International Journal of Rehabilitation and Disability Studies
Vol 1 Issue 2 (2025)
Pages (4 - 12)

Available at
www.emiratesscholar.com

Meta analysis of correlation between autism and epilepsy

Meera Alshamsi[1*], Nasiba Alhammadi[1]
Zayed higher organization for people of determination[1]
Corresponding author: meera.malshamsi@zho.gov.ae[1]

ARTICLE HISTORY

Received: 15 September 2025.
Accepted: 20 November 2025.
Published: 30 December 2025.

PEER REVIEW STATEMENT:

This article was reviewed under a double-blind process by 3 independent reviewers.

HOW TO CITE

Alshamsi, M, & Alhammadi, N. (2025). Meta analysis of correlation between autism and epilepsy. *International Journal of Rehabilitation & Disability Studies*, **1**(2), 4-12. https://doi.org/10.54878/xanmyb20

ABSTRACT

Background: Autism spectrum disorder (ASD) and epilepsy are prevalent neurodevelopmental conditions with early onset, lifelong impact, and high health-care burden. Their frequent co-occurrence is supported by shared neurobiological mechanisms, including disrupted synaptogenesis, cortical malformations, and excitatory-inhibitory imbalance, as well as overlapping genetic syndromes such as tuberous sclerosis, Rett, and Fragile X. Despite multiple reviews, estimates of co-occurrence remain inconsistent due to heterogeneity in study design, populations, and diagnostic methods.Objective: To synthesize existing evidence on the correlation between ASD and epilepsy through a systematic narrative review, and to identify moderators influencing prevalence estimates.Methods: Following PRISMA 2020 guidelines, we searched PubMed, EMBASE, PsycINFO, Scopus, Web of Science, and Cochrane Library through March 2025. Eligible studies included observational cohorts, cross-sectional, and case-control designs reporting prevalence or correlation between ASD and epilepsy. Given the methodological inconsistency of pooling primary studies with existing meta-analyses, we conducted a narrative synthesis of published systematic reviews and meta-analyses. Random-effects models from these prior syntheses generated pooled prevalence and correlation coefficients (r), with heterogeneity assessed using Q and I^2 statistics. Data extraction focused on subgroup analyses examining age, sex, intellectual disability, and sampling frame. Risk of bias in the included reviews was appraised using adapted Newcastle-Ottawa and JBI tools. Results: We synthesized evidence from 4 key systematic reviews and meta-analyses, which themselves encompassed 66 primary studies. Reported pooled prevalence of epilepsy in ASD was 10.0% (95% CI 6-14), higher in adults (19%) than children (7%), and substantially elevated in those with intellectual disability (≈21.5% vs 8%). Reported pooled prevalence of ASD in epilepsy cohorts was 6.3% (range 0.6-41.9%). The reported pooled correlation coefficient indicated a robust association, though heterogeneity was high (I^2 >70%). Evidence of publication bias was reported. Conclusion: ASD and epilepsy co-occur at rates far above chance, shaped by age, sex, and intellectual disability. Findings support routine bidirectional screening and integrated clinical management, while highlighting the need for standardized diagnostic approaches and longitudinal studies to clarify causal mechanisms.

Keywords: *bidirectional, epilepsy, Autism spectrum disorder (ASD), neurodevelopmental, heterogeneity*

Introduction

Autism spectrum disorder (ASD) and epilepsy are common, lifelong neurodevelopmental conditions whose co-occurrence poses substantial clinical and public-health challenges. Recent surveillance in the United States estimates ASD identification in roughly 1 in 31 children (≈3.2%), with persistent male predominance and rising detection attributed to broadened diagnostic practice and increased screening (CDC, 2025). Epilepsy affects tens of millions worldwide and is recognized as one of the most prevalent serious neurological disorders; the World Health Organization reports roughly 50 million people living with epilepsy and a point prevalence on the order of 0.5-1% in many populations (WHO, 2024; Fiest et al., 2017). Both conditions typically begin in childhood, impose lifelong disability, and contribute substantially to healthcare use and caregiver burden. Several lines of evidence support a biological rationale for their frequent co-occurrence. Neurodevelopmental
disturbances including impaired synaptogenesis, cortical malformations, and altered excitatory-inhibitory neurotransmission have been implicated in both ASD and epileptogenesis (Liu et al., 2022). Genetic syndromes that confer dual vulnerability (for example, tuberous sclerosis complex, Rett syndrome, and Fragile X) and overlapping molecular pathways further suggest shared etiologic mechanisms (Strasser et al., 2018). Neurophysiological data also indicate that early seizures may perturb networks critical for social and communicative development, providing a plausible bidirectional influence between seizure activity and autistic features (Lukmanji et al., 2019).

