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The co-occurrence of anorexia nervosa and autism spectrum condition – implications on
treatment of anorexia nervosa

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Abstract

Evidence suggests a high prevalence of autism spectrum condition (ASC) among individuals with anorexia nervosa (AN). Despite the growing evidence surrounding the treatment of anorexia nervosa, approximately twenty percent of patients develop a chronic course illness. Previous research has associated the co-occurrence of autism spectrum condition with worse long-term psychosocial outcomes and a chronic course of anorexia. Little evidence surrounding the treatment adaptations for this subgroup exists; although patients with co-occurring ASC are likely to benefit from treatment adaptations addressing neurodiversity.

This systematic review examines the clinical effectiveness of treatment methods for patients with co-occurring AN and ASC. Articles were identified by systematic search through the following databases: Scopus, ProQuest, EBSCOhost, and PubMed. Twelve (12) peer-reviewed articles were included in this systematic review.

Results of the synthesis implicate that patients with co-occurring anorexia nervosa and ASC seem to present more severe psychological eating disorder symptoms and have an elevated need for psychiatric care. There is mixed evidence about treatment effectiveness for the subgroup with co-occurring autism spectrum condition. Many studies report similar patterns of eating disorder symptom reduction in the patient groups with and without ASC, yet evidence of poorer response to treatment exists. Preliminary evidence of the effectiveness of cognitive remediation therapy and family-based therapy exists for this subgroup of patients. Inpatient treatment can be more efficient for this patient group than day-patient programmes. Patients with ASC might benefit from individual therapy sessions rather than group sessions.

There is preliminary evidence of suitable interventions for this comorbidity, yet more evidence of clinical effectiveness is required. Future research surrounding this topic is warranted to accommodate neurodiversity in eating disorder services.

Keywords: autism spectrum disorder, anorexia nervosa, co-occurrence, comorbidity, treatment, systematic review

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1 Introduction

Anorexia nervosa (AN) is a severe restrictive eating disorder (American Psychiatric Association, 2013). The severity of this disorder is characterised by significant individual psychosocial burden and long-term negative effects on quality of life even after recovery (Jenkins et al., 2020; Pohjolainen et al., 2016). Despite the growing evidence surrounding the treatment of anorexia approximately 30 % of patients show long-term difficulties in weight restoration (Berends et al., 2018) and 20 % of patients have a chronic course of illness (Dobrescu et al., 2020). During recent years, there has been increasing attention to the patient group with prolonged courses of illness.

Characteristics of autism spectrum disorder have been associated with a prolonged course of anorexia and poorer psychosocial outcomes (Nielsen et al., 2015, 2022; Saure et al., 2020). According to the DSM-5 autism spectrum disorder (ASD) is a neurodevelopmental disorder that is characterised by socio-communicative difficulties as well as rigid patterns of thinking and behaving (American Psychiatric Association, 2013). Anorexia and ASD are two distinct conditions, yet they are thought to overlap in multiple characteristics related to neuropsychological, sensory, and socio-emotional processing (Saure et al., 2021) It has been estimated that 20 % of anorexia patients show elevated levels of autistic traits (Huke et al., 2013) and autistic individuals are twice as likely to have ED than non-autistic individuals (Sedgewick et al., 2021). Even though there has been a growing body of research surrounding this co-occurrence, little is known of effective treatment adaptations for patients with anorexia nervosa that are on the spectrum. Due to the high prevalence of this comorbidity and findings of worse outcomes, the effect of autistic traits on treatment processes warrants further research. Furthermore, qualitative evidence has highlighted the substantial need for treatment adaptations for patients with anorexia and autism spectrum disorder (Babb et al., 2021; Kinnaird et al., 2019)

This systematic review aims to explore whether the co-occurrence of ASD or elevated ASD trait levels is associated with the effectiveness of treatment of anorexia nervosa. Clinical outcomes are explored to review whether autistic traits are affecting the course of treatment and outcomes among patients with anorexia nervosa. The systematic review aims to explore treatment options and their clinical significance for individuals with anorexia nervosa and co-occurring elevated ASD trait levels. Since this is a new area of research, implications for future research will be presented.

The research question of this review is two-fold. The research question is as follows:

- a. Are elevated autism spectrum traits associated with the effectiveness of treatment of anorexia nervosa?
- b. What kind of treatment would be especially beneficial for patients with anorexia nervosa and elevated autism spectrum traits?

2 Theoretical background

2.1 Anorexia nervosa

Anorexia nervosa (AN) is a severe eating disorder characterised by restriction of energy intake, severe fear of weight gain and a compromised view of own body image or low insight into low body weight (American Psychiatric Association, 2013). According to the DSM-5 anorexia nervosa is classified as restrictive (R-AN) and binge-eating/purging subtypes (BP-AN): in BP-AN there is a presence of compensatory behaviours relating to energy intake within the last three months (e.g. use of laxatives, vomiting) whereas in restrictive condition weight loss is aimed primarily by substantial amount of physical activity and restriction of eating (American Psychiatric Association, 2013). Atypical anorexia nervosa is categorised as “other specified eating and feeding disorder” but the symptomatic picture includes the same symptoms as anorexia nervosa without the presence of significantly low body weight (Moskowitz & Weiselberg, 2017). In a meta-analysis investigating global prevalence rates, the lifetime prevalence rate was found to be 0.16 % in the general population (Qian et al., 2022). A meta-analysis primarily including studies from Western countries found a lifetime prevalence of 0.8-6.3 % for women and 0,1-0,2 % for men: AN being significantly more prevalent among women (Silén & Keski-Rahkonen, 2022). Eating disorder research has often focused on binary definitions of gender; although it has been noted that gender-diverse individuals are at especially high risk for having an eating disorder (Romano et al., 2022).

Anorexia nervosa has been found to have the highest mortality rates of eating disorders, due to suicidality or physical health causes (Fichter & Quadflieg, 2016) Anorexia nervosa has been associated with elevated mortality rates, especially with longer duration and chronic course of illness (Franko et al., 2013). There is a 57-fold risk of suicide (Keel et al., 2003) and a 10-fold risk of early death (Button et al., 2010) among patients with anorexia nervosa compared to the general population. Having an ED is associated with a significantly elevated risk of being diagnosed with a wide range of physical conditions (Momen et al., 2022). Anorexia has been associated with notably high healthcare costs due to the elevated need for intensive inpatient treatment and lifespan health effects (Agras, 2001; de Oliveira et al., 2017). Due to the severity of this disorder; more research is needed to improve the treatment of this disorder.

2.2 Autism spectrum condition

By the diagnostic guideline of DSM-5 autism spectrum disorder (ASD) is a life-long neurodevelopmental condition that is characterized by individual socio-communicative challenges [e.g. difficulties in nonverbal communication, back-and-forth relationships, and emotional reciprocity] as well as rigid and repetitive patterns of thinking and behaving [e.g. restricted interests, hypo-/hypersensitivity to stimulus, importance of routines, stereotyped motor movements] (American Psychiatric Association, 2013). For the past years, defining the autism spectrum by the medical paradigm has been challenged by the neurodiversity model. The neurodiversity model conceptualises the autism spectrum as a variation of traits occurring in the population; manifesting with strengths and difficulties as well as widely varying support needs (Bottema-Beutel et al., 2021; Happé & Frith, 2020; Waizbard-Bartov et al., 2023). Among autism research the use of the term autism spectrum condition (ASC) has been recommended, since the term “disorder” has been reported as stigmatising and not capturing the set of strengths and difficulties experienced among individuals on the spectrum (Lai & Baron-Cohen, 2015). From here on the term ASC is used when referring to autism.

A systematic review found a prevalence rate of 1 % for ASC and that ASC would be 4.2 times more likely to occur among males than among females (Zeidan et al., 2022). Even though the male-to-female ratios of ASC have declined during the recent years (M. Solmi et al., 2022), late diagnosis of autistic women and non-binary individuals is still an evident issue in the field (Kavanaugh et al., 2023). It has been suggested that women and non-binary individuals are more likely to have a presentation of autism that is atypical, compensated, and masked (Lai et al., 2015; McQuaid et al., 2022). Masking or camouflaging refers to coping strategies autistic individuals may use to suppress their autistic traits in social contexts: high levels of camouflaging have been associated with the late onset of ASD diagnosis (Lai et al., 2015). The effect of “diagnostic overshadowing” has been proposed: autism might have been left unrecognised due to the predominance of depression and anxiety symptoms (Green et al., 2019).

Being on the spectrum has been associated with lower quality of life: this has been suggested to mainly be due to social difficulties and the strain of using compensatory strategies (Braden et al., 2022; Øverland et al., 2022). Psychiatric conditions are more prevalent among autistic individuals than in the general population: including eating disorders (Lai et al., 2019). In a sample from outpatient psychiatric services, at least 19 % of the patients fulfilled the criteria for autism spectrum disorder and in addition, 5–10 % of patients presented elevated autism

spectrum traits (Nyrenius et al., 2022). Particularly autistic women are at higher risk of obtaining psychiatric diagnoses and being admitted for psychiatric inpatient care (Martini et al., 2022).

