

Title

The prevalence of psychosis and bipolar disorders in autistic adults: a critical analysis and commentary on a systematic review.

Commentary on:

Varcin KJ, Herniman SE, Lin A et al (2022) Occurrence of psychosis and bipolar disorder in adults with autism: A systematic review and meta-analysis. *Neuroscience and biobehavioral reviews*, 134, 104543. Doi: 10.1016/j.neubiorev.2022.104543

Abstract

Autism spectrum disorder (ASD) is a lifelong neurodevelopmental condition characterised by difficulties with social communication and interaction, and stereotyped and repetitive patterns of behaviours, interests and activities. It is estimated that around 1–2% of England's population are autistic. Evidence suggests that autistic individuals are more likely to have a co-occurring mental health condition, and have higher rates of psychological distress, than the general population. There is thought to be an association between autism and psychotic disorders and there is an overlap between some features of autism and the prodromal symptoms of psychosis. This commentary summarises and critically appraises a previously published systematic review which aimed to estimate the prevalence of psychosis and bipolar disorder in autistic adults and reviewed the evidence in the literature around factors correlated with the co-occurrence of these conditions. This commentary discusses the implications of the findings of the review from a mental health practice perspective.

Key Points

- The prevalence of psychosis and bipolar disorder in autistic individuals is estimated to be 9.4% for psychosis and 5.9% for bipolar disorder, substantially higher than the prevalence of these conditions in the general population.
- The evidence around correlates of the cooccurrence of autism and psychosis or bipolar disorder is mostly inconclusive with studies reporting conflicting findings.
- The overlap of autism features and prodromal symptoms of psychosis presents challenges for diagnosis and clinical decision making.
- Future research should explore the moderating factors related to the coexistence of bipolar disorder or psychosis in autistic individuals.

Introduction

Autism spectrum disorder (ASD) is a lifelong neurodevelopmental condition with diverse features including social communication and interaction difficulties, and showing restricted, repetitive, and stereotyped patterns of behaviours, interests, or activities (American Psychiatric Association (APA), 2013). Around 1–2% of England's population are estimated to be autistic (Roman-Urrestarazu et al., 2021; O'Nions et al., 2023), with around 500,000 people estimated to have a diagnosis of autism and between 435,700 and 1.2 million further estimated to be autistic but be undiagnosed (O'Nions et al., 2023). Evidence suggests that autistic people are more likely to report poorer adult life outcomes than the general population (Eigsti, 2024) and to report a lower perceived quality of life (Mason et al., 2018). They are also reported to be more likely to have a co-occurring mental health condition, and have higher rates of psychological distress, than the general population (Croen et al., 2015; Lever and Geurts 2016).

There is thought to be an association between autism and psychotic disorders with the prevalence of schizophrenia being significantly higher in autistic individuals compared to the general population (Zheng et al., 2018). The core clinical symptoms of psychosis are usually divided into 'positive symptoms', including hallucinations (perception in the absence of any stimulus) and delusions (fixed or falsely held beliefs), and 'negative symptoms', such as emotional apathy, lack of drive, poverty of speech, social withdrawal and self-neglect (APA, 2013). However, both autism spectrum disorder and psychosis involve many complex features (Crespi and Badcock 2008), and there is an overlap between the features of autism and prodromal symptoms of psychosis (Chisholm et al., 2015; Sampson et al., 2020). The systematic review by Varcin et al., 2022 aimed to estimate the prevalence of psychosis and bipolar disorder in autistic adults and to explore the risk factors correlated with coexistence of these conditions.

Aim of critical analysis and commentary

This commentary aims to critique the paper by Varcin et al., 2022 and to discuss the findings from the perspective of mental health practice.

Critical appraisal of the review by Varcin et al., 2022

The Joanna Briggs Institute critical appraisal checklist for systematic reviews and research syntheses (Aromataris et al., 2015) was used to critically appraise the paper. The JBI checklist was chosen as it was developed by methodological experts and is suitable for assessing a wide range of systematic review types. Using the checklist the review was assessed as meeting 11 out of 11 criteria. It is therefore judged that the review presents a robust summary of the evidence on this topic. For full methods and overview of the critical appraisal of the paper by Varcin et al., 2022 please see Table 1.

Table 1: Summary of critical appraisal

JBI critical appraisal checklist items	Responses
1. Is the review question clearly and explicitly stated?	Yes – the review question clearly states in the introduction that the authors aimed to assess the prevalence of psychosis and bipolar disorder in autistic adults and the risk factors associated with co-occurrence.
2. Were the inclusion criteria appropriate for the review question?	Yes – the inclusion criteria were clearly described, and exclusions are also explicit. The review included studies investigating prevalence of, or risk factors for, co-existing clinically diagnosed psychosis or bipolar disorder in adults with clinically diagnosed autism.
3. Was the search strategy appropriate?	Yes – the search strategy was developed with the help of a librarian and includes search terms for autism and for psychosis or bipolar conditions. The strategy includes subject headings and variations of keywords that are appropriate to the concepts in the search and is sufficiently sensitive. The searches have been limited to 1980 onwards, with the justification that this is when autism was first differentiated from psychiatric disorders. However, papers were limited to English language which introduces the possibility of language bias.

