International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Autism Spectrum Disorders and Purinergic Signaling: A Systematic Review of Emerging Insights from Clinical Studies

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ADMINISTRATIVE INFORMATION

Support - N/A.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 8 March 2026 and was last updated on 8 March 2026.

INTRODUCTION

Review question / Objective Review question What clinical evidence supports purinergic signaling dysfunction in individuals with autism spectrum disorder?
Objective To systematically evaluate human clinical studies investigating purinergic signaling alterations, including purine metabolism and adenosine pathway changes, in individuals with autism spectrum disorder.

Condition being studied ASD.

METHODS

Participant or population ASD.

Intervention Alterations in purinergic signaling pathways, including:
• purine metabolism
• adenosine signaling
• purinergic receptor activity (e.g., P2X, P2Y)
• purine-related biomarkers (e.g., uric acid, ATP signaling)
• therapeutic interventions targeting purinergic signaling (e.g., suramin).

Comparator Comparisons may include:
• neurotypical control participants
• baseline measurements in ASD participants
• placebo groups (in clinical trials)
• comparisons across ASD severity levels.

Study designs to be included RCTs, cohort, case-control, cross sectional.

Eligibility criteria Inclusion:
Clinical human studies involving individuals with autism spectrum disorder that evaluate purinergic signaling pathways (e.g., purine metabolism, adenosine signaling, purinergic receptors) or related biomarkers. Eligible designs include randomized controlled trials, cohort studies, case-control studies, and cross-sectional studies.
Exclusion:

Preclinical studies (animal or in vitro), reviews, editorials, conference abstracts without full data, and studies not assessing purinergic signaling in ASD.

Information sources Electronic databases to be searched include:
• PubMed / MEDLINE
• Scopus
• Web of Science
• Embase.

Main outcome(s) Primary outcomes:
• alterations in purinergic signaling pathways in individuals with ASD
• changes in purine metabolism biomarkers (e.g., ATP, uric acid, adenosine)
Secondary outcomes:
• associations between purinergic signaling and ASD symptom severity
• effects of purinergic-targeted therapies on behavioral or clinical outcomes.

Quality assessment / Risk of bias analysis JBI.

Strategy of data synthesis A qualitative narrative synthesis will be performed summarizing study characteristics, methodologies, and key findings related to purinergic signaling alterations in ASD. Due to anticipated heterogeneity in study designs, outcome measures, and methodologies, quantitative meta-analysis may not be feasible.

Subgroup analysis If sufficient data are available, subgroup analyses may be conducted based on:

• age group (children vs adults)
• type of purinergic pathway evaluated (adenosine vs purine metabolism)
• study design
• type of biomarker or clinical outcome measured.

Sensitivity analysis N/A.

Country(ies) involved United States.

Keywords Autism spectrum disorder; purinergic signaling; purine metabolism; adenosine; metabolomics; biomarkers; clinical studies; autism.

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