2.3 The co-occurrence of autism spectrum condition and anorexia nervosa

The co-occurrence of autism spectrum condition and anorexia nervosa became an interest as early as 1980's when it was suggested that anorexia nervosa could be a female phenotype of autism (Gillberg, 1985). Since then, there has been a growing amount of research surrounding this co-occurrence. Even though there seems not to be evidence for the hypothesis of anorexia nervosa being the female phenotype of autism, the current evidence suggests a significant association between anorexia nervosa and autism spectrum condition.

2.3.1 Prevalence of the co-occurrence

Prevalence rates of the co-occurrence of anorexia and autism seem to vary on the assessment methods used. When clinical information of parental reports of childhood development is taken into consideration, prevalence rates for this co-occurrence are 4-10 % (Pooni et al., 2012; Rhind et al., 2014; Westwood et al., 2018). Studies that do not include retrospective information about ASC traits report higher prevalence rates: of individuals with AN, 10-52.5 per cent show clinically significant traits of ASC (Bentz et al., 2020; Postorino et al., 2017; Pruccoli, Solari, et al., 2021; Westwood et al., 2018) In register studies prevalence rates seem to be significantly lower: 1.3-3.5 % of individuals have co-occurring confirmed diagnoses of AN and ASC (Dinkler et al., 2021; Zhang et al., 2021). In a retrospective analysis of a patient cohort of autistic individuals, the prevalence of AN was found to be 6,8 % among women and 1 % among men; with a significantly higher prevalence among autistic women (Margari et al., 2019).

It has been argued that patients with anorexia have high rates of unrecognised autism (Mandy & Tehanturia, 2015) and ASC traits might become more prominent when eating disorders emerge (Huke et al., 2013). In qualitative has been noted that a considerable proportion of women receive a late ASC diagnosis only when they are admitted for ED services; in some cases, years after first admitted for psychiatric services (Babb et al., 2021; Brede et al., 2020; Kinnaird et al., 2019; Li et al., 2022). Groups of AN have an overrepresentation of women. Generally, it is more common for women to receive a late diagnosis of ASD (Kavanaugh et al.,

2023) and have psychiatric conditions co-occurring with ASC (Green et al., 2019). Yet it has been proposed that observed ASC characteristics might rather be associated with the illness phase of the eating disorder. For instance, it has been proposed that these characteristics might be due to starvation-related neurocognitive alterations of the brain (Katzman et al., 2001). However, the effect of starvation remains unspecific since patients with AN continue to present clinically significant ASC traits even after recovery (Kerr-Gaffney, Hayward, et al., 2021).

2.3.2 Shared characteristics

Research has noted that individuals suffering from anorexia often exhibit ways of behaving and thinking that are thought to be characteristic of autism spectrum disorders [eg. compromised neuropsychological processing, socioemotional characteristics, theory of mind and alexithymia] (Carpita et al., 2022). Furthermore, eating difficulties and sensory sensitivities are observed in both disorders (Saure, Lepistö-Paisley, et al., 2022; Spek et al., 2020). Understanding the commonalities and characteristics of these disorders is key to developing more efficient treatment methods.

Eating disturbances and sensory sensitivities

In both AN and ASC, there are compromises in eating behaviours and sensory processing. Patients with anorexia are found to have more atypical sensory processing in general and it has been thought to be an underlying factor behind eating disturbances present in this disorder (Saure, Lepistö-Paisley, et al., 2022). Longitudinal trajectories of disordered eating and sensory sensitivities are noted among autistic individuals. It has been estimated that ninety per cent of individuals on the spectrum have sensory sensitivities related to visual, auditory, olfactory and taste stimuli (Leekam et al., 2007). Eating disturbances and eating-related sensory sensitivities are common among both children and adults on the spectrum (Chistol et al., 2018; Spek et al., 2020). Early food selectivity in autism has been associated with eating disorder symptoms later in life (Carter Leno et al., 2022). Especially autistic women seem to show high amounts of eating-related routines, difficulties with social and sensory aspects of eating as well as heightened levels of ED symptoms (Lai et al., 2015; Spek et al., 2020) Presented findings highlight the likelihood of eating disturbances and sensory sensitivities in both anorexia and autism. For the treatment of this patient group with co-occurring ASC, it should be noted that it is likely that eating disturbances and sensory sensitivities have been present throughout the lifespan.

Neuropsychological characteristics

Literature suggests somewhat similar neuropsychological performance profiles between ASD and AN (Ghiotto et al., 2022; Westwood et al., 2017). Prominent overlapping neuropsychological characteristics in AN and ASC have been thought to be weak central coherence and cognitive inflexibility (Renwick et al., 2015; Saure et al., 2020). Weak central coherence refers to cognitive processing that is biased towards details and lacks the ability to integrate detailed information into bigger concepts (Lang et al., 2014). Cognitive flexibility refers to the ability to switch between different tasks and mental sets (Westwood et al., 2017). It has been suggested that ASC-related neuropsychological characteristics might affect the course of anorexia; since these characteristics might contribute to the course of illness together with previously mentioned eating disturbances (Saure et al., 2020). In autism spectrum conditions there is often a presence of intense and restricted interests (American Psychiatric Association, 2013). It could be that interests are ED-related topics: nutrition, exercise, and calorie content. Inflexible thinking patterns during anorexia might underline the importance of strict food-related routines and make it more difficult to obtain different ways of thinking; furthermore, weak central coherence may highlight the focus on nutrition-related details. (Brede et al., 2020)

Socioemotional and socio-cognitive characteristics

Compromises in socioemotional and socio-cognitive function seem to be present in both conditions. It has been proposed that there is a subgroup of anorexia nervosa patients that show elevated levels of social difficulties characteristic of ASC; this group of patients show difficulties in social interaction and non-verbal communication (Anckarsäter et al., 2012). Elevated autistic social traits in childhood have been found to be a risk factor behind disordered eating behaviours in adolescence (F. Solmi et al., 2021). Alexithymia, poor emotion recognition, compromises in “theory of mind” and poor social attention have been thought to be shared characteristics between individuals with ASC and AN (Bora & Köse, 2016; Kerr-Gaffney et al., 2020; Kerr-Gaffney, Mason, et al., 2021; Saure, Raevuori, et al., 2022). It has been proposed that these social characteristics would affect the treatment of AN (Saure, Raevuori, et al., 2022). Especially the effect of alexithymia has been noted. Alexithymia refers to an inability to identify and verbalize emotions and compromises in introspection (Vuillier et al., 2020). Alexithymia has been associated with more severe eating disorder pathology among individuals with anorexia nervosa (Lukas et al., 2022). It has been proposed that interventions targeted towards

alexithymia might be especially beneficial for patients of anorexia, for alexithymia seems to be a mediator of autistic traits and ED pathology (Moseley et al., 2023).

2.4 Treatment of anorexia nervosa

Even though there has been a growing body of evidence surrounding the treatment of anorexia: it has been noted that a significant number of individuals with eating disorders do not receive evidence-based treatment (Kazdin et al., 2017). In the treatment of AN, there has been a presence of relatively high drop-out rates and an occurrence of treatment resistance (Halmi et al., 2005). Treatment of AN is complex because it combines psychiatric care to manage psychological ED symptoms and psychiatric comorbidities and somatic care to minimize physical health risks (Mitchell & Peterson, 2020). Due to this, care is often multidisciplinary: integrating medical and dietic risk management, nutrition therapy, occupational therapy, physiotherapy, psychoeducation, and psychotherapies. (National Institute for Health and Care Excellence, 2017). Even though weight restoration is necessary at the beginning of the treatment; the role of intensive psychological evidence-based treatment methods is crucial to prevent relapses and chronicity of AN (Murray et al., 2019).

2.4.1 The possible effect of autism spectrum condition on treatment of anorexia nervosa

It appears that the shared characteristics of AN and ASC are likely to affect treatment processes of anorexia nervosa, since in a 30-year follow-up study comparing recovery trajectories among individuals with anorexia; feasible well-being outcomes were only limited to those without co-occurring ASC (Nielsen et al., 2022). Existing evidence suggests the presence of a subtype of anorexia characterised by elevated autistic traits, more severe eating disorder pathology and psychopathological concerns (Li et al., 2023) as well as a prolonged course of illness (Saure et al., 2020). Previously presented findings imply that there seem to be similar compromises in interpersonal and neurocognitive functioning observed in ASC and AN. “Cognitive-Interpersonal Maintenance Model” of AN proposes that issues of interpersonal functioning together with neurocognitive characteristics are factors maintaining the range of symptoms of anorexia and are likely to make recovery more difficult (Treasure & Schmidt, 2013) This model suggests that treatment noting social characteristics and cognitive styles are likely to be demanded for this patient group of AN with elevated autistic traits. In qualitative studies autistic patients have disclosed that the symptomatic picture of their AN is somewhat different: less characterised by

weight and body image concerns and maintained by autism-specific cognitive styles and social challenges (Brede et al., 2020; Kinnaird et al., 2019). Patients with ASC are likely to benefit from treatment adaptations and individualised treatment plans as well as an adapted service environment where autistic traits are taken into consideration. In qualitative studies, autistic participants with AN have highlighted the importance of individual sessions, communicational support, emotional skills training, and consideration of sensory sensitivities (Babb et al., 2021; Kinnaird et al., 2019; Li et al., 2022).