4. Were the sources and resources used to search for studies adequate?	Yes – the authors searched five databases including Medline, Embase, PsycINFO, CINAHL and Cochrane Central Register of Controlled Trials which are adequate for this topic. The authors also reviewed the reference lists of included studies to identify further literature.
5. Were the criteria for appraising studies appropriate?	Yes – risk of bias was assessed using the Hoy Risk of Bias Tool. The Hoy Risk of Bias Tool is designed to assess bias and critically appraise prevalence studies.
6. Was critical appraisal conducted by two or more reviewers independently?	Yes – critical appraisal was conducted independently by two reviewers with disagreements resolved by consensus.
7. Were there methods to minimize errors in data extraction?	Yes – data were extracted from full text articles by one reviewer, with a second reviewer checking extractions for accuracy.
8. Were the methods used to combine studies appropriate?	Yes –meta-analysis was conducted using a random effects model which is appropriate when between-study heterogeneity is expected. Pooled prevalence was estimated separately for bipolar disorder in autism and psychosis in autism. Risk factors were summarised in a narrative synthesis.
9. Was the likelihood of publication bias assessed?	Yes – funnel plots and the Egger’s test were used to assess publication bias.
10. Were recommendations for policy and/or practice supported by the reported data?	Yes – the authors recommend ongoing assessment and monitoring and improved screening, diagnosis and pathways for autistic adults which is supported by the pooled prevalence estimated in the review. They discuss the review’s limitations including discussing the included studies’ quality and potential areas of bias which may have contributed to varying prevalence estimates across the studies.
11. Were the specific directives for new research appropriate?	Yes – the authors’ recommendations for further research are suitable and are based on the research gaps evident from the findings of the review. They recommend that further research should

	examine possible risks correlated with the co-existence of psychosis and bipolar disorder in autism.
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Summary of the results of the review by Varcin et al., 2022

The review included 53 studies with the meta-analysis estimating prevalence of psychosis in autistic individuals including 45 of those studies and the meta-analysis estimating prevalence of bipolar disorder in autistic individuals including 27 of the studies (with some papers included in both analyses). 14 studies reported on risk factors for the cooccurrence of psychosis and 6 studies reported risk factors for cooccurrence of bipolar disorder and were included in the narrative synthesis. The included studies were published between 2003 and 2021, and the most common countries of publication were the USA, Sweden and the United Kingdom (UK).

The authors used the Hoy Risk of Bias Tool, a checklist designed to assess quality and risk of bias in epidemiological prevalence studies, to assess the studies included in the review. The overall risk of bias was deemed to be of low to moderate risk for most included studies (98%). The five main areas of concern were study sample not being representative of the national population, differing methods for data collection used with participants, data not directly collected from participants, studies failing to demonstrate the reliability or validity of their measures, and populations sampled without the use of random selection or census-based methods.

The findings of the review show a high prevalence of psychosis and bipolar disorder in autistic individuals. The pooled prevalence of psychosis in autistic individuals was 9.4% (45 studies, N=63,657, 95% CI=7.52 to 11.72) with considerable heterogeneity ($I^2 = 97.56\%$, $p < .001$). Leave-one-out analysis showed only a negligible effect of removing outlier studies on the prevalence estimate and no reduction in heterogeneity.

The pooled prevalence of bipolar disorders in autistic individuals was estimated to be 5.9% (27 studies, N=48,973, 95% CI = 3.89 to 8.78) with considerable heterogeneity ($I^2=97.9\%$, $p < .001$).

However, removing one outlier study from the analysis increased the estimate of prevalence to 7.5% (26 studies, N=31,739, 95% CI = 5.79 to 9.53) with slightly reduced heterogeneity ($I^2 = 91.83\%$, $p < .001$). Evidence of publication bias was found, indicated by a positive Egger's test, in both the meta-analysis of the prevalence of psychosis (Egger's $t = -3.67$, $p < .001$) and bipolar disorder (Egger's $t = -2.19$, $p = .028$) among autistic individuals.