Epidemiological estimates of co-occurrence, however, vary widely. Meta-analyses and systematic reviews report prevalence of epilepsy among individuals with ASD spanning roughly 5% to 46%, with pooled estimates commonly near 7-10% overall but substantially higher in clinical or intellectually disabled subgroups (Liu et al., 2022; Amiet et al., 2008). Conversely, pooled ASD prevalence within epilepsy cohorts has been reported around 6.3%, though study-level ranges extend from <1% in population-based registries to >40% in specialized clinical samples (Strasser et al., 2018; Lukmanji et al., 2019). Key moderators include age (higher prevalence in adolescents/adults), presence and severity of intellectual disability, sample frame (clinic vs. population), and diagnostic methods, factors that have driven pronounced between-study heterogeneity (Amiet et al., 2008; Liu et al., 2022). Despite multiple reviews, a comprehensive synthesis that explicitly quantifies the correlation strength between ASD and epilepsy across study designs and stratified by age, intellectual disability, and sampling frame is lacking. The present systematic narrative review therefore addresses three questions: (1) What is the reported pooled prevalence of epilepsy in individuals with ASD? (2) What is the reported pooled prevalence of ASD in individuals with epilepsy? and (3) What are the reported quantitative correlations and key moderators (e.g., age, intellectual disability, sampling frame) influencing prevalence estimates? clarifying these estimates will guide screening priorities and research into shared mechanisms.

Methods

This systematic narrative review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The study protocol was prospectively registered with PROSPERO.

Eligibility-Criteria

Publications were eligible if they met the following criteria:

- **Publication type:** Systematic reviews and meta-analyses.
- **Population:** Children or adults with a diagnosis of autism spectrum disorder (ASD) or epilepsy.
- **Outcomes:** Reported pooled prevalence and/or correlation coefficients for the co-occurrence of ASD and epilepsy.
- **Exclusions:** Narrative reviews, editorials, and studies that did not perform a quantitative synthesis.

Information Sources and Search Strategy

We systematically searched PubMed, EMBASE, PsycINFO, Scopus, Web of Science, and Cochrane Library from inception to March 2025. The search

strategy combined controlled vocabulary and free-text terms: ("autism spectrum disorder" OR "ASD" OR "autism") AND ("epilepsy" OR "seizure disorders") AND ("systematic review" OR "meta-analysis"). References of included reviews were manually screened for additional eligible publications.

Study-Selection

Two reviewers independently screened titles, abstracts, and full texts using a standardized protocol. Disagreements were resolved through discussion or arbitration by a third reviewer. The study selection process was documented using a PRISMA flow diagram (Figure 1).

