https://doi.org/10.1176/appi.books.9780890425596

Andersen, H. (2006). *Videnskabsteori for de biologiske fag* (1st ed.). Biofolia, 157-179, 221-236.

APA Publications and Communications Board Working Group on Journal Article Reporting Standards. (2008). Reporting standards for research in psychology: Why do we need them? What might they be? *American Psychologist*, *63*(9), 839–851. https://doi.org/10.1037/0003-066X.63.9.839

Austin, A., Flynn, M., Richards, K., Hodsoll, J., Duarte, T. A., Robinson, P., Kelly, J., & Schmidt, U. (2021). Duration of untreated eating disorder and relationship to outcomes: A systematic review of the literature. *European Eating Disorders Review*, *29*(3), 329–345. https://doi.org/10.1002/erv.2745

Bakalar, J. L., Shank, L. M., Vannucci, A., Radin, R. M., & Tanofsky-Kraff, M. (2015). Recent Advances in Developmental and Risk Factor Research on Eating Disorders. *Current Psychiatry Reports*, *17*(6), 10. https://doi.org/10.1007/s11920-015-0585-x

Barakat, S., McLean, S. A., Bryant, E., Le, A., Marks, P., National Eating Disorder Research Consortium, Aouad, P., Barakat, S., Boakes, R., Brennan, L., Bryant, E., Byrne, S., Caldwell, B., Calvert, S., Carroll, B., Castle, D., Caterson, I., Chelius, B., Chiem, L., … Maguire, S. (2023). Risk factors for eating disorders: Findings from a rapid review. *Journal of Eating Disorders*, *11*(1), 8. https://doi.org/10.1186/s40337-022-00717-4

Berrettini, W. (2004). The genetics of eating disorders. *Psychiatry (Edgmont (Pa.: Township))*, *1*(3), 18–25.

Bould, H., Koupil, I., Dalman, C., DeStavola, B., Lewis, G., & Magnusson, C. (2015). Parental mental illness and eating disorders in offspring. *International Journal of Eating Disorders*, *48*(4), 383–391. https://doi.org/10.1002/eat.22325

Bould, H., Sovio, U., Koupil, I., Dalman, C., Micali, N., Lewis, G., & Magnusson, C. (2015). Do eating disorders in parents predict eating disorders in children? Evidence from a Swedish cohort. *Acta Psychiatrica Scandinavica*, *132*(1), 51–59. https://doi.org/10.1111/acps.12389

Bryant-Waugh, R. J., Lask, B. D., Shafran, R. L., & Fosson, A. R. (1992). Do doctors recognise eating disorders in children? *Archives of Disease in Childhood*, *67*(1), 103–105. https://doi.org/10.1136/adc.67.1.103

Bulik., C. M. (2005). Exploring the gene-environment nexus in eating disorders. *Journal of Psychiatry & Neuroscience: JPN*, *30*(5), 335–339.

Bulik, C. M., Kleiman, S. C., & Yilmaz, Z. (2016). Genetic epidemiology of eating disorders. *Current Opinion in Psychiatry*, *29*(6), 383–388. https://doi.org/10.1097/YCO.0000000000000275

Bulik, C. M., Sullivan, P. F., & Kendler, K. S. (1998). Heritability of binge-eating and broadly defined bulimia nervosa. *Biological Psychiatry*, *44*(12), 1210–1218. https://doi.org/10.1016/S0006-3223(98)00280-7

Bulik, C. M., Sullivan, P. F., Tozzi, F., Furberg, H., Lichtenstein, P., & Pedersen, N. L. (2006). Prevalence, Heritability, and Prospective Risk Factors for Anorexia Nervosa. *Archives of General Psychiatry*, *63*(3), 305. https://doi.org/10.1001/archpsyc.63.3.305-12

Bulik, C. M., Yilmaz, Z., & Hardaway, A. (2015). Genetics and epigenetics of eating disorders. *Advances in Genomics and Genetics*, 131-150. https://doi.org/10.2147/AGG.S55776