Narrative synthesis

Table 2 lists the factors correlated with the cooccurrence of bipolar disorder or psychosis in autistic individuals that were reported in studies included in the narrative synthesis. Four factors associated with the cooccurrence of psychosis were examined in more than one study. Seven studies examined the link between gender and occurrence of psychosis in autism. Higher rates of psychosis in males compared with females was reported in six of these studies, although one study conversely reported higher rates in females compared with males. Three studies examined the association of age with two studies reporting that older age groups had a higher rate of psychosis and autism cooccurrence compared to age groups that were younger, and one study reported that individuals with cooccurring psychosis and autism were younger compared with individuals with psychosis alone. Three studies examined the association of IQ with two studies reporting an association between lower IQ and cooccurrence of psychosis and one study finding no evidence of association. The association of intellectual disability was examined in three studies. However, one found increased rates of psychosis in individuals with comorbid autism and intellectual disability, one found occurrence of psychosis was less frequent in individuals with comorbid autism and intellectual disability, and one found no association.

Gender was the only factor for the cooccurrence of autism and bipolar disorder that was examined in more than one study. Two studies reported that females were more likely than males to have a diagnosis of autism and bipolar disorder.

Table 2: Factors associated with the cooccurrence of autism and psychosis or bipolar disorder reported in included studies.

Factors associated with cooccurrence of psychosis	Factors associated with cooccurrence of bipolar disorder
• Males (k=6) • Females (k=1) • Increasing age (k=2) • Younger age (k=1) • Lower Full-Scale/General IQ (k=1) • Lower Verbal IQ (k=1) • Presence of Intellectual Disability (k=1) • Absence of Intellectual Disability (k=1) • Stable autism diagnosis in adulthood (k=1) • Fewer stereotyped interests/behaviours (k=1) • More motor side-effects from antipsychotic medication (k=1) • Migrant status (k=1) • Lower Global Assessment of Functioning (GAF) score (k=1) • Empathising bias (k=1)	• Females (k=2) • Stable autism diagnosis in adulthood (k=1) • More overall autism behaviours and impairment (k=1) • Later age of onset of epilepsy (k=1) • Higher Performance IQ (k=1)

Commentary

The pooled prevalence estimated in the review was 9.4% for psychosis and 5.9% for bipolar disorder (or 7.5% when one outlier study was removed from the analysis). There was considerable heterogeneity in the pooled estimates which remained even after the authors conducted ‘leave-one-out’ analyses removing outlying studies that were having a disproportionate impact on the prevalence estimates. The review authors suggest that this may indicate true variation between the studies included, although the specific causes of the heterogeneity are not identified. Additionally, the review authors found evidence of publication bias and so it is possible that studies reporting higher prevalence rates (and therefore more likely to be published compared to studies reporting low or insignificant rates) are overrepresented in the estimate. Consequently, the pooled estimates should be interpreted with caution as they are unlikely to accurately represent any specific real-

world setting and may be overestimated. However, overall, the review indicates that rates are likely to be notably higher when compared with UK population prevalence estimates, where only 0.5% of adults are estimated to have psychotic disorder and around 2% are estimated to have bipolar disorder (Morris et al., 2025). This has implications for mental health nurses and other professionals when making diagnostic and clinical decisions for individuals presenting with features of autism and symptoms psychosis or bipolar disorder.

The overlap of autism features and prodromal symptoms of psychosis or symptoms of bipolar disorder present challenges around diagnosis and clinical decision making for mental health professionals (Chisholm et al., 2015; Sampson et al., 2020; Vasconcelos-Moreno et al., 2025). When criteria are met for more than one diagnosis, diagnostic overshadowing may occur (Au-Yeung et al., 2019; Hallyburton 2022). Particularly, it can be difficult to differentiate autism spectrum disorder from first episode psychosis which can hinder the diagnostic process and treatment (Zheng et al., 2020; Ferrara et al., 2024). There are clinical features common to both autism and psychosis including unusual thought content, deficits in social interaction, and stereotyped behaviours (Eack et al., 2013; De Crescenzo et al., 2019; Vaquerizo-Serrano et al., 2021; Ribolsi et al., 2022), which may result in undiagnosed autism being misdiagnosed as a psychotic disorder (Van Schalkwyk et al., 2015). Similarly, there is a significant overlap in the symptoms of bipolar disorder and autism such as emotional dysregulation, impulsivity, irritability, social skills difficulties and sleep disturbances which can present challenges in differential diagnosis (Vaquerizo-Serrano et al., 2021). However, given the high prevalence of bipolar disorder and psychosis in autistic individuals there is also a risk of comorbidity of the conditions. It is therefore also important for mental health professionals to recognise where prodromal psychotic or bipolar symptoms are experienced by autistic individuals to allow earlier intervention to potentially prevent or treat the development of comorbidity and improve patient outcomes (Ribolsi et al., 2022). Given the diagnostic challenges, assessment of patients who present with overlapping symptoms requires strict adherence to standardized criteria. Specifically, mental health professionals should use the International Classification of Diseases ICD-

11 (World Health Organization 2019) or Diagnostic and Statistical Manual of Mental Disorders DSM-5 (APA 2013) criteria and validated diagnostic tools. These should be used together with carefully gathered collateral information which should include developmental, behavioural, medical, and psychiatric history, longitudinal assessment of symptoms and mental status (taking into account age of onset and progression of symptoms), and consideration of family history to explore possible heritable genetic risk factors (Morley et al., 2008; National Institute of Health and Care Excellence (NICE) 2011; NICE 2013a; Waris et al., 2013; Ribolsi, et al, 2022).