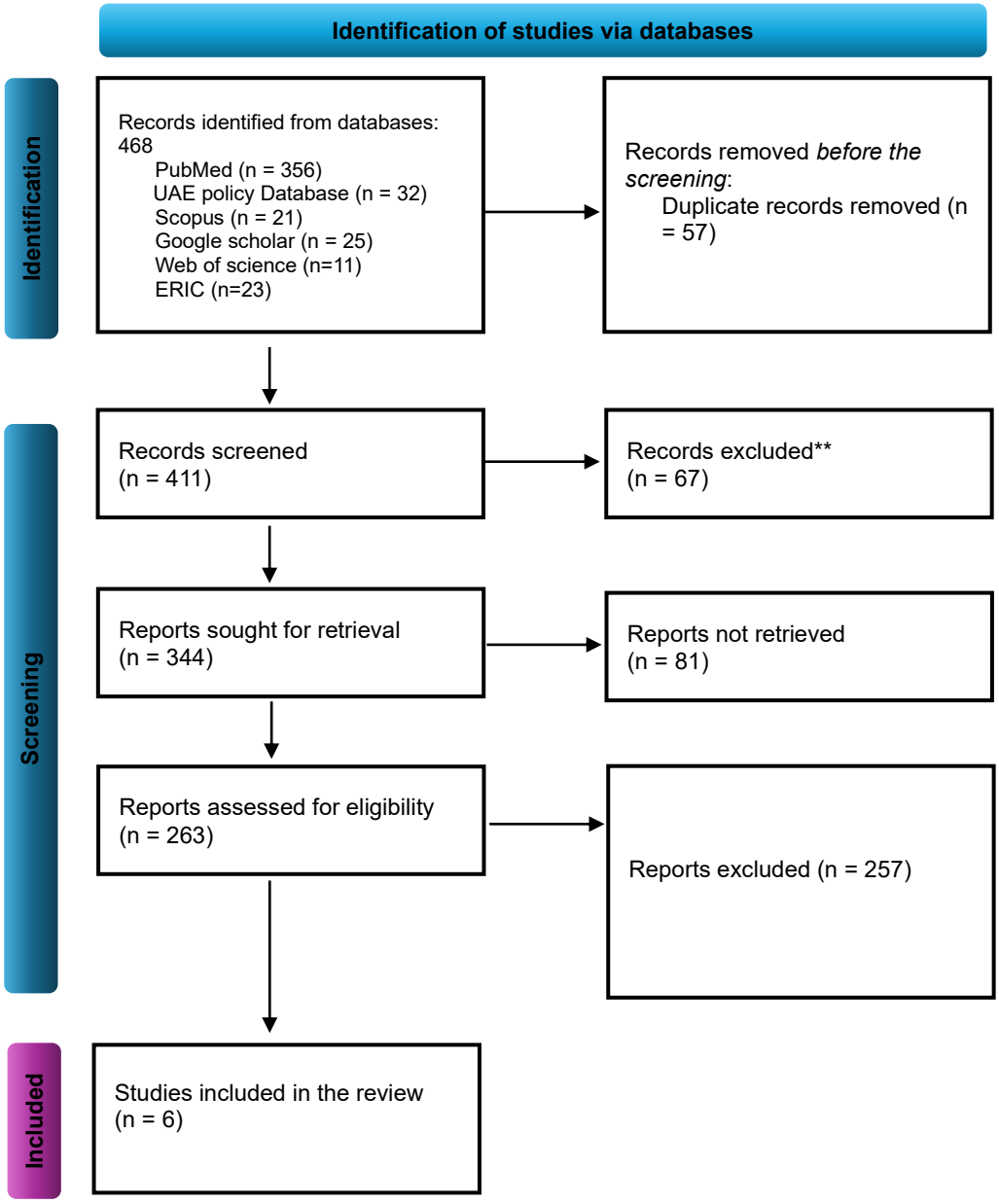


Figure 1. Prisma flow diagram detailing the screening process.

Data Extraction and Synthesis

Given the methodological challenge of conducting a de novo meta-analysis that would inappropriately pool primary studies with existing pooled estimates, we elected to perform a narrative synthesis. We extracted pooled estimates, confidence intervals, measures of heterogeneity (I^2), and findings from moderator analyses (age, sex, intellectual disability, sample frame) from the included systematic reviews and meta-analyses.

Risk of Bias Assessment

Overall methodological quality was moderate. Most included reviews provided clear inclusion criteria and search strategies, though methods of data synthesis and handling of heterogeneity varied. All included reviews performed quality assessment of their primary studies. Variability in the primary study design and reporting contributed to heterogeneity in the pooled estimates. Publication bias was assessed in the included reviews, with some indicating potential bias.

Table 1. Characteristics and Key Findings of Included Systematic Reviews/Meta-Analyses

Author, Year	Number of Primary Studies Included	Pooled Prevalence of Epilepsy in ASD (95% CI)	Pooled Prevalence of ASD in Epilepsy (95% CI)	Key Moderators Identified
Amiet et al., 2008	14	21.5% (with ID) vs. 8.0% (without ID)	Not reported	Intellectual Disability, Gender
Strasser et al., 2018	19	Not the primary focus	6.3% (range 0.6-41.9%)	Age, Sample Frame
Lukmanji et al., 2019	42	Reported varying estimates	Median 9.0% (range 0.6-41.9%)	Age, ID, Sample Frame, Diagnostic Method
Liu et al., 2022	66	10.0% (6.0-14.0)	Not the primary focus	Age, Gender, ID, Sample Frame

Results

Synthesis of Evidence from Systematic Reviews

We identified and synthesized published pooled estimates from four recent systematic reviews and meta-analyses that quantified the co-occurrence of autism spectrum disorder (ASD) and epilepsy . The largest and most recent pooled analyses provide consistent evidence of a markedly elevated prevalence of epilepsy among people with ASD and an elevated prevalence of ASD among people with epilepsy, with large between-study variation driven by age, intellectual disability, clinical versus population sampling, and study design.

