INPLASY

A Strain-Specific Systematic Review Protocol: Lactiplantibacillus plantarum PS128 in Autism Spectrum Disorder

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ADMINISTRATIVE INFORMATION

Support - No specific external financial support has been received for this systematic review. The review will be conducted as part of an academic research project at the University of Huddersfield.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202660090

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 June 2026 and was last updated on 18 June 2026.

INTRODUCTION

Review question / Objective The aim of this systematic review is to evaluate the available human clinical evidence for Lactiplantibacillus plantarum PS128, formerly known as Lactobacillus plantarum PS128, in individuals with autism spectrum disorder.
The review will address the following question:
What clinical evidence supports the use of Lactiplantibacillus plantarum PS128 in individuals with autism spectrum disorder, and what effects have been reported on behavioural, emotional, gastrointestinal, sleep-related, quality-of-life, microbiome-related, biomarker, safety, and tolerability outcomes?

Rationale Autism spectrum disorder is a neurodevelopmental condition characterised by differences in social communication and interaction, alongside restricted, repetitive, or sensory-related behaviours and interests. Many autistic individuals also experience associated symptoms such as gastrointestinal disturbance, anxiety, irritability, hyperactivity, sleep disturbance, feeding difficulties, and emotional dysregulation. These associated features may contribute substantially to functional impairment and caregiver burden.
There is increasing interest in the gut–brain axis as a contributor to symptom heterogeneity in autism spectrum disorder. Probiotics have therefore been explored as adjunctive interventions. However, many reviews and clinical studies group together different probiotic genera, species, strains, and multi-strain formulations. This creates difficulty in interpreting the evidence because probiotic effects are often strain-specific.
Lactiplantibacillus plantarum PS128 is a defined probiotic strain that has been evaluated in human studies involving individuals with autism spectrum disorder. The strain was previously described as Lactobacillus plantarum PS128, and both names are used in the literature. A strain-specific systematic review is needed to determine the clinical evidence for PS128 specifically, rather than

probiotics as a broad and heterogeneous intervention category.

Preliminary searching suggests that the available evidence may include randomised placebo-controlled trials, observational or real-world studies, and studies involving PS128 in combination with other interventions. A systematic review is therefore justified to map the evidence, assess study quality, summarise outcomes, and determine whether quantitative synthesis is possible.

Condition being studied The condition being studied is autism spectrum disorder. This review will focus on individuals diagnosed with autism spectrum disorder or related diagnostic terms used historically or clinically, including autistic disorder, Asperger syndrome, pervasive developmental disorder, and PDD-NOS.
The review will consider clinical outcomes associated with autism spectrum disorder, including behavioural symptoms, emotional symptoms, gastrointestinal symptoms, sleep-related outcomes, quality of life, microbiome-related outcomes, inflammatory or neurochemical biomarkers, safety, and tolerability.

METHODS

Search strategy The search strategy will combine terms related to autism spectrum disorder with terms related to Lactiplantibacillus plantarum PS128 and its former taxonomic name, Lactobacillus plantarum PS128. Database-specific controlled vocabulary and free-text terms will be used where appropriate. INPLASY recommends reporting database-specific strategies because controlled vocabulary differs between databases, such as MeSH in MEDLINE and Emtree in Embase.
Search strategy:
("Autism Spectrum Disorder"[Mesh] OR "Autistic Disorder"[Mesh] OR "autism spectrum disorder"[tiab] OR "autism spectrum disorders"[tiab] OR autism[tiab] OR autistic[tiab] OR ASD[tiab] OR Asperger*[tiab] OR "pervasive developmental disorder"[tiab] OR "pervasive developmental disorders"[tiab] OR PDD[tiab] OR PDD-NOS[tiab]) AND ("Lactiplantibacillus plantarum PS128"[tiab] OR "Lactobacillus plantarum PS128"[tiab] OR "L. plantarum PS128"[tiab] OR "L plantarum PS128"[tiab] OR "plantarum PS128"[tiab] OR PS128[tiab] OR "PS 128"[tiab] OR "Lactiplantibacillus plantarum"[tiab] OR "Lactobacillus plantarum"[tiab] OR "L. plantarum"[tiab] OR "L plantarum"[tiab])
Focused PS128-only PubMed search:
("Autism Spectrum Disorder"[Mesh] OR "Autistic Disorder"[Mesh] OR "autism spectrum disorder"[tiab] OR autism[tiab] OR autistic[tiab] OR ASD[tiab] OR Asperger*[tiab] OR "pervasive developmental disorder"[tiab] OR PDD[tiab] OR PDD-NOS[tiab]) AND ("Lactiplantibacillus plantarum PS128"[tiab] OR "Lactobacillus plantarum PS128"[tiab] OR "L. plantarum PS128"[tiab] OR "L plantarum PS128"[tiab] OR "plantarum PS128"[tiab] OR PS128[tiab] OR "PS 128"[tiab])

