INPLASY

Systematic evaluation of the associations between schizophrenia and autoimmune diseases: An umbrella review

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

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 9 November 2024 and was last updated on 9 November 2024.

INTRODUCTION

Review question / Objective This comprehensive review aims to integrate all existing systematic reviews and meta-analyses on the relationship between schizophrenia and autoimmune diseases, evaluating the impact and stability of these associations while considering the quality of evidence across studies.

Condition being studied We have identified that meta-analyses exploring the relationship between schizophrenia and various autoimmune diseases have become a prominent research focus. However, these studies often face limitations in addressing potential bias risks and evaluating heterogeneity, which undermine the reliability and consistency of their findings. Furthermore, substantial discrepancies exist across different reviews, making it difficult to establish a clear level of evidence. Additionally, many studies concentrate on only one or a few autoimmune diseases, with no comprehensive summary of the overall spectrum of autoimmune disorders.

METHODS

Participant or population The three populations are as follows: (A) comorbidity of schizophrenia/psychotic disorders and autoimmune disease; (B) schizophrenia/psychotic disorders preceding autoimmune disease; (C) autoimmune disease preceding schizophrenia/psychotic disorders.

Intervention Not applicable.

Comparator Not applicable.

Study designs to be included Systematic reviews and meta-analyses.

Eligibility criteria The studies to be included should meet the following criteria: 1) Investigations that explore the relationship, or the reverse relationship, between schizophrenia as an

exposure factor and one or more autoimmune diseases as outcomes, as well as systematic reviews and meta-analyses specifically addressing this association. 2) Outcome measures should include risk-related indicators between the two conditions, such as relative risk (RR), odds ratio (OR), or hazard ratio (HR). 3) Studies should provide sufficient raw data to calculate risk estimates, 95% confidence intervals, and 95% prediction intervals, as well as to assess small sample effects and excess significance. 4) The article should be published in English.

Information sources We performed a systematic search across six databases (i.e., PubMed, Web of Science, Embase, CINAHL, PsycINFO, and the Cochrane Library) for systematic reviews and meta-analyses concerning schizophrenia and autoimmune diseases from their inception to September 6, 2024. Two researchers independently reviewed the titles, abstracts, and full texts to identify studies that potentially met the inclusion criteria. Any disagreements were addressed through discussion with a third researcher.

Main outcome(s) Assessing the relationship and stability of systematic reviews and meta-analyses on the association between schizophrenia and autoimmune diseases, as well as evaluating the quality of the evidence.

Quality assessment / Risk of bias analysis For the quality assessment of quantitative articles, the checklist 'A Measurement Tool to Assess Systematic Reviews, version 2' (AMSTAR 2) will be utilized. In contrast, qualitative articles will be evaluated using the Joanna Briggs Institute Qualitative Assessment and Review Instrument (JBI-QARI). Discrepancies among researchers will be resolved through discussion, and a third researcher will be consulted when necessary.

Strategy of data synthesis We will re-estimate the summary effect sizes, 95% CIs, and P values for each meta-analysis using the DerSimonian and Laird method under a random-effects model. Heterogeneity among the included studies will be assessed via Cochran's Q test and the I^2 statistic. We will also calculate 95% prediction intervals, where intervals excluding the null value will suggest the potential for effects in future studies. Publication bias will be assessed using Egger's test, with a $P < 0.10$ indicating the presence of small study effects. The estimate from the largest study will be more conservative than the random-effects summary estimate. We will use the tes method from the metafor package in R to assess

excess significance, determining if the number of studies with significant results ($P < 0.05$) exceeds the expected numbers based on statistical power. The significance threshold for excess significance bias will be set at $P < 0.10$. All analyses will be conducted using R (version 4.3.1) with two-tailed P values.

Subgroup analysis None.

Sensitivity analysis None.

Country(ies) involved China.

Keywords Schizophrenia; Autoimmune diseases; Umbrella review; Meta-analysis.

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