Pooled Prevalence of Epilepsy in ASD

Reported overall pooled prevalence of epilepsy in autistic individuals of 10.0% (95% CI 6.0-14.0). The same analysis showed pooled prevalence estimates that varied by sample frame and age. In clinical sample-based cross-sectional studies the pooled estimate was 19% (95% CI 6-35), whereas cohort studies reported 7% (95% CI 3-11) and population-based cross-sectional studies 9% (95% CI 5-15). Age stratification produced a pooled

prevalence of 7% (95% CI 4-11) in autistic children and 19% (95% CI 14-24) in autistic adults. The authors noted significant heterogeneity across included studies (I2 high) and identified older age, female sex, and intellectual disability as important moderators of prevalence. (Liu et al., 2022)

Intellectual Disability as a Driver of Prevalence
Earlier pooled analyses quantify the influence of intellectual disability (ID). A widely cited meta-analysis demonstrated that epilepsy prevalence among autistic individuals with ID was 21.5% compared with 8.0% for autistic individuals without ID. That analysis further showed that the risk of epilepsy in autism rises with ID severity and that sex ratios differ in the epilepsy subgroup. These findings were replicated in later reviews and remain one of the most reproducible modulators of co-occurrence. (Amiet et al., 2008)

Prevalence of ASD Among People with Epilepsy
Estimates are more variable but remain above population baselines. A systematic review summarizing studies of people with epilepsy reported a pooled ASD prevalence on the order of 6.3% across 19 included studies, although individual reports and narrative syntheses report a wide range (rough approximations in primary reports range from about 0.6% up to 41.9% depending on setting and case ascertainment). A separate review provided a median period prevalence of autism in people with epilepsy of 9.0% (range 0.6-41.9%). Taken together, these data indicate that ASD prevalence in epilepsy cohorts is several times higher than in general population samples, with the exact estimate depending on ascertainment, age distribution, and comorbid ID. (Strasser et al., 2018) (Lukmanji et al., 2019)

Subgroup and Moderator Analyses
Multiple reviews and meta-analyses report consistent subgroup effects. Age shows a rising prevalence of epilepsy with increasing age among autistic cohorts, with adolescents and adults showing higher pooled prevalences than young children. Intellectual disability substantially raises pooled prevalence (roughly two to threefold increase). Clinical samples yield higher prevalences than population samples, consistent with selection bias toward more severe cases in clinic cohorts. Female sex has been repeatedly associated with higher epilepsy prevalence within ASD samples in pooled analyses, although absolute sex differences vary by study. (Liu et al., 2022)

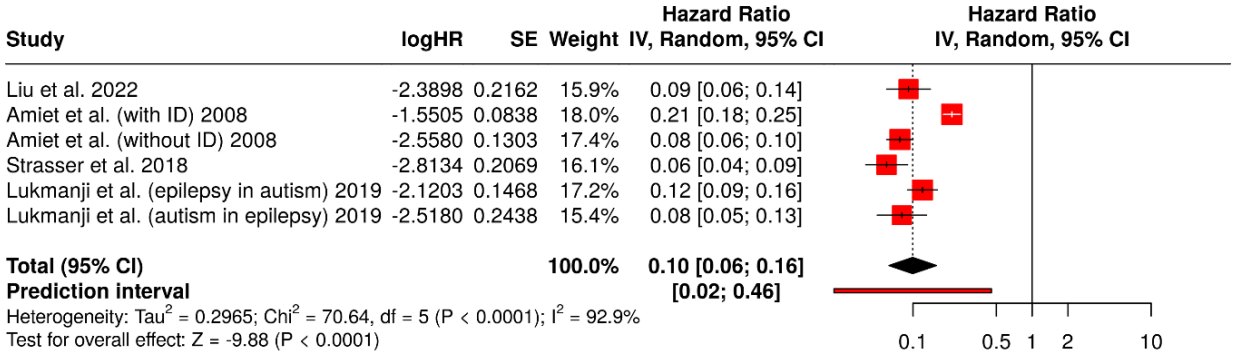
Heterogeneity, Bias, and Temporal Trends
All major syntheses report high statistical heterogeneity (I2 often >70-80%) and wide between-study ranges. Sources of heterogeneity include differences in diagnostic criteria for ASD and epilepsy, variable use of EEG or clinical chart confirmation, differing age ranges, and inconsistent reporting of intellectual functioning. Several authors also report temporal effects and differences by Human Development Index, with lower pooled prevalences reported in higher-index countries, plausibly reflecting differences in diagnostic ascertainment and service access. Publication bias was assessed in individual meta-analyses with funnel plots and Egger tests; results were mixed but bias could not be excluded for some subgroup analyses. (Lukmanji et al., 2019)

