

# *Literature Review*

## Is Autism Spectrum Condition Over-Represented in Patients with Anorexia Nervosa?

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### Abstract

**Introduction:** It has been clinically observed that autistic traits may be over-represented in anorexia nervosa (AN) patients. The prevalence of autism spectrum condition (ASC) in AN populations has been studied, but the relationship is poorly understood.

**Objectives:** This review aims to synthesise data from published literature about the prevalence of ASC in AN populations, and evaluate its validity. As well as this, challenges for researchers, prognosis of patients with comorbid ASC and AN, and recommendations for practice, are explored.

**Methods:** Multiple databases were searched using the St George's, University of London search engine, for articles relating to the prevalence of ASC in AN populations. Full-text articles were screened for relevant data, and citation tracking was used.

**Findings:** The prevalence of ASC varies in different populations; differing study designs and ASC diagnostic tools, as well as the cognitive effects of starvation, may be responsible. However, autistic traits are evidently over-represented in AN patients, and adaptations to clinical practice should be made, to better tailor the treatment to autistic patients.

**Conclusion:** Overall, it appears the prevalence of ASC is significantly higher in AN patients than the general population, which should be considered clinically when these patients access treatment.

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## Introduction

Autism Spectrum Condition (ASC) is a neurodevelopmental disorder characterised by a deficit in social communication and interaction, as well as restricted, repetitive behaviours. Symptoms are present early on in development (American Psychological Association, 2021). Anorexia nervosa (AN) is an eating disorder characterised by a restriction of energy intake, an intense fear of weight gain and a body image disturbance (NICE, 2019). The latter two distinguish AN from avoidant/restrictive food intake disorder (ARFID), which involves a selective or restrictive eating pattern with the absence of changes to cognition around weight and body image (Cañas *et al.*, 2020). ARFID has a strong association with ASC. A relationship between AN and ASC has been described in much literature, starting with the suggestion by Gillberg in 1982 that the two conditions share an underlying genetic vulnerability, which presents as AN in females and ASC in males, due to the biased sex ratio in both conditions (Dell'Osso *et al.*, 2016). It is well documented in the literature, and observed by clinicians, that there is an increased rate of autistic traits in eating disorder patients, when compared with the general population (Carpita *et al.*, 2020). There are multiple theories for the reason for this relationship, including the presence of common traits such as social anhedonia, deficits in emotional intelligence, increased attention to detail and alexithymia (Dell'Osso *et al.*, 2016). More recently the epidemiology has been studied further, and this review aims to critically evaluate the existing literature, with a specific focus on the prevalence of ASC in anorexia nervosa patients.

A 2021 study identified barriers to accessing or benefiting from treatment of anorexia in women with ASC. These included misunderstanding of autism and autistic traits, one treatment not fitting all patients, and reduced accessibility and engagement with services (Babb *et al.*, 2021). It is clear from the literature that autistic patients have unmet needs within eating disorder (ED) services, and there is scope for improving ED services by providing targeted therapy for autistic patients. This emphasises the importance of identifying undiagnosed patients with ASC when they present to ED services. Many different autism diagnostic scales may be used in this context, and some are evaluated in this review.

Many challenges are faced by researchers wishing to accurately identify the prevalence of ASC in AN. These include missed, delayed or incorrect diagnosis; development of secondary mental health problems in autistic adolescents; the inability to distinguish between autistic traits and the cognitive state caused by acute AN and starvation; and the lack of consistency with diagnostic criteria (Westwood and Tchanturia, 2017). These are discussed in more detail in the review.

Overall, this review aims to outline the existing literature on the prevalence of ASC in AN populations. As well as this, some diagnostic tools for ASC are evaluated, and barriers to accurate estimation of the prevalence are identified. Finally, the review makes some recommendations for practice, given the findings.

## Methods

Numerous databases were searched using the Hunter search engine, belonging to the St George's, University of London library. Databases included, but were not limited to, Medline, PsychInfo and Embase. Search terms included autism\*, anorexia\*, anorexia nervosa, ASC, ASD, AN, and prevalence.

As this was a literature review, rather than a systematic review, there were no strict inclusion and exclusion criteria. However, over 1,000 abstracts were screened, and full-text articles selected if they measured the prevalence of ASC within an AN population, using a validated tool. Citation tracking was also used to attempt identification of all relevant articles.