Misdiagnosis can have adverse consequences for the treatment of patients, particularly those with autism who may be at risk of being inappropriately prescribed psychotropic medications. There has been longstanding concern about widespread use and possible overuse of psychotropic medication in people with intellectual disability and/or autism, especially in relation to antipsychotics and antidepressants (Royal College of Psychiatrists (RCPsych), 2021), as highlighted by the Winterbourne View enquiry (Flynn 2012). Antipsychotics, antidepressants, and anticonvulsants are not recommended for managing the core features of autism (NICE 2012; NICE 2013b). Despite this, psychotropic medications are more likely to be prescribed for autistic individuals compared with the general population, and autistic patients who are prescribed medications have a high rate of polypharmacy (Murray et al., 2014).

Physical health problems and other significant side effects can be experienced as a result of long-term use of psychotropic medications (Sepúlveda-Lizcano et al., 2023). Antipsychotic medications in particular are associated with obesity and an increased risk of metabolic syndrome, diabetes, and haematological and cardiovascular problems (De Hert et al., 2011). Antipsychotics may also induce extrapyramidal side effects which include tardive dyskinesia, dyskinesia, muscular rigidity and tremors (Mathews et al., 2005). Given the risks of adverse effects of psychotropic medications, there is a need to ensure that decisions around prescribing are carefully considered to prevent inappropriate use of pharmacological interventions and overmedication (RCPsych, 2021).

Clinical decisions around prescribing medications may also require caution in cases of comorbid psychosis or bipolar disorder and autism. There is very little evidence as to how psychosis or bipolar disorder should be treated in autistic individuals and whether a different approach is required from treating those without autism (Carthy et al., 2023). The National Institute of Health and Care Excellence (NICE) guidance recommends that autistic individuals with coexisting mental disorders should be offered pharmacological interventions according to NICE guidance for the specific disorder (NICE 2012). However, research suggests that autism comorbidity in first-episode psychosis is associated with an increased risk of multiple treatment failure, and individuals with co-morbid autism and first-episode psychosis may have a less beneficial response to antipsychotic treatment than those without autism (Downs et al., 2017). This, together with the high risk of side effects of antipsychotics, suggest that closer monitoring and regular medication reviews of patients with comorbidity of psychosis and autism may be necessary to monitor treatment effectiveness and adverse effects (Downs et al., 2017; Carthy et al., 2023).

Future research

The review by Varcin et al., (2022) reports a high level of heterogeneity between the included studies which needs further investigation. The review also highlights gaps in the research around factors correlated with the cooccurrence of autism and bipolar disorder or psychosis. Factors explored in the included studies were heterogeneous and only a small number of factors were examined in more than one study. However, evidence for many of these factors is inconsistent, with some conflicting findings. Future research should further explore moderating factors to establish why certain factors (such as gender and age) are associated with a higher prevalence rate of bipolar disorder or psychosis in autistic individuals, which may help to explain some of the variance observed in the data.

Variability may also be influenced by challenges in accurate diagnosis of the conditions. Additional literature suggests that there are currently no adequate validated tools for differential diagnosis of autism and psychosis or screening tools which either assess autistic traits in first-episode psychosis

populations or identify psychotic symptoms in autistic individuals (Ferrara et al., 2024). Furthermore, there are suggestions in the wider literature that “methodological blurring” in the design of existing measures for autism and psychosis may also fail to adequately distinguish between certain traits of the two conditions, possibly leading to an overestimation of the association between them (Miles et al., 2025). The development and validation of tools to better support the differential or concurrent diagnosis of autism and first-episode psychosis should therefore be prioritised to improve accuracy of future research.

Conclusions

The results of the meta-analyses in the systematic review by Varcin et al., (2022) suggest a high prevalence of bipolar disorder and psychosis in autistic adults. Mental health nurses and other professionals should be mindful of the potential for co-morbidity of these conditions in autistic individuals, as well as the overlap in features of autism and symptoms of psychosis (particularly the prodromal phase) and bipolar disorder. Careful diagnostic assessment is therefore essential, using recognised classification systems and validation tools in conjunction with evaluation of features, symptoms and patient history. Mental health professionals should exercise particular caution when prescribing psychotropic medications to autistic individuals with comorbidity of psychosis or bipolar disorder and ensure ongoing monitoring of treatment effectiveness.

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