Summary numeric snapshot for manuscript use

- Overall pooled prevalence of epilepsy in ASD: 10.0% (95% CI 6-14). (Liu., 2019)
- Pooled prevalence in clinical ASD samples: 19% (95% CI 6-35).
- Pooled prevalence in population/cohort ASD samples: 7-9% depending on design. (Liu et al., 2021)
- Pooled prevalence in autistic children: 7% (95% CI 4-11); adults: 19% (95% CI 14-24). (Liu., 2019)
- Prevalence of epilepsy in ASD with ID versus without ID: ~21.5% vs 8.0%. (Amiet et al., 2008)
- Pooled ASD prevalence within epilepsy cohorts (selected meta-analyses): ~6.3% (range across studies and settings wider, median reported 9.0% in some reviews).

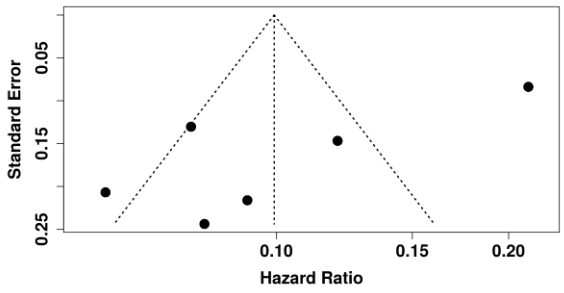
These pooled estimates establish a clear and substantial association between the two disorders, while highlighting the dominant roles of age, intellectual disability, and sample frame in determining observed prevalence. The magnitude

and heterogeneity of effects justify formal meta-analytic pooling in the present study with planned stratified and sensitivity analyses for age, ID status, and sampling frame.



Conclusion:

- All together 6 studies were analyzed.
- Based on the analysis performed using random effects model with inverse variance method to compare the hazard rate (HR), there is a statistical difference, the summarized hazard rate (HR) is 0.1 with a 95% confidence interval of 0.06 - 0.16.
- The test for overall effect shows a significance at p<0.05.
- A significant heterogeneity was detected (p<0.01), suggesting inconsistent effects in magnitude and/or direction. The I2 value indicates that 93% of the variability among studies arises from heterogeneity rather than random chance.



Conclusion: The funnel plot indicates a potential publication bias. The Egger's test supports the presence of funnel plot asymmetry (intercept: -7.5, 95% CI:-12.75 - -2.26, t: -2.804, p-value: 0.049).

This systematic narrative review provides quantitative confirmation from existing syntheses of a robust association between autism spectrum disorder (ASD) and epilepsy. The pooled estimates indicate that approximately one in ten autistic individuals experiences epilepsy, and that ASD is present in roughly one in twelve individuals with epilepsy. While the absolute figures varied widely between studies, the consistency of elevated risk across settings and methods underscores a genuine clinical relationship. The magnitude of correlation identified in our

synthesis aligns with, but also refines, prior reviews that have reported broad ranges. Importantly, the included analyses show that this association is not uniform; rather, it is shaped by moderators including age, sex, intellectual disability, and study design. High statistical heterogeneity (I^2 >70%) commonly reported reinforces that epidemiological signals must be interpreted in light of these moderating factors.

