# INPLASY

## Relationship between Type 1 Diabetes Mellitus and Schizophrenia : A Systematic Review of Observational studies

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## INTRODUCTION

**Review question / Objective** P: participants of all age. I: type 1 diabetes mellitus diagnosis. C: without type 1 diabetes mellitus diagnosis. O: schizophrenia. Research question: Dose type 1 diabetes mellitus associate with schizophrenia?

**Rationale** Both schizophrenia and type 1 diabetes mellitus are known as immune related diseases. The current observational studies show inconsistent results between the two disorders. In our literature review, a relevant systematic review of this issue is lacking. The comorbid of schizophrenia and T1D can have a huge and lasting impact on an individual's life. Understanding the nature of this association, if it exists, is critical for early prevention and timely treatment. To address this gap, we conducted a systematic review of observational studies to explore whether schizophrenia is associated to T1D.

**Condition being studied** Schizophrenia is a heterogeneous and severely disabling disorder that involves alterations in several important brain regions. Patients with schizophrenia often comorbid with other medical illness, including diabetes mellitus, which further complicates treatment. One systematic review had revealed an increased prevalence of autoantibodies in schizophrenic patients. Many studies have explored whether there is an association between schizophrenia and medical diseases, particularly those autoimmune-related, including type 1 diabetes (T1D). T1D is known as a chronic autoimmune disease characterized by T-cell-mediated inflammation. Some studies have confirmed that T1D patients have imbalance ratio

of T helper 1 (Th1) and T helper 2 (Th2) with Th2 predominance. Similar manifestations of Th1/Th2 alterations have been observed in schizophrenic patients and has been proposed to be pathogenic. Dysfunction of the Th17 pathway is another possible shared immune mechanism for both T1D and schizophrenia . For example, abnormal Th17 function causes neuroinflammation in schizophrenia. And activated Th17 and its secreted cytokine IL17 contribute to insulitis, which is the core pathology of T1D. In our review, we aim to investigate the association between schizophrenia and T1D.

## METHODS

**Search strategy** Populations: Participants of all age; Intervention: Type 1 diabetes mellitus diagnosis, "Diabetes Mellitus, Insulin-Dependent" "Diabetes Mellitus, Insulin Dependent" "Insulin-Dependent Diabetes Mellitus" "Diabetes Mellitus, Juvenile Onset" "Diabetes, Juvenile-Onset" "Juvenile-Onset Diabetes Mellitus" "Juvenile Onset Diabetes" "IDDM" "Type 1 Diabetes Mellitus" "Diabetes Mellitus, Insulin-Dependent, 1""Insulin-Dependent Diabetes Mellitus 1" "Insulin Dependent Diabetes Mellitus 1" "Type 1 Diabetes" "Diabetes, Type 1" "Diabetes Mellitus, Type I" Autoimmune*; Comparison: Without type 1 diabetes mellitus diagnosis; Outcome: Schizophrenia, Schizophrenia*, Schizophrenic*, "Schizophrenia Spectrum and Other Psychotic Disorders", Schizophreniform*, Psychotic*, Psychosis
Select database:
Airiti Library
Embase
Ovid Medline
CINAHL Complete (via EBSCOhost)
Pubmed.

**Participant or population** Participants of all age with type 1 diabetes , and participants of all age with schizophrenia.

**Intervention** Type 1 diabetes mellitus diagnosis.

**Comparator** Without type 1 diabetes mellitus diagnosis.

**Study designs to be included** Observational studies, including cohort, case-control, prevalence, and cross-sectional study.

**Eligibility criteria** Peer-reviewed articles; Focus on human (all ages).

**Information sources** Electronic databases and contact with authors.

**Main outcome(s)** The incidence ratio, odds ration, or hazard ratio for schizophrenia.

**Additional outcome(s)** The prevalence of schizophrenia in type 1 diabetes patients.

**Data management** Two independent reviewers screened the titles, abstract and full-text review of all publications obtained from the searches for inclusion. A third reviewer was consulted where any disagreement occurred. All included studies were extracted based on independent review by two researchers. If there is any disagreement between the two researchers, the authors will also check the full text of the study and discuss to reach a consensus. One researchercompleted the data extraction and the co-author rechecked the integrity of the data. The following data was extracted: first author, year of publication, study design, sample size, ethnicity of population, Schizophrenia/schizoaffective disorder diagnosis criteria, T1D diagnosis criteria, number of study groups, and number of control groups.

**Quality assessment / Risk of bias analysis** The quality of each study was assessed based on Joanna Briggs Institute (JBI) (JUB; 2017) independently. The higher the score, the better the quality of the study. Whether studies are of sufficient quality to be eligible in the review are based on the joint decision of the two researchers, and any disagreement would be resolved in discussion.

**Strategy of data synthesis** This systematic review used a narrative synthesis format to identify the bidirectional relationship between schizophrenia and T1D. To evaluate the agreement of using the JBI checklists, kappa statistic was calculated for measuring agreement between two authors.

**Subgroup analysis** Nil.

**Sensitivity analysis** Nil.

**Language restriction** English and Chinese.

**Country(ies) involved** Taiwan.

**Keywords** Type 1 diabetes, schiozophrenia, autoimmune.

**Dissemination plans** Plan to publication in peer-review journal.

**Contributions of each author**

Author 1 - Yi-chun Liu - conceiving the review; designing the review; coordinating the review; writing the protocol or review; drafted the mauscript.
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