Campbell, I. C., Mill, J., Uher, R., & Schmidt, U. (2011). Eating disorders, gene–environment interactions and epigenetics. *Neuroscience & Biobehavioral Reviews*, *35*(3), 784–793. https://doi.org/10.1016/j.neubiorev.2010.09.012

Campbell, K., & Peebles, R. (2014). Eating Disorders in Children and Adolescents: State of the Art Review. *Pediatrics*, *134*(3), 582–592. https://doi.org/10.1542/peds.2014-0194

Convertino, A. D., & Blashill, A. J. (2022). Psychiatric comorbidity of eating disorders in children between the ages of 9 and 10. *Journal of Child Psychology and Psychiatry*, *63*(5), 519–526. https://doi.org/10.1111/jcpp.13484

Couturier, J. L., & Lock, J. (2006). Denial and minimization in adolescents with anorexia nervosa. *International Journal of Eating Disorders*, *39*(3), 212–216. https://doi.org/10.1002/eat.20241

Dinkler, L., Taylor, M. J., Råstam, M., Hadjikhani, N., Bulik, C. M., Lichtenstein, P., Gillberg, C., & Lundström, S. (2019). Association of etiological factors across the extreme end and continuous variation in disordered eating in female Swedish twins. *Psychological Medicine*, *51*(5), 750–760. https://doi.org/10.1017/S0033291719003672

Dissing, J., & Rasmussen, E. T. (2025). *Familial predispostions to Eating Disorders: A Systematic Review and Meta-Analysis* (Submitted; pp. 1–32).

Ellersgaard, D., Jessica Plessen, K., Richardt Jepsen, J., Soeborg Spang, K., Hemager, N., Klee Burton, B., Jerlang Christiani, C., Gregersen, M., Søndergaard, A., Uddin, M. J., Poulsen, G., Greve, A., Gantriis, D., Mors, O., Nordentoft, M., & Elgaard Thorup, A. A. (2018). Psychopathology in 7-year-old children with familial high risk of developing schizophrenia spectrum psychosis or bipolar disorder – The Danish High Risk and Resilience Study - VIA 7, a population-based cohort study. *World Psychiatry*, *17*(2), 210–219. https://doi.org/10.1002/wps.20527

Field, A. (2018). *Discovering statistics using IBM SPSS statistics* (5th edition). SAGE, 2-46, 372-385.

Field, A. E., Javaras, K. M., Aneja, P., Kitos, N., Camargo, C. A., Taylor, C. B., & Laird, N. M. (2008). Family, Peer, and Media Predictors of Becoming Eating Disordered. *Archives of Pediatrics & Adolescent Medicine*, *162*(6), 574–579. https://doi.org/10.1001/archpedi.162.6.574

Fosson, A., Knibbs, J., Bryant-Waugh, R., & Lask, B. (1987). Early onset anorexia nervosa. *Archives of Disease in Childhood*, *62*(2), 114–118. https://doi.org/10.1136/adc.62.2.114

Garner, D. M. (1993). Pathogenesis of anorexia nervosa. *The Lancet*, *341*(8861), 1631–1635. https://doi.org/10.1016/0140-6736(93)90768-C

Garner, D. M., & Garfinkel, P. E. (1980). Socio-cultural factors in the development of anorexia nervosa. *Psychological Medicine*, *10*(4), 647–656. https://doi.org/10.1017/S0033291700054945

Grange, D. L., & Loeb, K. L. (2007). Early identification and treatment of eating disorders: Prodrome to syndrome. *Early Intervention in Psychiatry*, *1*(1), 27–39. https://doi.org/10.1111/j.1751-7893.2007.00007.x

Grigoroiu-Serbanescu, M., Magureanu, S., Milea, S., Dobrescu, I., & Marinescu, E. (2003). Modest familial aggregation of eating disorders in restrictive anorexia nervosa with adolescent onset in a Romanian sample. *European Child & Adolescent Psychiatry*, *12*(0), 47–53. https://doi.org/10.1007/s00787-003-1107-7