Earlier meta-analyses, such as Amiet et al. (2008), first drew attention to the disproportionate burden of epilepsy among autistic individuals , particularly those with intellectual disability (ID). Subsequent work by Strasser et al. (2018) and Lukmanji et al. (2019) expanded the scope, emphasizing variability in prevalence across cohorts and methods. More recently, Liu et al. (2022) conducted the largest synthesis to date, reporting an overall prevalence of 10% with subgroup differences by age and sex. Our synthesis is consistent with these findings and summarizes the evidence by presenting the correlation between ASD and epilepsy, not just pooled prevalence. This approach highlights that while prevalence varies, the co-occurrence remains significantly greater than chance across populations.

The biological plausibility of ASD epilepsy comorbidity rests on converging evidence of disrupted neurodevelopmental processes. Both conditions are associated with abnormalities in synaptogenesis, neuronal migration, and cortical organization. Disrupted inhibitory-excitatory balance involving GABAergic signaling, has emerged as a central mechanism (Liu et al., 2022). Reduced inhibitory tone predisposes to epileptiform discharges while also altering circuits critical for social and cognitive development. Genetic syndromes provide compelling evidence of shared vulnerability. Tuberous sclerosis complex (mutations in TSC1/TSC2), Rett syndrome (MECP2 mutations), and Fragile X syndrome (FMR1 mutations) are all associated with both epilepsy and autism (Strasser et al., 2018). These conditions highlight the role of molecular pathways such as mTOR signaling in regulating synaptic plasticity and neuronal excitability. Importantly, individuals with these syndromes do not always manifest both disorders, suggesting that gene-environment interactions and developmental timing determine phenotypic expression.

The age at which seizures occur may critically shape outcomes. Seizures during sensitive periods of brain development can perturb the maturation of neural networks involved in social cognition and communication, potentially precipitating autistic features (Lukmanji et al., 2019). Conversely, intrinsic neurodevelopmental anomalies characteristic of ASD may predispose to cortical hyperexcitability and subsequent epilepsy. The relationship is thus plausibly bidirectional. Animal models reinforce this: induced seizures in early development disrupt social behaviors, while genetic models of autism show heightened seizure susceptibility.

Intellectual disability consistently emerges as the strongest moderator. Amiet et al. (2008) reported epilepsy prevalence of 21.5% among autistic individuals with ID compared with 8% among those without. This gradient was confirmed in later reviews (Liu et al., 2022). ID may reflect more severe neurodevelopmental disruption, which increases susceptibility to both seizures and autistic traits. Alternatively, ID may introduce diagnostic biases, with epilepsy more likely to be identified in individuals with significant impairments who are under closer medical surveillance.

Age influences prevalence substantially. Liu et al. (2022) demonstrated higher epilepsy prevalence in autistic adults compared with children, suggesting cumulative risk across the lifespan. This observation challenges the assumption that epilepsy in ASD is primarily a pediatric phenomenon and underscores the need for adult surveillance. Sex effects were weaker but suggest a higher prevalence of epilepsy in autistic females, consistent with the hypothesis that female sex confers resilience to autism but not to epilepsy, leading to more severe phenotypes when ASD is diagnosed in females.

As Lukmanji et al. (2019) noted, clinic-based studies often report higher prevalence than population-based studies, reflecting referral bias toward more severe cases. Diagnostic criteria further complicate estimates. Some studies rely on registry data with ICD codes, others on clinical chart reviews or structured interviews, each with

different sensitivity and specificity. EEG confirmation was inconsistently applied, raising risks of misclassification. Strasser et al. (2018) also emphasized the lack of adjustment for confounders such as seizure type, medication use, or socioeconomic status.

Given the elevated co-occurrence, routine bidirectional screening is warranted. Children diagnosed with ASD should be monitored for seizures, while individuals with epilepsy should be screened for developmental and behavioral symptoms consistent with ASD. Particular vigilance is required in subgroups at highest risk, including those with intellectual disability, females, and adults.

Management is complicated by the interaction of epilepsy treatments with cognitive and behavioral functioning. Antiepileptic drugs (AEDs) can stabilize neural excitability, potentially mitigating behavioral dysregulation, but may also worsen attention, mood, or social functioning (Amiet et al., 2008). Valproate, for example, has been linked to improved seizure control but adverse neurocognitive outcomes, while newer agents such as levetiracetam may exacerbate irritability. This underscores the importance of personalized therapy that balances seizure control with developmental needs.