2.4.2 Addressing neurodiversity in eating disorder treatment

In terms of service use, in qualitative studies, autistic individuals have highlighted the importance of individual encounters, accessibility of services, respect and acknowledging neurodiversity (Cascio & Racine, 2022). There is still a significant need for knowledge surrounding neurodiversity and giving patients with autism and anorexia a voice when making treatment adaptations is extremely crucial. Although positive experiences from accommodating autistic traits are also brought forward, patients with this comorbidity do often report feeling misunderstood in the ED services due to their autistic traits (Babb et al., 2021). Qualitative studies highlight the significant need for treatment adaptations for the subgroup of anorexia nervosa with elevated autistic traits (Babb et al., 2021; Kinnaird et al., 2019; Li et al., 2022). Whilst there is a consensus about the importance of accommodating this comorbidity, qualitative evidence from the UK notes that the majority of clinicians working in the ED services feel like they lack the confidence in helping patients with co-occurring autism (Kinnaird et al., 2017). Even though lack of confidence has been put into words; clinicians express their knowledge on this co-occurrence by naming the same treatment targets and differences in anorexia symptoms as autistic participants themselves (Brede et al., 2020). Lack of resources and time limits have been thought to make it more difficult for clinicians to address this comorbidity in such an individualised approach that they have wished (Babb et al., 2021).

2.4.3 Psychosocial treatment methods

Treatment of anorexia can include outpatient, day-patient and inpatient treatment; where different psychosocial treatment methods such as therapy sessions are offered (Zipfel et al., 2015). Day-patient treatment after short inpatient care treatment has been suggested to be a cost-effective treatment with similar symptom reduction in comparison to longer inpatient treatment

(Herpertz-Dahlmann et al., 2014). Currently, no clear superiority over one specific treatment is supported by international treatment guidelines. For adult patients latest NICE guidelines suggest CBT-ED [cognitive behavioural therapy targeted to eating disorders], MANTRA (Maudsley model of Anorexia Nervosa Treatment) and SSCM [specialist supportive clinical management] and for young patients it is suggested to provide CBT-ED or family-based therapy (National Institute for Health and Care Excellence, 2017). There is still a lack of international treatment guidelines addressing the co-occurrence of ASC and anorexia. Although the first regionally implemented treatment guideline for this co-occurrence has been presented, there has been preliminary evidence for its effectiveness (Li et al., 2024; Tchanturia et al., 2020, 2021).

Cognitive remediation therapy is still an experimental treatment method which is targeted to neuropsychological challenges such as cognitive inflexibility weak central coherence (Zipfel et al., 2015). A meta-analysis suggested CRT to be a feasible intervention in raising awareness of personal cognitive styles and increasing treatment motivation among AN patients (Marchesi et al., 2024). Preliminary evidence of autistic individuals benefiting from CRT exists; although individuals on the spectrum likely benefit from modifications of the intervention (Dandil, Smith, Kinnaird, et al., 2020). A component of emotional skills training can be added to CRT, intervention is referred to as CREST; intervention has been found to reduce social anhedonia and alexithymia and improve personal motivation among patients with AN (Tchanturia et al., 2015).

2.4.4 Conceptualization of treatment effectiveness

The effectiveness of treatment can be referred to as patient-specific clinical effectiveness or cost-effectiveness. In this systematic review, the focus is on the clinical effectiveness of treatment. Effectiveness of treatment refers to the odds of a certain treatment method or protocol being beneficial for a certain patient population: effectiveness is defined by comparisons of baseline and outcome measures (Andrews, 1989). Recovery of anorexia nervosa can be conceptualized as psychological recovery as well as reduction of psychological/cognitive ED symptoms; efficient treatment leads to reductions of these (Bardone-Cone et al., 2018). The clinical effectiveness of AN treatment is measured by weight restoration, reduction of psychological/cognitive ED symptoms as well as measures of quality of life and daily life functioning

(Monteleone et al., 2022). Treatment effectiveness and can be assessed by analysing the frequency and length of service use, intensity of treatment and treatment completion rates (Gaskell et al., 2023).

When weight restoration is considered in efficiency research, the used measure is most likely BMI or percentual BMI (Zipfel et al., 2015). As a measure of ED pathology, questionnaire EDE-Q (*eating disorder examination questionnaire*) is the most used (Monteleone et al., 2022). Since in AN there is often a presence of neuropsychological symptoms, symptoms are often measured if treatment is targeted to these. Central coherence is often measured with ROCF (*Rey-Osterrich Figure*), and cognitive flexibility is measured by Brixton test, WCST (*Wisconsin card sorting task*) or self-reported D-Flex. (Saure et al., 2020). The effectiveness of treatment can be assessed by improvements in socioemotional factors: such as alexithymia and social anhedonia. Alexithymia is most often measured with TAS (*Toronto Alexithymia Scale*) and social anhedonia with SAS (*Social Anhedonia Scale*) (Saure, Raevuori, et al., 2022). Treatment efficiency can also be characterized by improvements in treatment motivation, which is often measured by the “*Motivational ruler*”; scale including components of ability and motivation to change (Adamson et al., 2018). In anorexia there is often a co-occurring presence of psychiatric concerns such as depression, anxiety, and OCD symptoms; anorexia treatment is targeted to the reduction of these symptoms (Zipfel et al., 2015). Measures of psychopathology, overall functioning, and quality of life at the beginning and the end of the treatment are reflecting treatment effectiveness (Monteleone et al., 2022).

3 Methods

3.1 Systematic review as a method

This thesis is performed as a systematic review, and it is conducted to answer the research question. Systematic reviews are characterized by transparency and replicable methodology (Siddaway et al., 2019). The idea of a systematic review is to gather existing evidence by performing systemized literature searches: based on formulated research question, systemized search strategy and defined inclusion and exclusion criteria (Boland et al., 2017). Systematic review aims to synthesize existing quality evidence, link the evidence to existing theoretical evidence and highlight future areas of research (Siddaway et al., 2019).

3.2 Literature searches

Literature searches for this systematic review were performed in 5.1.2024. The searches were carried out on Scopus, ProQuest, EBSCOhost databases and PubMed. It was defined in the search that the articles must be peer-reviewed and written in English. Articles published after 1.1.2004 were included in the search. Only academic articles were searched. These definitions were added into search phrases or otherwise defined in the database system. The search terms are presented by databases (table 1).

Table 1: *Search terms used by databases.*

EBSCOhost databases	("autism spectrum disorders" OR asd OR autism OR autistic) AND (anorexia OR anorexic OR "anorexia nervosa") AND (comorbidity or comorbidities or cooccurrence or comorbid or co-occurring or co-morbid or concurrent) AND (treatment OR intervention OR therapy OR management OR rehabilitation OR hospitalization)
Scopus	(TITLE-ABS-KEY (autism OR "autism spectrum disorder" OR asd OR autistic) AND TITLE-ABS-KEY(anorexia OR "anorexia nervosa") AND TITLE-ABS-KEY(treatment OR therapy OR rehabilitation OR intervention OR management OR hospitalization) AND TITLE-ABS-KEY (comorb*))
Pubmed	("autism spectrum disorders" OR asd OR autism OR autistic) AND (anorexia OR anorexic OR "anorexia nervosa") AND (comorbidity OR comorbidities OR co-occurrence OR comorbid) AND (treatment OR intervention OR therapy OR management OR rehabilitation)
Proquest	noft(autism OR autistic OR asd) AND noft(anorexia) AND noft(treatment OR intervention OR therapy OR hospitalization OR rehabilitation OR management)

3.3 Eligibility criteria

For inclusion criteria, it was defined that an article must be an academic peer-reviewed article written in the English language and published after 1.1.2004. This systematic review was planned to include 10-20 academic articles. Quantitative data was warranted to better respond to the research question considering treatment effectiveness since treatment outcome measures are quantitative scales. Literature reviews, treatment guidelines, letters, qualitative studies, and conference publications were excluded. For quality control of the articles, it was defined that the journal where the article has been published must have a Jufo Classification of at least 1 at the time of the publication. Jufo-Classification ranges from 1 to 3: from basic quality to highest quality of the journal. Jufo-Classification of 0 implies that the publication does not fulfil the baseline criteria for quality journals (*User Guide for the Publication Forum Classification*, 2020).