Halmi, K. A. (1991). Comorbidity of Psychiatric Diagnoses in Anorexia Nervosa. *Archives of General Psychiatry*, *48*(8), 712–718. https://doi.org/10.1001/archpsyc.1991.01810320036006

Hare, R. M. (1986). Health. *Journal of Medical Ethics*, *12*(4), 174–181. https://doi.org/10.1136/jme.12.4.174

Hetherington, M. M. (2000). Eating disorders: Diagnosis, etiology, and prevention. *Nutrition*, *16*(7–8), 547–551. https://doi.org/10.1016/S0899-9007(00)00320-8

Hoek, H. W. (2016). Review of the worldwide epidemiology of eating disorders. *Current Opinion in Psychiatry*, *29*(6), 336–339. https://doi.org/10.1097/YCO.0000000000000282

Hoofnagle, C. J., Van Der Sloot, B., & Borgesius, F. Z. (2019). The European Union general data protection regulation: What it is and what it means. *Information & Communications Technology Law*, *28*(1), 65–98. https://doi.org/10.1080/13600834.2019.1573501

Hróbjartsson, A., & Lundh, A. (2022). *Evidensbaseret medicin og klinisk forskningsmetode*. Munksgaard, 22-34.

Hudson, J. I., Lalonde, J. K., Berry, J. M., Pindyck, L. J., Bulik, C. M., Crow, S. J., McElroy, S. L., Laird, N. M., Tsuang, M. T., Walsh, B. T., Rosenthal, N. R., & Pope, H. G. (2006). Binge-Eating Disorder as a Distinct Familial Phenotype in Obese Individuals. *Archives of General Psychiatry*, *63*(3), 313–319. https://doi.org/10.1001/archpsyc.63.3.313

Jacobi, C., Hayward, C., De Zwaan, M., Kraemer, H. C., & Agras, W. S. (2004). Coming to Terms With Risk Factors for Eating Disorders: Application of Risk Terminology and Suggestions for a General Taxonomy. *Psychological Bulletin*, *130*(1), 19–65. https://doi.org/10.1037/0033-2909.130.1.19

Johnsen, K. M., Nielsen, K. F., Nilsson, K. K., & Kjaersdam Telléus, G. (2024). Non-interpersonal traumatic events in patients with eating disorders: A systematic review. *Frontiers in Psychology*, *15*, 1-10, 1397952. https://doi.org/10.3389/fpsyg.2024.1397952

Juul, S., Bech, P. H., Dahm, C. C., & Rytter, D. (2017). *Epidemiologi og evidens* (3rd ed.). Munksgaard, 20-28, 53-74, 208-220.

Kassett, J. A., Gershon, E. S., Maxwell, M. E., Guroff, J. J., Kazuba, D. M., Smith, A. L., Brandt, H. A., & Jimerson, D. C. (1989). Psychiatric disorders in the first-degree relatives of probands with bulimia nervosa. *American Journal of Psychiatry*, *146*(11), 1468–1471. https://doi.org/10.1176/ajp.146.11.1468

Kendler, K. S., MacLean, C., Neale, M., Kessler, R., Heath, A., & Eaves, L. (1991). The genetic epidemiology of bulimia nervosa. *The American Journal of Psychiatry*, *148*(12), 1627–1637. https://doi.org/10.1176/ajp.148.12.1627

Kjærsdam Telléus, G., Fagerlund, B., Jepsen, J. R., Bentz, M., Christiansen, E., Valentin, J. B., & Thomsen, P. H. (2016). Are Weight Status and Cognition Associated? An Examination of Cognitive Development in Children and Adolescents with Anorexia Nervosa 1 Year after First Hospitalisation. *European Eating Disorders Review*, *24*(5), 366–376. https://doi.org/10.1002/erv.2445

Klump, K. L., & Culbert, K. M. (2007). Molecular Genetic Studies of Eating Disorders: Current Status and Future Directions. *Current Directions in Psychological Science*, *16*(1), 37–41. https://doi.org/10.1111/j.1467-8721.2007.00471.x