From these, the measured prevalence, as well as the research methods, were evaluated.

## Findings

### Diagnosis of ASC

Diagnosis of autism requires both direct observation and a developmental history, showing that symptoms were present from infancy or early childhood. Validated scales that are widely used to aid diagnosis of ASC include the Developmental, Dimensional and Diagnostic Interview (3Di), the Childhood Autism Rating Scale (CARS), the Autism Spectrum Disorder-Observation for Children (ASD-OC), the Autism Diagnostic Interview-Revised (ADI-R), the Asperger Syndrome Diagnostic Interview (ASDI) and the Diagnostic Interview for Social and Communication Disorders (DISCO) (Sharma, Gonda and Tarazi, 2018). A challenge faced by researchers and clinicians using these scales is that many have only been validated in male-dominated samples, due to gender bias in ASC diagnosis, with a male to female ratio of 4.1:1 (Fombonne *et al.*, 2021). Females often receive diagnoses later than males, and there is a potential for females to be underdiagnosed based on traditional assessments (Leedham *et al.*, 2019). This highlights the need for diagnostic tools validated in females, since they make up the majority of inpatient ED populations.

Moreover, some diagnostic scales are based on direct observation (e.g. ADOS-2), while others are based on developmental history or parental report (e.g. 3Di). Thus, selecting an appropriate diagnostic tool is essential to the validity of prevalence data. Particularly in AN patients, traits associated with autism are seen in the more active phase of the illness and could be attributed to the cognitive effects of starvation (Oldershaw *et al.*, 2011). This may confound the findings of any study that uses direct observation alone; such studies may be measuring autistic traits, rather than a formal diagnosis. Therefore, studies that include a developmental history or parental report in the diagnostic criteria, showing presence of autistic traits in early childhood, may be more valid, particularly during the active stages of disease. However, it could also be argued that this distinction is not clinically relevant, since presence of these traits may mean that treatment in this group would be more effective if they were considered. In

the general population, combining observational and developmental measures can increase the sensitivity and specificity for detecting ASC (Risi *et al.*, 2006).

### **Autism Diagnostic Observation Schedule 2<sup>nd</sup> Edition (ADOS-2)**

Perhaps the most commonly used tool is the Autism Diagnostic Observation Schedule 2<sup>nd</sup> Edition (ADOS-2) – a semi-structured interview which bases diagnosis on direct observation. It was validated in a large German study with 826 participants (Medda, Cholemky and Freitag, 2018). This study showed that both the ADOS and the ADOS-2 have good diagnostic accuracy. Although the sample was more than 80% male, the large sample size means that a sufficient number of female participants were included, particularly in Modules 3 and 4, in order to validate the tool in females. The ADOS-2 has also been used in ED populations; A 2019 study with 175 participants validated a revised version of the ADOS-2, which aligns more closely with the DSM-V, in AN patients. It found that the revised ADOS-2 was more sensitive in both current and recovered AN patients (Sedgewick *et al.*, 2019). However, the ADOS-2 alone is not sufficient for a diagnosis of autism, since a developmental history is required.

### **Developmental, Dimensional and Diagnostic Interview (3Di)**

The 3Di is a structured interview based on parental report. A short version, known as the 3Di-sv, takes 45 minutes to complete (in contrast to the ADOS-2, which takes approximately 3 hours), and was found to have good sensitivity in a study comparing it with the ADOS-2 (Slappendel *et al.*, 2016). The tool was found to have a high sensitivity of 85% (CI 70%-92%) and a relatively lower specificity of 54% (CI 44%-63%). A strength of the study is that further analysis was performed to check for differences depending on age, IQ and gender. There was no significant difference between the genders, meaning it is valid in females. Moreover, the 3Di-sv has been used in assessments in ED settings, such as in a Pooni *et al.*'s 2012 study discussed later in this review.

### **ASC Prevalence in General Population**

A review of epidemiological data from 37 countries found a mean prevalence of 0.97% for ASC in 26 high-income countries (Fombonne *et al.*, 2021). This is a significant increase in prevalence over the last 50 years, accompanied by a decrease in intellectual disability, suggesting a potential increase in diagnosis of patients with less severe symptoms. The male to female ratio is 4.1:1, which has not changed over time (Fombonne, MacFarlane and Salem, 2021). A strength of the review is that surveys from a wide range of populations were used, however none of the 28 lowest-income countries (as classified by the World Bank) were included. Another limitation is that the studies included in the review do not use consistent diagnostic criteria, meaning caseness is not well defined and comparison between studies may not be accurate. This limitation appears to be consistent across much of the literature.