Articles were included in the review if they examined the treatment of anorexia nervosa in cases where there was co-occurring ASC or elevated ASC traits. Comparisons of treatment groups of AN patients with and without elevated ASC traits were warranted. Articles that covered only the treatment of AN without a mention of co-occurring autism, were not included in this review. Because research surrounding this topic is still sparse, the literature was not limited to certain age groups of the patient groups investigated.

All articles must answer research question a; whether autistic traits are associated with the effectiveness of treatment of anorexia. In addition, they may also respond to research question b; what kind of treatment would be especially beneficial for this patient group? For research question a, clinical treatment effectiveness measures such as weight normalisation, reductions of ED pathology, general psychopathology, neuropsychological symptoms as well as service use are examined. Research question b was included to gather existing evidence of certain treatment methods for AN by comparing two subgroups with and without elevated ASC traits. It was required that studies were examining psychological treatment methods for anorexia nervosa: including psychosocial interventions, therapy formats, hospitalisation periods or rehabilitation processes. Articles that included only pharmacological treatment interventions or considered only somatic care for AN were excluded.

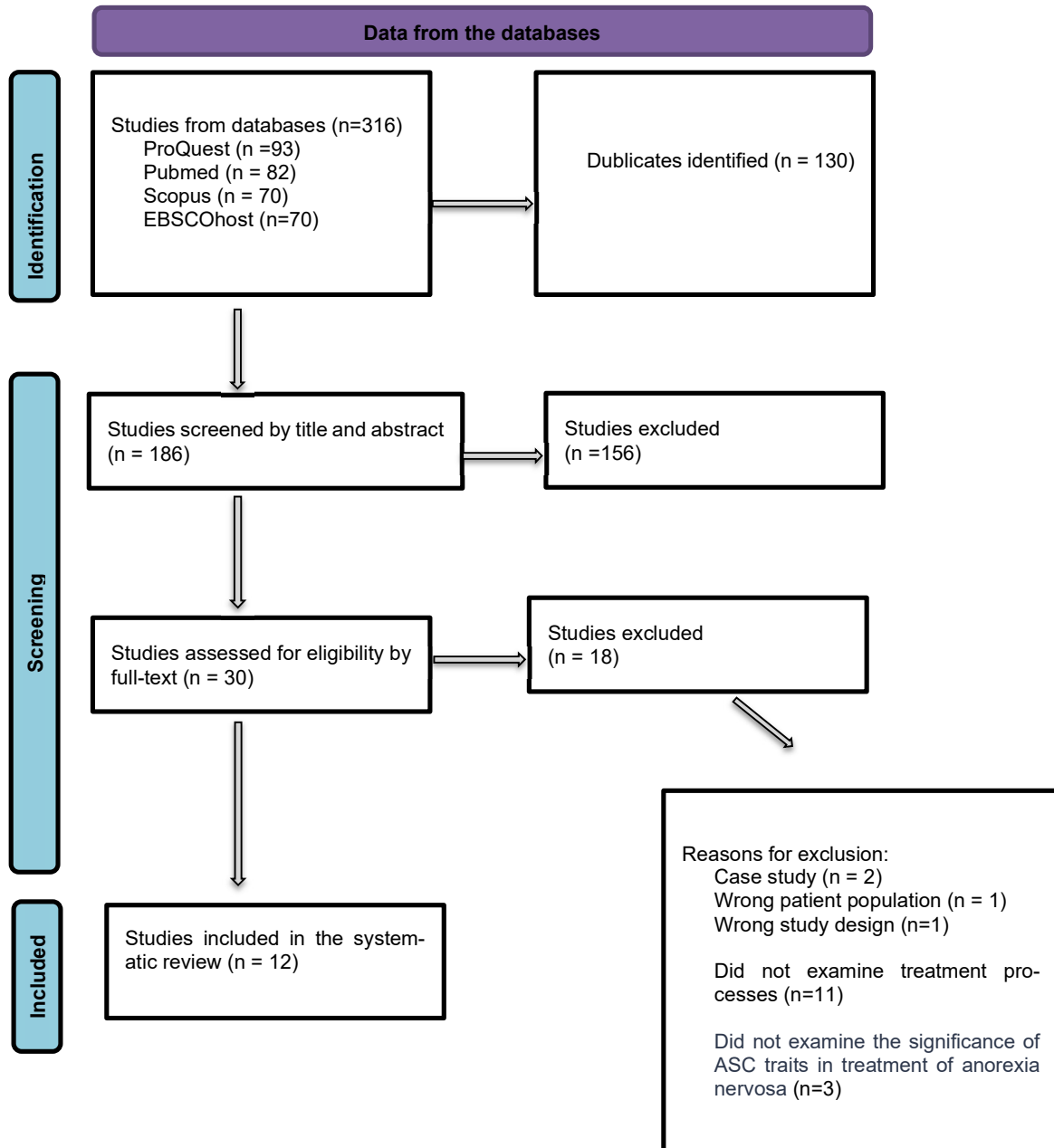
Clinically determined diagnoses of restrictive-type and binge-purging-type anorexia nervosa by criteria of DSM-IV or DSM-V, ICD-9, or ICD-10 were included. Articles that were focused on the treatment of eating disorders other than anorexia were excluded. Yet was decided to include

articles that were investigating atypical anorexia. This decision was made by the fact that individuals with this “other specified eating and feeding”-disorder exhibit similar psychological symptoms to anorexia nervosa. Autism spectrum diagnostic criteria have changed in the DSM-V diagnostic classification system. However, it was decided to include articles that have included patients with ASD diagnosis based on previous diagnostic guidelines. Assumption can be made that DSM-IV, ICD-9 and ICD-10 diagnoses can capture most features of the autism spectrum and by including these diagnoses also, the collected data will nevertheless have advantages. Therefore, articles including assessment methods or diagnostic guidelines based on DSM-IV, DSM-V, ICD-9, or ICD-10 criteria are included in this review. Articles that included anorexia patients with previous clinically verified autism diagnoses were included. Articles that tested autistic traits with appropriate methods such as AQ-10 (*autism spectrum quotient*) and ADOS-2 2 (*autism diagnostic observation schedule 2*) were included. Studies using SRS-2 (*social responsiveness scale*) were also decided to be included because it has been found to be a psychometrically appropriate tool for detecting autistic traits in clinical settings; and its advantage is representative norms (Kerr-Gaffney et al., 2020). Studies using SAS (*social amplitude scale*) with additional clinical interviews were also included: SAS combined with DAWBA (*the developmental and well-being assessment*) is thought to be an appropriate combination of methods for detecting ASC traits (Kaiser et al., 2023).

3.4 Study selection & screening process.

By search terms (See Table 1), in total 316 results were found, of which 130 duplicates were identified. After duplicates were excluded, 186 articles were left for title and abstract screening. If the title or abstract did not include a reference to both autism and anorexia, the article was excluded. Literature reviews, treatment guidelines, letters, qualitative studies, and conference publications were excluded in the first screening process. If both anorexia and ASC were mentioned and implications for treatment were presented in the abstract, articles were analysed by full text. In full-text analysis, 30 articles were screened. Yet some of the articles were excluded in full-text analyses because they did not investigate treatment processes, did not include treatment outcome measures, did not specify anorexia nervosa or other eating disorders in statistical analysis, or did not investigate the significance of ASC traits for treatment. Twelve articles were included in this systematic review. The screening process is presented. (See Figure 1).

Figure 1: Screening process according to the PRISMA guidelines (Page et al., 2021).



4 Results

4.1 Study characteristics

Studies included in this systematic review examined implications for treatment from different perspectives and responded to defined research questions. All articles in this review were peer-reviewed. Journals where the articles were published had a Jufo-Classification of 1 (eleven articles) or of 2 (one article). Two of the journals received a Jufo-classification of 2 after the publication date of the articles. For the research question a. focus of interest was whether autistic traits affect clinical outcome measures such as BMI, eating disorder pathology, psychopathology, neuropsychological performance, and overall functioning. It was also explored whether ASC traits affect the intensity of treatment. For research question b it was examined what treatment would be especially beneficial. Interventions investigated were family-based therapy, cognitive remediation therapy (CRT), cognitive and emotional skills training (CREST) as well as psychiatric inpatient and day-patient programmes were examined. All articles responded to research question a. Research question b was answered by eight studies.