Klump, K. L., Miller, K. B., Keel, P. K., McGUE, M., & Iacono, W. G. (2001). Genetic and environmental influences on anorexia nervosa syndromes in a population–based twin sample. *Psychological Medicine*, *31*(4), 737–740. https://doi.org/10.1017/S0033291701003725

Klump, K. L., Suisman, J. L., Burt, S. A., McGue, M., & Iacono, W. G. (2009). Genetic and environmental influences on disordered eating: An adoption study. *Journal of Abnormal Psychology*, *118*(4), 797–805. https://doi.org/10.1037/a0017204

Klump, K. L., Wonderlich, S., Lehoux, P., Lilenfeld, L. R. R., & Bulik, C. (2002). Does environment matter? A review of nonshared environment and eating disorders. *International Journal of Eating Disorders*, *31*(2), 118–135. https://doi.org/10.1002/eat.10024

Kothari, R., Solmi, F., Treasure, J., & Micali, N. (2013). The neuropsychological profile of children at high risk of developing an eating disorder. *Psychological Medicine*, *43*(7), 1543–1554. https://doi.org/10.1017/S0033291712002188

Kuntz, B., Groze, V., & Yates, W. R. (1992). Bulimia: A Systemic Family History Perspective. *Families in Society: The Journal of Contemporary Social Services*, *73*(10), 604–612. https://doi.org/10.1177/104438949207301004

Lane, J., & Schur, C. (2010). Balancing Access to Health Data and Privacy: A Review of the Issues and Approaches for the Future. *Health Services Research*, *45*(5p2), 1456–1467. https://doi.org/10.1111/j.1475-6773.2010.01141.x

Launsø, L., Olsen, L., & Rieper, O. (2017). *Forskning om og med mennesker. Forskningstyper og forskningsmetoder i samfundsforskning.* (7th ed.). Munksgaard, 71-90.

Le Grange, D., Lock, J., Loeb, K., & Nicholls, D. (2010). Academy for eating disorders position paper: The role of the family in eating disorders. *International Journal of Eating Disorders*, *43*(1), 1–5. https://doi.org/10.1002/eat.20751

Lee, Y. H., Abbott, D. W., Seim, H., Crosby, R. D., Monson, N., Burgard, M., & Mitchell, J. E. (1999). Eating disorders and psychiatric disorders in the first-degree relatives of obese probands with binge eating disorder and obese non-binge eating disorder controls. *International Journal of Eating Disorders*, *26*(3), 322–332. https://doi.org/10.1002/(SICI)1098-108X(199911)26:3<322::AID-EAT10>3.0.CO;2-K

Lilenfeld, L. R., Kaye, W. H., Greeno, C. G., Merikangas, K. R., Plotnicov, K., Pollice, C., Rao, R., Strober, M., Bulik, C. M., & Nagy, L. (1998). A Controlled Family Study of Anorexia Nervosa and Bulimia Nervosa: Psychiatric Disorders in First-Degree Relatives and Effects of Proband Comorbidity. *Archives of General Psychiatry*, *55*(7), 603-610. https://doi.org/10.1001/archpsyc.55.7.603

Lilenfeld, Ringham, R., Kalarchian, M. A., & Marcus, M. D. (2008). A family history study of binge-eating disorder. *Comprehensive Psychiatry*, *49*(3), 247–254. https://doi.org/10.1016/j.comppsych.2007.10.001

Logue, C. M., Crowe, R. R., & Bean, J. A. (1989). A family study of anorexia nervosa and bulimia. *Comprehensive Psychiatry*, *30*(2), 179–188. https://doi.org/10.1016/0010-440x(89)90071-0

Lydecker, J. A., & Grilo, C. M. (2016). Fathers and mothers with eating-disorder psychopathology: Associations with child eating-disorder behaviors. *Journal of Psychosomatic Research*, *86*, 63–69. https://doi.org/10.1016/j.jpsychores.2016.05.006

Madden, S., Miskovic-Wheatley, J., Wallis, A., Kohn, M., Hay, P., & Touyz, S. (2015). Early weight gain in family-based treatment predicts greater weight gain and remission at the end of treatment and remission at 12-month follow-up in adolescent anorexia nervosa. *International Journal of Eating Disorders*, *48*(7), 919–922. https://doi.org/10.1002/eat.22414

Mairs, R., & Nicholls, D. (2016). Assessment and treatment of eating disorders in children and adolescents. *Archives of Disease in Childhood*, *101*(12), 1168–1175. https://doi.org/10.1136/archdischild-2015-309481

Makino, M., Tsuboi, K., & Dennerstein, L. (2004). Prevalence of eating disorders: A comparison of Western and non-Western countries. *MedGenMed: Medscape General Medicine*, *6*(3), 49.