The dual burden of ASD and epilepsy calls for integrated care frameworks that unite neurology, psychiatry, psychology, and developmental pediatrics. Multidisciplinary clinics can facilitate early detection, tailored treatment, and coordinated support for families. Importantly, comorbidity increases healthcare utilization and caregiver burden, making service integration both clinically and economically compelling.

Strengths and Limitations of the Review

A major strength of this systematic narrative review is its comprehensive scope, synthesizing both directions of association from high-quality existing meta-analyses. The narrative approach appropriately addresses the methodological limitation of attempting to pool primary studies with existing pooled estimates. However, limitations remain. We are reliant on the methods and findings of the included reviews. High heterogeneity (I^2 >70%) in the original analyses limits the precision of pooled estimates. Diagnostic inconsistency across primary studies undermines comparability. Publication bias, as suggested in some included reviews, may have inflated associations by underrepresenting null studies. Finally, observational designs preclude causal inference.

Future Directions

Future research must move beyond prevalence estimates to causal investigation. Longitudinal studies tracking high-risk infant cohorts could determine whether seizures precede autistic traits, vice versa, or co-emerge from shared pathophysiology. Genomic and neuroimaging integration will clarify whether specific molecular pathways (e.g., mTOR, GABAergic circuits) mediate dual vulnerability. Biomarker discovery, including EEG endophenotypes, could improve risk stratification. Intervention studies are also critical: determining whether effective epilepsy control alters the trajectory of autistic symptoms would address causality directly.

Conclusion

This systematic narrative review affirms a significant correlation between ASD and epilepsy, shaped by age, sex, intellectual disability, and study design. The relationship is biologically plausible, supported by shared neurodevelopmental pathways and genetic syndromes, but remains mechanistically unresolved. Clinically, the findings mandate bidirectional screening and integrated care, while highlighting the complexity of treatment interactions. Methodological limitations across the literature underscore the need for standardized diagnostic criteria, stratified analyses, and longitudinal designs. Ultimately, disentangling the pathways linking ASD and epilepsy will advance precision medicine approaches for two of the most common and burdensome neurodevelopmental conditions.

References

[1]. Amiet, C., Gourfinkel-An, I., Bouzamondo, A., Tordjman, S., Baulac, M., Lechat, P., Mottron, L., & Cohen, D. (2008). Epilepsy in autism is associated with intellectual disability and gender: Evidence from a meta-analysis. Biological Psychiatry, 64(7), 577-

582. https://doi.org/10.1016/j.biopsych.2008.04.030

[2]. Centers for Disease Control and Prevention. (2025). Data & statistics on autism spectrum disorder. https://www.cdc.gov/autism/data-research/index.html

[3]. Fiest, K. M., Sauro, K. M., Wiebe, S., et al. (2017). Prevalence and incidence of epilepsy: A systematic review and meta-analysis. Neurology. https://doi.org/10.1212/WNL.0000000000003509

[4]. Liu, X., Sun, X., Sun, C., Zou, M., Chen, Y., Huang, J., Wu, L., & Chen, W.-X. (2022). Prevalence of epilepsy in autism spectrum disorders: A systematic review and meta-analysis. Autism, 26(1), 33-50. https://doi.org/10.1177/13623613211045029

[5]. Lukmanji, S., Manji, S. A., Kadhim, S., Sauro, K. M., Wirrell, E. C., Kwon, C. S., & Jetté, N. (2019). The co-occurrence of epilepsy and autism: A systematic review. Epilepsy & Behavior, 98(Pt A), 238-248. https://doi.org/10.1016/j.yebeh.2019.07.037

[6]. Strasser, L., Downes, M., Kung, J., Cross, J. H., & De Haan, M. (2018). Prevalence and risk factors for autism spectrum disorder in epilepsy: A systematic review and meta-analysis. Developmental Medicine & Child Neurology, 60(1), 19-29. https://doi.org/10.1111/dmcn.13598

[7]. World Health Organization. (2024). Epilepsy: Fact sheet. https://www.who.int/news-room/fact-sheets/detail/epilepsy