Most articles included in this systematic review were naturalistic studies in inpatient or outpatient programmes. Three articles included a follow-up examination of the treatment of outcomes. The data included one RCT study and one case series study. All articles fit the inclusion criteria by the time frame they were published. All articles were published after 2016 and the latest was published in 2022. All articles identified a group with elevated autistic traits. Three studies included participants who had clinically verified autism diagnoses before the treatment of anorexia. In most studies, autistic traits were measured in patient groups by AQ-10 or ADOS-. In one study autistic traits were measured by SRS-2. In one article SAS was used to categorise participants into a group with elevated ASD trait levels and some participants received probable ASD diagnosis by the ASD module of DAWBA (Nazar et al., 2018). Anorexia nervosa diagnoses had been administered by clinicians according to the criteria of DSM-IV, DSM-V, ICD-9, ICD-10, or ICD-11. Diagnoses of anorexia nervosa included mostly restrictive subtype of anorexia nervosa (*R-AN*) but also binge-purge subtype of anorexia nervosa (*BR-AN*) and atypical anorexia nervosa (*AAN*). Overall sample sizes ranged from 35 to 3189. The size of the ASC group ranged from 16 to 149. Study characteristics are shown more in detail (see Table 2)

Table 2: Study characteristics

Study	Study setting	Intervention	Sample characteristics		Sample size		Autism assessment method	Outcome measures	Main results
			Age	Proportion of women	Overall sample	ASC group			
Adamson et al. (2018)	Naturalistic study	Individual and group CREST	18-63 (M=25.5)	100 %	Individual CREST n=66 Group CREST n=62	Individual CREST n=21 Group CREST N=21	AQ-10	SAS, TAS, Motivational ruler	No significant difference in treatment response between groups
Bentz et al. (2022)	Case series	Family-based therapy	10–17	87.1 %	n=157	N=16	Clinically verified diagnosis	IEBW, need of intensified care, successful treatment completion	No difference in weight normalisation or successful treatment competition between groups. Elevated need for intensified care in the ASC group.
Dandil et al. (2020)	Naturalistic study	Individual CRT	M=23.9	100 %	N=99 All measures n=61	n=25	AQ-10	ROCF, Brixton test, D-flex	CRT seems to be a feasible intervention among patients with elevated ASC traits
Giombini et al. (2022)	Single-centre RCT	Individual CRT & TAU/TAU only	10–18 M=14.49	93.8 %	n=80	n=18	SRS-2	WCST, ROCF, Brixton test, D-Flex, EDE-Q, RCADS, SCQ, Motivational ruler	CRT seems to be a feasible intervention among patients with elevated ASC traits, although patients might benefit from alterations in the treatment program.
Zhang et al. (2022)	Register-study	Outpatient and inpatient care	Age > 16	98 %	n = 3189	n = 134	Clinically verified diagnosis	29 outcome measures (eg. eating disorder pathology, overall functioning, treatment intensity)	Having co-occurring ASD was associated with significantly worse outcomes on 22 measures
Leppänen et al. (2022)	Naturalistic study (2-year follow-up)	Inpatient care	12–27	100 %	n = 118	Above cut-off: AQ-10 n=30, ADOS-2 n=35, both n=9	ADOS-2, AQ-10	BMI, EDE-Q, HADS, OCI, WSAS	Patients with elevated ASC traits showed more severe eating disorder symptoms in terms of psychopathology and eating disorder pathology across time points.
Li et al. (2020)	Naturalistic study	Inpatient and day-patient care, step-up programme	Age>18	97.9 %	n = 476 IP 306 86 SU 82 20 DC 88 20	n=126 IP 86 SU 20 DC 20	AQ-10	EDE-Q, HADS, WSAS, Motivational Ruler, BMI	Inpatient treatment was effective for patients with high autistic traits.

Abbreviations: BMI=Body Mass Index; EDE-Q=Eating Disorder Examination Questionnaire; OCI=Obsessive-Compulsive Inventory; ROCF=Rey-Osterrich Complex Figure; RCADS=revised children’s anxiety and depression scale; SAS=Social Amplitude Scale; TAS=Toronto Alexithymia Scale; SCQ=Social Communication Questionnaire; WSAS=Work and Social Adjustment Scale; HADS=Hospital Anxiety and Depression Scale; AQ=Autism Spectrum Quotient; ADOS=Autism Diagnostic Observation Schedule; SRS=Social Responsiveness Scale; D-Flex=Detail and Flexibility Questionnaire; IEBW=mean expected body weight z-score; IP=Inpatient care; DC= Day-patient care; SU=Step-up

Study	Study setting	Intervention	Sample characteristics		Sample size		Autism assessment method	Outcome measures	Main results
			Age	Proportion of women	Overall sample	ASC group			
Nazar et al. (2018)	Naturalistic study (1-year follow-up)	Inpatient care	13–21 M=16.9	91.4 %	N = 149	n=23 Probable ASD diagnosis n=6	DAWBA, SAS	BMI, DASS-21, SDQ, SEED, medication use	Patients with ASC show a similar reduction of eating disorder pathology in treatment. Yet patients have an elevated need for treatment and more severe residual difficulties after treatment
Prucoli, et al. (2021)	Naturalistic study (45-day follow-up)	Inpatient care	11–17 M=14,6	95,1 %	N=82	N=22	ADOS-2, AQ-10 & clinical interview	EDI-3, SAFA, %BMI, treatment intensity	The patient group with suspected ASD diagnosis did not differ by treatment intensity, weight normalisation, reduction of eating disorder pathology, or psychopathological concerns.
Stewart et al. (2017)	Naturalistic study	Inpatient care (mainly family-based therapy)	9–18 M=14,6	100 %	N=286	N= 20	AQ, DAWBA	EDE-Q, SAS, Morgan Russel Scale, %mBMI, Self- and parent-reported MFQ, SCARED, CHOOCI	Less reduction of eating disorder pathology in the ASC group. No difference in physical outcomes or length of treatment periods between patient groups.
Tchanturia et al. (2016)	Naturalistic case series study	Group CRT	M=26,2	n/a	N=35	N=14	AQ-10, ADOS-2	Self-reported D-flex, Motivational ruler	Significant improvements in motivation or self-reported cognitive styles in group CRT were limited to patients with low autistic traits
Tchanturia et al. (2019)	Naturalistic study	Inpatient care	18–55 M=27,3	100 %	N=171	<i>size of the group not specified</i>	AQ-10	BMI, HADS, EDE-Q, WSAS	Elevated AQ-10 scores were associated with more severe eating disorder symptoms, psychopathology, and occupational difficulties. Elevated AQ-10 scores were not associated with treatment effectiveness.

Abbreviations: AQ=Autism Spectrum Quotient; ADOS=Autism Diagnostic Observation Schedule; BMI=Body Mass Index; EDE-Q=Eating Disorder Examination Questionnaire; SAS=Social Amplitude Scale; WSAS=Work and Social Adjustment Scale; HADS=Hospital Anxiety and Depression Scale; DASS-21=Depression, Anxiety and Stress Scale; SDQ=Strengths and Difficulties Questionnaire; SEED=The Short Evaluation of Eating Disorders; EDI=Eating Disorder Inventory; SAFA=The Self-Administered Psychiatric Scales for Children and Adolescents; DAWBA=The Development and Well-Being Assessment; SCARED=Screen for Child Anxiety Related Disorders; CHOCCI=Child Obsessional Compulsive Inventory; %m BMI=Percentage median Body Mass Index; %BMI Percentage Body Mass Index; MFQ=Moods and Feelings Questionnaire; D-Flex=Detail and Flexibility Question

4.2 Synthesis

4.2.1 Are elevated autism spectrum traits associated with the effectiveness of treatment of anorexia nervosa?

Reduction of eating disorder pathology

Eight studies examined eating disorder pathology on EDE-Q and in seven studies trajectories of reduction of eating disorder pathology were examined. In five studies AN patients with co-occurring ASD diagnosis or with elevated ASC trait levels showed more severe ED pathology on EDE-Q (Leppanen et al., 2022; Li et al., 2020; Tchanturia et al., 2019; Zhang et al., 2022). In four studies there were no significant differences at baseline in ED pathology were found between groups (Giombini et al., 2022; Nazar et al., 2018; Pruccoli, Rosa, et al., 2021; Stewart et al., 2017). It was examined whether elevated ASC traits are associated with a reduction of eating disorder pathology. In five studies no significant difference in patterns of reduction of ED pathology among patients with elevated ASC traits compared to controls was found (Giombini et al., 2022; Leppanen et al., 2022; Nazar et al., 2018; Pruccoli, Rosa, et al., 2021; Tchanturia et al., 2019). Yet in one study patients with high ASC traits showed less improvement on EDE-Q on the subscale of weight and shape concerns (Stewart et al., 2017). In a study examining treatment effectiveness of different treatment programmes: participants with high ASC traits showed more reduction of ED pathology in inpatient care compared to participants with low ASC trait levels; this effect was reversed in day-patient care (Li et al., 2020).