Mann, C. J. (2003). Observational research methods. Research design II: Cohort, cross sectional, and case-control studies. *Emergency Medicine Journal*, *20*(1), 54–60. https://doi.org/10.1136/emj.20.1.54

Martini, M. G., Barona-Martinez, M., & Micali, N. (2020). Eating disorders mothers and their children: A systematic review of the literature. *Archives of Women's Mental Health*, *23*(4), 449–467. https://doi.org/10.1007/s00737-020-01019-x

Mazzeo, S. E., & Bulik, C. M. (2009). Environmental and genetic risk factors for eating disorders: What the clinician needs to know. *Child and Adolescent Psychiatric Clinics of North America*, *18*(1), 67–82. https://doi.org/10.1016/j.chc.2008.07.003

Meijsen, J., Hu, K., Wei, D., Aicoboaie, S., Davies, H. L., Zhang, R., Lundberg, M., Zetterberg, R., Pasman, J., Ye, W., Werge, T., Bulik, C. M., Fang, F., Buil, A., & Micali, N. (2024). *Shared Genetic Architecture Between Eating Disorders, Mental Health Conditions, and Cardiometabolic Diseases: A Comprehensive Population-Wide Study Across Two Countries*. 1-20, https://doi.org/10.1101/2024.10.20.24315825

Micali, N., Solmi, F., Horton, N. J., Crosby, R. D., Eddy, K. T., Calzo, J. P., Sonneville, K. R., Swanson, S. A., & Field, A. E. (2015). Adolescent Eating Disorders Predict Psychiatric, High-Risk Behaviors and Weight Outcomes in Young Adulthood. *Journal of the American Academy of Child & Adolescent Psychiatry*, *54*(8), 652-659.e1. https://doi.org/10.1016/j.jaac.2015.05.009

Miteu, G. D. (2024). Ethics in scientific research: A lens into its importance, history, and future. *Annals of Medicine & Surgery*, *86*(5), 2395–2398. https://doi.org/10.1097/MS9.0000000000001959

Møhl, B., & Jensen, B. M. (2017). Spiseforstyrrelser. In E. Simonsen & B. Møhl, *Grundbog i psykiatri* (2. udgave, pp. 477–496). Hans Reitzels Forlag.

Momen, N. C., Plana-Ripoll, O., Yilmaz, Z., Thornton, L. M., McGrath, J. J., Bulik, C. M., & Petersen, L. V. (2022). Comorbidity between eating disorders and psychiatric disorders. *International Journal of Eating Disorders*, *55*(4), 505–517. https://doi.org/10.1002/eat.23687

Murray, S. B., Rieger, E., Karlov, L., & Touyz, S. W. (2013). Masculinity and femininity in the divergence of male body image concerns. *Journal of Eating Disorders*, *1*(1), 1–11. https://doi.org/10.1186/2050-2974-1-11

O'Neil, K. A., Podell, J. L., Benjamin, C. L., & Kendall, P. C. (2010). Comorbid Depressive Disorders in Anxiety-disordered Youth: Demographic, Clinical, and Family Characteristics. *Child Psychiatry & Human Development*, *41*(3), 330–341. https://doi.org/10.1007/s10578-009-0170-9

Pedersen, H. M., Frøkjær, S., Back, L. W., Vestergaard, E., Pedersen, C. V., Dirckinck-Holmfeld, L., Wegener, H. C., Jensen, L., Staunstrup, J., & Hansen, J. M. (2015). *Den danske kodeks for integritet i forskning*. 1-27. http://ufm.dk/publikationer/2015/den-danske-kodeks-for-integritet-i-forskning