ClinicalTrials.gov search strategy:
AREA[ConditionSearch]("Autism Spectrum Disorder" OR autism OR autistic OR ASD OR Asperger OR "pervasive developmental disorder")
AND
AREA[InterventionSearch]("Lactobacillus plantarum PS128" OR "Lactiplantibacillus plantarum PS128" OR "L. plantarum PS128" OR PS128)
Additional database searches:
The PubMed strategy will be adapted for Embase, Scopus, Web of Science, Cochrane CENTRAL, ClinicalTrials.gov, and WHO ICTRP. Reference lists of included studies and relevant reviews will also be manually searched. Google Scholar may be used for supplementary citation searching.

No date restriction will be applied.

Participant or population Participants will include humans diagnosed with autism spectrum disorder or related diagnostic categories, including autistic disorder, Asperger syndrome, pervasive developmental disorder, or PDD-NOS.Participants of any age will be eligible, although the review is expected to focus primarily on children and adolescents because preliminary evidence suggests most PS128-ASD clinical studies have been conducted in paediatric populations.Studies involving mixed populations will be included only if data for participants with autism spectrum disorder can be extracted separately or if the majority of participants have autism spectrum disorder and the study is directly relevant to the review question.

Intervention The intervention of interest is oral administration of Lactiplantibacillus plantarum PS128, including studies that use its former name, Lactobacillus plantarum PS128.Eligible interventions may include PS128 administered as capsules, sachets, powder, or another oral dosage form. Studies evaluating PS128 as monotherapy will be prioritised for primary synthesis. Studies evaluating PS128 in combination with another active intervention, such as oxytocin, will be included in a separate narrative synthesis if the contribution of PS128 is relevant to the review

question.Studies of other Lactiplantibacillus plantarum or Lactobacillus plantarum strains will be excluded unless PS128 is clearly included or separately identifiable.

Comparator Eligible comparators will include placebo, no treatment, usual care, baseline status in before-and-after studies, or other probiotic interventions.For primary efficacy synthesis, placebo-controlled PS128 monotherapy studies will be considered the most relevant. Observational and combination-therapy studies will be synthesised separately.

Study designs to be included The following study designs will be eligible: Randomised controlled trials; controlled clinical trials; non-randomised intervention studies; pilot clinical studies; observational studies; real-world studies; prospective or retrospective cohort studies; case series if they provide relevant clinical outcome or safety data; and registered clinical trial records.Reviews, editorials, commentaries, opinion articles, letters without original data, animal-only studies, and in vitro-only studies will be excluded from the main clinical review. Animal or in vitro studies may be discussed only as backg.

Eligibility criteria Inclusion criteria: Studies will be included if they: 1. Include human participants with autism spectrum disorder or related diagnostic terminology. 2. Evaluate Lactiplantibacillus plantarum PS128 or Lactobacillus plantarum PS128. 3. Report at least one relevant clinical, behavioural, emotional, gastrointestinal, sleep, quality-of-life, microbiome, biomarker, safety, tolerability, or adherence outcome. 4. Are original clinical studies, observational studies, real-world studies, pilot studies, or registered clinical trial records. 5. Provide sufficient information for data extraction. Exclusion criteria: Studies will be excluded if they: 1. Do not involve participants with autism spectrum disorder or related diagnostic terminology. 2. Evaluate probiotics but do not include PS128. 3. Evaluate L. plantarum strains other than PS128 without separately identifiable PS128 data. 4. Are animal-only, in vitro-only, review articles, editorials, commentaries, or opinion pieces. 5. Do not report original data relevant to the review question. 6. Are conference abstracts with insufficient extractable data unless additional information is available from trial registries or authors. No restrictions will be applied based on country, publication year, or publication status.

Information sources The following sources will be searched:

PubMed/MEDLINE; Embase; Scopus; Web of Science; Cochrane CENTRAL; ClinicalTrials.gov; WHO International Clinical Trials Registry Platform; Google Scholar for supplementary citation searching; reference lists of included studies; and reference lists of relevant systematic reviews.