Weight normalisation

Eight studies used weight normalisation (measured with BMI, %mBMI or IEBW) as a treatment outcome measure. It was found that individuals having ASD diagnosis had lower minimum BMI during anorexia nervosa (Zhang et al., 2022). In another study, it was found that patients with elevated ASD trait levels had significantly higher BMI at the beginning of treatment (Li et al., 2020). In most of the studies, no association between elevated ASD traits and weight was found and similar patterns of weight normalisation among adult and young patients with high and low autistic traits were observed (Bentz et al., 2022; Leppanen et al., 2022; Nazar et al., 2018; Pruccoli, Rosa, et al., 2021; Stewart et al., 2017; Tchanturia et al., 2019). One study found that in inpatient care patients with high ASC traits showed more weight normalisation compared to patients with low ASC traits (Li et al., 2020).

Reduction of psychopathology

Six studies considered the co-occurring psychopathology (anxiety, depression, OCD) during AN; yet psychopathology was measured with various measures (see Table 2: see Table 3). Five studies found an association between ASC and more severe psychopathology (Leppanen et al., 2022; Li et al., 2020; Stewart et al., 2017; Tchanturia et al., 2019). In two studies no significant differences in psychopathological symptoms were noted between the groups with high and low autistic traits (Giombini et al., 2022; Pruccoli, Rosa, et al., 2021). Yet in most of the studies, no significant differences in treatment effectiveness in patterns of reduction of psychopathological symptoms were observed between patient groups with high ASC and low ASC trait levels (Giombini et al., 2022; Leppanen et al., 2022; Li et al., 2020; Pruccoli, Rosa, et al., 2021; Stewart et al., 2017; Tchanturia et al., 2019). In the study of Nazar and colleagues' patients with co-occurring ASC reported more impairment on SDQ (*strengths and difficulties questionnaire*), indicating a higher risk for psychopathology. Although the patients with ASC showed similar improvement on SDQ compared to the non-ASC group, difficulties remained more severe in the ASC group (Nazar et al., 2018). Overall, it was noted that individuals with ASC continued to present more severe psychopathology; and more often clinically severe pathology after treatment (Leppanen et al., 2022; Li et al., 2020; Stewart et al., 2017; Tchanturia et al., 2019).

Outcomes on socioemotional and overall functioning

Six studies investigated social and overall functioning in the patient groups. Elevated ASC traits were associated with more severe impairment in socioemotional and functional domains at baseline (Adamson et al., 2018; Leppanen et al., 2022; Li et al., 2020; Nazar et al., 2018; Tchanturia et al., 2019; Zhang et al., 2022). Adult and adolescent patients in ASC groups showed more impairment on the "work and social scale" (Leppanen et al., 2022; Li et al., 2020; Tchanturia et al., 2019) and young patients showed more social difficulties on SDQ (Nazar et al., 2018) across time points. Patients with co-occurring ASD reported more clinical impairment on CIA and CGI and lower general and social functioning on GAF at admission and discharge. (Zhang et al., 2022). Participants with high ASC traits had significantly higher levels of social anhedonia and alexithymia across time-points (Adamson et al., 2018). Yet no significant differences of improvement in socio-emotional functioning were observed between patient groups with high and low autistic traits (Adamson et al., 2018; Leppanen et al., 2018; Li et al., 2020; Nazar et al., 2018; Tchanturia et al., 2019).

Four studies considered motivation as a treatment outcome measure and patient group characteristic; a self-reported Motivational Ruler was used as a measure. Two studies reported no differences in motivation at baseline or improvement in motivation among patient groups with high and low ASC traits (Adamson et al., 2018; Giombini et al., 2017). Although different responses in improvement of motivation have been noted. In one study participants with high autistic traits reported to have lower readiness to change and less improvement on this measure (Li et al., 2020). In one study significant improvement on treatment motivation was only limited to patients with low ASC traits (Tchanturia et al., 2016).

Neuropsychological outcomes

Three studies examined neuropsychological outcomes of central coherence and cognitive flexibility. In all studies, the ASC group showed more difficulties in neuropsychological domains at baseline (Dandil, Smith, Adamson, et al., 2020; Giombini et al., 2022; Tchanturia et al., 2016). Self-reported cognitive flexibility was measured by D-flex. In one study clinically significant improvements on self-reported cognitive styles of cognitive flexibility and central coherence were limited to patients with low ASC traits (Tchanturia et al., 2016). In another study, significant improvement in self-reported cognitive flexibility was found in both ASC and non-ASC group (Dandil, Smith, Adamson, et al., 2020). Generally, the ASC group showed high self-reported D-Flex scores at baseline (indicating higher cognitive inflexibility) and the non-ASD group showed low scores; although the high scores reduced and the low baseline scores increased after CRT (Giombini et al., 2022).

Performance-based measures were ROCF (Rey-Osterrich figure) for central coherence and for cognitive flexibility WSCT (Wisconsin card sorting task) and Brixton test. When comparing performance-based measures, both ASC and non-ASC subgroups showed significant improvements in central coherence measured with ROCF: with no significant difference in improvement between these groups (Giombini et al., 2022). In another study: no improvement was found on central coherence measured with ROCF in either of the groups; no significant difference in treatment response was noted between groups. (Dandil, Smith, Adamson, et al., 2020). In the same study, no significant difference in improvement in cognitive flexibility was noted between the ASC and non-ASC groups on the Brixton test (Dandil, Smith, Adamson, et al., 2020). However, in the other study, the non-ASC group showed more improvement in cognitive flexibility measured with WSCT and Brixton test compared to the ASC group (Giombini et al., 2022).

Treatment augmentation and treatment completion

Five studies compared treatment augmentation between ASD and non-ASD groups. In one study no significant difference in treatment duration or frequency of hospital admissions was found between the groups of participants with high or low autistic traits (Prucoli, Rosa, et al., 2021). Yet in four studies ASC was associated with heightened need and use of psychiatric inpatient and day-patient care (Bentz et al., 2022; Nazar et al., 2018; Stewart et al., 2017; Zhang et al., 2022): although in one of the studies, treatment augmentation was rather predicted by depressive symptoms (Stewart et al., 2017).

There was no difference in treatment completion rates between groups (Nazar et al., 2018; Tchanturia et al., 2016). No differences in rates of patients having successful treatment completion in 12 months were found between groups of high and low autistic traits (Bentz et al., 2022). However, in one study association between a chronic course of illness and co-occurring ASD was noted. Of patients with co-occurring ASD, 67 per cent had a severe and prolonged course of AN compared to 37 per cent in the group without ASD (Zhang et al., 2022).

4.2.2 What kind of treatment would be especially beneficial for anorexia nervosa?

Cognitive remediation therapy with or without emotional skills training

The outcomes of cognitive remediation therapy were evaluated in three studies. Outcomes were defined by neuropsychological characteristics and motivation. A similar response to individual cognitive remediation therapy was observed between ASC and non-ASC (Dandil, Smith, Adamson, et al., 2020). In a study of Giombini and colleagues (2022) examining individual CRT, poorer treatment response was noted in the ASC group. Patient age and timing of therapy sessions were affecting treatment response in the ASC group; CRT was more effective for patients with older age and patients with high ASC traits benefitted from the intervention more if it was offered later in the inpatient treatment programme (Giombini et al., 2022). When outcomes of brief group format CRT were measured, improvements on cognitive thinking styles and perceived abilities to change were limited to patients with low ASC trait levels (Tchanturia et al., 2016). In a study examining CREST in both individual and group formats participants with elevated ASD traits showed similar responses to treatment: improvements on motivation and reduction of alexithymia in individual format were comparable between groups (Adamson et al., 2018).

Family-based interventions

Among young anorexia patients with and without co-occurring diagnosis of ASC, no differences in rates of patients having successful treatment completion or weight normalisation were found (Bentz et al., 2022). The study of Stewart and colleagues primarily investigated family-based interventions; the ASC subgroup did not differ in terms of physical outcomes, reduction of psychopathological concerns or treatment duration, yet the ASC group showed less reduction of ED symptoms (Stewart et al., 2017). In the study of Nazar and colleagues, carer intervention had been added to treatment as usual: reduction of ED pathology was comparable between groups and treatment completion rates did not differ (Nazar et al., 2018). Preliminary evidence suggests that family-based interventions would be feasible interventions for young anorexia nervosa patients with co-occurring autism since similar patterns in treatment completion and weight normalisation were found (Bentz et al., 2022; Nazar et al., 2018; Stewart et al., 2017). Although family-based interventions warrant further examinations of effectiveness since ASC was found to affect treatment effectiveness (Stewart et al., 2017).

Hospitalisation: inpatient, day-patient treatment, and outpatient treatment

Among autistic patients there was an elevated need and duration of inpatient care; autistic patients had a mean of 121.9 days spent in inpatient care compared to 28.36 days in the group without co-occurring ASD (Zhang et al., 2022). Fifty per cent of patients with ASC received intensive care compared to 16 per cent in the non-ASC group (Bentz et al., 2022). When the treatment response of ASC and non-ASC subgroups was considered; the ASC subgroup did benefit from CRT more if it was offered later in the treatment programme (Giombini et al., 2017). In a study investigating treatment programmes of inpatient care, step-up programme, and day-patient care: the key finding was that patients with high levels of autistic traits seemed to benefit more from inpatient care than patients with low autistic traits in terms of weight normalisation and reduction of eating disorder pathology; although this effect was reversed in day-patient care (Li et al., 2020). The step-up programme is targeted to improvement in social and overall functioning, and reduction of ED pathology is rather a side target of treatment; at the end of this programme patients with high ASC traits showed significantly more social impairment and anxiety symptoms as well as weaker motivation compared to patients with low ASC trait, although statistical analyses lacked power to show significant effects due to small sample size (Li et al., 2020).