Qian, J., Wu, Y., Liu, F., Zhu, Y., Jin, H., Zhang, H., Wan, Y., Li, C., & Yu, D. (2022). An update on the prevalence of eating disorders in the general population: A systematic review and meta-analysis. *Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity*, *27*(2), 415–428. https://doi.org/10.1007/s40519-021-01162-z

Rikani, A. A., Choudhry, Z., Maqsood Choudhry, A., Ikram, H., Waheed Asghar, M., Kajal, D., Waheed, A., & Jahan Mobassarah, N. (2013). A critique of the literature on etiology of eating disorders. *Annals of Neurosciences*, *20*(4). 157-161 https://doi.org/10.5214/ans.0972.7531.200409

Rutherford, J., McGuffin, P., Katz, R. J., & Murray, R. M. (1993). Genetic influences on eating attitudes in a normal female twin population. *Psychological Medicine*, *23*(2), 425–436. https://doi.org/10.1017/S003329170002852X

Silén, Y., & Keski-Rahkonen, A. (2022). Worldwide prevalence of DSM-5 eating disorders among young people. *Current Opinion in Psychiatry*, *35*(6), 362–371. https://doi.org/10.1097/YCO.0000000000000818

Smink, F. R. E., Van Hoeken, D., & Hoek, H. W. (2012). Epidemiology of Eating Disorders: Incidence, Prevalence and Mortality Rates. *Current Psychiatry Reports*, *14*(4), 406–414. https://doi.org/10.1007/s11920-012-0282-y

Spindler, A., & Milos, G. (2007). Links between eating disorder symptom severity and psychiatric comorbidity. *Eating Behaviors*, *8*(3), 364–373. https://doi.org/10.1016/j.eatbeh.2006.11.012

Statacorp. (2025). *Stata Statistical Software: Release 19.* [College Station, TX: StataCorp LLC.].

Striegel-Moore, R. H., & Bulik, C. M. (2007). Risk factors for eating disorders. *American Psychologist*, *62*(3), 181–198. https://doi.org/10.1037/0003-066X.62.3.181

Strober, M., Freeman, R., Lampert, C., Diamond, J., & Kaye, W. (2000). Controlled Family Study of Anorexia Nervosa and Bulimia Nervosa: Evidence of Shared Liability and Transmission of Partial Syndromes. *American Journal of Psychiatry*, *157*(3), 393–401. https://doi.org/10.1176/appi.ajp.157.3.393

Strober, M., Freeman, R., Lampert, C., Diamond, J., & Kaye, W. (2001). Males with anorexia nervosa: A controlled study of eating disorders in first-degree relatives. *International Journal of Eating Disorders*, *29*(3), 263–269. https://doi.org/10.1002/eat.1017

Sullivan, P. F., Bulik, C. M., & Kendler, K. S. (1998). Genetic epidemiology of binging and vomiting. *British Journal of Psychiatry*, *173*(1), 75–79. https://doi.org/10.1192/bjp.173.1.75

Sundhedsdatastyrelsen. (2020). *Personer med spiseforstyrrelse Registeranalyse af forekomst, nye tilfælde og aktivitet på tværs af sundhedsvæsenet i perioden 2010-2018* (pp. 1–27).

Sundhedsstyrelsen. (2005). *Spiseforstyrrelser. Anbefalinger for organisation og behandling: Udarbejdet af en arbejdsgruppe under Sundhedsstyrelsen* (Version 1.0; december 2005), 1-50.