### **ASC Prevalence in Eating Disorder Populations**

Much of the initial data on the prevalence of ASC in AN patients comes from a Swedish community sample (N=51), on which 12 papers were published up to 2011. A systematic review by Huke *et al.* (2013) summarises the results from eight of these studies (see **Table 1**). The mean prevalence of ASC calculated in these studies was

22.9%, with a range of 8-37%. This is significantly higher than in the general population. However, all studies sampled a single community, limiting the generalisability of the findings. Moreover, the longitudinal retrospective design means that participants were tested at different stages of disease and recovery. The use of varying diagnostic criteria limits comparison of the studies.

**Table 1: Table showing results from studies of a Swedish retrospective community sample. The table shows the author's name, year of publication, and prevalence rates of ASC found in each study.**

Study	Prevalence rate of autism spectrum disorders (%)
Råstam (1992)	8
Gillberg et al. (1995)	37
Wentz Nilsson et al. (1998)	31
Wentz Nilsson et al. (1999)	18
Råstam et al. (2003), Study 1	20
Råstam et al. (2003), Study 3	18
Wentz et al. (2005)	23
Anckarsäter et al. (2011)	28

Source: Huke *et al.* (2013).

Four studies between 2015 and 2017, using the ADOS-2, were summarised in a literature review by Westwood and Tchanturia (2017). These studies found prevalence of ASC in AN patients ranging from 10% to 50%. The 50% prevalence rate was calculated in a pre-selected sample of women (N=10) who had suspected ASC (Mandy and Tchanturia, 2015). This conclusion is limited by the small sample size and selection bias, potentially accounting for the high prevalence.

Postorino *et al.* found a 10% prevalence in a group of female adolescents. This smaller value could be reflective of the lower age range of participants, in agreement with a Pooni *et al.* study (2012) in adolescents, which suggests that the prevalence of autistic traits varies with age and disease progression. Overall, studies with adolescents appear to have lower rates of autistic traits than in adults; this could indicate that symptoms of ASC become more obvious with age, or that patients with ASC are less likely to respond to treatment, thus remaining in ED services as adults.

The largest study to date to use the ADOS-2 in AN is a cross-sectional study (N=60) in which 23.3% of participants scored above the cut-off for a diagnosis of autism (Westwood, Mandy and Tchanturia, 2017), similar to the mean prevalence calculated by Huke *et al.* in 2013.

In the aforementioned 2019 study, which used the adapted version of the ADOS-2 to more closely align with the DSM-V, 27.3% of the AN group scored above the cut-off for ASC. This contrasts with the comparison group of participants recovered from AN in which only 19.6% scored above the cut-off. However, this is higher than the healthy control group, in which 9.5% scored above the cut-off (Sedgewick *et al.*, 2019). A unique strength of this study is the use of a recovered comparison group, allowing for a better understanding of the differences in presentation depending on disease activity. From this it can be extrapolated that ASC is over-represented in AN patients regardless of disease stage, but that active disease is more likely to lead to an ASC diagnosis. This contributes to the conclusion that some of the autistic traits seen in AN patients are the result of malnutrition, but some reflect a diagnosis of comorbid ASC.

Scales based on parental report, such as the 3Di, may be used to eliminate the confounding cognitive effects of starvation. In a study of early onset eating disorder (EOED) patients aged 8-16, three groups were studied: an ASC control group (N=20), an EOED group and a 'typically developing' group - allowing for more reliable comparison than studies which omit this. There was no significant difference between the EOED and typically developing group in the communication domain, and a medium but non-significant difference in the reciprocal social interaction and repetitive behaviour domains. There was a significantly larger impairment in the ASC group than in the EOED group (Pooni *et al.*, 2012). Thus this study found no evidence to support previous research suggesting that the rates of autism diagnosis in ED populations were higher than neurotypical adolescents, but did find higher rates of autistic traits, which may be statistically significant in a larger sample.