5 Discussion

5.1 Discussion of the results

This systematic review aimed to respond to a two-fold research question. The aim was to explore whether elevated ASC traits are associated with the effectiveness of anorexia treatment and to explore the findings of different interventions for the subgroup of anorexia patients with elevated ASC traits. A two-fold research question was responded to by existing up-to-date evidence yet partly limited evidence. It would have been expected that elevated ASC traits or ASC diagnosis would be associated with poorer treatment effectiveness and warrant treatment adaptations. This was assumed by the literature reviewed for the thesis. By shared characteristics of anorexia and ASC (e.g. sensory sensitivities, compromises in socio-emotional functioning, neuropsychological characteristics) it was expected that these would influence treatment response.

Psychopathology and eating disorder pathology

Evidence presented in the synthesis suggests that the reduction of psychopathological concerns shows similar patterns among patients with and without elevated autistic traits. In other words, elevated ASC traits do not seem to be associated with treatment effectiveness on this measure (Giombini et al., 2022; Leppanen et al., 2022; Li et al., 2020; Pruccoli, Rosa, et al., 2021; Stewart et al., 2017; Tchanturia et al., 2019). In addition, most of the studies included in the synthesis found no difference in patterns of reduction of eating disorder symptoms (Giombini et al., 2022; Leppanen et al., 2022; Nazar et al., 2018; Pruccoli, Rosa, et al., 2021; Tchanturia et al., 2019). These are unexpected findings since previous research shows that patients with co-occurring AN and ASC are more likely to obtain a chronic course of illness (Nielsen et al., 2015, 2022). However, two studies noted the differences in the reduction of eating pathology between the groups with high and low autistic traits (Li et al., 2020; Stewart et al., 2017). Furthermore, studies that included wider follow-up measurements after treatment found that participants in the ASC group had more residual difficulties after treatment. One study found an association between a more likely chronic course of illness and ASD diagnosis (Zhang et al., 2022). These imply that treatment effectiveness for the ASC group remains somewhat unspecific. Further longitudinal studies examining treatment effectiveness with larger sample sizes are likely warranted.

In the synthesis, it was noted patients with ASC have more severe psychological eating disorder symptoms across time points (Leppanen et al., 2022; Li et al., 2020; Tchanturia et al., 2019; Zhang et al., 2022) yet in a few studies, the association between ED symptom severity and autism was not observed (Giombini et al., 2022; Nazar et al., 2018; Pruccoli, Rosa, et al., 2021; Stewart et al., 2017). Interestingly there was a significantly higher age of participants in the studies that had found an association with the severity of psychological ED symptoms and ASC. This implies that differences are noted due to age in the patient groups that exhibit autistic traits. The co-occurrence should be examined separately among young and adult patients.

It is noteworthy that patients with ASC are more likely to present severe psychopathology at admission and discharge (Leppanen et al., 2022; Li et al., 2020; Stewart et al., 2017; Tchanturia et al., 2019). More severe psychopathology across time points in the ASC is considerable since individuals on the spectrum are more likely to obtain comorbid psychiatric conditions (Lai et al., 2019). In the synthesis, the elevated risk for self-harm and suicidality was noted (Zhang et al., 2022). A significantly higher proportion of patients with co-occurring ASD had received tube feeding during their treatment (Zhang et al., 2022) and patients in the ASC group had more psychotropic medication use at admission and during treatment (Nazar et al., 2018; Pruccoli, Rosa, et al., 2021). These are likely to reflect more severe ED symptoms and co-occurring psychopathology in the ASC group. This is in line with research suggesting a subgroup of AN with elevated ASC traits and a more severe symptomatic picture of an ED (Li et al., 2023). These highlight the importance of noting the more severe symptomatic picture of anorexia in treatment contexts when there is a co-occurrence of ASC.

Social and occupational functioning

Generally, patients with elevated levels of autistic traits have more severe impairment in social functioning compared to peers with low autistic traits across time points. In terms of treatment effectiveness, autistic traits did not seem to be associated with different treatment responses in terms of improvements in social and overall daily functioning. Although the presence of social difficulties is considerable due to the nature of ASC (Lai & Baron-Cohen, 2015). It can be questioned whether measures of social and functioning are appropriate measures of treatment outcomes when there is a co-occurrence of ASC. Social difficulties may be more pronounced in the acute illness phase, although a level of social challenges is characteristic of ASC. It has been suggested that measures of quality of life would better reflect intervention outcomes among autistic individuals (Movsessian & Osoba, 2022).

Physical outcomes

In response to the research question of treatment effectiveness, elevated autistic traits did not seem to be associated with treatment effectiveness in terms of weight restoration or physical outcomes (Bentz et al., 2022; Leppanen et al., 2022; Nazar et al., 2018; Pruccoli, Rosa, et al., 2021; Stewart et al., 2017; Tchanturia et al., 2019). However, in one study it was noted that participants with ASC obtained clinically more significant weight restoration than patients with low ASC traits (Li et al., 2020). Yet on the results of this review, the association with BMI remains low. The low association between BMI and autistic traits is considerable due to possible different presentations of anorexia when there is a co-occurrence of ASC. In qualitative studies, autistic patients have disclosed that a symptomatic picture of their anorexia nervosa is less characterised by weight concerns (Babb et al., 2021; Kinnaird et al., 2019; Li et al., 2022). Overall BMI as a clinical severity indicator for anorexia has been questioned. In studies that have grouped patients into groups by BMI; ED pathology or treatment outcomes between groups have been found to be independent of BMI (Machado et al., 2017; Toppino et al., 2022). In studies included in the synthesis even though ASC traits were not associated with BMI, there was a significant association with psychological ED symptoms and psychopathological concerns (Leppanen et al., 2022; Nazar et al., 2018; Stewart et al., 2017; Tchanturia et al., 2019). These imply that measuring treatment outcomes by BMI is less significant when examining the impact of ASC traits. Other clinical outcomes should rather be the focus when examining treatment outcomes in this comorbidity.

Treatment targets

Clinically severe anxiety, depression and social impairment have shown to be significantly more often present in the ASC subgroup even upon discharge on different treatment programmes (Li et al., 2020); this implies the need for continuing support after treatment. Overall, the results presented in the synthesis highlight the elevated need for psychiatric care in terms of duration and frequency of service use in the patient group with ASC traits. Yet it remains unspecific, to what extent more severe psychopathology in the ASC group predicts the heightened need for psychiatric services. It should be investigated further what factors account for the elevated service use. The elevated need for services likely reflects the more severe symptomatic picture of anorexia. It could be that now existing treatment methods in services lack the effectiveness for treating this comorbidity.

This systematic review included studies of cognitive remediation therapy, CRT with emotional skills training, family-based therapy as well as day-patient and inpatient care. Family-based treatment seemed to be a feasible intervention in terms of clinical symptom reduction (Bentz et al., 2022; Nazar et al., 2018; Stewart et al., 2017); yet the difference noted in one study in ED symptom reduction between ASC and non-ASC warrants further investigation (Stewart et al., 2017). Maudsley model treatment and cognitive behavioural therapy targeted to the treatment of eating disorders (CBT-ED) are commonly offered for anorexia nervosa, yet there is still a lack of studies investigating these interventions for the co-occurrence of AN and ASC; due to this, these interventions were not included in this review. Studies investigating a wider set of commonly used interventions among this comorbidity could be beneficial.

Outcomes of cognitive remediation therapy

Theoretically, cognitive remediation therapy could be an appropriate treatment method for patients with elevated autistic traits due to shared characteristics of cognitive rigidity noted in both ASC and AN (Leppanen et al., 2018; Treasure & Schmidt, 2013). Results were somewhat mixed in three studies included in the synthesis of this systematic review. In response to the research question: preliminary evidence of the feasibility of CRT for the ASC group exists (Dandil, Smith, Adamson, et al., 2020), although the ASC group might benefit from the treatment modifications (Giombini et al., 2022). Yet two studies implicated an association with ASC and somewhat poorer treatment effectiveness of CRT (Giombini et al., 2022; Tchanturia et al., 2016). The intervention of CRT should be investigated further with larger sample sizes in the ASC patient group. These studies had a focus on neuropsychological treatment outcomes. Yet to some extent, cognitive rigidity and detail-focused cognitive style are characteristic of the neurodevelopmental condition of ASC. For this, examining outcomes by ED pathology and quality of life could be useful.