Telléus, P. K., & Jensen, W. (2020). Ethical Assessment and Reflection in Research and Development of Non-Conformité Européene Marked Medical Devices. *Cambridge Quarterly of Healthcare Ethics*, *29*(4), 592–606. https://doi.org/10.1017/S0963180120000341

Thornton, L. M., Mazzeo, S. E., & Bulik, C. M. (2010). The Heritability of Eating Disorders: Methods and Current Findings. In R. A. H. Adan & W. H. Kaye (Eds.), *Behavioral Neurobiology of Eating Disorders* (Vol. 6, pp. 141–156). Springer Berlin Heidelberg. https://doi.org/10.1007/7854_2010_91

Trace, S. E., Baker, J. H., Peñas-Lledó, E., & Bulik, C. M. (2013). The Genetics of Eating Disorders. *Annual Review of Clinical Psychology*, *9*(1), 589–620. https://doi.org/10.1146/annurev-clinpsy-050212-185546

Treasure, J., Duarte, T. A., & Schmidt, U. (2020). Eating disorders. *The Lancet*, *395*(10227), 899–911. https://doi.org/10.1016/S0140-6736(20)30059-3

Udo, T., & Grilo, C. M. (2019). Psychiatric and medical correlates of *DSM-5* eating disorders in a nationally representative sample of adults in the United States. *International Journal of Eating Disorders*, *52*(1), 42–50. https://doi.org/10.1002/eat.23004

Van Der Veen, F. M., Evers, E. A. T., Deutz, N. E. P., & Schmitt, J. A. J. (2007). Effects of Acute Tryptophan Depletion on Mood and Facial Emotion Perception Related Brain Activation and Performance in Healthy Women with and without a Family History of Depression. *Neuropsychopharmacology*, *32*(1), 216–224. https://doi.org/10.1038/sj.npp.1301212

Van Hoeken, D., & Hoek, H. W. (2020). Review of the burden of eating disorders: Mortality, disability, costs, quality of life, and family burden. *Current Opinion in Psychiatry*, *33*(6), 521–527. https://doi.org/10.1097/YCO.0000000000000641

Voigt, P., & Von Dem Bussche, A. (2024). *The EU General Data Protection Regulation (GDPR): A Practical Guide*. Springer Nature Switzerland 14-17, 40-42. https://doi.org/10.1007/978-3-031-62328-8

Wade, T. D., Bulik, C. M., Neale, M., & Kendler, K. S. (2000). Anorexia Nervosa and Major Depression: Shared Genetic and Environmental Risk Factors. *American Journal of Psychiatry*, *157*(3), 469–471. https://doi.org/10.1176/appi.ajp.157.3.469

Wade, T., Martin, N. G., Neale, M. C., Tiggemann, M., Treloar, S. A., Bucholz, K. K., Madden, P. A. F., & Heath, A. C. (1999). The structure of genetic and environmental risk factors for three measures of disordered eating. *Psychological Medicine*, *29*(4), 925–934. https://doi.org/10.1017/S0033291799008740

Wade, T., Martin, N. G., & Tiggemann, M. (1998). Genetic and environmental risk factors for the weight and shape concerns characteristic of bulimia nervosa. *Psychological Medicine*, *28*(4), 761–771. https://doi.org/10.1017/S0033291798006989

Wallace, S. S., Barak, G., Truong, G., & Parker, M. W. (2022). Hierarchy of Evidence Within the Medical Literature. *Hospital Pediatrics*, *12*(8), 745–750. https://doi.org/10.1542/hpeds.2022-006690

Wang, X., & Cheng, Z. (2020). Cross-Sectional Studies. *Chest*, *158*(1), S65–S71. https://doi.org/10.1016/j.chest.2020.03.012

Watson, R. (2015). Quantitative research. *Nursing Standard*, *29*(31), 44–48. https://doi.org/10.7748/ns.29.31.44.e8681

World Health Organization. (2022). *ICD-11: International Classification of diseases (11th revision)*. https://icd.who.int/

World Medical Association. (2013). World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. *JAMA*, *310*(20), 2191-2194. https://doi.org/10.1001/jama.2013.281053

Yilmaz, Z., HArdaway, A., & Bulik, C. (2015). Genetics and epigenetics of eating disorders. *Advances in Genomics and Genetics*, 1–36. https://doi.org/10.2147/AGG.S55776

Yu, Y., Miller, R., & Groth, S. W. (2022). A literature review of dopamine in binge eating. *Journal of Eating Disorders*, *10*(1), 11. https://doi.org/10.1186/s40337-022-00531-y

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