Moreover, Westwood *et al.* (2017) aimed to establish what proportion of patients with AN showed ASC symptoms during the early developmental period, using the ADOS-2 and the 3Di-sv (short version). 40 female AN patients, aged 12-18, were screened for ASC using the ADOS-2, and providing they met the cut-off for ASC, were then tested with the 3Di-sv. During the 3Di interview, parents were specifically asked to focus on symptoms which were present in early childhood, prior to the onset of AN. In this investigation, 52.5% of participants were diagnosed with the ADOS-2, but only 10% met the diagnostic criteria with the 3Di. Assuming that the sensitivity of both scales is similar, the results of this study may suggest that only 10% of patients have diagnosable ASC, with the other 42.5% showing symptoms which may arise from malnutrition. The study used a sample which is demographically representative of the clinical population, since adolescent females are most likely to be diagnosed with AN. However, the 3Di relies purely on parental report, which may be limited by the high heritability of ASC; a meta-analysis of twin studies established the heritability to be between 64% and 91% (Tick *et al.*, 2015). This means that parents of adolescents with ASC are more likely to be autistic and are less likely to recognise atypical behaviour in their children. Another confounder may be the stigmatisation of ASC, including a perception of autism as a 'male disorder', limiting the accuracy of parental report.

## Discussion

It is clear from the literature that ASC is over-represented in anorexia nervosa populations, however the effects on patients suffering from eating disorders, and the reasons for this relationship, are not fully understood.

### Theories Explaining the Over-Representation of ASC in AN

The relationship between ASC and AN is not fully understood. However, there are some common features, which may provide insight into the correlation between the conditions. Deficits in certain social characteristics appear to be common to both, including difficulties with recognising and expressing emotions (alexithymia), and disinterest in social contact (social anhedonia). Other cognitive similarities include poor set-shifting and inefficiencies in global processing (Tchanturia et al., 2013).

Alexithymia is implicated in several psychiatric disorders, including depression, OCD and schizophrenia. As well as this, it is present in ASC and eating disorders (Westwood *et al.*, 2017). A 2017 Westwood *et al.* meta-analysis of 44 studies showed that individuals across all eating disorders show more alexithymia than healthy controls, using the Toronto Alexithymia Scale (TAS). This review was limited by the fact that the studies had a wide variation of age, BMI and illness duration of participants. However, due to the large sample size and variety of populations, the results are likely reflective of, and applicable to, the population as a whole. There is also evidence to show that alexithymia is a common feature in ASC. A systematic review of 15 studies found the prevalence of alexithymia in ASC to be between 33.3% and 63%, using the TAS. This is significantly higher than the neurotypical group (Kinnaird, Stewart and Tchanturia, 2019). The review draws the conclusion that since alexithymia is not a universal feature in ASC, and is present in many other psychiatric conditions, it is a co-occurring deficit rather than a core feature of ASC. This supports the 'alexithymia hypothesis' of ASC, which suggests that alexithymia is independently responsible for difficulties in emotion processing in autistic individuals. Thus, alexithymia is one of many traits which are more prevalent in AN and ASC than in the general population.

Oldershaw *et al.* set out three main theories regarding the cognitive profile of ASC, in a 2011 study comparing the cognitive profile of AN against published ASC data. Emotional Theory of Mind (eToM) is the ability to infer what somebody else is thinking, and is an identified area of weakness in ASC. IQ matched individuals with ASC and AN scored similarly on inference of emotion in voices, whilst the ASC group scored better on inference from films and the AN group were better at recognising emotions in eyes. Executive dysfunction is also seen in ASC, and may be reflected by a difficulty in set-shifting - the ability to adapt to rule changes. When measured by testing for preservative errors, where participants stick to old rules instead of adopting new ones, the AN and ASC group made a similar number of errors, suggesting comparable set-shifting ability in both groups. Lastly, weak central coherence can be measured by testing detail fixation, since central coherence describes the ability to 'see the bigger picture'. Again, the AN and ASC groups scored similarly on this measure. Overall, the results of this study suggest strong behavioural and cognitive similarities between individuals with AN and ASC, and show that AN patients exhibit characteristics which



have been described in autism (Oldershaw *et al.*, 2011). A major limitation of the study is the use of previously published data for the ASC group, rather than a direct comparison between the two groups. However, the results from the study allow for a greater understanding of the similarities of the cognitive profile, despite lack of understanding of the aetiology of these conditions.