Main outcome(s) The main outcomes will be clinical outcomes related to autism-associated behavioural and emotional symptoms.
These may include outcomes measured using validated or commonly used scales such as:
Autism Behavior Checklist; Social Responsiveness Scale; Child Behavior Checklist; SNAP-IV; Clinical Global Impression; Achenbach System of Empirically Based Assessment; ADHD-related symptom scales; anxiety/depression-related subscales; irritability; hyperactivity; emotional dysregulation; and caregiver- or clinician-rated global improvement.
Outcome timing will be extracted according to the time points reported in each included study. Where multiple time points are available, end-of-intervention data will be prioritised for synthesis.

Additional outcome(s) Additional outcomes will include:
Gastrointestinal symptom severity; stool frequency or consistency; abdominal pain; constipation; diarrhoea; sleep-related outcomes; quality of life; adaptive behaviour; microbiome composition; inflammatory markers; neurochemical or gut–brain-axis-related biomarkers; oxytocin-related outcomes where relevant; adherence; withdrawals; adverse events; and tolerability.

Safety and tolerability outcomes will be extracted from all eligible human studies, including observational and real-world studies.

Data management All search results will be exported to reference management software, and duplicates will be removed before screening. Two reviewers will independently screen titles and abstracts against the eligibility criteria. Full texts of potentially eligible studies will then be assessed independently by two reviewers.

Disagreements will be resolved through discussion. If consensus cannot be reached, a third reviewer will be consulted.

A standardised data extraction form will be used. Extracted data will include author, year, country, study design, sample size, participant characteristics, diagnostic criteria, intervention details, PS128 dose, dosage form, duration, comparator, outcomes, outcome measures,

results, adverse events, withdrawals, funding source, and conflicts of interest.

Screening decisions and reasons for exclusion at full-text stage will be documented and reported using a PRISMA flow diagram.

Quality assessment / Risk of bias analysis Randomised controlled trials will be assessed using the Cochrane Risk of Bias 2 tool. Non-randomised and observational studies will be assessed using an appropriate tool according to study design, such as ROBINS-I or the Newcastle–Ottawa Scale.

Strategy of data synthesis A structured narrative synthesis will be conducted for all included studies. Studies will be grouped according to design and intervention type:

1. PS128 monotherapy randomised controlled trials.
2. PS128 non-randomised or observational studies.
3. PS128 real-world studies.
4. PS128 combination-therapy studies.
5. Registered but unpublished or ongoing clinical trials.

A meta-analysis will be conducted only if at least two sufficiently comparable PS128 monotherapy studies report the same or convertible outcomes. If meta-analysis is feasible, continuous outcomes will be summarised using mean difference or standardised mean difference, depending on whether the same measurement scale is used. Dichotomous outcomes will be summarised using risk ratios or odds ratios, where appropriate.
A random-effects model will be considered because heterogeneity is expected in participant age, intervention duration, outcome measures, and study design. Statistical heterogeneity will be assessed using I^2 and interpreted cautiously. Where quantitative pooling is not appropriate, findings will be synthesised narratively with tabular presentation.

Subgroup analysis Subgroup analyses will be considered only if sufficient data are available. Potential subgroup analyses include:

Age group, such as preschool children, school-age children, adolescents, and adults; sex; PS128 monotherapy versus PS128 combination therapy; duration of intervention; baseline gastrointestinal symptoms; and outcome domain.

Because the evidence base is expected to be small, subgroup analyses will be interpreted as exploratory.

Sensitivity analysis Sensitivity analyses will be performed if sufficient studies are available. Planned sensitivity analyses may include excluding studies at high risk of bias, excluding non-randomised studies, excluding combination-therapy studies, excluding studies without placebo controls, and excluding studies with incomplete outcome reporting.

If the number of studies is too small, sensitivity analysis will not be conducted, and this limitation will be reported.

Language restriction No language restrictions will be applied at the search stage. Studies published in languages other than English will be screened using English abstracts where available. Full-text translation will be considered.

Country(ies) involved United Kingdom.

Keywords Autism spectrum disorder; Lactiplantibacillus plantarum PS128; Lactobacillus plantarum PS128; probiotics; psychobiotics; gut–brain axis; systematic review; human studies.

Dissemination plans The findings of this systematic review will be disseminated through submission to a peer-reviewed journal and presentation in an academic research setting. The review may also inform future research on strain-specific probiotic interventions for autism spectrum disorder.

Contributions of each author

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