Reflections on inpatient care

One study in the synthesis noted, that inpatient care seemed more efficient than day-patient programmes for the ASC group: in terms of weight restoration and reduction of psychological ED symptoms (Li et al., 2020). This could be due to individualised treatment plans and secure routines in inpatient treatment. Autistic patients have considered inpatient treatment beneficial but have noted the importance of structure, routines and rigid timetables (Babb et al., 2021). These results preliminarily suggest that patients with high autistic traits might not benefit from

day-patient care as much as peers with low autistic traits. Since day-patient care is the more cost-effective option with similar clinical effectiveness in the treatment of AN (Herpertz-Dahlmann et al., 2014), the effectiveness of day-patient care among the ASC group should be investigated further and the possible modifications to day-patient care could be considered to address neurodiversity better.

Reflections on group therapy sessions

Day-patient and step-up care included a lot of group participation. These treatment programmes were found to be less beneficial than inpatient treatment in ASC group (Li et al., 2020). This result could be due to the involvement of group work. It could be that group-based therapy could be less advantageous for the group in the ASC group due to the social burden of group work (Kinnaird et al., 2019). Positive effects of group format CRT were only limited to patients with low ASC traits (Tchanturia et al., 2016). However, conclusions about the significance of group-based intervention cannot be drawn by this study since the effectiveness of group and individual formats of treatment were not compared. In the study investigating CREST group format intervention seemed to be a feasible intervention in improving motivation; although significant reductions of alexithymia in the ASC subgroup were only noted in the individual format of CREST (Adamson et al., 2018). These results do not allow us to conclude the effectiveness of group work in the subgroup with elevated ASC traits due to discrepancies in the assessment methods used. Yet they pose a question of whether group-based therapy is less useful in this subgroup with elevated autistic traits. Difficulties with group work have been disclosed in qualitative studies including the experiences of patients with co-occurring ASC and AN (Babb et al., 2021; Kinnaird et al., 2019; Li et al., 2022). Together these qualitative findings propose the importance of individualised treatment considerations.

Unrecognised autism in eating disorder populations

In the studies included in the synthesis: approximately one-fourth of participants scored above the cut-off on autistic diagnostic measures, although the number of confirmed diagnoses was relatively low. High levels of autistic traits could to some extent be due to unrecognised autism among ED patients. In a register-based study in the synthesis, four per cent of the participants had confirmed ASD diagnosis and the median age for autism diagnosis was 23 years (Zhang et al., 2022). This implies a high age of first recognition of autism. In a meta-analysis, the global mean age for receiving ASD diagnosis was estimated to be 5 years; with males being more

likely to receive early diagnosis (van 't Hof et al., 2021). A study investigating the co-occurrence of anorexia and autism using a Swedish population-based sample; found a median age for females receiving diagnosis of ASD was 17 years (Dinkler et al., 2021). In the study of Zhang and colleagues' 86 per cent of patients had received their autism diagnosis only after their eating disorder diagnosis (Zhang et al., 2022). It has been noted that receiving an ED diagnosis is more likely when an autism diagnosis has been set in late childhood, compared to cases of earlier recognition of autism (Rødgaard et al., 2021). This indicates that early recognition of autism potentially provides required support earlier in life, and possibly reduces the risk of later eating disorders.

5.2 Strengths and limitations

This thesis presents implications for anorexia nervosa treatment when there is a co-occurrence of ASC and ASD. A strength of this review is the exploration of a relatively new but important area of research and its implications for future research. In the literature searches, articles were searched from 2004 to the beginning of 2024, a relatively broad time frame for inclusion. This decision was made by the presumption that evidence surrounding this comorbidity is limited, and even earlier data would be advantageous. This definition produced possibly more literature search results than necessary. Nevertheless, the articles included in this review were relatively recently published. The novelty of the data poses strengths for this review: the articles include recent diagnostic criteria, and recently validated assessment methods and offer treatment supported by recent guidelines.

The main limitations of this systematic review are the relatively low study samples. Many of the studies included had small samples of participants with high autistic traits. Due to small samples, some outcome measures might lack the power to show significant effects. Other limitations are related to the characteristics of the samples. For the large part participants included in the studies were women. It has been noted that the effect of gender is associated with different presentations of both autism and anorexia (Lai et al., 2015; Raevuori et al., 2014). Due to these varying presentations, these results might not be generalisable to males and non-binary individuals. The sample included participants from middle childhood to adulthood; heterogeneity of age groups might affect interpretation of the results. A large proportion of the studies included in this review were conducted by the same research group from the same geographical area. Furthermore, many studies were conducted in single-centre settings. Socioeconomic context

and treatment centre-related protocols may influence the generalizability of these results. In addition, most of the studies had included participants with both restrictive and binge-purging subtypes of anorexia as well as atypical anorexia; although a great majority had restrictive AN. Binge-purging and restrictive type anorexia show similar impairment, but the symptomatic picture somewhat differs between subtypes (Reas & Rø, 2018). Due to this, investigating the subtypes separately in the context of ASC could be beneficial.

The second main limitation was the high heterogeneity of study designs and outcome measures. Most of the studies were naturalistic studies. Only one study used a controlled study setting. The heterogeneity of different treatment interventions examined weakens the comparability of the results. In the majority of the studies, treatment-as-usual was offered, although protocols of TAU might differ across treatment centres. A large proportion of the studies included in this review were conducted in cross-sectional settings which prevents from drawing causal conclusions. Yet three studies included in this review examined treatment outcomes in follow-up examinations, which provides advantageous data. A limitation and a strength of this systematic review was the exploration of effectiveness by diverse outcome measures. This is a strength due to the multifaceted exploration of the co-occurrence of the conditions of anorexia and autism in treatment contexts. Although diverse outcome measures limit drawing strong conclusions.

The third main limitation is related to the autism assessment methods used. Only in three studies did the participants obtain confirmed ASD diagnosis based on wider diagnostic protocols. In the majority of the studies, there was a use of self-reported measures and autistic traits were measured during inpatient treatment of anorexia nervosa. Self-reported measures of autism have been criticised for low sensitivity, lack of retrospectivity of the items and likeliness to detect false positives due to current anxiety symptoms (Ashwood et al., 2016). It has been argued that high autistic traits observed among anorexia nervosa patients may reflect internalising psychopathology and acute phase of illness rather than a neurodevelopmental condition of autism (Calderoni et al., 2015; Westwood et al., 2016). The somewhat unstable nature of ASC traits was noted in the studies since there was a significant reduction of ASC traits during treatment (Li et al., 2020; Tchanturia et al., 2019). In most of the studies included in the synthesis, there was a presence of psychiatric comorbidities in the samples which could have possibly led to overestimation of ASC. Yet ADOS-2 and AQ-10 have been found to be reliable assessment methods among patients with AN: not falsely identifying autism due to anxiety-related behaviours and depression (Adamson et al., 2022; Barnett et al., 2021; Sedgewick et al., 2019). Yet

further studies investigating this comorbidity with a set of questionnaires together with retrospective data, diagnostic interviews and validated observation are warranted.

5.3 Conclusions

In the anorexia patient group with co-occurring ASD diagnosis or elevated autistic traits there seems to be a severe range of eating disorder symptoms: in terms of eating disorder pathology, comorbid psychopathology as well as social and occupational challenges. However when treatment effectiveness is considered: patients with and without elevated autistic traits generally show similar patterns of weight restoration, neuropsychological improvement as well as reduction of eating disorder-related and psychopathological concerns. Yet some studies have reported a poorer response to treatment in the subgroup with elevated autistic traits (Giombini et al., 2022; Li et al., 2020; Stewart et al., 2017; Tchanturia et al., 2016; Zhang et al., 2022). One study included in the synthesis found an association between a chronic course of illness and co-occurring autism spectrum condition (Zhang et al., 2022).

Co-occurring autism seems to be associated with an elevated need for inpatient and outpatient care and longer treatment periods. Preliminary evidence of the effectiveness of cognitive remediation therapy and family-based therapy exists for the anorexia patient group with elevated autistic traits, yet future research on these treatment methods is warranted. There is evidence of inpatient treatment being more efficient for this patient group than day-patient programmes. Individuals with co-occurring ASC might benefit more from individual therapy sessions than group sessions.

5.4 Implications for future research

This area of research is still relatively new. More research surrounding this topic is needed to acknowledge the co-occurrence of anorexia nervosa and autism spectrum conditions better in treatment contexts. Research across treatment centers is needed and larger sample sizes are warranted to draw more reliable conclusions. Studies using clinically verified diagnoses of ASD are warranted. While studies investigating the effectiveness of treatment adaptations for this co-occurrence are required: making treatment adaptations comes with the need for resources. In this systematic review, the cost-effectiveness of treatment methods was not examined. Further studies examining the cost-effectiveness and long-term effects of treatment adaptations for this subgroup are likely warranted.

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