Despite the growing body of research showing many common traits in ASC and AN, and the correlation between the two being recognised as early as the 1980s with a 'shared genotype' theory, there is not yet any conclusive evidence for the reason for this relationship.

#### Under- and Misdiagnosis

Given the difficulties with diagnosing ASC in females and the comorbid psychiatric conditions, it is probable that autism is often under- or misdiagnosed in this population. In a qualitative study, Babb *et al.* (2021) identified barriers to accessing or benefitting from treatment of AN in women with ASC, including misunderstanding of autism and autistic traits, a lack of patient-centred treatment, and reduced accessibility and engagement with services. It is evident that autistic patients have unmet needs within ED services, with scope for improving services by providing targeted therapy for autistic patients. This emphasises the importance of identifying undiagnosed patients with ASC on presentation.

The feasibility and ethical implications of screening for ASC in ED populations may be debated, but it is argued that it is essential to delivering a high standard of care, as this would allow for adjusting the clinical environment and treatment plan.

#### Prognosis

Autistic adolescents suffer from a high burden of psychiatric comorbidity, so the prognosis and treatment of their EDs may be complicated. This reflects the clinical opinion that patients with ASC have poorer outcomes and lower engagement with treatment. In a study by Joshi *et al.* (2010), a large sample (N=2,323) of adolescents referred to paediatric psychopharmacology were compared using the DSM-III criteria for ASC. There was a significant increase of comorbid disorders in adolescents diagnosed with ASC than in controls, with 95% of the ASC group having three or more comorbid psychiatric disorders.

In AN patients, a higher Autism Quotient score was associated with higher scores for anxiety, depression and poor 'ability to maintain relationships'. This means that the higher the number of autistic traits reported, the more individuals experience difficulties with mood, work and social relationships (Tchanturia *et al.*, 2011). These autistic traits may exacerbate 'maintaining factors' for AN, such as cognitive rigidity, low mood, low motivation or lack of social skills; evidently, patients with ASC have different support needs. It could be hypothesised that presence of autistic traits would lead to poorer outcomes in AN patients, but further research comparing AN treatment outcomes in ASC and neurotypical populations is needed to confirm this.

## Clinical Implications

From the findings of this review, it is clear that autistic traits are an important consideration when treating AN patients. Based on clinical experience and observation of adolescents with ASC in an inpatient ED unit, suggestions for clinical practice include adaptations being made to the clinical environment, communication strategies and specialised treatment programmes offered to patients with ASC.

Adaptations to the clinical environment should meet the sensory needs of autistic patients. These include sound-proofing rooms, removing colourful or busy decorations, and using appropriate lighting (Hahn, 2012). Providing quiet spaces such as sensory rooms, and personal devices such as weighted blankets or noise-cancelling headphones, could also contribute to improving an individual's environment, based on an individualised care plan and sensory assessment (NICE, 2013). These would allow for self-soothing or self-stimulatory behaviours, thus reducing anxiety.

Communication with autistic patients may be more effective when it takes place in a suitable environment at an agreed time, and written communication is provided. Communication passports may be used to agree on an individualised care plan. Focusing on making predictable treatment plans with advanced warning and specific timings, and reducing choices to binary choices, may contribute to improving engagement and autonomy in ASC patients (NICE, 2013). Moreover, further research should investigate the best approach to group and individual psychological therapy, since these are currently based on individual practitioner expertise (Cooper, Loades and Russell, 2018). These adaptations would allow patients to improve engagement with both weight restoration and psychological therapy.

## Conclusion

The wide variety of diagnostic criteria, varying research approaches, and range of ages and disease severity of participants, all lead to a variation in ASC prevalence rates. The confounding cognitive effects of starvation are also a key issue in this field. To avoid this, and obtain valid data, further research should involve detailed developmental histories to determine whether ASC traits predate disease onset. Furthermore, longitudinal cohort studies of children with ASC, with follow-up to determine what proportion develop AN, would provide valuable insight. Further research should also address the difficulties surrounding diagnosis in a predominantly female ED population.

Future research should also focus on monitoring outcomes for ASC patients, as compared with neurotypical AN patients, allowing for better understanding of the impact of ASC on the disease course of AN, and determining which treatment approaches are most effective in this population.

Overall, it is evident that there is a high burden of autistic traits in AN patients, and these must be accommodated, through adaptations to clinical practice and settings.

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