

## Gut microbiota changes in patients with Alzheimer's disease spectrum based on 16S rRNA sequencing: a systematic review and meta-analysis

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**ADMINISTRATIVE INFORMATION****Support** - STI2030-Major Projects (Grant number: 2021ZD0201802).**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202460067**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 June 2024 and was last updated on 17 June 2024.**INTRODUCTION**

**Review question / Objective** This study aims to characterize the alterations in the gut microbiota of Alzheimer's disease spectrum patients compared to healthy individuals.

**Condition being studied** The gut microbiota is hypothesized to play roles in Alzheimer's disease pathogenesis. In recent years, many gut microbiota composition and abundance investigations in Alzheimer's disease patients have been conducted; however, despite this work, some results remain controversial. Therefore, we conducted a systematic review and meta-analysis using 16S rRNA sequencing to explore gut microbiota alterations between patients with Alzheimer's disease spectrum and healthy controls.

**METHODS**

**Participant or population** Alzheimer's disease spectrum patients.

**Intervention** 16S rRNA sequencing technique is employed to test the taxonomy of gut bacteria between Alzheimer's disease spectrum patients and healthy controls.

**Comparator** Healthy subjects were selected as controls based on age, sex, and body mass index matching those of the Alzheimer's disease spectrum patients.

**Study designs to be included** Randomized controlled trials, cohort studies, or case-control studies.

**Eligibility criteria** (1) Alzheimer's disease spectrum patients diagnosed using validated criteria (Diagnostic and Statistical Manual of Mental Disorders or National Institute on Aging and Alzheimer's Association guidelines); (2) gut microbiota comparisons conducted between Alzheimer's disease spectrum and healthy controls using 16S rRNA sequencing; (3) gut microbiota samples came from stool samples; (4) Accessible

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raw data were, such as relative gut microbiota abundance at distinct levels, microbial composition, and community structures; and (5) Studies not limited by language type.

**Information sources** PubMed, Web of Science, Embase, the Cochrane Library, China National Knowledge Infrastructure, China Biology Medicine disc database, WanFang database and Social Sciences Citation Index databases.

**Main outcome(s)** Compared to the healthy controls, Alzheimer's disease spectrum patients exhibited specific characteristics in their gut microbiota, including alpha diversity and the relative abundance of microbial taxa at the phylum to genera levels.

**Quality assessment / Risk of bias analysis** Based on extracted data, the Cochrane Risk of Bias Assessment Tool was used for RCTs which had five domains: randomization, deviation from intervention, missing data, outcome measurements, and selective reporting. The Newcastle–Ottawa scale was used for observational/non-randomized studies with domain selection, comparability, and exposure/outcomes.

**Strategy of data synthesis** This meta-analysis was conducted using Stata 14.0 software. Standardized mean differences and 95% confidence intervals came from fixed effects or random effects models for quantitative synthesis. Heterogeneity was evaluated using the Cochran Q statistic and quantified by  $I^2$  tests, with an  $I^2 > 50\%$  indicating moderate-to-high heterogeneity.

**Subgroup analysis** The subgroups can be based on demographic characteristic--country.

**Sensitivity analysis** The sensitivity analysis will be conducted by the Stata 14.0 if necessary.

**Country(ies) involved** China.

**Keywords** Alzheimer's disease, gut microbiota, 16S rRNA sequencing, biomarkers, meta-analysis.

#### **Contributions of each author**

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Author 2 - Xiaopan Cui.

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